Stability and Plasticity of Inhibitory Control

– Kumulative Arbeit –

Inaugural-Dissertation

zur Erlangung der Doktorwürde

der

Philosophischen Fakultät

der

Rheinischen Friedrich-Wilhelms-Universität zu Bonn

vorgelegt von

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aus Wermelskirchen

Bonn, 2024

Gedruckt mit der Genehmigung der Philosophischen Fakultät

der Rheinischen Friedrich-Wilhelms-Universität Bonn

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Tag der mündlichen Prüfung: 29.11.2023

"Inhibition is (…) not an occasional accident; it is an essential and unremitting element of our cerebral life."

(James, 1890, p. 583)

"Inhibitory control makes it possible for us to change and for us to choose how we react and how we behave rather than being unthinking creatures of habit. It doesn't make it easy. Indeed, we usually are creatures of habit and our behavior is under the control of environmental stimuli far more than we usually realize, but having the ability to exercise inhibitory control creates the possibility of change and choice**. It can also save us from making fools of ourselves."**

(Diamond, 2013, p. 137)

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ACKNOWLEDGEMENTS

I sincerely thank all those who have supported and accompanied me on my way here and have thus significantly contributed to the completion of this thesis!

First and foremost, my sincere thanks go to my supervisor Ulrich Ettinger, who has always inspired me with his enthusiasm for research. His knowledge, experience, and insightful suggestions have shaped this research work, and I am deeply grateful for his support and that he has always believed in me and my abilities. I am looking forward to our future research projects.

I would also like to thank Prof. Dr. André Beauducel, Prof. Dr. Henning Gibbons and PD Dr. Dr. Cornelia McCormick for being part of my examination board. I want to thank Prof. Veena Kumari and her team in London for their valuable input during my stay at Brunel University and for their ongoing support within our joint research projects. Furthermore, I want to thank Wolf Harmening for the enjoyable collaboration, Inga Meyhöfer for motivating me to learn programming and all our research assistants for their tremendous support in the lab.

A big thank you goes to my colleagues, Celina, Eli, Jule, Kristof, Mirko, Philine, Pia, Rebekka, and Yaira, for the many great moments we have shared. A birthday without a trashed office can only be a bad one, and working with you guys is not only work but also a lot of fun. A very special thank you goes, of course, to Rebekka, the world's best office colleague. We had constructive discussions, motivating talks, and perfectly timed coffee breaks during our PhDs. Even though our academic paths are now, unfortunately, parting after such a long time, she will remain a friend and will be eternally immortalised in my variable names. At this point, I would also like to thank Annika, with whom I found my way into research and with whom I discovered the joy of programming (in the smallest basement office in the world), and Judith, with whom I discovered the most creative and fun ways of learning that still help me today.

Most of the rest of my friends and family have pretty little to do with this thesis and probably don't even exactly know what it is about, and that's precisely what I'm thankful for: they always help me to come back to work in a good mood and with a clear head.

And even though I mostly inhibit my unbridled enthusiasm for cognitive control in my private environment in the sense of social agreeableness, one person probably knows more about inhibition than he would like to - Steffen. Thank you for everything, for listening, thinking along, and unconditionally keeping my options open.

And last but not least, Jonne, whose gentle kicks in my belly in the final phase pushed me to finish this thesis.

ABSTRACT

Throughout life and in various situations, people are required to control their behaviour, suppress automatic responses, resist distraction, and selectively direct their attention. However, they are not always equally successful. Thus, an important question that has not been addressed sufficiently is to what extent behavioural inhibitory control is determined by stable traits or time-varying states. Furthermore, how can inhibitory control be influenced deliberately, and what processes underlie this ability? In particular, the influence of inhibitory neurotransmitters on inhibitory control is mostly unknown, and it has not yet been clarified whether inhibitory control is a unitary construct at all or comprises multiple unrelated subcomponents. This thesis aims to address these research gaps regarding the stability and plasticity of inhibitory control.

To this end, results from four studies are presented. In all studies, data from healthy adult students were assessed, and within-subject designs with measurement occasions at one-week intervals were applied. Data analyses include latent state-trait modelling (Study 1) and distributional analyses such as delta plots (Study 2, 4) and Stochastic Early Reaction, Inhibition, and late Action (SERIA) models (Study 3).

In Study 1, data from different inhibitory control tasks (antisaccade, Eriksen flanker, go-/no-go, Simon, stop-signal and Stroop tasks) were decomposed into stable traits and time-varying states. While performance in individual tasks was found to be mainly influenced by traits, those task-specific traits were mostly unrelated. Task-specific results were also evident in the pharmacological studies (Studies 2 – 4). In Study 2, the effect of lorazepam administration on antisaccade, Eriksen flanker, and Simon tasks was investigated. Lorazepam increases the neural activity of the major inhibitory neurotransmitter γ-aminobutyric acid (GABA). The results clearly suggest a role of inhibitory neurotransmitters in inhibitory control. To better understand task-specific results, data from the antisaccade and Simon tasks were further analysed using SERIA models that distinguish between automatic and controlled responses (Study 3) and lorazepam effects in the Eriksen flanker task were examined more closely in Study 4. Therefore, the task was slightly modified while keeping the study design similar to

Study 2. The results from Studies 3 and 4 indicate that increased inhibitory neurotransmitter activity may impair suppressing automatic responses and widen the focus of selective attention, causing distractors to interfere more strongly.

In conclusion, the results reported here suggest that inhibitory control tasks are determined mainly by stable – yet task-specific – traits and that inhibitory control is worsened by increased neural inhibition.

ZUSAMMENFASSUNG

Im Laufe des Lebens sowie in verschiedenen Situationen müssen Menschen ihr Verhalten kontrollieren, automatische Reaktionen unterdrücken, Ablenkungen widerstehen und ihre Aufmerksamkeit selektiv lenken. Dies gelingt jedoch nicht immer gleich gut. Eine wichtige Frage, die noch nicht ausreichend untersucht wurde, ist daher, inwiefern inhibitorische Verhaltenskontrolle durch stabile Merkmale bzw. Dispositionen (Traits) oder zeitlich instabile Merkmale (States) bestimmt wird. Außerdem, wie lässt sich die inhibitorische Kontrolle gezielt beeinflussen, und welche Prozesse liegen dieser Fähigkeit zugrunde? Insbesondere der Einfluss inhibitorischer Neurotransmittern auf inhibitorische Kontrolle ist weitgehend unbekannt, und es bleibt unklar, ob inhibitorische Kontrolle überhaupt ein einheitliches Konstrukt darstellt oder aus mehreren, nicht miteinander zusammenhängenden Teilfähigkeiten besteht. Die vorliegende Arbeit zielt darauf ab, diese Forschungslücken hinsichtlich Stabilität und Plastizität inhibitorischen Kontrolle zu adressieren.

Dazu werden die Ergebnisse von vier Studien vorgestellt. In allen Studien wurden Daten gesunder erwachsener Studierender erhoben, wobei Messwiederholungsdesigns mit einwöchigen Abständen verwendet wurden. Zu den Datenanalysen gehören Latent-State-Trait-Modelle (Studie 1) und Verteilungsanalysen wie Delta-Plots (Studie 2, 4) und SERIA (Stochastic Early Reaction, Inhibition, and late Action) Modelle (Studie 3).

In Studie 1 wurden Daten aus verschiedenen Aufgaben zur Messung inhibitorischer Kontrolle (Antisakkaden, Eriksen-Flanker, Go/No-Go, Simon, Stop-Signal und Stroop Aufgaben) in Traits und States zerlegt. Auch wenn die Leistungen in einzelnen Aufgaben hauptsächlich durch Traits beeinflusst wurden, gab es nur wenig Gemeinsamkeit zwischen diese aufgabenspezifischen Traits. Aufgabenspezifische Ergebnisse zeigten sich auch in den pharmakologischen Studien (Studien 2 - 4). In Studie 2 wurde zunächst der Effekt einer Lorazepam-Gabe auf die Antisakkaden, Eriksen-Flanker und Simon Aufgaben untersucht. Lorazepam erhöht die neuronale Aktivität des wichtigsten inhibitorischen Neurotransmitters γ-Aminobuttersäure (GABA). Die Ergebnisse deuten eindeutig auf eine Rolle inhibitorischer Neurotransmitter bei inhibitorischer Kontrolle hin. Zum besseren Verständnis

aufgabenspezifischer Ergebnisse wurden die Daten der Antisakkaden und Simon Aufgaben mit Hilfe von SERIA-Modellen, die zwischen automatischen und kontrollierten Reaktionen unterscheiden, weiter analysiert (Studie 3), und die Lorazepam-Effekte in der Eriksen-Flanker Aufgabe wurden in Studie 4 genauer untersucht. Dazu wurde bei ähnlichem Studiendesign wie in Studie 2, die Aufgabe leicht modifiziert. Die Ergebnisse von Studie 3 und 4 lassen vermuten, dass eine erhöhte inhibitorische Neurotransmitteraktivität die Unterdrückung automatischer Reaktionen beeinträchtigt und den Fokus selektiver Aufmerksamkeit weitet, so dass Distraktoren stärker interferieren.

Zusammenfassend deuten die hier berichteten Ergebnisse darauf hin, dass Aufgaben zur Messung inhibitorischer Kontrolle hauptsächlich durch stabile - jedoch aufgabenspezifische - Traits bestimmt werden und dass inhibitorische Kontrolle durch erhöhte neuronale Inhibition verschlechtert wird.

1 INTRODUCTION

1.1 Models, Measurement and Mechanisms of Inhibitory Control

1.1.1 Theoretical Approaches

The term *inhibition* has been used for over 100 years to describe a variety of phenomena (see Figure 1), ranging from particular processes, such as inhibitory mechanisms in the neurotransmitter system, to the general prevention of undesirable behaviour (Aron, 2007; Dempster, 1995; MacLeod et al., 2003; Smith, 1992). While at the beginning of the 19th century, observations of inhibitory processes in controlled experiments were ignored or dismissed as errors (Howell, 1921; Meltzer, 1899), the term became established in the second half of the century (Bari & Robbins, 2013; Macmillan, 1992, 1996). Clark (1996) defined inhibition comprehensively as "any mechanism that reduces or dampens neuronal, mental, or behavioral activity" (p.128). As a core function of cognitive control, behavioural inhibitory control constitutes the main focus of the present thesis.

Cognitive control mechanisms enable goal-directed responses to relevant stimuli and ignoring irrelevant ones (Miyake & Friedman, 2012). Without this ability, we would often be helpless in the face of the multitude of stimuli in our environment and be unable to adapt to changing environments. Therefore, control mechanisms are essential characteristics of human behaviour, especially when intentions are incompatible with automatic behaviour. Furthermore, it is known that some people can better control their behaviour than others (Friedman & Miyake, 2017) and that this ability may vary within a person depending on external circumstances (e.g. Killgore, 2010). However, research on the stability and plasticity of inhibitory control is still incomplete.

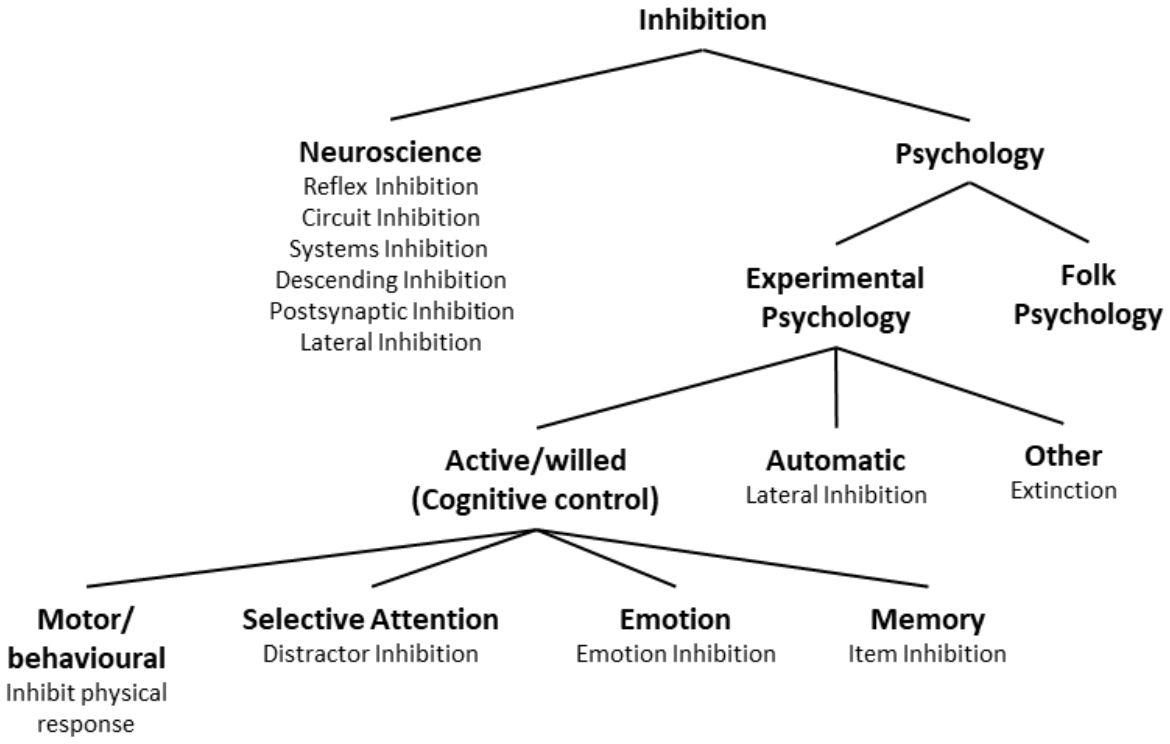


Figure 1. Overview of Research and Application Fields using the Term *Inhibition*.

Adapted from: Aron, A. R. (2007). The neural basis of inhibition in cognitive control. *The Neuroscientist*, 13(3), 214–228, Copyright © (2007).

To begin, despite a large body of research, there is a lack of agreement on the definition of cognitive control (Baggetta & Alexander, 2016; Karr et al., 2018), also termed executive functions (Diamond, 2013). A very well-known model that also addresses controlled processes is the multi-component model of working memory (Baddeley, 2012; Baddeley & Hitch, 1974). While this model, as well as other earlier models (e.g. Shallice, 1982), initially assumed a unitary control system (cf. the central executive; Baddeley & Hitch, 1974), there has been a later shift to considering several sub-domains of cognitive control (Baddeley, 1996; Smith, 1999). Miyake et al. (2000) established the widely used classification comprising "*inhibition* of dominant or prepotent responses", "*shifting* between tasks or mental sets", and "*updating* and monitoring of working memory representations" (Miyake et al., 2000, p. 54).

The subdomain of inhibition is not a uniform construct either (Dempster, 1993), and many subcomponents contribute to successful behavioural inhibitory control. First, relevant

aspects must be selected during the perception of a stimulus, and irrelevant stimuli or responses must be ignored or suppressed. When information is processed in working memory, memory intrusions of older, now irrelevant information must be prevented. Finally, an appropriate response must be selected and executed, whilst undesired reactions must be avoided or stopped (Friedman & Miyake, 2004). In addition, there are proactive stop mechanisms. Proactive inhibition results from internal goals preparing for the possible impending reactive inhibition that is triggered by external signals (Aron, 2011; Ballanger, 2009).

It is still debated whether, and if so, which aspects of this entire process belong to one or more distinct inhibitory control abilities. One of the early classifications of inhibitory control was suggested by Harnishfeger (1995), distinguishing between behavioural inhibition and cognitive inhibition, e.g. inhibiting thoughts, and between cognitive inhibition and resistance to interference, e.g. preventing interference by distracting stimuli. This structure has subsequently been adopted (e.g. Hasher et al., 2007; Stahl et al., 2014), sometimes with slight modifications, including the separation of behavioural and oculomotor inhibition (Nigg, 2000) and extensions, such as adding the delaying of responses in the face of reward (Cyders & Coskunpinar, 2011). In addition, there is overlap with other constructs or cognitive processes, for instance, selective visual attention, which is the ability to selectively direct perception and responses to relevant objects and ignore objects or events that are not currently relevant (Treisman, 1969).

At present, the taxonomy provided by Friedman and Miyake (2004) is widely used. They distinguished between prepotent *response inhibition,* which is "the ability to deliberately suppress dominant, automatic, or prepotent responses", resistance to *distractor interference*, which is "the ability to resist or resolve interference from information in the external environment that is irrelevant to the task at hand" and resistance to *proactive interference*, which is "the ability to resist memory intrusions from information that was previously relevant to the task but has since become irrelevant" (Friedman & Miyake, 2004, pp. 104–105). The present thesis will focus solely on response inhibition and distractor interference, as these two closely related dimensions were shown to be separable from proactive

interference (Friedman & Miyake, 2004). An overview of different taxonomies used to describe these constructs is given in Table 1.

Table 1. Overview of Taxonomies on Inhibitory Control.

Present thesis	Dempster (1993)	Harnishfeger (1995)	Nigg (2000)	Friedman and Miyake (2004)	Hasher et al. (2007)	Diamond (2013)	Stahl et al. (2014)	Kane et al. (2016)
Response Inhibition	Control of Motor Interference	Behavioural Inhibition	Behavioural Inhibition / Oculomotor Inhibition	Prepotent Response Inhibition	Restraint	Self Control	Behavioural Inhibition	Attention Restraint
Distractor Interference	Control of Perceptual Interference	Resistance to Interference	Interference Control	Resistance to Distractor Interference	Access	Interference Control	Stimulus Interference	Attention Constraint

1.1.2 Assessment

> "How did the American secret service CIA manage to reveal Soviet spies during the cold war? **Legend has it that suspects had to perform a classical color-word Stroop task** (…) with Russian color words (…) which were shown in an incompatible print color (…) if the suspect showed a prolonged reaction or even made a reading mistake (…) the **CIA agents knew they found a Russian-speaking spy."**
>
> (Haciahmet et al., 2022, pp. 1–2)

Many tasks and variations have been constructed and implemented to measure inhibitory control in both research and application. Inhibitory control tasks are usually based on the presentation of a stimulus to be responded to or not responded to. Responses are typically verbal, oculomotor, or manual. Some tasks address inhibitory control by requiring the suppression of an automatic response; others present competing stimuli or stimulus features. In general, the former tasks are assigned to response inhibition, the latter to distractor interference. However, this subdivision is sometimes ambiguous. The following sections explain all tasks relevant to this thesis and the respective theories. Table 2 provides schematic depictions of the tasks and a summary of the key dependent variables and their

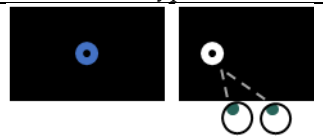
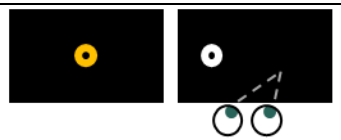
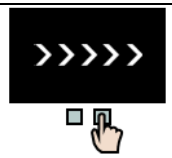
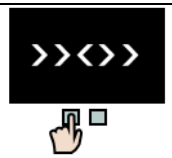
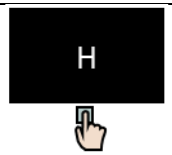
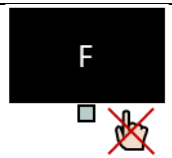
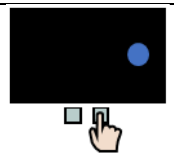
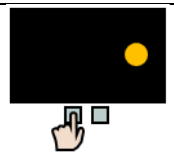
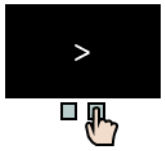
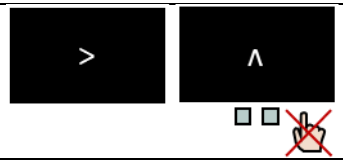
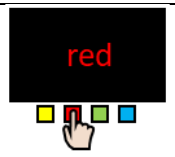
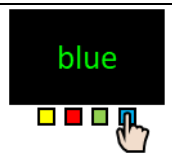
respective constructs. This thesis considers these dependent variables as measures of inhibitory performance, also referred to as primary inhibitory control variables.

Antisaccade Task

The antisaccade task (Hallett, 1978) is based on eye movement detection and measures response inhibition (Gärtner & Strobel, 2021; Rey-Mermet et al., 2018; Stahl et al., 2014). In this task, a central fixation stimulus is followed by a peripheral target on the right or left half of the screen. Participants are instructed to inhibit the prepotent saccade towards the appearing target and instead generate a saccade to the diametrically opposite position (Hutton & Ettinger, 2006). Typically, there is a control condition in which participants perform prosaccades, i.e. they are instructed to look towards the stimulus. Eye-tracking technology (section 2.1) allows precise measurement of eye movements during the task.

Common dependent variables are direction errors and latencies, i.e. the time from the target's appearance to the onset of a correctly executed saccade (Holmqvist et al., 2011). Antisaccade error rate is considered as the primary inhibitory variable. Typically, healthy people have an antisaccade error rate of about 20 – 30% (Coors et al., 2021; Smyrnis et al., 2002), and incorrect trials are usually followed by corrective saccades (Fischer et al., 2000; Hallett, 1978; Hutton & Ettinger, 2006). The simple manipulation of the instruction allows contrasting performance in voluntary antisaccades with performance on highly automated, reflex-like prosaccades. In general, responses in antisaccade trials are slower and contain more errors than in prosaccade trials (Pierce et al., 2019). Additionally, responses are affected by trial history (e.g. previous trial was a prosaccade or antisaccade trial; Cherkasova et al., 2002; Manoach et al., 2007) when pro- and antisaccades are presented in a mixed design instead of a block-wise presentation.

Table 2. Inhibitory Control Tasks.

Task	Graphical depiction of trial types			Primary Inhibitory Variable	Construct
antisaccade	prosaccade		antisaccade 	antisaccades error rate	response inhibition
Eriksen flanker	congruent		incongruent 	congruency effect	distractor interference
go-/no-go	go		no-go 	no-go error rate	response inhibition
Simon	congruent		incongruent 	congruency effect	unclear
stop-signal	go		stop 	SSRT	response inhibition
Stroop	congruent		incongruent 	congruency effect	response inhibition or distractor interference

Note. The schematic graphical depictions and assigned primary inhibitory variables of the tasks are the variants and measures used in the studies of this thesis. For more detailed information on task variants and measured constructs, see section 1.1.2. SSRT = stop-signal reaction time

The nature of underlying cognitive mechanisms in antisaccade performance is an ongoing debate (Hutton & Ettinger, 2006). A variety of theoretical models describe processes involved in the antisaccade task. Early models assumed a serial process when correctly executing antisaccades: The tendency to perform an automatic prosaccade is suppressed, there is a spatial transformation of the stimulus location into a motor command to the opposite side, and, finally, the volitional saccade is performed (Everling & Fischer, 1998; Olk & Kingstone, 2003; Pierce et al., 2019).

More recent models suggest a race between automatic pro- and deliberate antisaccades in a parallel competition. The correct execution of an antisaccade occurs if it is generated fast enough. If, in contrast, the prosaccade reaches the critical response threshold first, an incorrect prosaccade is performed (Cutsuridis, 2017; Cutsuridis et al., 2007; Massen, 2004; Noorani & Carpenter, 2013; Trappenberg et al., 2001). Parallel programming seems reasonable as prosaccade errors are usually followed by corrective saccades, many of which are executed too quickly to be sequentially generated after the incorrect response (Pierce et al., 2019). Furthermore, Massen (2004) showed that a manipulation slowing down correct antisaccades also leads to higher error rates. Thus, the prosaccade process had more time to reach the threshold.

According to these models, the prosaccade programme is cancelled as soon as the correct antisaccade is performed, which can be explained in several ways (Hutton, 2008). On the one hand, it is possible that a fast activation of the antisaccade automatically inhibits the prosaccade execution. In other words, there is a competitive integration of two signals, and the antisaccade response necessarily prevents the generation of the prosaccade through latent inhibition without a specific stop process being necessary (Cutsuridis et al., 2007). On the other hand, there are models, such as the linear approach to threshold with ergodic rate (LATER) model, which postulate that the race requires a specific stop process that suppresses the incorrect prosaccade (Noorani & Carpenter, 2013, 2016). The stochastic early reaction, inhibition, and late action (SERIA) model (Aponte et al., 2017) builds on the LATER model and is of particular relevance to this thesis. It additionally takes into account that there are both early failures of inhibition with short latencies and late ones with longer

latencies (Coe & Munoz, 2017). The model includes an early race between a fast prosaccade and an inhibition unit and a later secondary race between controlled pro- and antisaccades (section 2.3.2).

Eriksen Flanker Task

The Eriksen flanker task (Eriksen & Eriksen, 1974) is, like most inhibitory control tasks, based on the assessment of manual responses. Participants categorise a central target (e.g. arrow, letter, or symbol) flankered by either congruent or incongruent stimuli, thus, stimuli that are associated with the same or opposite response as the target. Incongruent compared to congruent flankers increase reaction time (RT) and error rate, referred to as congruency or flanker effects, serving as the primary inhibitory variables.

The task is a measure of resistance to distractor interference (Friedman & Miyake, 2004; Gärtner & Strobel, 2021; Pettigrew & Martin, 2014; Rey-Mermet et al., 2018; Stahl et al., 2014). However, interference is raised due to at least two different conflicts, impairing the explicit interpretation of task results: On the one hand, there is a conflict on stimulus level, i.e. between the codes of target and distractor, and on the other hand, there is a conflict on the response level, i.e. between responses assigned to target and distractor (Fournier et al., 1997; Kornblum et al., 1990; Stahl et al., 2014). Furthermore, the congruency effect also reflects selective attentional effects. Although the targets position for all upcoming trials is exactly predictable, adjacent positions are processed and impact task performance. Apparently, the selectivity of the visual system is limited in its capacity (Eriksen & Eriksen, 1974). Thus, the task is studied both as a measure of distractor interference and in the context of selective visual attention.

The limitation of attention is often explained by attentional filtering processes. Initial models of attention compare attention to a spotlight that highlights a particular location, which is then processed more intensely (Posner, 1980; Posner, Snyder, & Davidson, 1980). Based on findings from the Eriksen flanker task, this model has been superseded by the variable zoom lens metaphor, assuming that the position of attention and its size and shape are adjustable. As time from target onset (or cue onset, depending on task design) passes, the focus

narrows, and the narrower it is, the less influential distractors are (Eriksen & St. James, 1986; LaBerge et al., 1991).

Temporal parameters of the build-up in attentional selectivity are also subject to dual route or dual process models, which suggest a deliberate and a direct route leading to responses. The slower, deliberate route favours the correct response, and the fast, automatic, direct route leads to either the correct or incorrect response (Ridderinkhof et al., 2021). Accordingly, there are more errors in fast incongruent responses than in slow ones (Gratton et al., 1992). This idea is also taken up by the Activation-Suppression model (Figure 2; Ridderinkhof, 2002). This model assumes a gradual build-up in selective suppression that reduces activation by the direct route. When selective suppression is strong, the direct route loses relevance more quickly, thus the deliberate route gains relevance more quickly, resulting in faster incongruent RT. Therefore, RT distributions reflect temporal dynamics of activation and suppression processes (Wildenberg, Burle et al., 2010). A typical finding in the Eriksen flanker task is that for slow responses, the corresponding congruency effect for RT increases. That is, when analysing trials with slow responses, the RT difference between incongruent and congruent conditions is larger than for fast responses. However, when selective suppression is built up, this increased congruency effect for RT in slow responses is reduced, indicating that the influence of the direct route has been suppressed (Burle et al., 2005; Jong et al., 1994; Ridderinkhof, 2002).

The idea of gradually increasing selectivity of attention to the target is taken up in many theoretical concepts regarding the Eriksen flanker task (Kinder et al., 2022; White et al., 2011). However, there are also considerations on whether the build-up in selectivity takes place not gradually but in two distinct stage-like phases (Hübner et al., 2010). Temporal parameters in selective attention seem to depend on task characteristics (such as the selected stimuli, presentation order, and times). Therefore, it is crucial to consider these in interpreting results (Hübner & Töbel, 2012; Pratte, 2021). So-called delta plots visualise concepts of the Activation-Suppression model by plotting congruency effects as a function of RT distribution, which is addressed in more detail in section 2.3.1.

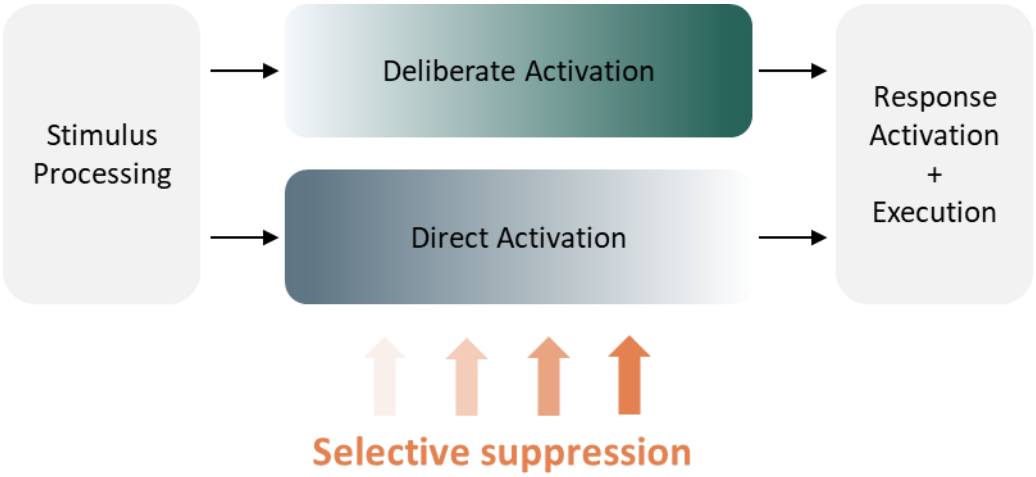


Figure 2. Activation-Suppression Model.

The deliberate route (top) correctly transfers the stimulus into the required response and is slower than the direct route (bottom), which is also influenced by irrelevant stimulus features/dimensions. Over time, selective suppression builds up, represented by increasing arrow intensity, and inhibits direct activation, thereby facilitating the correct response in incongruent trials.

Go-/No-Go Task

The go-/no-go task (Drewe, 1975; Luria, 1973) requires participants to respond quickly to predefined frequently presented go stimuli and to withhold the response on infrequent no-go stimuli. Usually, a manual keypress is required, but there are also eye-tracking-based versions of the task (Noorani & Carpenter, 2016; Talanow et al., 2020). The primary inhibitory control variable is the no-go (commission) error rate. A higher rate of no-go errors is assumed to indicate a lower degree of response inhibition (Aichert et al., 2012; Stahl et al., 2014). Importantly, the involved cognitive mechanisms are affected by task parameters such as stimulus presentation speed and go stimulus frequency. The higher frequency of go compared to no-go stimuli leads to an automatised tendency to respond. A higher prepotency to respond may enhance the requirement to cancel a preactivated process, whereas under lower prepotency, decisional processes may affect performance more strongly (Aron, 2011). However, task parameters are typically not standardised (Young et al., 2018).

It has also been questioned whether reactive inhibition caused by the presentation of the no-go stimulus is the only inhibitory mechanism affecting task performance (Criaud & Boulinguez, 2013). Uncertainty about the subsequent trial causes participants to control their behaviour throughout the entire task to have enough time to process perceptual information and respond appropriately (Jaffard et al., 2007). Thus, the go-/no-go task requires withholding responses (Wright et al., 2014) and successful performance also relies on mechanisms of proactive inhibition (Aron, 2011; Ballanger, 2009). Stronger proactive control is associated with slower go RT and usually improves reactive inhibition of the response in no-go trials.

Simon Task

In the Simon task (Simon & Rudell, 1967), a manual spatial response (e.g. left/right button press) to a stimulus is made depending on a non-spatial feature (e.g. stimulus colour or shape) while its position is ignored. Although stimulus location is irrelevant to the task, non-corresponding stimulus and response locations increase RT and error rates compared to corresponding locations. These congruency or Simon effects (Simon, 1990) are considered the primary inhibitory variables. There is no consensus as to whether the Simon task is a measure of distractor interference or response inhibition (Rey-Mermet et al., 2018; Verbruggen et al., 2005). On the one hand, a distracting stimulus feature, i.e. its location, is to be ignored, similar to how distracting stimuli are to be ignored in the Eriksen flanker task, suggesting the task is a measure of distractor interference; on the other hand, there are indications that the task may be a measure of response inhibition: In contrast to the Eriksen flanker task, there is no interference at stimulus level, but only at response level. In incongruent trials, the location triggers an action tendency that opposes the response triggered by the stimulus. Thus, the Simon effect is solely due to a stimulus-response conflict, whereas the Eriksen flanker task is also impacted by a stimulus-stimulus conflict (Fournier et al., 1997; Kornblum et al., 1990).

The Simon effect can also be explained by dual-route models (Jong et al., 1994; Kornblum et al., 1990). The irrelevant stimulus location activates the automatic direct route that supports the corresponding spatial response. The deliberate route activates the correct response

according to stimulus-response mapping. Again, analysing congruency effects as a function of RT offers insights into temporal components of these underlying mechanisms (Burle et al., 2014; Proctor, 2011).

Interestingly, compared to other congruency effects for RT, the Simon effect is more pronounced in faster than slower RTs (Burle et al., 2005; Hommel, 2011; Wildenberg, Wylie et al., 2010). In distributional analyses, this is reflected in reduced congruency effects for slow responses (section 2.3.1). One reason could be a spontaneous decay of spatial information (Hommel, 1993; Jong et al., 1994). However, for very slow RTs, the congruency effect in the Simon task becomes negative, i.e. congruent responses are processed more slowly than incongruent ones. This finding contradicts the hypothesis of spontaneous decay and suggests an active inhibitory mechanism as it is part, for example, of the Activation-Suppression model (Figure 2) that has also been discussed in relation to the Eriksen flanker task (Ridderinkhof, 2002). Such a suppressing mechanism could build up slowly over time and therefore be more effective for slow than early responses. Reversed late Simon effects could result from a possible overshoot due to the build-up of inhibition.

These temporal dynamics can also be reproduced in modelling. Ulrich et al. (2015) showed that the direct activation of spatial information increases rapidly and then decreases again when relevant activation increases, which leads to smaller congruency effects for slow RTs. This assumption is also supported by other studies showing that stimulus location is processed faster than the relevant dimension in the Simon task (Cespón et al., 2020). The temporal overlap between relevant and irrelevant activation is smaller than in the Eriksen flanker task, where target and distractors are processed equally fast. If the temporal lag between relevant and irrelevant activation is increased in an Eriksen flanker task, reduced congruency effects for slow responses can also be obtained for this task (Hübner & Töbel, 2019). Thus, task-related differences may result from different onsets and strengths of suppression mechanisms (Baroni et al., 2011; Burle et al., 2005; Pratte et al., 2010; Ulrich et al., 2015).

Stop-Signal Task

The stop-signal task (Lappin & Eriksen, 1966; Logan & Cowan, 1984) can be considered a variant of the go-/no-go task. A manual response is chosen based on a centrally presented go stimulus with typically two categories mapped onto different responses. In a minority of trials, the stimulus is unpredictably followed by a visual or auditory stop-signal. When a stop-signal appears, the response must be withheld. An important difference is that in the go-/no-go task, no-go trials immediately start with the presentation of the no-go stimulus. However, in the stop-signal task, stop trials begin with the presentation of a go signal, which is later followed by the stop-signal. Therefore, the response must be inhibited after motor programming mechanisms have been initiated. Instead of not programming a response or generating an alternative action (like in the antisaccade task), an already initiated action, the response to the go signal, is cancelled (Eagle et al., 2008). Thus, the stop-signal task demands a later-stage inhibition than the go-/no-go task (Rubia et al., 2001).

Similar to the go-/no-go task, proactive inhibition mechanisms play a role in the stop-signal task. The participant must find a balance between slow and fast responses in go trials. While the instruction requires a fast response, at the same time, a fast response makes it difficult to stop in time. Proactive inhibition is essential for this balance (Verbruggen & Logan, 2009b, 2017). The central idea of the stop-signal task is that separate stop and go processes are activated; successfully stopping indicates a faster stop than go process (Verbruggen et al., 2008).

The primary inhibitory variable is the stop-signal reaction time (SSRT, Figure 3), which is an estimate of the speed of stopping an initiated response and which is used as a measure of response inhibition (Rey-Mermet et al., 2018; Verbruggen & Logan, 2009a). The shorter the time between go and stop-signal (stop-signal delay; SSD), the more likely a successful inhibition. As successful inhibition results in the absence of a response, SSRT cannot be measured directly. Estimation methods underlying the SSRT are based on the independent horse race model (Logan & Cowan, 1984). This model assumes that there is an independent race between the go and stop processes (Ollman, 1973), which are triggered by the respective signal. In a stop trial, completing the stop process in time results in successful response

inhibition. However, a response is executed incorrectly when the go process is completed before the stop process.

There are different methods for designing stop-signal tasks and estimating the end of the stop process (Verbruggen & Logan, 2009a). SSRT is calculated by subtracting the mean SSD from the end of the stop process (Verbruggen et al., 2019). The original SSRT calculation was based on the mean method, in which the end of the stop process equals the mean RT in go trials, thereby assuming that p(respond | signal) is .50. Recent recommendations, however, prefer the more complex integration method as it is more reliable and less biased, for example, by the skewness of the RT distribution (Verbruggen et al., 2019). This method estimates the end of the stop process as n^{th} RT, where n is the number of RTs in the go RT distribution multiplied by p(respond | signal).

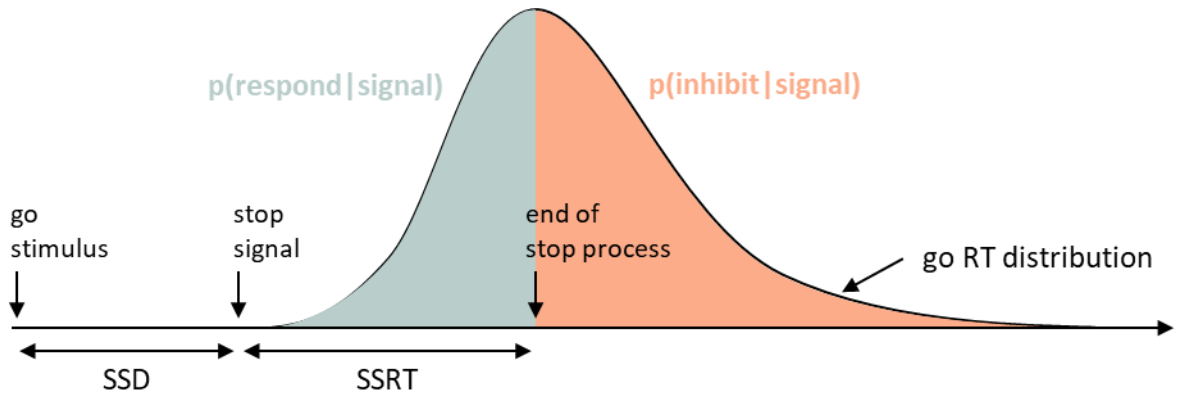


Figure 3. Stop-Signal Task – The Independent Race Model.

The probability of responding to a stop-signal corresponds to the part of the go RT distribution that is too fast to be inhibited. The remaining part of the distribution corresponds to slower responses that can be inhibited. SSD = stop-signal delay; SSRT = stop-signal reaction time; RT = reaction time

The SSRT has also been criticised for not capturing all the inhibition mechanisms involved (e.g. the ability to initiate the stop process) and for being a cumulative statistic that subsumes several processes into a single value per participant (Skippen et al., 2019). Furthermore, the independent horse race model is limited by the fact that it only describes processes but does

not explain them (Schall et al., 2017; Verbruggen & Logan, 2017). In addition, for comparisons between studies and the evaluation of reliability (section 1.2.1) in the stop-signal task, it should be kept in mind that task versions, especially in old publications, were not standardised. Since changes in task and estimation methods substantially affect the stop process and the task's reliability (Band et al., 2003), this can be considered a major shortcoming in past research. However, by now, many of the effects of heterogeneity in task construction and execution have been well studied, and recommendations on how the task should best be implemented have been developed (Verbruggen et al., 2019).

Stroop Task

In the Stroop task (Stroop, 1935), colour words are presented in different font colours. The instruction is to identify the font colour and not the written word. RTs and error rates are higher when word and font colour are incongruent compared to congruent or neutral (e.g. colour patch) conditions. The very robust (MacLeod, 1991) congruency effect for RT is also referred to as the Stroop effect and serves as the primary inhibitory variable. Typically, the task is used to measure response inhibition (Friedman & Miyake, 2004; Gärtner & Strobel, 2021; Pettigrew & Martin, 2014; Rey-Mermet et al., 2018; Stahl et al., 2014). However, it is sometimes also assigned to distractor interference (e.g. Nigg, 2000).

Response inhibition is evident in the task as reading is a more automated response than naming the colour. This automated response must be suppressed in incongruent trials, leading to a time delay. Thus, the Stoop task is also used to study automatic and controlled processes, as first described by Posner and Snyder (1975). While the former processes are unconscious, without intention, and undisturbed by other cognitive processes, controlled processes are conscious and have limited capacity (Schneider & Shiffrin, 1977; Shiffrin & Schneider, 1977). Posner and Snyder (1975) assume that automatic and controlled processes are processed in parallel until shortly before the response is executed, an assumption shared by theories of other task processes (see above). Like many response inhibition tasks, the Stroop task also demands working memory capacities. While congruent trials can be solved correctly without attention to the task instruction, in incongruent trials, the correct task set

must be maintained to recall that the colour is to be named and not the word to be read (Kane et al., 2016).

However, the Stroop task may also be regarded as a measure of distractor interference because, similar to the Eriksen flanker task, there is a conflict that may be the result of stimulus-stimulus conflict and stimulus-response conflict (Kornblum et al., 1990; van Veen & Carter, 2005; van Veen et al., 2001; Whitehead et al., 2020). The stimulus-stimulus conflict arises when the irrelevant stimulus dimension opposes the relevant stimulus dimension, i.e. written word and font colour. The stimulus-response conflict arises when the irrelevant stimulus dimension opposes the required response, i.e. written word and mapping of colour and button-press. The task can either be solved by inhibiting an automated response or by ignoring distracting task aspects of the stimuli (Stahl et al., 2014). Thus, both automatic encoding processes and response selection contribute to the Stroop effect (Houwer, 2003).

Following these considerations, the question arises as to whether, in reverse, congruent trials lead to facilitation processes. Congruent trials were first used about 30 years after the introduction of the task. Until then, the Stroop effect was based only on comparing incongruent and neutral trials (Langer & Rosenberg, 1966). Indeed, in congruent trials, facilitation has been observed, but it is highly dependent on how the neutral condition is designed (e.g. colour blocks or irrelevant words), and overall facilitation effects are much smaller than the Stroop effect itself (MacLeod, 1991). Another aspect in which Stroop tasks differ is the response modality. Initially, the task required vocal responses. However, today there are also versions in which the answer is given by pressing keys previously assigned to the colours. It has been shown that the assignment is learned quickly (Houwer, 2003) and that phonological processing takes place in both modalities (Parris et al., 2019). The Stroop effect may be reduced in magnitude for manual responses but remains robustly present (MacLeod, 1991).

1.1.3 Unity and Diversity

As discussed in the previous section, inhibitory control tasks capture different subcomponents of inhibition. Since, in practice, often only one task is used and then taken as an indicator of inhibitory control in general, the critical question arises to what extent performance in variables in different tasks is interrelated.[1]

Correlations Between Tasks

One approach to study the unity of the inhibitory control is the investigation of correlations between primary inhibitory variables of different tasks. The strongest significant positive correlations in previous studies were shown between go-/no-go and stop-signal tasks, which may be expected as both are considered to measure response inhibition (r = .28 – .88; Bender et al., 2016; Enge et al., 2014; Hedge et al., 2018; Reynolds et al., 2006; Tiego et al., 2018). However, some studies reported non-significant correlations (Aichert et al., 2012; Cheung et al., 2004). In addition to the go-/no-go and stop-signal tasks, the antisaccade task is also considered a measure of response inhibition. Accordingly, significant positive yet mostly small correlations between antisaccade and stop-signal tasks were shown (r = .16 – .19; Friedman & Miyake, 2004; Gärtner & Strobel, 2021; Miyake et al., 2000) and fewer non-significant correlations (Aichert et al., 2012; Rey-Mermet et al., 2018). However, research on correlations between antisaccade and go-/no-go tasks is limited and seems to support non-significant correlations (Aichert et al., 2012).

The Stroop task is also often interpreted as a measure of response inhibition and, accordingly, showed significant positive correlations with the antisaccade task (r = .13 – .23; Aichert et al., 2012; Friedman & Miyake, 2004; Miyake et al., 2000; Rey-Mermet et al., 2018). However, correlations were very small, and one study also reported a non-significant correlation (Gärtner & Strobel, 2021). In addition, there is no evidence of significant

[1] In this thesis, results reported on inhibitory control tasks refer to primary inhibitory variables unless otherwise stated.

correlations between go-/no-go and Stroop tasks (Aichert et al., 2012; Bender et al., 2016; Cheung et al., 2004; Enge et al., 2014; Hedge et al., 2018; Noreen & MacLeod, 2015; Tiego et al., 2018). Findings on correlations between Stroop and the stop-signal tasks are mixed, including mostly non-significant (Aichert et al., 2012; Bender et al., 2016; Cheung et al., 2004; Enge et al., 2014; Enticott et al., 2006; Gärtner & Strobel, 2021; Hedge et al., 2018; Tiego et al., 2018) but also few significant correlations (r = .15 – .21; Friedman & Miyake, 2004; Miyake et al., 2000; Rey-Mermet et al., 2018). Thus findings support theoretical considerations that question whether both tasks measure the same construct (Khng & Lee, 2014). However, again correlations were small, and in line with the potential role of distractor interference in the Stroop task (section 1.1.2), there are studies reporting significant correlations between Stroop and Eriksen flanker tasks (r = .13 – .18; Friedman & Miyake, 2004; Hedge et al., 2018; Rey-Mermet et al., 2018; Whitehead et al., 2020) but also some that do not (Bender et al., 2016; Gärtner & Strobel, 2021; Pettigrew & Martin, 2014).

There seems to be little in common between the Eriksen flanker task and the response inhibition tasks: All studies summarised here found non-significant relations of the Eriksen flanker task with antisaccade, go-/no-go and stop-signal tasks (Bender et al., 2016; Friedman & Miyake, 2004; Gärtner & Strobel, 2021; Hedge et al., 2018; Rey-Mermet et al., 2018; Tiego et al., 2018). The only exception is one study reporting a significant correlation between the Flanker and stop-signal tasks (r = .15; Friedman & Miyake, 2004).

Finally, regarding the Simon task, there are only few findings on significant correlations between the Simon task and other inhibitory control tasks: Tiego et al. (2018) reported a significant positive correlation between Simon and Stroop tasks (r = .27) and Whitehead et al. (2020) reported a significant correlation between Simon and Eriksen flanker tasks (r = .18). All other correlations between those tasks as well as between Simon and go-/no-go or stop-signal tasks were non-significant (Paap & Sawi, 2016; Rey-Mermet et al., 2018; Tiego et al., 2018). Those findings might suggest the Simon task to be a measure of distractor interference rather than response inhibition. However, this statement should be evaluated with great caution, as it is based on far too few studies.

To summarise, findings on correlations between different tasks were heterogenous, and even significant correlations were usually in a very low range. The only tasks with fairly consistent correlations are the stop-signal and go-/no-go tasks.

There are several possible reasons to explain the absence of correlations between the primary inhibitory variables of the tasks. On the one hand, low or non-significant correlations could indicate that task performance includes unrelated abilities; on the other hand, there are several measurement issues that could have contributed to the results. First, it would be possible that the lack of consideration of possible speed-accuracy trade-offs reduces correlations between tasks. Therefore, so-called inverse efficiency scores can be calculated for some tasks that combine speed and accuracy. However, the use of this measure seems to increase correlations only slightly (Gärtner & Strobel, 2021; Wolff et al., 2016), suggesting that speed-accuracy trade-offs are not the main driver of the small correlations. Another reason could be the aggregation across trials to individual task scores, where much information is lost. However, assessing trial-by-trial variability does not result in higher correlations between Flanker and Stroop task scores, as shown by Rouder and Haaf (2019). Furthermore, low reliability could have decreased correlations (Spearman, 1904). It has been shown that congruency effects often do not have satisfactory reliability (section 1.2.1; Hedge et al., 2018). Accordingly, correlations are increased when purely incongruent RTs are considered, for example, in the Stroop and Eriksen flanker tasks, instead of congruency effects (e.g. Gärtner & Strobel, 2021). Moreover, low correlations may be the result of task impurity. Task impurity describes that different tasks capture idiosyncratic task requirements and do not exclusively measure inhibitory control processes (Burgess, 1997; Miyake et al., 2000). These task-specific processes might generate more variance than cross-task inhibitory control processes, thus masking commonalities (Shilling et al., 2002) and reducing convergent validity (Duckworth & Kern, 2011).

Both latter problems, namely unreliability and task impurity, can be addressed using latent variable approaches. Latent variable approaches extract common variance between tasks, resulting in purer measurements. In addition to the task-specific variance, the variance of

random measurement errors is considered separately, leading to correlations between tasks being corrected for unreliability (Bollen, 1989).

Latent Variable Approaches

Latent variable approaches usually do not focus on individual correlations between tasks but allow the investigation of which tasks form a common construct and how different constructs are related. For example, despite low correlations, Aichert et al. (2012) demonstrated that antisaccade, Stroop, go-/no-go, and stop-signal tasks load on a common response inhibition factor.

The subdivision of inhibition into response inhibition, distractor interference and proactive interference by Friedman and Miyake (2004), introduced in 1.1.1, also results from confirmatory factor analysis using latent variables. In their seminal, often-cited study on the unity and diversity of inhibitory control, they identified commonalities between tasks, extracted the three factors, and showed that the latent factors response inhibition and distractor interference are closely related (r = .67), whereas neither is associated with proactive interference. Friedman and Miyake (2004) concluded that there is at least some commonality within inhibition. Kane et al. (2016) confirmed the close relationship (r = .60) between attention restraint (i.e. response inhibition) and attention constraint (i.e. distractor interference) in a better-powered study, again showing that the constructs are similar but not interchangeable. Other studies also report an overlap of different aspects of inhibition using latent variable approaches (Pettigrew & Martin, 2014), and the unity and diversity pattern could even be replicated in non-human primates (Loyant et al., 2022).

However, recent studies challenge inhibitory control as a psychometric construct or question the closeness of the relationship between response inhibition and distractor interference. Stahl et al. (2014) were able to identify the two factors, which, however, were not related. They pointed out that the Eriksen flanker task was often used as a measure of distractor interference in past studies and the Stroop task as a measure of response inhibition. Since both tasks involve stimulus-response and stimulus-stimulus conflicts (section 1.1.2), the relation between the two constructs may have been artificially increased.

Tiego et al. (2018) showed that response inhibition and distractor interference are unrelated when working memory capacity is included in the model. Thus, common reliance on other processes, such as working memory or processing speed, might partly explain the relationship between both constructs (Hedge et al., 2021). Furthermore, some studies do not find any evidence for the underlying factors proposed by Friedman and Miyake (2004), and there are studies reporting model results without high informative value (Gärtner & Strobel, 2021; Rey-Mermet et al., 2018). Rey-Mermet et al. (2018) thus question the interpretation of earlier studies. In those, as in their own data, often only one task had a strong factor loading, i.e. the factor mainly measured variance in one task. They conclude that inhibitory control tasks do not measure a common construct.

It has even been questioned whether inhibition is a distinct factor within cognitive control at all, as a line of studies was not able to extract a separate inhibitory factor (Gignac & Kretzschmar, 2017; Huizinga et al., 2006; Hull et al., 2008; Krumm et al., 2009). Instead, they found variance to be explained by general speed (Jewsbury et al., 2016; van der Sluis et al., 2007) or showed that inhibition and updating are not separable (Klauer et al., 2010). Also, even a study by Friedman et al. (2008) has questioned their initial division into three cognitive control functions. Their data resulted in a bifactor model in which variance in inhibitory control tasks was fully explained by an overarching Common EF (executive function) factor rather than an inhibition-specific factor. The Common EF factor may reflect the ability to form, maintain, manage and, most importantly, use goals to adjust ongoing processes. This ability is essential when dealing with prepotent or contradictory information and may, therefore, explain variance in inhibitory control tasks (Friedman & Miyake, 2017). A Common EF factor could explain difficulties in identifying separate factors and ambiguities regarding their attribution. However, it cannot account for the fact that in some studies there is evidence for tasks not to measure a common construct at all (Rey-Mermet et al., 2018).

To summarise, using latent variable analyses reduces task impurity and has contributed to a more differentiated view of different subcomponents of inhibitory control and their interrelationships. However, a unified framework on inhibitory control and its

subcomponents is still lacking to date. Using latent variable analyses does not solve all methodological problems, e.g. a very high measurement error leads to little possible common variance remaining and thus may still be problematic (Draheim et al., 2021). In addition, little attention has been paid to the fact that tasks are often presented in a specific context, and the resulting systematic variance across tasks could be misinterpreted as inhibitory control.

1.1.4 Neural Basis

"For more than a century, scientists have attempted to solve "the riddle of the frontal lobes" -that is, to unravel the "hidden secrets" relating the frontal lobes to intellectual functioning."

(Dempster, 1993, p. 13)

The previous sections have shown the absence of a unified concept of inhibitory control. In this section, the focus is shifted to investigating the neural basis of inhibitory control by first addressing cortical structures involved in inhibitory control and then the underlying neurotransmitter systems.

Insights into the neural basis of inhibition come from lesion studies in humans (e.g. Aron et al., 2003; Pierrot-Deseilligny et al., 2003), primate research (e.g. Burman & Bruce, 1997; Sasaki et al., 1989), functional magnetic resonance imaging (fMRI; e.g. Ettinger, Ffytche et al., 2008; Wager et al., 2005), electroencephalography and magneto-encephalography (EEG/MEG; e.g. Allen et al., 2018; McDowell et al., 2005) and transcranial magnetic stimulation (TMS; e.g. Sohn et al., 2002; Wildenberg, Burle et al., 2010) studies.

Performance in inhibitory control tasks is associated with activity in an extensive cortical network. Early reports on the famous case of Phineas Gage, who suffered a lesion in the frontal cortex in an accident and showed impairments in goal-directed behaviour as a result, suggested that the prefrontal cortex (PFC) has a unique role in the voluntary control of our behaviour (Macmillan, 2000). Whereas in the past, frontal functions were often equated with cognitive control, today, a more differentiated view is taken of the individual areas of the frontal lobe and their interactions with other cortical and subcortical structures (Alvarez &

Emory, 2006), although it is undisputed that the PFC is substantially engaged in inhibitory control (Bari & Robbins, 2013; Munoz & Everling, 2004; Stuss, 2011; Stuss & Alexander, 2000). It is assumed that there is a hierarchical neural control along the rostro-caudal axis, in which the PFC, in particular, has control over lower levels (Badre & D'Esposito, 2009; Koechlin et al., 2003; Ridderinkhof et al., 2004).

Within the PFC, especially the ventrolateral (VLPFC) and dorsolateral (DLPFC) prefrontal cortices are involved in the control of higher cognitive functions, such as the integration of perception and action planning in order to translate a learned rule into behaviour (Bari & Robbins, 2013; McDowell et al., 2008; Sweeney et al., 2007). The right inferior frontal cortex (rIFC) is sometimes referred to as "the main locus of inhibitory control" (Bari & Robbins, 2013, p. 63). However, its exact function has not yet been conclusively clarified (Aron et al., 2004; Banich & Depue, 2015). While some studies attribute a role to the rIFC in behavioural monitoring, updating of action plans, selection of appropriate action plans, and control of motor output (Aron, 2011; Chikazoe et al., 2007), there is also evidence that the rIFC may rather be involved in attending to unexpected stimuli and that the pre-supplementary motor area (pre-SMA) may be responsible for the suppression of unwanted motor behaviour (Sharp et al., 2010). The strong functional connectivity between rIFC and pre-SMA could be why lesions in rIFC also lead to deficits in inhibition (Allen et al., 2018; Bari & Robbins, 2013).

In further progression, information is processed in the supplementary motor area (SMA), where responses are initiated or selected and forwarded to the pre-motor cortex (Bari & Robbins, 2013). The frontal eye fields (FEF) and supplementary eye fields (SEF) play a special role in the behavioural monitoring of saccadic inhibition tasks (Ettinger, Ffytche et al., 2008; Jamadar et al., 2013). Other areas that contribute to the successful inhibition of unwanted behaviours include the anterior cingulate cortex (ACC), which is critical for conflict and error monitoring (Botvinick et al., 2001), the supramarginal gyrus (SMG; Brown et al., 2006; Ettinger, Ffytche et al., 2008), the insula (Bari & Robbins, 2013), and subcortical areas such as the subthalamic nucleus (STN) or striatum (Aron, 2011).

In addition to well-supported findings on the brain areas generally involved in inhibitory control, there are both cross-task and task-specific activation patterns (Liu et al., 2004; Nee

et al., 2007; Sebastian et al., 2013; van Veen & Carter, 2005; van Veen et al., 2001; Wager et al., 2005) that will not be further elaborated in this thesis. However, at the neural level, these studies support the idea of different tasks measuring different aspects of inhibitory control (section 1.1.3).

While macroscopic neural mechanisms and the cortical network underlying inhibitory control have been well and extensively studied, microscopic neural mechanisms, such as the neurotransmitters involved in behavioural inhibition, are far less well-characterised (Pauwels et al., 2019). Most findings on cortical structures involved in inhibitory control come from fMRI studies. However, fMRI results are based on blood oxygen level-dependent (BOLD) signals and may not distinguish whether neural signals are excitatory or inhibitory (Buzsáki et al., 2007; Logothetis, 2008). Methodologically, excitatory and inhibitory neurotransmitter systems are often investigated with pharmacological methods (section 1.3.2), magnet resonance spectroscopy (MRS) and positron emission tomography (PET; e.g. Badgaiyan & Wack, 2011; O'Driscoll et al., 1995).

Successful inhibitory control has been shown to involve the excitatory neurotransmitter systems of dopamine (DA), norepinephrine (NE), serotonin (5-HT), and acetylcholine (ACh). DA influences motor readiness for inhibition and activation, and it is involved in error monitoring and selecting a required response (Badgaiyan & Wack, 2011; Bari & Robbins, 2013). DA may also influence the stability of attentional focus and top-down attentional processes (Noudoost & Moore, 2011). NE is also involved in attention by facilitating attention to task-relevant stimuli (Bari & Robbins, 2013; Chamberlain et al., 2006). In addition, NE and 5-HT have been associated with inhibiting an already-initiated response (Cools et al., 2008; Hahn, 2015; Logue & Gould, 2014). However, there are also findings suggesting that the 5-HT system has little influence on inhibitory control (Bari & Robbins, 2013). ACh is known as a neurotransmitter of attention control (Coull, 1998; Moore & Zirnsak, 2017; Noudoost & Moore, 2011). Inhibitory control may be indirectly enhanced by increasing attention through ACh (Ettinger & Kumari, 2019; Sarter & Paolone, 2011). Similar to the cortical networks, there are task-specific effects related to neurotransmitter activity (Eagle et al., 2008), again supporting the idea of different underlying mechanisms. These

differences have implications for developing drug treatments for disorders associated with different deficits in inhibitory control tasks (Eagle et al., 2008).

Even though there is evidence of interaction between excitatory and inhibitory neurotransmitters (Garbutt & van Kammen, 1983), the role of inhibitory neurotransmitters in inhibitory control is less well characterised. The most important inhibitory neurotransmitter in the human brain is γ-aminobutyric acid (GABA; Uusi-Oukari & Korpi, 2010). About 10–40 % of the cerebral cortex and a large part of subcortical structures are innervated by GABAergic neurons (Fonnum, 1987; Rubenstein & Merzenich, 2003). There are $GABA_A$ and $GABA_B$ receptors (Owens & Kriegstein, 2002). Figure 4 shows the distribution of $GABA_A$ receptor in the human brain. There is evidence that GABA activity in the primary motor cortex may contribute to stopping speed (Chowdhury et al., 2019). Furthermore, there is evidence for correlations between GABA levels in the pre-SMA and age-related deterioration of reactive inhibition (section 1.3; Hermans et al., 2018; Nikitenko et al., 2020). In addition, there is preliminary evidence for interactions between ACh and GABA: ACh release in rats was reduced by inhibitory neurotransmitters, which in turn reduced attention thereby suggesting a role for GABA in attention and inhibitory control (Burk et al., 2018).

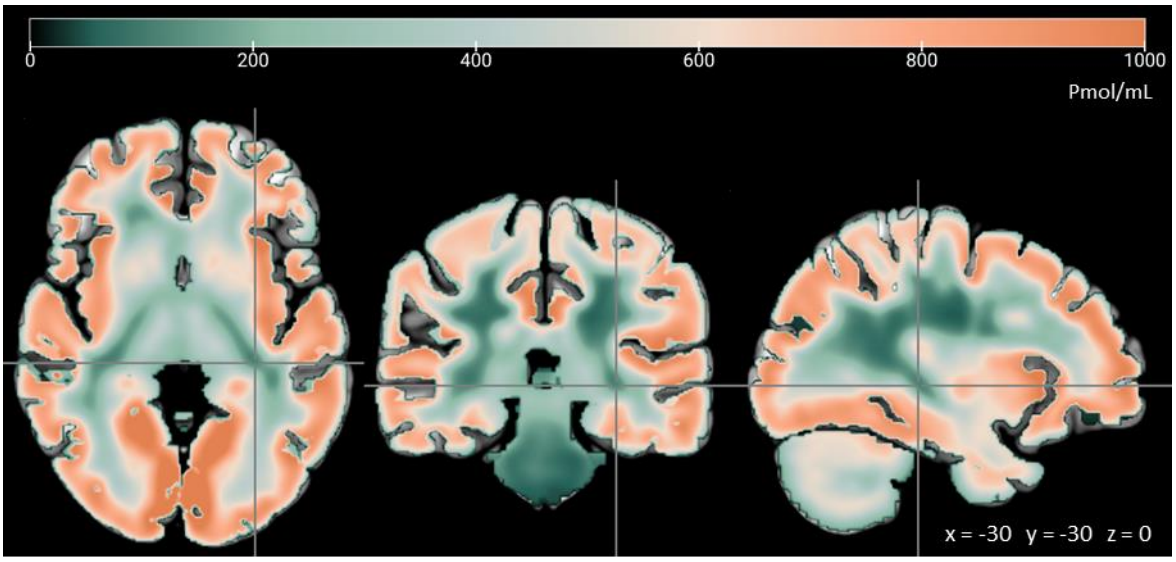


Figure 4. $GABA_A$ Receptor Density (pmol/mL) in the Human Brain.

The figure was created using the Benzodiazepine Receptor Atlas provided by Nørgaard et al. (2020).

GABAergic influences on cognition can be investigated by administering benzodiazepines, anxiolytic drugs known to modulate $GABA_A$ receptors (section 1.3.2). Such pharmacological studies may be used to examine influences on neurotransmitter systems affecting task performance. Changes in inhibitory control, e.g. when administering pharmacological substances, will be discussed in section 1.3. However, before addressing plasticity, the next section will focus on stability, as there are facets of stability that constitute an important prerequisite for studying performance changes.

1.2 Stability of Inhibitory Control

In this thesis, the term *stability* is used in the context of stable measurements. A measurement is considered stable if interindividual differences are temporally stable. Importantly, stability, in this sense, does *not* contradict changes in performance (*plasticity*; see section 1.3) on average (Figure 5). However, the term stability is also used in the stability-flexibility dilemma (Dreisbach & Fröber, 2019), where it refers to processes of goal maintenance and shielding. The dilemma arises from fundamentally antagonistic demands in cognitive control: On the one hand, there is a need for constantly shielding from disturbing stimuli to avoid conflicts; on the other hand, there is a need for *flexibility*, which is the ability to adapt behaviour and thoughts to changing task requirements (Dreisbach & Fröber, 2019).

The importance of stable measurements, thus little interindividual changes over time, becomes apparent, for example, against the background of clinical research. Specifically, there are consistent findings of inhibitory control deficits in mental disorders, for example, attention deficit hyperactivity disorder (ADHD; Barkley, 1997, 1999; Lipszyc & Schachar, 2010; Munoz et al., 2003; Nigg, 2001), autism (Robinson et al., 2009), bipolar disorder (Quraishi & Frangou, 2002; Solé et al., 2011), eating disorders (Bartholdy et al., 2016), obsessive-compulsive disorder (OCD; Chamberlain et al., 2005; Lipszyc & Schachar, 2010), Parkinson's disease (Cameron et al., 2012; Chan et al., 2005), substance abuse (Smith et al., 2014), schizophrenia (Ettinger, Aichert et al., 2018; Kaladjian et al., 2011; Lipszyc & Schachar, 2010), and Tourette's syndrome (Jahanshahi & Rothwell, 2017). It is crucial for clinical research to understand whether these deficits are random time-varying or stable changes, which is important, e.g., when aiming to identify so-called endophenotypes.

Endophenotypes are measurable components, at first sight unrecognisable, that provide clues to the genetic underpinnings of diseases, which are more subtle than disease syndromes (Gottesman & Gould, 2003). Criteria for an endophenotype are heritability, association with illness, independence of clinical state, co-segregation and measurement reproducibility (Glahn et al., 2014). Thus, only when deficits in performance can be measured with high stability and do not fluctuate depending on the situation, a measurement can be suitable to indicate clinical characteristics.

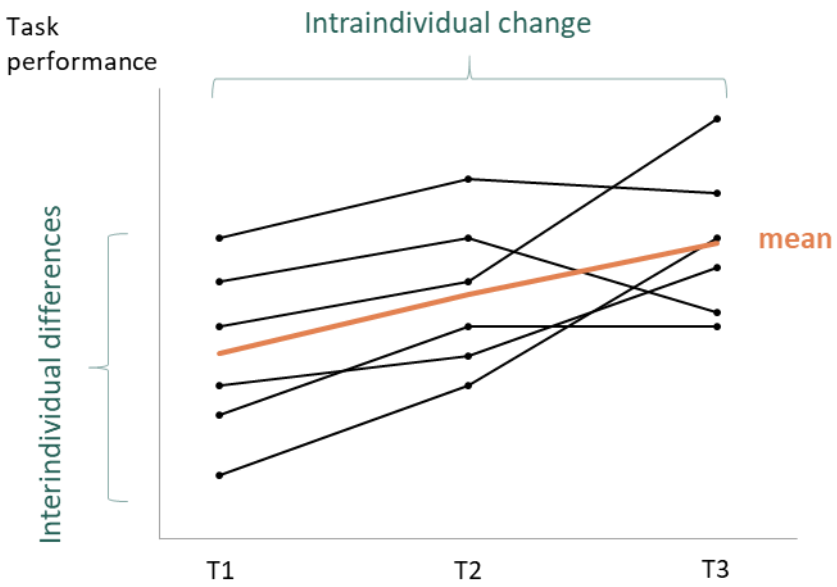


Figure 5. Interindividual Differences, Intraindividual Change and Stability.

The example illustrates high stability between measurement occasions T1 and T2 and lower stability between measurement occasions T2 and T3. In addition, there are changes over time from measurement occasions T1 to T2 and from measurement occasions T2 to T3. Measurement errors are not considered in this figure.

In healthy adults, it was shown that the Common EF factor is highly heritable and hereditary influences remained stable in participants between the age of 17 and 23 (Friedman et al., 2016). It is important to note, however, that high heritability, as well as stability, do not imply invariability or predetermination (Friedman & Miyake, 2017). Individual differences in the Common EF factor are almost entirely driven by genetic influences. Thus, individual variability around a mean is explained but not the mean itself. For example, better

population nutrition could affect the population mean in EF despite high heritability. This aspect is also relevant in the context of other stability and plasticity studies as elaborated above: A measurement providing high stability, i.e. there are little interindividual changes over time, does not imply that there are no (systematic) intraindividual changes at sample level.

Stability is often reported using reliability coefficients. Reliability calculations are based on classical test theory, which divides a measure into variance due to the true value and variance due to measurement error (DeVellis, 2006).

1.2.1 Reliability

"Robust experimental effects do not necessarily translate to optimal methods of studying individual differences."

(Hedge et al., 2018, p. 1182)

Regarding reliability, there is a distinction between internal consistency and temporal stability (Figure 6). Internal consistency (e.g. split-half correlations or Cronbach's α) indicates how different items or trials are related within a measurement. On the other hand, temporal stability (e.g. test-retest or intra-class correlations; ICC) indicates how measured values from different measurement occasions are related. Reliabilities are labelled as excellent (≥.80), good (≥.60), moderate (≥.40) and poor (Hedge et al., 2018). Table 3 gives an overview of previously reported reliabilities of primary inhibitory variables.

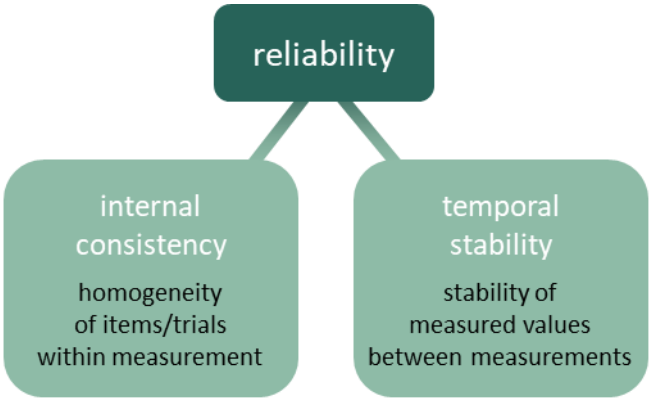


Figure 6. Different Types of Reliability.

Internal consistency for antisaccade and go-/no-go error rate was excellent in all reported studies, and temporal stability for antisaccade error rate was also predominantly good to excellent. For go-/no-go error rate, reported temporal stability was less consistent, but especially test-retest reliability also appeared to be good to excellent. Poor ICCs were only reported by Jones et al. (2016) in a condition including 80% no-go trials. In their condition with less frequent no-go trials (20%), reliability was higher, underlining the importance of no-go frequency in the go-/no-go task (section 1.1.2). Thus, overall, measurements of inhibitory control in both tasks were stable within one measurement and over periods from 1 week to several months. For antisaccade error rate, even at 19 months interval, temporal stability was still good (Klein & Fischer, 2005).

Difference scores help to separate relevant variance from variance that is not of interest (Draheim et al., 2019). In the case of congruency effects, they allow extracting variance due to the conflict alone. Congruency effects have also proven to be highly robust but not necessarily reliable. The Stroop effect shows the highest internal consistency and temporal stability among the congruency effects summarised here. Studies that reported only moderate reliability were exclusively studies that calculated the Stroop effect using the difference between congruent and incongruent trials (Bender et al., 2016; Stahl et al., 2014; Whitehead et al., 2020). For studies with neutral trials as a reference category, the internal consistency was higher (e.g. Siegrist, 1995; Tiego et al., 2018). However, Rey-Mermet et al. (2018) found excellent internal consistencies for both calculation methods, indicating that there is not a clear relationship between calculation method and reliability. For Flanker and Simon effects, previously reported reliabilities were in the range between poor and excellent, although negative ICCs were only reported by White et al. (2019), using no more than 40 trials per task.

Table 3. Summary of Reported Reliabilities for Inhibitory Control Variables.

		Poor	Moderate	Good	Excellent
antisaccade task	α				.81–.94[a,b,c]
antisaccade error rate	$r_{split\text{-}half}$				.86–.97[d,e,f,g]
	ICC			.69–.79[a,b,h]	.92[c]
	$r_{test\text{-}retest}$		.44[i]	.60–.68[j,f]	.89–.92[a,c]
Eriksen flanker task	α		.53[c]	.68[c]	
RT congruency effect	$r_{split\text{-}half}$	.26–.31[k,l]	.54–.59[d,g]	.71–.74[g,m]	
	ICC	-.51–.39[n,o]	.40–.57[p]		.91[c]
	$r_{test\text{-}retest}$			.51–.75[q,r]	.94[c]
go-/no-go task	α				.87–.89[c]
no-go error rate	$r_{split\text{-}half}$				.82–.84[k,m]
	ICC	.25[n]	.55[n]	.76[p]	.84 [c]
	$r_{test\text{-}retest}$			.62–.65[q,s,t]	.84 [c]
Simon task	α				.87–.89[c]
RT congruency effect	$r_{split\text{-}half}$	.14[u]	.56–58[m,u]	.61–.73[g,l,u]	
	ICC	-.19–.39[o]	.49–.53[o]	.69[c]	
	$r_{test\text{-}retest}$		.43[r]	.71 [c]	
stop-signal task	α	.29 [c]		.61 [c]	
SSRT	$r_{split\text{-}half}$			.72–.76[d,e]	. 94[m]
	ICC	.03–.36[c,p]	.43–.49[p]	.71[v]	
	$r_{test\text{-}retest}$	.03 [c]		.60–.65[q,t]	
Stroop task	α				.87–.88[w]
RT congruency effect	$r_{split\text{-}half}$		.50[k,l]	.72[x]	.80–.91[d,e,g,m]
	ICC			60–.66[p]	
	$r_{test\text{-}retest}$		.57[q]	.68–.73[w,y]	

Note. RT = mean reaction time; SSRT = stop-signal reaction time; α = Cronbach's α; ICC = interclass correlation coefficient; Labels are classified according to Hedge et al., 2018: excellent ≥.80, good ≥.60, moderate ≥.40, poor <.40.

[a] Ettinger et al., 2003, [b] Meyhöfer et al., 2016, [c] Wöstmann et al., 2013, [d] Friedman & Miyake, 2004, [e] Friedman et al., 2008, [f] Klein & Fischer, 2005, [g] Rey-Mermet et al., 2018, [h] Płomecka et al., 2020, [i] Klein & Berg, 2001, [j] Talanow & Ettinger, 2018, [k] Stahl et al., 2014, [l] Whitehead et al., 2020, [m] Tiego et al., 2018, [n] Jones et al., 2016,[o] White et al., 2019, [p] Hedge et al., 2018, [q] Bender et al., 2016, [r] Paap & Sawi, 2016, [s] Kertzman et al., 2008, [t] Weafer et al., 2013, [u] Borgmann et al., 2007, [v] Congdon et al., 2012, [w] Siegrist, 1995, [x] Miyake et al., 2000, [y] Siegrist, 1997

Problems regarding low reliabilities in difference scores have long been discussed (Bereiter, 1963; Webster & Bereiter, 1963). One reason seems to be that the calculation combines error components of congruent/neutral and incongruent trials and reduces between-subject variability (Crawford et al., 2008; Whitehead et al., 2020). Hedge et al. (2018) point out that the more strongly congruent and incongruent trials correlate, the more variance they share and the lower the reliability of congruency effects. In experimental research, it is desirable for an effect (e.g. Stroop effect) to be robust and of similar size across participants. Thus, researchers aim for small between-subject variability. On the other hand, high reliability requires large variability between individuals (Fisher et al., 2018; Hedge et al., 2018;

Whitehead et al., 2018). In addition to the slowdown in incongruent trials compared to congruent trials, congruency effects are larger when the previous trial contained little conflict (i.e. congruent trials), also referred to as conflict adaptation, Gratton or sequential congruency effect (Gratton et al., 1992). The sequential congruency effect thus forms a difference score at two points. In agreement with reliability problems in difference scores, Whitehead et al. (2018) reported poor internal consistency of sequential congruency effects in Eriksen flanker, Simon and Stroop tasks ($r_{split\text{-}half}$ = -.07 – .17). Thus, the problem is compounded when differences are taken from differences, again highlighting the paradox between the robustness of experimental effects and the reliability of interindividual differences: A robust effect at the group level does not necessarily lead to reliable effects at the individual level (Hedge et al., 2018) and low reliability reduces possible correlations between tasks (section 1.1.3).

SSRT in the stop-signal task is also based on the calculation of differences and only provides one measurement per participant, aggregated across all trials. As expected, this variable also showed low reliability. While internal consistency, except for the study by Wöstmann et al. (2013), was in the good to excellent range, temporal stability was the lowest of the tasks reported here (Table 3). In addition to the use of a difference score, another reason for low reliability may be that the stop-signal task is sensitive to the instruction, and participants often slow down their response despite instructions not to (Barch et al., 2009; Sylwan, 2004). Furthermore, using different response strategies seems to influence the measurement (Leotti & Wager, 2010).

In addition to the primary inhibitory variables, other task outcomes are frequently reported from inhibitory control tasks. On the one hand, there are variables from congruent or non-inhibition-related conditions that reflect processes such as processing speed (e.g. congruent RT) and those from incongruent or control-related conditions that also capture aspects of inhibitory control (e.g. incongruent error rate). Good to excellent temporal stability over at least one week and good to excellent internal consistency were observed for latencies/RTs in all conditions of antisaccade, Eriksen flanker, go-/no-go, Simon and Stroop tasks (ICC = .58 – .93, $r_{test\text{-}retest}$ = .65 – .93, Cronbach's α = .84 – .97, $r_{split\text{-}half}$ = .72 – .97; Borgmann et al., 2007;

Ettinger, Kumari et al., 2008; Hedge et al., 2018; Jones et al., 2016; Kertzman et al., 2008; Klein & Berg, 2001; Klein & Fischer, 2005; Martínez-Loredo et al., 2017; Meyhöfer et al., 2016; Miyake et al., 2000; Paap & Sawi, 2016; Płomecka et al., 2020; Roy-Byrne et al., 1995; Saville et al., 2011; Siegrist, 1995, 1997; Strauss et al., 2005; Talanow & Ettinger, 2018; Tiego et al., 2018; Versino et al., 1993; White et al., 2019; Wöstmann et al., 2013). Regarding the stop-signal go RT, recent studies showed lower and less consistent temporal stability (ICC = .35 – .60, $r_{test\text{-}retest}$ = .60 – .83, Cronbach's α = .92 – .93; Hedge et al., 2018; Saville et al., 2011; Wöstmann et al., 2013). For error rates in prosaccades and congruent and incongruent conditions in Eriksen flanker, Simon and Stroop tasks, however, only poor to good temporal stability and poor to excellent internal consistency was reported (ICC = .36 – .78, $r_{test\text{-}retest}$ = .22 – .78, Cronbach's α = -.17 – .86; Franzen, 1987; Hedge et al., 2018; Martínez-Loredo et al., 2017; Płomecka et al., 2020; Talanow & Ettinger, 2018; Wöstmann et al., 2013). These low reliabilities likely result from low error rates and ceiling effects in those conditions.

In addition to the influences on reliability mentioned so far, it has also been shown that task design (e.g. test length), sample (e.g. size, age, IQ), or context of the measurement impact reliability (Wöstmann et al., 2013). Therefore, reliability should not be considered an inherent task characteristic (Parsons et al., 2018; Rouder et al., 2019).

In summary, there have been many studies on the reliability of inhibitory control. Especially error rates in antisaccade and go-/no-go tasks show high internal consistency and temporal stability. Measures based on the calculation of difference scores seem to be less reliable. A lack of reliability causes problems particularly in repeated measures designs and makes it difficult to obtain information about individual abilities in inhibitory control. However, that information would be desirable, especially in clinical settings where test scores may be used in diagnosis and treatment decisions. In section 1.1.3, it was shown that latent variable approaches can be used to extract task-specific and common variance across tasks in developing taxonomies of inhibitory control. Similarly, when studying stability, it is possible to use structural equation modelling (SEM) and decompose true variance into stable and situation-dependent variance using so-called latent state-trait (LST) models (Geiser et al., 2015; Steyer et al., 1992; Steyer et al., 2015; Steyer & Schmitt, 1990). In addition,

it is possible to include trait changes and thus consider plasticity (for details on modelling, see section 2.2). These models thus go beyond the classical calculation of consistency and stability by considering short-term, situational fluctuations that do not last long, e.g. mood or tiredness, underlying stable differences between individuals and trait change, e.g. learning effects. However, so far, they have received little attention in inhibition research and were mainly used in questionnaires (e.g. Schmitt & Steyer, 1993; Schmukle & Egloff, 2005; Schuler et al., 2014) and, in some cases, in other cognitive tasks (e.g. Bonnefon et al., 2007; Danner et al., 2011). A first study on LST models in eye movement assessment by Meyhöfer et al. (2016) indicates that performance in antisaccade (and prosaccade) tasks can be reliably measured and is primarily due to stable traits instead of state components. These analyses are a promising approach to further elucidate the stability of inhibitory control and will be addressed in Study 1.

1.3 Plasticity of Inhibitory Control

In the previous section, it has become clear that it is not only stability that is desirable in cognition. However, it is equally important for an individual to be able to change cognitive abilities. The desire for improvements or enhancement of inhibitory control does not only play a role in clinical samples. High inhibitory ability is a helpful skill in almost all areas of life, and better cognitive control, in general, is associated with positive aspects such as higher perceived quality of life, health, wealth, career, success (from school to work), or perceived happiness (Diamond & Ling, 2016).

The term *plasticity* was initially used in the context of neural reorganisation (Quentin et al., 2019). For example, if there are failures in individual brain regions, other areas can partially take over the failed functions (Leblanc et al., 2006; Thompson et al., 2009), and training/experience can influence the size of individual brain areas (Maguire et al., 2000). Accordingly, behavioural plasticity describes changes in performance resulting from an experience, thereby including, for example, learning or changes due to development over the lifespan (Binder et al., 2009; Mermillod et al., 2013).

The latter, i.e. the development over the lifespan, probably contains the most remarkable human inhibitory control changes (Kang et al., 2022). There are first indications of developing cognitive control functions between the 6th and 30th month of life. However, during early childhood, inhibitory control is difficult to detect and probably not very pronounced (Holmboe et al., 2018; Holmboe et al., 2021). In the following years, an enormous and decisive development occurs, reaching adult level at the age of 12 to 15 (Bucci & Seassau, 2012; Cragg, 2016; Huizinga et al., 2006; Luna et al., 2004; van de Laar et al., 2014). Afterwards, there are only slight improvements, and inhibitory control abilities remain on a plateau until the first deteriorations occur in the late 30s (Ferguson et al., 2021; Kang et al., 2022). In late adulthood, more substantial deficits in inhibitory control become apparent (Bedard et al., 2002; Klein et al., 2000; Munoz et al., 1998; Sweeney, 2001).

In this thesis, two aspects of the plasticity of inhibitory control are particularly important and will be examined in more detail in the following sections. First, are there systematic intraindividual improvements across different measurements when tasks are presented repeatedly? And second, can changes in inhibitory control be induced by the administration of drugs that act on neurotransmitter systems with relevance to cognition and motor control?

1.3.1 Repeated Measurement and Training Effects

Plasticity can be seen, for example, in changes that occur as a result of repeated measurements or in changes induced by specific training. Repeated measures designs usually do not explicitly aim to provoke changes in performance and significant effects of measurement occasion are often considered confounding factors in those designs. In addition, studies of reliability or without targeted intervention also frequently report results on significant intraindividual changes in inhibitory control at group level over time.

For inhibition in the antisaccade, Eriksen flanker, and stop-signal tasks, some studies found performance improvements over time (Ettinger et al., 2003; Meyhöfer et al., 2016; Paap & Sawi, 2016; Weafer et al., 2013), and others did not report significant changes (Jones et al., 2016; Klein & Berg, 2001; White et al., 2019; Wöstmann et al., 2013). The periods between the

measurement occasions in those studies mentioned here vary from about one week (e.g. Paap & Sawi, 2016) to over two months (e.g. Wöstmann et al., 2013). However, except for antisaccades, significant changes were only found in studies using relatively short test-retest intervals. For longer intervals, such as 77 days, Paap and Sawi (2016) reported no significant changes in inhibition. In the Simon task, there seemed to be no change over time at all (Paap & Sawi, 2016; White et al., 2019; Wöstmann et al., 2013). Inhibitory control improvements in repeated measurement over short (several days) and even very long intervals (one year) were most pronounced in the Stroop effect (Beglinger et al., 2005; Davidson et al., 2003; Martínez-Loredo et al., 2017; Strauss et al., 2005; Wöstmann et al., 2013). Interestingly, in the go-/no-go task, there was even evidence of impairments over time (Jones et al., 2016; Weafer et al., 2013). Jones et al. (2016) showed not only impairments in no-go error rate but also faster go RTs. Thus, findings could result from a speed-accuracy trade-off.

The reported changes could be true performance changes, i.e. improvements in inhibitory control. Alternatively, they might reflect insufficient practice before task admission. Performance changes may also occur within one test session (Wöstmann et al., 2013), so integrating a sufficient number of practice sessions before starting the assessment is particularly important.

In addition to such unintended changes in inhibitory control, some studies explicitly address the trainability of inhibitory control. Mostly, training consists of a series of practice sessions, i.e. measurement repetitions or strategy transmission (Jolles & Crone, 2012). One potential area of research is the training of inhibitory control in clinical samples, which aims to investigate whether training may also positively affect other areas of life (Irwin Harper et al., 2022). So far, however, only few studies have been dedicated to this topic, and there is no strong evidence for effective improvements (e.g. Johnstone et al., 2010). Moreover, such studies cannot answer whether possible improvements in clinical samples result from compensating for deficient abilities or if there is also plasticity of inhibitory control in the healthy spectrum.

In healthy adults, improvements in inhibition in an antisaccade task were shown by daily training over two weeks (Dyckman & McDowell, 2005) and in a Simon task by repeating the

task daily for three days (Millner et al., 2012). Again, the most consistent findings of improvements relate to the Stroop effect, which improved significantly with 6 – 8 training sessions over periods of up to three weeks (Maraver et al., 2016; Talanow & Ettinger, 2018). In older participants, such training (Wilkinson & Yang, 2012) even persisted over three years (Wilkinson & Yang, 2016). Potentially, such training could help to counteract age-related degradation processes. Findings are mixed for training in go-/no-go and stop-signal tasks (Li et al., 2022). For instance, Zhao et al. (2018) and Maraver et al. (2016) showed improvements in go-no/go error rate due to training, but these did not last longer than three weeks (Zhao et al., 2018). Berkman et al. (2014) found improvements in SSRT that were not accompanied by improvements in go RT, i.e. there was no strategy adaptation. In contrast, data from Enge et al. (2014) suggest that training improves RT in go-/no-go and stop-signal tasks but at the cost of error rate, and SSRT does not improve either. Therefore, they concluded that these are not true improvements in inhibition but stem from a speed-accuracy trade-off similar to that already found in repeated measurement studies. Talanow and Ettinger (2018) also showed improved performance in trained tasks but also in untrained tasks from pre- to post-measurement, which raises the question of whether active training is necessary to improve performance in inhibitory control tasks.

Moreover, if tasks are indeed measuring a common construct (section 1.1.3), learning effects in one task should also positively affect performance in other tasks in the construct. Studies have investigated so-called near transfer effects, e.g. from one inhibitory control task to another, untrained inhibitory control task, and far transfer effects, e.g. from one inhibitory control task to another, untrained cognitive task. However, evidence for true transfer effects is not compelling. Maraver et al. (2016) showed near transfer from response inhibition and distractor interference training (using Stroop-like, conflict resolution and go-/no-go-like tasks) to Stroop and stop-signal tasks. Similarly, Millner et al. (2012) reported near transfer from Simon and emotional go-/no-go tasks to an Eriksen flanker task. Others found no near transfer, such as Enge et al. (2014), who assessed transfer from go-/no-go and stop-signal tasks to a Stroop task. In addition, there was no far transfer to a fluid intelligence task. Similarly, Talanow and Ettinger (2018) reported no near transfer from Stroop training to an antisaccade task nor far transfer to shifting, working memory, or planning.

In summary, study results suggest that if there are true training effects, they are smaller than expected and probably no more effective than simple measurement repetition. Thus, inhibitory control was found to improve to some extent with repetition. Still, no one has investigated trait changes while considering situational effects, i.e. does inhibitory control improve with repeated measurements regardless of situational fluctuations? This research gap is addressed in Study 1. In addition, data on absent transfer effects again raise the question of whether inhibitory control is a unitary construct.

1.3.2 Pharmacological Modulation

Changes in performance may also be deliberately induced by pharmacological influences. As improvements due to repeated measurements may confound with drug effects, administration order in pharmacological studies is usually randomised. Psychopharmacology studies the interaction between drugs or other chemical agents and sensation, thinking and behaviour. Two directions of action are distinguished. On the one hand, there is "what a drug does to the body" (Stolerman & Price, 2015, p. 1276), referred to as pharmacodynamics. Pharmacodynamics thus involves processes through which a substance acts in the body. On the other hand, there are pharmacokinetic mechanisms describing "what the body does to a drug" (Stolerman & Price, 2015, p. 1276), thus incorporating processes like drug absorption, distribution, metabolism and excretion.

Several studies have investigated the influence of pharmacological substances on inhibitory control. These include substances consumed in everyday life, such as nicotine (e.g. Ettinger et al., 2017) or caffeine (e.g. Tieges et al., 2009), but also prescription drugs used to treat psychological disorders. One aim of these investigations is to better understand typical neural functions as well as impairments in the context of neuropsychiatric disorders. Accordingly, findings from psychopharmacological studies may help to development strategies to prevent or treat cognitive dysfunction in such disorders. In addition, some substances may potentially enhance cognition in healthy participants (e.g. Dresler et al., 2019). Thus, psychopharmacology provides an opportunity to influence cognitive processes and investigate plasticity processes in inhibitory control.

So far, studies have mostly focused on substances that act on excitatory neurotransmitter systems. For example, the influence of nicotine on inhibitory control has been investigated. Nicotine is a nonselective acetylcholine receptor (nAChR) agonist and influences the dopaminergic neurotransmitter system (Dani & Bertrand, 2007; Kloet et al., 2015). The study of nicotine and inhibition is also of interest, given the high self-administration rates in clinical samples associated with inhibition deficits (e.g. ADHD; Lambert & Hartsough, 1998). Indeed, there is evidence for improved SSRT by nicotine in samples with impaired inhibition (Ettinger & Kumari, 2019) but not in healthy non-smokers (Ettinger et al., 2017; Schröder et al., 2021). In addition, there is evidence for nicotine-related improvements in antisaccades. However, evidence is little or unclear for other inhibitory control tasks (Ettinger & Kumari, 2019).

Research on prescription drugs for inhibitory control includes, for example, studies on methylphenidate. Methylphenidate, also known under the trade name Ritalin®, is used to treat ADHD and inhibits the monoamine transporters for DA and NE. Thus, the intake increases extracellular DA and NE levels (Faraone, 2018; Volkow et al., 2001). There are improvements in inhibition in ADHD samples (Coghill et al., 2014) but mixed results on improvements in healthy individuals (Allman et al., 2012; Costa et al., 2013; Nandam et al., 2011). Such studies emphasise the importance of better investigating complex interactions between cognition and behaviour in mental disorders such as ADHD. However, they do not strongly support using methylphenidate as a cognitive enhancer in healthy individuals, at least with regards to inhibitory control.

Sedative substances, on the other hand, have not been sufficiently studied regarding their association with inhibitory control mechanisms. The investigation of such substances could help to better understand the role of inhibitory neurotransmitter systems in behavioural inhibition (section 1.1.4). One focus of the present thesis is on benzodiazepines, particularly the benzodiazepine lorazepam, also known under the trade name Tavor®. Benzodiazepines are positive allosteric modulators of the $GABA_A$ receptor (Figure 7). As such, they enhance the agonist effect, provide more GABA activity and thereby reduce the excitability of a neuron (Knoflach & Bertrand, 2021; Uusi-Oukari & Korpi, 2010). Benzodiazepines are used

in psychiatry for the treatment of anxiety and are sometimes used for the short-term treatment of sleep disorders (Lader, 2011). Accordingly, benzodiazepines have anxiolytic, sleep-promoting, anticonvulsive, arousal-reducing, muscle-relaxing and sedative effects (Baldwin et al., 2013). The sedative effect of benzodiazepines is shown in experiments, for example, in reduced saccadic peak velocity. This effect is very robust, and peak velocity has thus the potential to be used as a biomarker for sedative effects (de Visser et al., 2003).

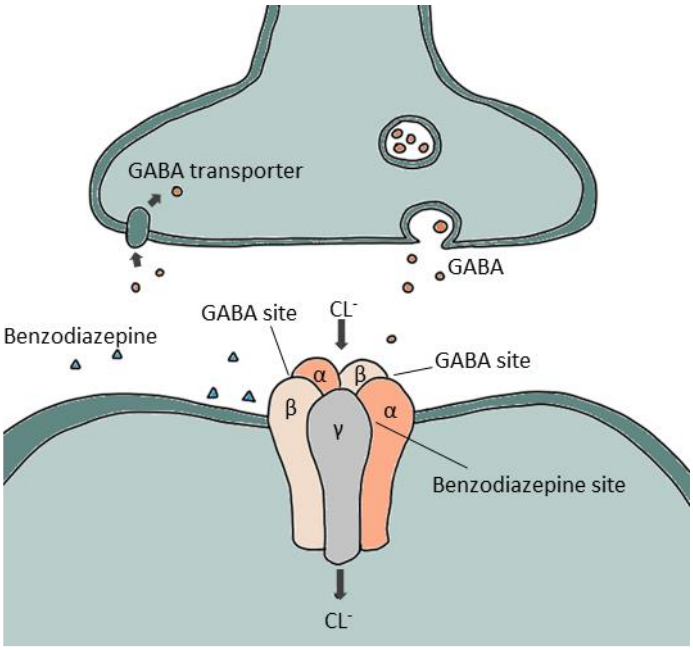


Figure 7. GABAergic Synapse Including a $GABA_A$ Receptor and its Binding Sites.

The $GABA_A$ receptor hat a pentagonal structure including two α and two β subunits and one γ subunit (Uusi-Oukari & Korpi, 2010; Zhu et al., 2018); GABA = γ-aminobutyric acid; CL^- = chloride

In experiments on the influence of benzodiazepines on attention, a cognitive function closely related to inhibitory control (section 1.1.1; Barkley, 1997; Moorselaar & Slagter, 2020; Verbruggen et al., 2008), benzodiazepines induced impairments in attentional switching, choice RT, encoding mechanisms, vigilance, or visual information processing (Duka et al., 1995; Giersch & Herzog, 2004; Jalava et al., 1995; Post et al., 1997; Wesnes et al., 1997). Given the anxiolytic effects of benzodiazepines, it is also interesting to note that higher state and trait anxiety are associated with narrower attentional focus (Caparos & Linnell, 2012; Wegbreit et al., 2015). It is, therefore, conceivable that benzodiazepines conversely widen

the attentional focus, which could also have implications for performance in distractor interference tasks.

There are only very few studies that explicitly examined benzodiazepine-induced changes in inhibitory control. Some studies have administered benzodiazepines and reported effects on performance of inhibitory control tasks. However, those studies often did not report results specifically on primary inhibitory control variables. An overview of these studies is given in Table 4.

In antisaccades, there was a significant increase in error rates and latencies under benzodiazepines (Green & King, 1998; Green et al., 2000; McCartan et al., 2001). However, the results were not evaluated in direct comparison with performance in prosaccades in that study. Therefore, it cannot be ruled out that effects may simply be due to a general slowing or deterioration in saccadic performance, as results from prosaccade tasks show that these were also slowed down under benzodiazepines (Chen et al., 2015; Ettinger et al., 2018; Haas et al., 2007; Masson et al., 2000). Reynolds et al. (2004) reported non-significant drug effects for no-go error rate and SSRT. One other study on SSRT confirmed this finding (Shadli et al., 2016), but one showed increased SSRT under the benzodiazepine Triazolam (Fillmore et al., 2001). However, in the latter study, go RT was also slowed down, which again could indicate that the effect was not inhibition specific. Benzodiazepine effects on congruency effects for RT in Eriksen flanker and Stroop tasks were either not significant (Bruijn et al., 2004; Riba et al., 2005; Seol et al., 2019) or not reported (Clariá et al., 2011; Deplanque et al., 2018; Puga et al., 2005). However, there was one study (Mercer et al., 1998) showing a significant increase in the Stroop effect under Lorazepam. That study was also the only one reporting results on manual responses in the Stroop task. Thus, response modality may have had an impact on the results. In addition, results on the Eriksen flanker task should be treated with caution. All reported studies used small sample sizes ($N \leq 12$) and a task version with a RT deadline to keep error rates constant across drug conditions. Furthermore, benzodiazepine effects on the flanker effect, reported by Bruijn et al. (2004), were close to significance ($p = .062$). To our knowledge, no studies reported benzodiazepine effects on a Simon task..

Table 4. Summary of Studies on Immediate Benzodiazepine Effects on Inhibitory Control.

Reference	Inhibitory Control Task	Benzodiazepine	Study Design	Dependent Variable	Drug effect
Green and King (1998)	**antisaccade** (54 antisaccades)	Lorazepam (2 mg)	*N* = 20 male, within-subject, 5 measurement occasions, interval 1 week, additional: 3 doses chlorpromazine	AS error rate AS latency	increased by drug increased by drug
Green et al. (2000)	**antisaccade** (54 antisaccades)	Lorazepam (0.5, 1, 2 mg)	*N* = 20 male, within-subjects, 5 measurement occasions, interval 1 week, additional: sertraline	AS error rate AS latency	increased by drug (1 and 2 mg) increased by drug (1 and 2 mg)
McCartan et al. (2001)	**antisaccade** (54 antisaccades)	Lorazepam (2 mg)	*N* = 46 male, between-subjects, additional: chlorpromazine	AS error rate	increased by drug
Bruijn et al. (2004)	**Eriksen flanker** (5 letters, 600 trials)	Lorazepam (2.5 mg)	*N* = 12, within-subjects, 4 measurement occasions, interval 1 week, additional: D-amphetamine, mirtazapine	RT[a] RT congruency effect	increased by drug n.s.
Clariá et al. (2011)	**Eriksen flanker** (5 letters, 480 congruent, 720 incongruent trials)	Alprazolam (0.25, 1 mg)	*N* = 11 male, within-subjects, 3 measurement occasions, interval 1 week	RT[a]	increased by drug (1 mg)
Riba et al. (2005)	**Eriksen flanker** (5 letters, 960 congruent, 1440 incongruent trials)	Alprazolam (0.25, 1 mg)	*N* = 12 male, within-subjects, 3 measurement occasions, interval 1 week	RT[a] RT congruency effect	increased by drug (1 mg) n.s.
Reynolds et al. (2004)	**go-/no-go**	Diazepam (5, 10 mg)	*N* = 35, within-subjects, 3 measurement occasions, interval 1 week	no-go error rate	n.s.

Reference	Inhibitory Control Task	Benzodiazepine	Study Design	Dependent Variable	Drug effect
Fillmore et al. (2001)	**stop-signal** (128 go, 48 stop trials, stop-signal sound, SSD random)	Triazolam (0.125, 0.25 mg)	*N* = 30 (10,10,10), between- subjects	SSRT Go RT	increased by drug (all doses) increased by drug (0.25 mg)
Reynolds et al. (2004)	**stop-signal** (stop-signal sound, staircase-like tracking SSD)	Diazepam (5, 10 mg)	*N* = 35, within-subjects, 3 measurement occasions, interval 1 week	SSRT	n.s.
Shadli et al. (2016)	**stop-signal** (288 go, 96 stop trials, visual stop-signal, staircase-like tracking SSD)	Triazolam (0.25 mg)	*N* = 26 (10 placebo, 9 Triazolam, 8 Buspirone), between-subjects	SSRT Go RT	n.s. n.s.
Deplanque et al. (2018)	**Stroop** (100 black words, 100 congruent, 100 incongruent, vocal response)	Lorazepam (2 mg)	*N* = 30, within-subjects, 3 measurement occasions, interval 2-4 weeks, additional: etifoxine	Incongruent RT[b] Error rate	increased by drug increased by drug
Mercer et al. (1998)	**Stroop** (96 trials, manual reaction)	Lorazepam (2 mg)	*N* = 11, within-subjects, 6 measurement occasions, interval >=1 week, additional: 4 doses zolmitriptan	RT congruency effect	increased by drug
Puga et al. (2005)	**Stroop** (black words, incongruent, vocal response)	Bromazepam (3 mg)	*N* = 15, within-subjects, 3 measurement occasions, including 2 placebos	Error rate	n.s.
Seol et al. (2019)	**Stroop** (30 neutral, 30 incongruent, vocal response)	Brotizolam (0.25 mg)	*N* = 29 male, within-subjects, additional: suvorexant, 3 measurement occasions, interval >=2 days, completed within 8 weeks	RT congruency effect Incongruent RT Congruent RT	n.s. n.s. n.s.

Note. All studies were placebo-controlled, randomised, double-blind, assessing healthy samples, including male and female (unless otherwise described). RT = mean reaction time; SSRT = stop-signal reaction time; n.s. = not significant

[a] Response time deadline was used to keep error rates constant in all drug conditions, [b] time to read 100 words

Altogether, these findings do not allow any clear conclusions to be drawn about benzodiazepine effects on response inhibition and distractor interference. While many studies reported increased RTs and error rates, effects on primary inhibitory control variables were rarely separated from effects of general slowing and sedation, and methodological limitations reduce the power of the studies to date. Studies 2 – 4 aim to address this issue

1.4 Goals of the Current Thesis

As described above, inhibitory control is an important cognitive control function not only because it is associated with many positive aspects of life (Diamond & Ling, 2016) but also because it is often deficient in clinical samples (Mirabella, 2021). This thesis aims to provide a better understanding of the construct of inhibitory control, including aspects of stability and plasticity. The experimental section includes one study (Study 1) on whether inhibitory control is mostly influenced by stable traits or time-varying states and three studies (Studies 2–4) on changes in inhibitory control due to increased neural inhibition. The studies have in common that young, healthy adults were studied using repeated measures designs, and the same inhibitory control tasks were applied. Specifically, the goals of these studies are as follows.

The first study applied LST modelling. Latent variable approaches have contributed to understanding the construct of inhibitory control and relationships between tasks while controlling for low reliability and task impurity (Friedman & Miyake, 2017). However, psychometric properties of inhibitory control tasks (Draheim et al., 2019; Hedge et al., 2018; Rouder & Haaf, 2019) and the existence of a unitary underlying inhibitory control construct (Rey-Mermet et al., 2018) have not yet been conclusively clarified. One approach that has been lacking so far is the investigation of the reliability of individual tasks and the construct of inhibitory control, considering situational (state) and temporally stable (trait) influences (Study 1).

The remaining three studies address inhibitory neurotransmitters. While the neural network of inhibitory control and the role of excitatory neurotransmitters in inhibitory control have been widely addressed, the role of inhibitory neurotransmitters has received little attention

so far. Research is needed to address this issue and gain a better understanding of neural mechanisms underlying inhibitory control and generate insights into pharmacological influences. Since the current knowledge on this topic is limited, one aim was to investigate whether increased GABAergic neural activity influences inhibitory control (Study 2). Subsequently, the effects found on response inhibition were further investigated using computational modelling, focussing on conflict adaptation, automatic and controlled processes (Study 3). Finally, given evidence in Study 2 of possible influences of inhibitory neurotransmitters on the focus of selective attention, in the last step, GABAergic processes in distractor interference were analysed in more detail using a modified version of the Eriksen flanker task (Study 4).

2 METHODS

The following section contains a brief outline of the methods used in the studies of this thesis. First, the general experimental procedure is described, including the recording and analysis of oculomotor data. Next, an overview of LST modelling is given, which can be used to calculate the extent of trait and state components in a measurement. The last part addresses distributional analyses, explaining the computation of delta plots and the study of inhibitory control using SERIA models.

2.1 General Experimental Approach

This thesis is based on behavioural studies, the basic procedure of which will be briefly outlined in the following. Healthy adult students performed different experimental tasks on the computer in a controlled laboratory setting. Specifically, these were the antisaccade, Eriksen flanker, go-/no-go, Simon, stop-signal and Stroop tasks (Table 2), whereby not all tasks were part of all studies. Manual responses were recorded in all tasks except the antisaccade task. The dependent variables for those tasks were calculated based on RTs of correct trials and error rates. For more details on primary inhibitory variables, see section 1.1.2.

In the antisaccade task, oculomotor responses were assessed using a table-mounted EyeLink1000 eye-tracker system (SR Research Ltd., Figure 8 (A)) which applies video-based

combined pupil and corneal reflection (VCPCR) recording (Duchowski, 2007; Holmqvist et al., 2011; Hutton, 2019; Young & Sheena, 1975). This eye-tracking method has the advantages that it is non-invasive, has a high temporal solution, can handle slight head movements and is relatively easy to implement. The position of the gaze on the screen (point of regard) is measured (Duchowski, 2007).

(A) (B)

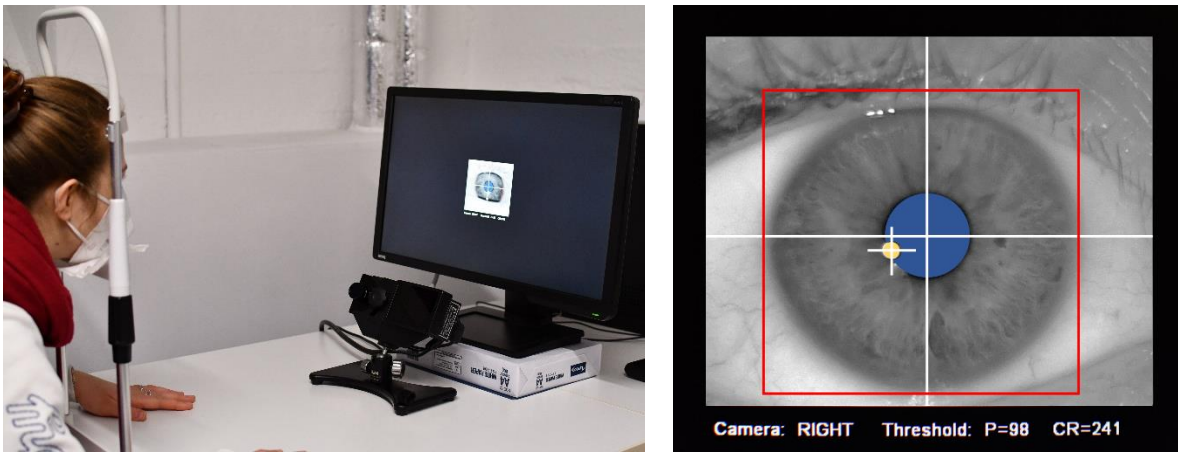


Figure 8. Eye-Tracking Setup (A) and Image of Recorded Eye (B).

The eye tracking set-up includes a table mounted EyeLink1000 system. The pupil (blue) and corneal reflection (yellow) are correctly identified. Source: private photograph

For this purpose, the centre of the pupil and the corneal reflection (first Purkinje image) of an infrared lamp shining on the eye are recorded. The pupil absorbs most of the light and is, therefore, the darkest area in the recorded image, whereas the reflection is the brightest area. Figure 8 (B) shows an example of a correctly identified pupil and corneal reflection. When the eye moves, the reflection remains stable while the position of the pupil shifts. The gaze position can be determined from the relative position of these two components (Holmqvist et al., 2011; Hutton, 2019). To do so, in the first step of calibration, stimuli are presented at different positions the participant looks at, and the relative positions of the reflection and pupil are stored. Feature-based or model-based approaches segment both positions and make it possible to use this data to determine gaze positions on the entire screen. In the second step, this prediction is checked in the validation process by comparing the prediction with the

actual gaze behaviour when the stimuli are presented the second time. Finally, during the task, it is thus possible to determine the x and y positions of the gaze over time, from which dependent variables such as latency can be derived (Hutton, 2019).

All studies have in common the application of within-subject designs using intervals between measurement occasions of exactly one week. Specifically, Study 1 included three measurement occasions, which were included in the analyses as an independent variable. Studies 2–4 were placebo-controlled, double-blind and randomised designs, considered the gold standard in pharmacological research (Karpouzian et al., 2019). At the beginning of each measurement occasion, a capsule was administered containing either lorazepam (1 mg in Studies 2–4; additionally 0.5 mg in Studies 2–3) or placebo. In pharmacological studies, drugs may be administered either between- or within-subjects. In this thesis, within-subject designs were used as these have low variability between drug conditions and high statistical power, even in smaller samples (Karpouzian et al., 2019). Both dose and administration period are critical parameters in the design of pharmacological studies, as they have a direct impact on the maximum blood concentration and elimination half-life, resulting in the "window of opportunity", i.e. the period during which plasma concentration is stable and which has optimal conditions for investigating drug effects (Karpouzian et al., 2019). Oral doses of 0.5 mg (Study 2, 3) and 1 mg (Study 2–4) of lorazepam were administered. Subsequently, there was a waiting period of at least 2 hours for the peak plasma concentration of lorazepam to be reached (Greenblatt, 1981; Kyriakopoulos et al., 1978).

Data were analysed using ANOVAs and classical reliability coefficients (Cronbach's α and ICC). In addition, LST models (Study 1) and distributional analyses (Study 2–4) were applied. These methods will be described in the following sections.

2.2 Latent State-Trait Modelling

LST theory takes into account that measurements do not take place in a situational vacuum. It extends classical test theory by assuming that sources of variance in a measure are not only the person and measurement error but also situational influences and the interaction between

person and situation (Geiser et al., 2015; Steyer et al., 1992; Steyer & Schmitt, 1990; Steyer et al., 1999).

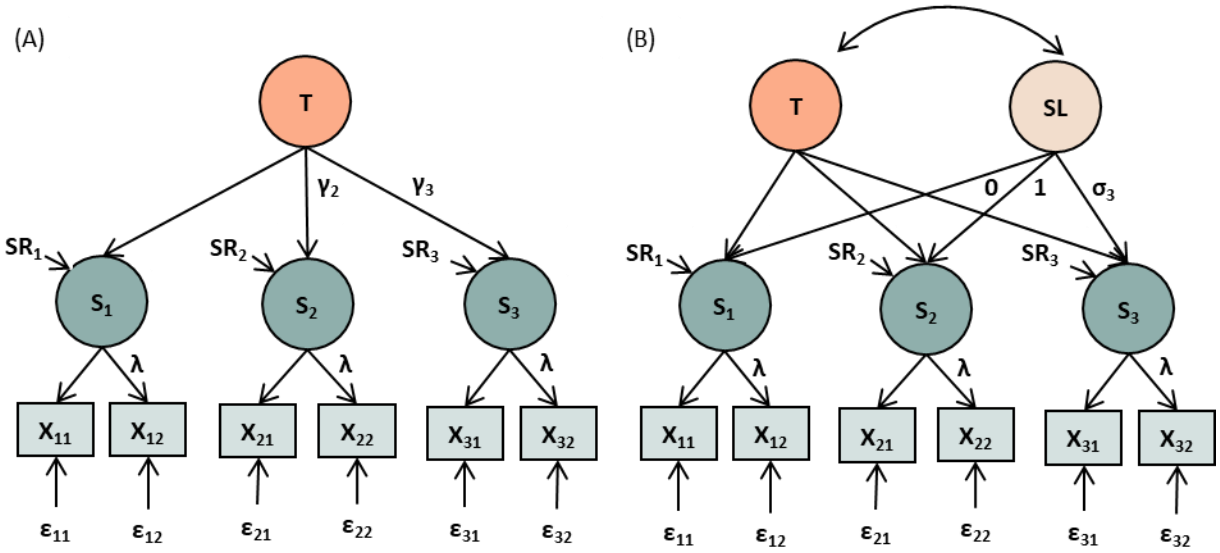


Figure 9. Latent State-Trait (A) and Latent Growth-Curve (B) Models.

In latent state-trait models (LST), state or alternatively trait means may be freely estimated. In latent growth-curve (LGC) models, trait and slope means are freely estimated. Remaining intercepts or means are set to zero. The example shows models including three measurement occasions *i* and two test sets *k*. Double arrows indicate correlations and loadings without a label are fixed to 1. T = latent trait; SL = latent slope; S_k = latent states; SR_k = latent state residuals; X_{ik} = manifest dependent variables; ε_{ik} = measurement error variances; γ_k = trait loadings; σ_k = slope loadings; λ_{ik} = state loadings.

The general approach of the LST theory is a two-step decomposition. First, observed variables are divided into two or more test halves and decomposed into latent states (S_k) and measurement error variances (ε_{ik}). Second, latent states are dismantled into a latent trait (T) and occasion-specific state residuals (SR_k). Model testing and the computation of relevant parameters can be conducted using SEM. States and traits are latent random variables that cannot be directly computed from the observed variables but have to be estimated (Steyer et al., 2015). In terms of content, the latent state variables represent characteristics of the person in a situation during one measurement occasion. The latent trait variable reflects variance that remains stable across measurement occasions and is thus considered an attribute of the person itself. Last, the occasion-specific state residual represents influences of the situation and the

interaction of the person and situation (Steyer et al., 1999). Situational influences may be, for example, stress (Shields et al., 2016), noise (Szalma & Hancock, 2011), motivation (Botvinick & Braver, 2015), emotion (Dreisbach, 2006), or level of arousal (Lo et al., 2016).

Importantly, traits are not necessarily immutable but may change over time (Geiser et al., 2015). To account for possible trait changes, intercepts of the states can be freely estimated or, alternatively, more complex models that model trait changes separately can be defined (Bollen, 2006). Therefore, in second-order latent growth-curve (LGC) models, the latent states are not only dismantled into a trait but also a latent slope factor (SL) accounting for variance caused by different rates of trait changes. Finally, LST models of different tasks or variables can be combined into hierarchical models, and correlations between the respective traits can be assessed. This way, relations between different measurements can be tested only considering the pure trait ability thereby significantly advancing previous taxonomies based on latent variables (Friedman & Miyake, 2004). Examples of LST and LGC models are depicted in Figure 9.

Finally, after testing the models with SEM and checking measurement invariance (Steyer et al., 2015) and model fit, models can be used to calculate common consistency, occasion specificity and reliability (Geiser et al., 2015; Steyer et al., 1992; Steyer & Schmitt, 1990). Common consistency represents the amount of variance explained by trait influences:

$$Con(X_{ik}) = \frac{{\lambda_{ik}}^2 {\gamma_{ik}}^2 Var(T)}{Var(X_{ik})} \quad (1)$$

In LGC models, common consistency comprises variance explained by stable trait influences and trait changes:

$$Con(X_{ik}) = \frac{{\lambda_{ik}}^2 {\gamma_{ik}}^2 Var(T) + {\lambda_{ik}}^2 {\sigma_{ik}}^2 Var(SL) + 2{\lambda_{ik}}^2 \gamma_{ik} \sigma_{ik} Cov(T, SL)}{Var(X_{ik})} \quad (2)$$

Occasion specificity is the amount of variance explained by the situation and the situation × person interaction:

$$Spe(X_{ik}) = \frac{\lambda_{ik}{}^2 Var(S)}{(X_{ik})} \quad (3)$$

Reliability represents the total amount of error-free variance explained by the model. Thus, common consistency and occasion specificity sum up to the reliability coefficient:

$$Rel(X_{ik}) = Con(X_{ik}) + Spe(X_{ik}) \quad (4)$$

2.3 Distributional Analyses

A better understanding of experimental findings may be achieved by not only using cumulative summary statistics for all trials (e.g. mean error rate) but by also looking at different time periods in trials (e.g. fast and slow responses) separately, which can be done, for example, with the help of delta plots (section 2.3.1). Another possibility to capture the entire distribution of responses is to apply generative models, which provide information about presumed computational or psychological causes of experimental findings (Heinzle et al., 2016; Huys et al., 2016). This thesis deals with results from the SERIA model (section 2.3.2).

2.3.1 Delta Plots

Delta plots illustrate congruency effects separately for slower and faster RTs. Therefore, trials are binned in equal parts (e.g. quintiles), and congruency effects are calculated for each bin. According to the Activation-Suppression model (Figure 2; Ridderinkhof, 2002), there are a deliberate and a direct route leading to responses. The strength of the direct response activation due to the irrelevant stimulus dimension/feature is reduced by the build-up in selective suppression (section 1.1.2). Initial and strong direct activation is reflected in delta plots for accuracy. If the deliberate route is slow, the direct activation has a strong influence. Accordingly, more fast errors in incongruent trials are made, reflected in high congruency effects for accuracy for fast responses (Figure 10 (A)). The build-up in suppression or selectivity is reflected in the course of delta plots for RT. When selective suppression is strong, the direct route has reduced impact, and RT becomes faster in incongruent trials. Thus,

reduced congruency effects for RT for slow responses reflect a fast build-up in selectivity (Figure 10 (B)). Reduced congruency effects for slow responses in the Simon task, as discussed in section 1.1.2, are reflected in negative-going delta plots for RT, similar to the red line in Figure 10 (B). In contrast, delta plots are typically positive-going for Eriksen flanker tasks and take the form of the blue example in Figure 10 (B).

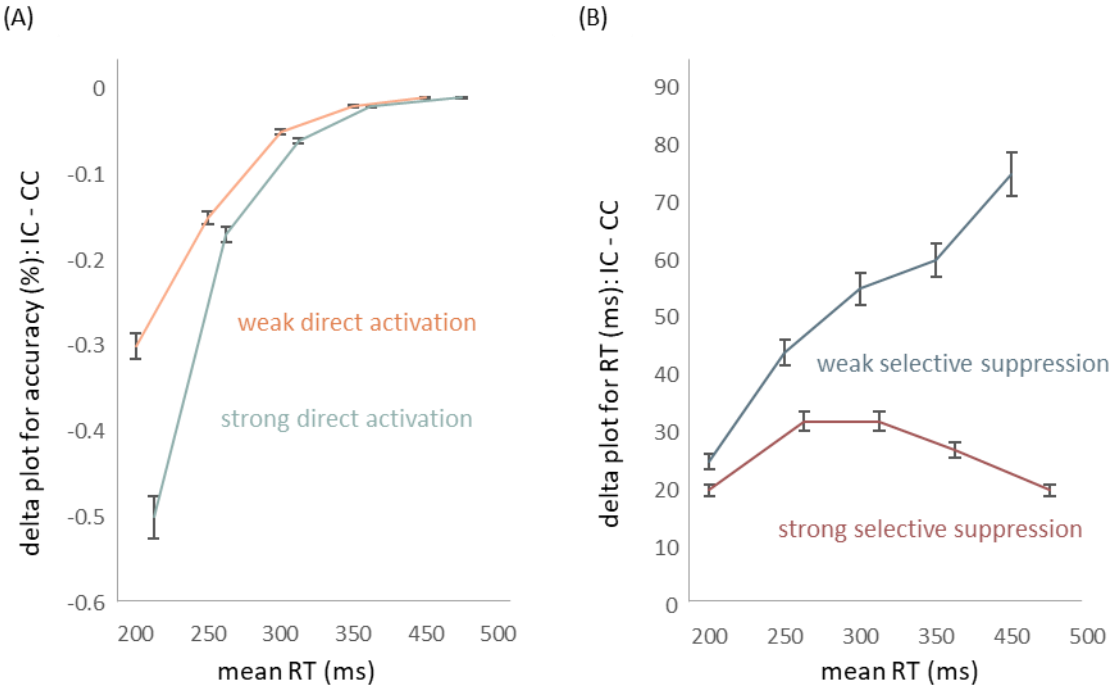


Figure 10. Exemplary Delta Plots for Accuracy (A) and for RT (B).

These illustrations show hypothetical delta plots. RTs are rank-ordered and separated into quintiles. For each quintile, the difference in accuracy and mean RT of correct trials between congruent and incongruent conditions are plotted against the mean RT of both conditions in the respective quintile. Delta plots for accuracy may differ depending on the strength of the direct activation, shown in the two hypothetical coloured examples. Delta plots for RT may reveal differences in the strength of selective suppression, again shown in two hypothetical coloured examples. IC = incongruent; CC = congruent; RT = reaction time.

2.3.2 SERIA Model

Similar to delta plots, the SERIA (stochastic early reaction, inhibition, and late action) model (Aponte et al., 2017) is not based on standard summary statistics (e.g. mean RT, mean error

rate) but captures entire response distributions. The model formalises ideas from Noorani and Carpenter (2016) and extends their formal probabilistic LATER (Linear Approach to Threshold with Ergodic Rate) model by considering that congruent responses such as prosaccades can not only be the result of an automated, fast response but can also result from a second late race between controlled congruent and incongruent responses.

More precisely, the SERIA model (Figure 11; Aponte et al., 2017; Aponte et al., 2018) assumes four race processes. These comprise the early congruent response[2] (u_e), inhibition (u_i), late congruent response (u_c) and late incongruent response (u_n) units. Automatic, i.e. early congruent responses, can be stopped by the latent, unobservable inhibition process if it hits the response threshold first. A second race then takes place between late congruent and incongruent responses. The times a unit hits the threshold are denoted by U_e, U_i, U_c and U_n. Random variables of interest are latency/RT $T \in [0, \infty[$ and the performed action $A \in \{congruent, incongruent\}$.
Formally, the processes can be described as follows:

A congruent response at time t (A = congruent, T = t) is performed if the early unit hits the threshold before the other three units

$$p(U_e = t)p(U_i > t)p(U_c > t)p(U_n > t) \tag{5}$$

when the late congruent unit hits the threshold before the other three units

$$p(U_c = t)p(U_e > t)p(U_i > t)p(U_n > t) \tag{6}$$

or when the late congruent unit hits the threshold before the incongruent unit while the inhibition unit stopped the early unit.

$$p(U_c = t)p(U_n > t)\int_0^t p(U_i = \tau)p(U_e > \tau)\, d\tau \tag{7}$$

[2] To simplify model explanations, the terms “prosaccades” and “congruent responses” are used synonymously in this section. The same applies to “antisaccades” and “incongruent responses”.

Accordingly, an incongruent response at time t (A = incongruent, T = t) is performed if the late incongruent unit hits the threshold before the other three units

$$p(U_n = t)p(U_e > t)p(U_i > t)p(U_c > t) \quad (8)$$

Or when the late incongruent unit hits the threshold before the congruent unit while the inhibition unit stopped the early unit.

$$p(U_n = t)p(U_c > t)\int_0^t p(U_i = \tau)p(U_e > \tau)\, d\tau \quad (9)$$

Two parameters describe each unit: the mean and variance until the threshold is hit. Eight (unit) parameters thus specify the distribution of actions and RTs in a condition. In addition, three further parameters are assumed: one for non-decision time, which is the time until the first race starts, one for the probability of low latency outliers, which is the probability of RT shorter than the non-decision time and one for delays before the start of the second race.

In the present thesis, when calculating SERIA models, trials were not only differentiated into congruent and incongruent, but it was also considered whether the previous trial was congruent (low conflict) or incongruent (high conflict). So far, the SERIA Model has only been used for antisaccades, but in this thesis it is applied to a Simon task for the first time.

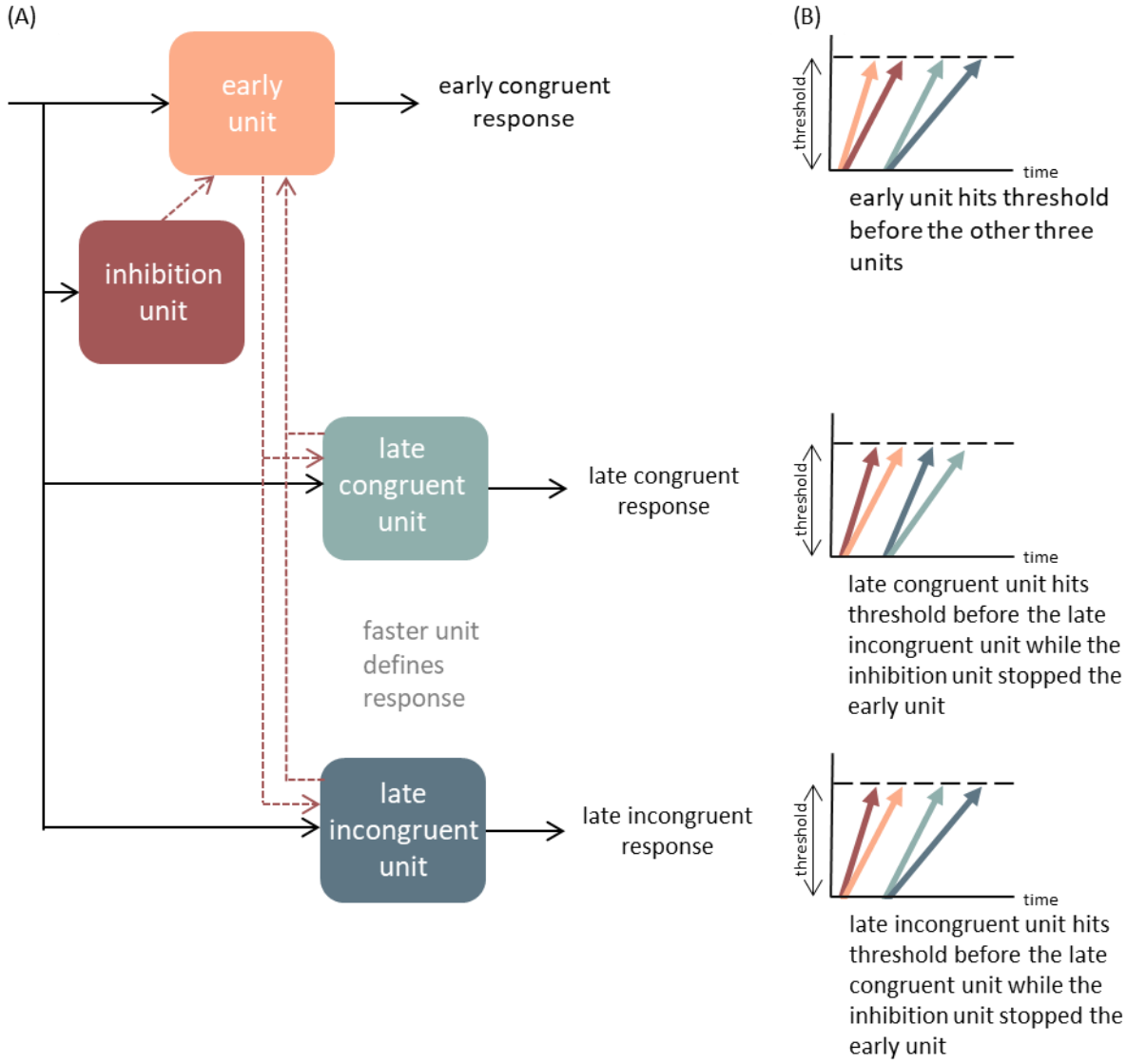


Figure 11. Stochastic Early Reaction, Inhibition, and late Action (SERIA) Model.

The SERIA model (A) includes four units. There is a first race between an early (light red) and an inhibition (red) unit, and a second race between a late congruent (green) and a late incongruent (blue) unit. When a unit hits the threshold, the other units no longer influence the outcoming response, indicated by the red dashed line. Thus, the order in which different units hit thresholds leads to different responses. In the examples shown (B), the colours of the arrows correspond to those in (A). For simplicity, it is assumed that the units have the same threshold. Adapted from: Aponte, E. A., Schöbi, D., Stephan, K. E., & Heinzle, J. (2017). The Stochastic Early Reaction, Inhibition, and late Action (SERIA) model for antisaccades. *PLoS Computational Biology*, *13*(8), licensed under CC BY 4.0.

3 STUDIES

Table 5. Overview of Studies Included in the Current Thesis.

Reference	Citation	Open Science	Status
Study 1	**Faßbender, K.**, Meyhöfer, I., & Ettinger, U. (2023). Latent State-Trait and Latent Growth Curve Modelling of Inhibitory Control. *Journal of Experimental Psychology: General*, 152(5), 1396–1419.	Preregistered, Open data, Open material	Published
Study 2	**Faßbender, K.**, Bey, K., Lippold, J. V., Aslan, B., Hurlemann, R., & Ettinger, U. (2021). GABAergic modulation of performance in response inhibition and interference control tasks. *Journal of Psychopharmacology*, *35*(12), 1496-1509.	Open data	Published
Study 3	Aponte, E. A., **Faßbender, K.**, Heinzle, J., & Ettinger, U. (2022). Gabaergic modulation of conflict adaptation and response inhibition. *BioRxiv*, 2022.03.03.482762.	Open data	Under Review
Study 4	**Faßbender, K.**, Baumert, P. M., Wintergerst, M. W., Terheyden, J. H., Aslan, B., M Harmening, W., & Ettinger, U. (2023). GABAergic Involvement in Selective Attention. *Journal of Cognitive Neuroscience*, *35*(6), 976-989.	Preregistered, Open data, Open material	Published

Note. The order of the studies corresponds to the order in which they are summarised in this thesis.

3.1 Study 1. State and Trait Components in Inhibitory Control

Faßbender, K., Meyhöfer, I., & Ettinger, U. (2022). Latent State-Trait and Latent Growth Curve Modelling of Inhibitory Control. Journal of Experimental Psychology: General, 152(5), 1396–1419.

Temporal stability of inhibitory control tasks is crucial, e.g. in pharmacological studies involving repeated measurements (Shaffer, 1979) or in studies addressing individual differences (Aichert et al., 2012; Stahl et al., 2014). However, reliability (Hedge et al., 2018) of inhibitory control remain unclear. Additionally, the interrelations of inhibitory control measures and their resultant taxonomies are still controversial (Stahl et al., 2014). A major shortcoming of previous research in this context is the implicit assumption of a trait-like inhibitory ability without formally testing it by separating reliable variance into stable trait and situationally varying state components.

Therefore, the first aim of the current study was to provide a detailed examination of latent state and trait components as well as trait changes over time of the most widely used tasks to measure inhibitory control. To our knowledge, no other study reports results from LST models for inhibitory control tasks, except for one study of antisaccades (Meyhöfer et al., 2016) and no study reports results on trait changes in inhibitory control. The second aim was to examine the trait-based structure of inhibitory control. Studies analysing the structure of inhibitory control have not yet assessed commonalities between tasks on trait level while controlling for measurement error and state effects.

A sample of N = 150 healthy participants performed antisaccade, Eriksen flanker, go-/no-go, Simon, stop-signal and Stroop tasks on three measurement occasions with an inter-session interval of exactly one week (±1 hour). In order to address state and trait influences, LST and LGC models were applied (Geiser et al., 2015; Steyer et al., 1992; Steyer et al., 2015; Steyer et al., 1999). We combined LST models of all primary inhibitory variables to investigate the trait-based structure of inhibitory control by adding higher-order latent factors that explained variance in task-specific traits. Finally, to provide comparability to previous studies (e.g. Friedman & Miyake, 2004), we analysed the structure of inhibitory control by applying SEM

on data from measurement occasion one without considering state and trait components. Results on congruency effects for error rate are not reported due to low error rates.

The first result was that the model fitting was successful, and excellent model fit was found for all inhibitory control variables except for the congruency effect for RT in the Simon task. There was no measurement invariance for this variable, which is why the task was not considered further for modelling at the trait level. LST and LGC models explained most of the variance in the dependent variables that measure inhibition (model-based reliability: .51 – .85). Antisaccade error rate revealed excellent reliability (.85). As expected, reliability was slightly lower for congruency effects for RT (.52 – .65) and lowest for SSRT (.51). Our study showed, for the first time, that the majority of explained variance was due to traits (consistency: .50 – .77, proportion of reliable variance explained by trait: mean 84%), except for SSRT (consistency: .28, proportion of reliable variance explained by trait: 54%). Of all dependent variables, SSRT was thus most strongly influenced by the situation and the interaction between person and situation. In the RT variables (e.g. congruent RT, incongruent RT) that do not or only indirectly measure inhibitory control, the variance explained by the models was excellent (model-based reliability: .89 – 1.0), and again the majority of the variance was determined by trait influences (consistency: .77 – .92).

In addition to this evidence of substantial stability, there was also plasticity at model level. There were trait changes in all primary inhibitory variables except SSRT. However, these changes occurred mainly between measurement occasion one and two and were relatively small. In most primary inhibitory variables, there were also interindividual differences in plasticity. Specifically, in no-go error rate and the Stroop task congruency effect for RT, trait changes were even more pronounced when participants showed low performance at measurement occasion one (correlation trait and slope: r = -.40, r = -.57 respectively).

In summary, regarding the study's first aim, most inhibitory control tasks were based on temporally stable cognitive processes that were only slightly influenced by situational factors.

For the second study objective, the results were less conclusive. First, there were relations between tasks on trait level, but the pattern of these relations was not consistent. A model in

which only the Eriksen flanker task was considered to measure distractor interference while all other tasks were explained by one common response inhibition factor led to a close relationship between distractor interference and response inhibition at trait level. However, when assigning the Stroop task to distractor interference too (sections 1.1.2 and 1.1.3), there was no longer any connection between the now-formed trait distractor interference and trait response inhibition factors. In addition to this model, describing all tasks with a common trait inhibition factor (Figure 12 (A)) also offered an excellent model fit. Irrespective of the chosen model, it was evident that common trait factors explained little variance in the respective tasks at any measurement, contradicting the existence of a common stable inhibition ability at trait level. Interestingly, compared to the other tasks, in the stop-signal task, only little variance was explained by a stable trait (see above). However, the part of variance explained by trait components was strongly associated with time-stable variance in the other tasks.

In addition, we analysed the structure of inhibition with data from measurement occasion one without considering states and traits. The only model with an acceptable model fit included two correlated factors (response inhibition: antisaccade, go-/no-go and stop-signal tasks; distractor interference: Flanker, Simon, and Stroop tasks; Figure 12 (B)). However, again, only little variance in the tasks was explained by the superordinate factors.

These results provide convincing evidence that previous reports questioning inhibition as a unitary construct (Gärtner & Strobel, 2021; Rey-Mermet et al., 2018) were not due to a lack of consideration of situational fluctuations. On the contrary, the tasks used here appeared to be primarily influenced by stable traits, with relatively little apparent commonality between tasks. Thus, in summary, the results suggest that the tasks do not measure a unified construct of inhibitory control.

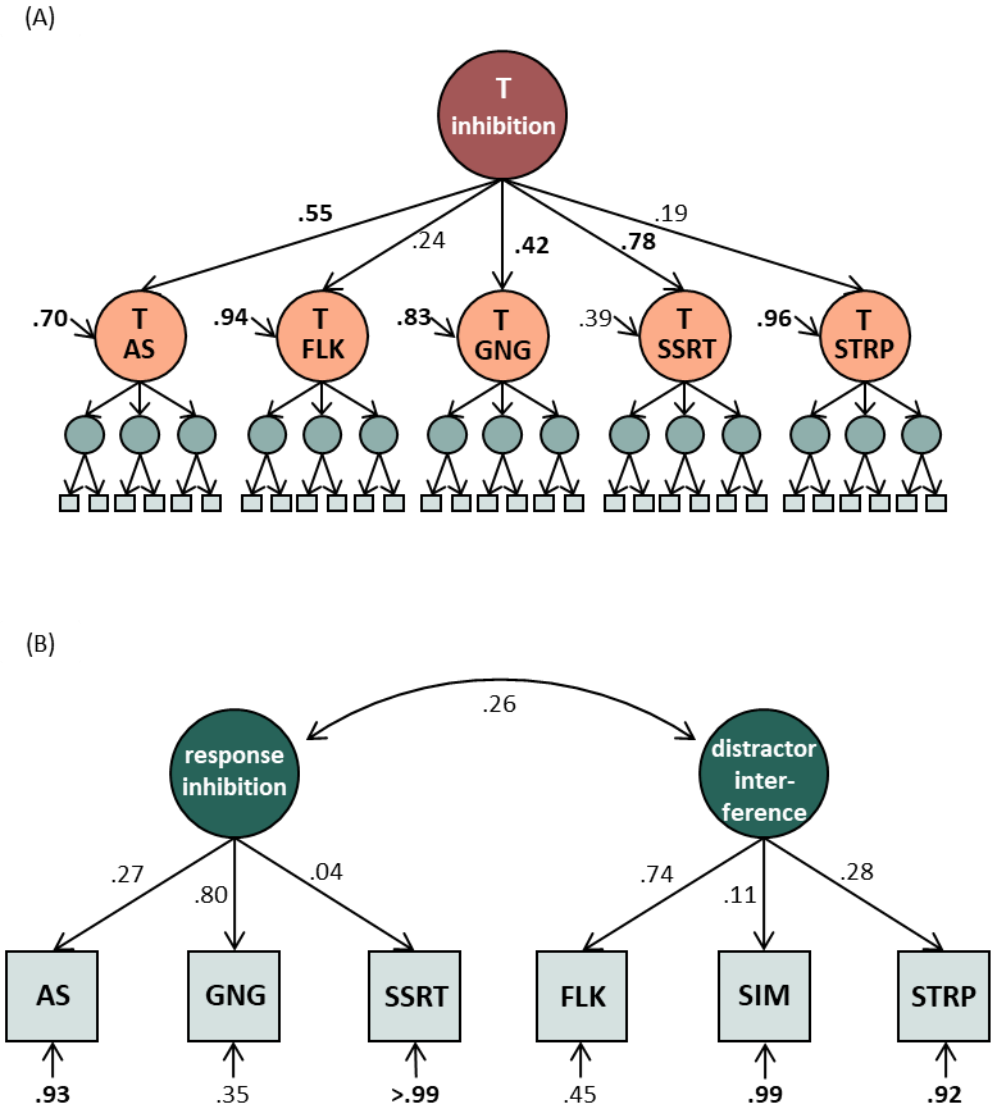


Figure 12. Key Findings from Study 1.

The trait-based structure of inhibitory control could be explained by a model including one common trait inhibition factor loading on all tasks (A). For reasons of clarity, this model is only presented in full up to the trait level. The structure of inhibition with data from measurement occasion one without considering states and traits could be explained by a two-factor model (B). Single-headed arrows from one circle to another indicate standardised factor loadings (interpretable as standardised regression coefficients). Remaining single-headed arrows indicate error variances. Double arrows indicate correlations. Numbers are printed in boldface when $p < .05$. T = latent trait; AS = antisaccade error rate, FLK = Eriksen flanker RT congruency effect; GNG = no-go error rate; SIM = Simon RT congruency effect; SSRT = stop-signal reaction time; STRP = Stroop RT congruency effect.

3.2 Study 2. GABA and Inhibitory Control

Faßbender, K., Bey, K., Lippold, J. V., Aslan, B., Hurlemann, R., & Ettinger, U. (2021). GABAergic modulation of performance in response inhibition and interference control tasks. Journal of Psychopharmacology, 35(12), 1496-1509.

Despite its importance for mental and physical well-being (Diamond & Ling, 2016), the underlying neural mechanism of inhibitory control as well as possible influences of psychotropic drug administration and associated plasticity processes are not yet fully understood. Inhibitory control is consistently associated with neural activity in frontoparietal and subcortical brain areas, and, at the cellular level, it is known to involve the DA, NA and Ach systems (Aron & Poldrack, 2006; Bari & Robbins, 2013). However, there is only little evidence on the role of the major inhibitory neurotransmitter GABA.

Therefore, the present study aimed to examine the effects of the benzodiazepine lorazepam on response inhibition and distractor interference. We hypothesised that lorazepam, by increasing GABAergic activity, impairs inhibitory control and that this effect goes beyond a general slowing of psychomotor processes. In addition, we explored whether the heterogeneity of inhibitory control measures observed in Study 1 is also reflected in different drug influences, and we calculated delta plots to examine in more detail the influence of lorazepam on build-up in selectivity and direct activation[3].

N = 50 healthy participants received 0.5 mg, 1 mg lorazepam, or placebo (within-subjects, double-blind, randomised) and performed the same antisaccade, Eriksen flanker and Simon tasks as in Study 1. The three measurement occasions were each separated by one week and took place at the same time of day in the same laboratory. The main results are shown in Figure 13.

[3] Initially, data from Study 2 were also evaluated using drift-diffusion models (Ulrich et al., 2015). Since these models did not yield reproducible conflict-related parameters (White et al., 2018), the results were discarded and are therefore not included in the present thesis.

In all three tasks, responses under drug became slower and more error-prone. In addition, lorazepam enhanced the congruency effect for error rates in all tasks and that for RT in the Eriksen flanker task. That is, in antisaccade/incongruent conditions, the drug effect was more pronounced than in prosaccade/congruent conditions, suggesting GABAergic involvement in inhibitory control. Drug-induced changes were not apparent in delta plots. Thus, there was no indication for lorazepam to have different effects on RT or error rate in early or late segments of the RT distribution. However, delta plots revealed typical task-specific patterns: Delta plots for RT were positive in slope for antisaccade and Eriksen flanker tasks and negative in slope for the Simon task. For late segments, the congruency effect was even reversed.

Comparisons of drug effects between tasks suggest that the drug-induced increase in congruency effects for error rate was stronger in the antisaccade tasks compared to both other tasks. Changes in error rate from placebo to drug (both doses) were significantly correlated between antisaccade and Simon tasks but not compared to the Eriksen flanker task.

Together, these results are the first to clearly indicate GABAergic involvement in response inhibition and distractor interference tasks. As the drug did not affect the three tasks in the same manner, the study further underscores the notion of heterogeneity in the construct of inhibitory control also regarding plasticity.

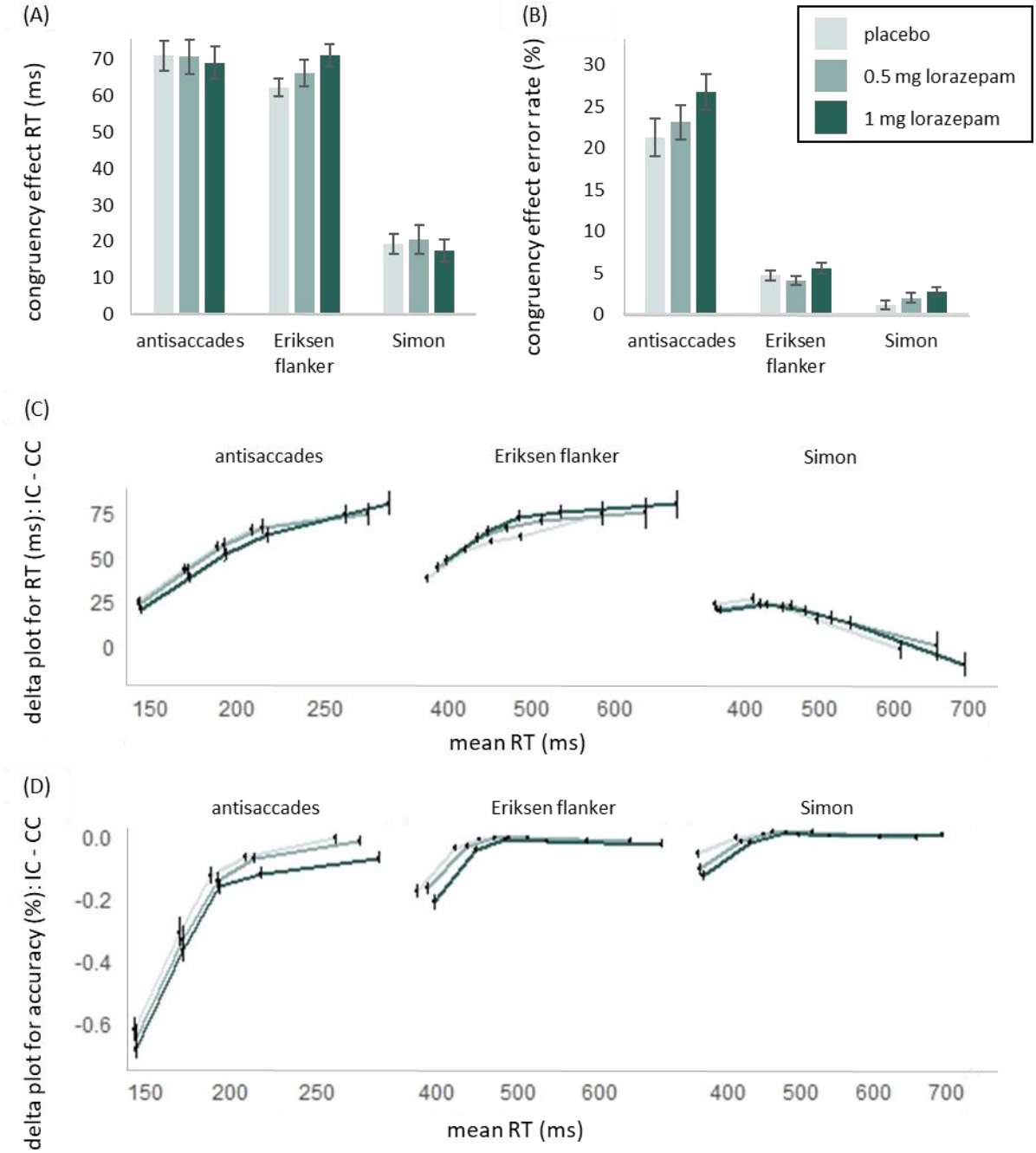


Figure 13. Key Findings from Study 2.

Lorazepam effects on congruency effects for reaction time (A) and error rate (B) and lorazepam effects on delta plots for reaction time (C) and accuracy (D) in antisaccade, Eriksen flanker and Simon tasks are shown. Error bars indicate the standard error. IC = incongruent; CC = congruent; RT = reaction time. Adapted from: Faßbender, K., Bey, K., Lippold, J. V., Aslan, B., Hurlemann, R., & Ettinger, U. (2021). GABAergic modulation of performance in response inhibition and interference control tasks. *Journal of Psychopharmacology*, 35(12), 1496-1509.

3.3 Study 3. GABA and Response Inhibition – SERIA Model

Aponte, E. A., Faßbender, K., Heinzle, J., & Ettinger, U. (2022). Gabaergic modulation of conflict adaptation and response inhibition. BioRxiv, 2022.03.03.482762.

One way to further dissect and better understand GABAergic processes in inhibitory control (Study 2) is to consider automatic and controlled processes separately. This division is part of dual process models. It can be formalised mathematically using models such as the SERIA model (Aponte et al., 2017) and may provide further insights into GABAergic involvement in the processes underlying response inhibition, going beyond the pure consideration of RT distributions.

Thus, the first aim of the present study was to apply the SERIA model to a Simon task for the first time, which is particularly interesting given that the SERIA model was initially designed for the antisaccade task, i.e. a classical response inhibition task (Hutton & Ettinger, 2006). In the Simon task, the roles of response inhibition and distractor interference have not been conclusively clarified (Verbruggen et al., 2005). In addition to these processes, conflict adaptation (Gratton et al., 1992) is observed in the Simon task. Using the SERIA model, conclusions about the interplay between conflict adaptation, automatic and controlled processes, and their effects on RT distributions may be drawn. The second aim of the study was to use the model-based data to specify GABAergic effects concerning the role of automatic and controlled processes, response inhibition and conflict adaptation in lorazepam-induced impairments in the two tasks.

For the first part of the study, antisaccade and Simon task data were used from N = 164 participants who had taken part in the first session of Study 1. For the second part, data were drawn upon from N = 50 participants from Study 2, including doses of 0.5 mg, 1 mg lorazepam, or placebo. SERIA models were fitted for the analyses.

Model fits of the first part showed that the SERIA model is suitable not only to describe processes of the antisaccade task but also those of a Simon task. As expected, negative delta plots were found in the Simon task. However, the subdivision into low and high conflict trials (based on whether the previous trial was congruent or incongruent) showed that positive

slopes were present for this task after low conflict trials. As the model fitting revealed, this was mainly due to a high proportion of slow, controlled responses in incongruent trials, contrasted with a higher proportion of automatic, fast responses in congruent trials. After high conflict trials, delta plots were negative-going, which according to the modelling, was due to conflict adaptation taking place. It was achieved by slowing down the controlled congruent responses while simultaneously facilitating controlled incongruent trials. In the antisaccade task, there was no conflict adaptation in the form of facilitation of controlled antisaccades (Figure 14 (A)).

When calculating delta plots that do not contain automated responses but only controlled responses, it is interesting to note that delta plots also became negative in antisaccades. These negative delta plots resulted from larger variance in controlled congruent trials compared to controlled incongruent trials. In classical delta plots, this effect is masked by fast, automatic congruent responses that are more frequent in antisaccades than in the Simon task.

In the second part of the study, all model results from the first part were replicated. Regarding drug effects, lorazepam slowed both controlled and automatic responses at all doses. In addition, in the Simon task, the proportion of automatic responses was significantly increased under 0.5 mg lorazepam. Lorazepam was also found to increase conflict adaptation in the Simon task, with controlled congruent responses becoming slower under high conflict than under low conflict. Again, high conflict facilitated controlled incongruent trials, but the drug did not modulate this effect. In the antisaccade task, the effect of lorazepam slowing down controlled prosaccades after high compared to low conflict was not significant but was observed at the descriptive level under 1 mg lorazepam (Figure 14 (B)).

In summary, the results show that increased neural GABAergic activity slowed down not only automatic responses but also controlled responses in both Simon and antisaccade tasks. In addition, increased GABAergic activity enhanced conflict adaptation in the Simon task by slowing down controlled congruent responses. Furthermore, it increased the proportion of automatic responses, indicating that increased neural inhibition could impair the inhibition unit or contribute to controlled units reaching the threshold later.

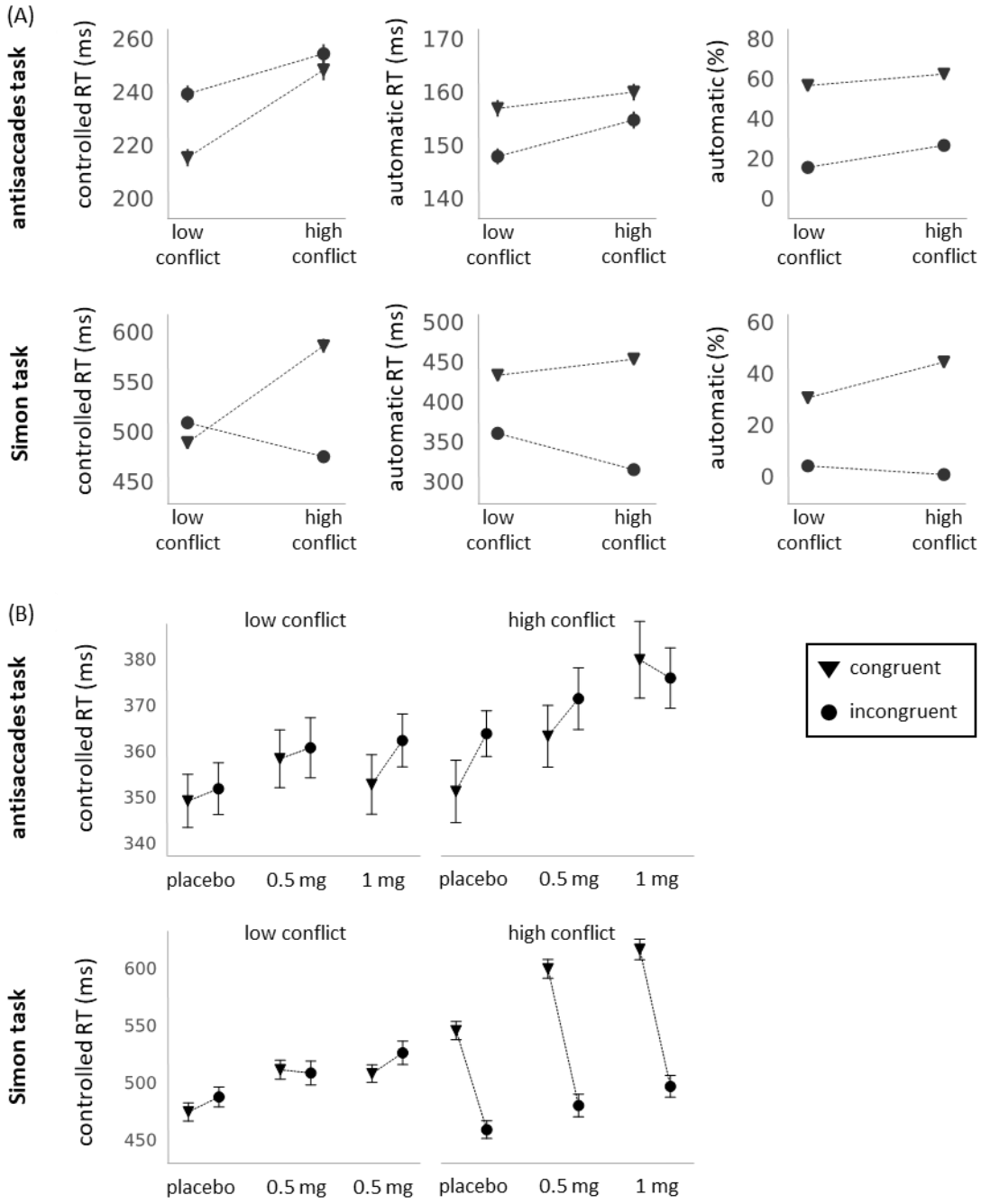


Figure 14. Key Findings from Study 3.

For the first part of the study (A), reaction times of controlled and automatic responses and the probability of an automatic response are shown. For the second part (B), reaction times of controlled responses are shown as a function of dose. Error bars indicate the standard error. Low conflict = previous trial was congruent/prosaccade; High conflict = previous trial was incongruent/antisaccade; RT = reaction time. Adapted from: Aponte, E. A., Faßbender, K., Heinzle, J., & Ettinger, U. (2022). Gabaergic modulation of conflict adaptation and response inhibition. *BioRxiv*.

3.4 Study 4. GABA and Distractor Interference

Faßbender, K., Baumert, P. M., Wintergerst, M. W. M., Terheyden, J. H., Aslan, B., Harmening, W., & Ettinger, U. (2023). GABAergic Involvement in Selective Attention. Journal of Cognitive Neuroscience, 35(6), 976-989.

The Eriksen flanker task is used to measure distractor interference and is also frequently applied in visual attention research. Many theories deal with how selective attention to the target is built up to process target-relevant information more intensively and reduce distractor influences in this task. At stimulus onset, selective attention is low, and mainly automatic responses are present. Over time, the contribution of controlled processes increases, and selectivity is built up. Study 2 showed that lorazepam increased distractor interference in the Eriksen flanker task, likely due to impaired selective attention. The present study was intended to substantiate whether this deterioration was mainly because the build-up in selectivity was slowed down or because the attentional focus was generally widened.

For this purpose, N = 29 participants received 1 mg lorazepam or placebo (within-subjects, double-blind, randomised) and completed an extended Eriksen flanker task. In this version of the task (White et al., 2011), there were outer and inner incongruent conditions in addition to the congruent and incongruent conditions (Figure 15). These allowed to examine how the influence of incongruent outer flankers decreases with narrower attentional focus compared to inner flankers, whilst the total number of incongruent flankers remains consistent. In addition, delta plots were calculated to explore the temporal course of attentional narrowing. The two measurements took place one week apart at the same time of day. The main results are shown in Figure 16.

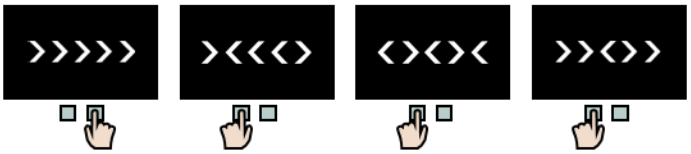


Figure 15. Illustration of the Modified Eriksen Flanker Task.

This task includes congruent, outer incongruent, inner incongruent and incongruent conditions (from left to right).

First, the results from Study 2 were replicated in the congruent and completely incongruent conditions, indicated by slower responses and an increased congruency effect for RT under drug. Furthermore, there was a linear increase in RT from congruent to outer incongruent, inner incongruent to incongruent under lorazepam. A similar trend was seen under placebo, but the pairwise comparison between outer and inner incongruent was not significant. Under placebo, the more incongruent distractors were present, the worse the participants' performance became; under lorazepam, the position of the distractors also played a role so that incongruent distractors that were closer to the target had a stronger influence. A possible explanation for this pattern can be found in Figure 17. Lorazepam may have widened the focus of attention, thereby making inner flankers more influential.

With the aim of replicating the results from the placebo group in the newly established extended task version, in a second online experiment, N = 25 participants completed the task on one measurement occasion, on their own electronic devices and without the influence of medication. The task effects found under placebo could be replicated, as again in this sample, there were no significant differences between the outer and inner incongruent conditions.

These analyses have not yet clarified whether lorazepam effects involve temporal or qualitative mechanisms. A purely temporal effect would mean that participants under lorazepam with a slower build-up in selectivity would show impairments particularly in fast responses. Instead, in slow responses, there would then have been enough time to build up selective attention. Thus, the drug effect should decrease in slow responses. The results from the delta plots speak against this assumption. On the one hand, there was no improvement in congruency effects for RT in slow segments, i.e. participants did not shift from responding slowly under lorazepam. Secondly, there were even larger congruency effects for error rate in slow segments under lorazepam. That is, when responding slowly, participants under lorazepam made even more errors when reacting to inner incongruent or incongruent trials than when responding faster.

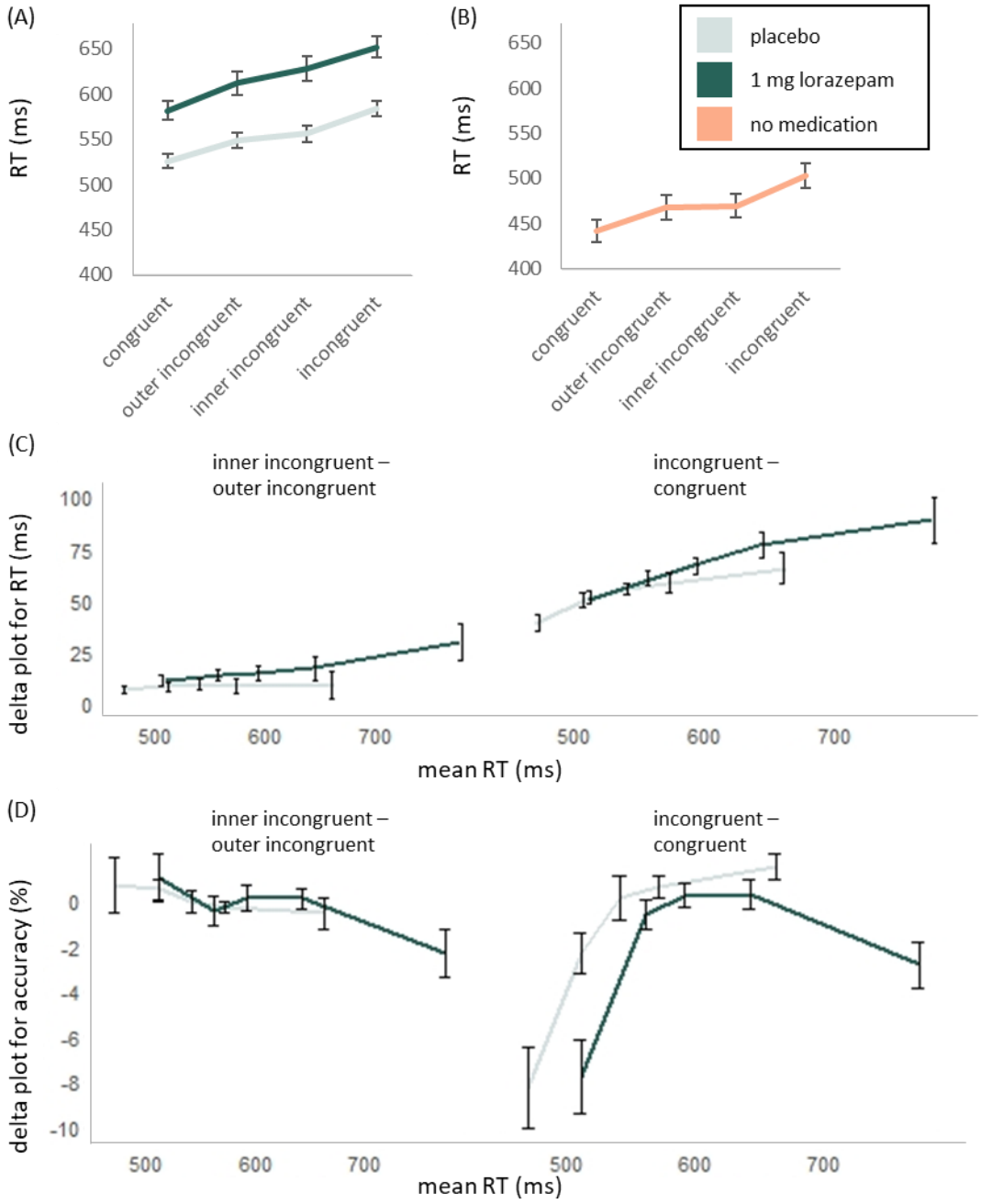


Figure 16. Key Findings from Study 4.

Lorazepam effects on reaction time (A), reaction times from online experiment (B), and lorazepam effects on delta plots for reaction time (C) and accuracy (D) in the modified Eriksen flanker task are shown. Classical delta plots, showing the difference between incongruent and congruent trials (right column) and delta plots showing the difference between inner and outer incongruent trials (left column) are included. Error bars indicate the standard error. RT = reaction time. Adapted from: Faßbender, K., Baumert, P. M., Wintergerst, M. W., Terheyden, J. H., Aslan, B., M Harmening, W., & Ettinger, U. (2023). GABAergic Involvement in Selective Attention. *Journal of Cognitive Neuroscience*, 35(6), 976-989.

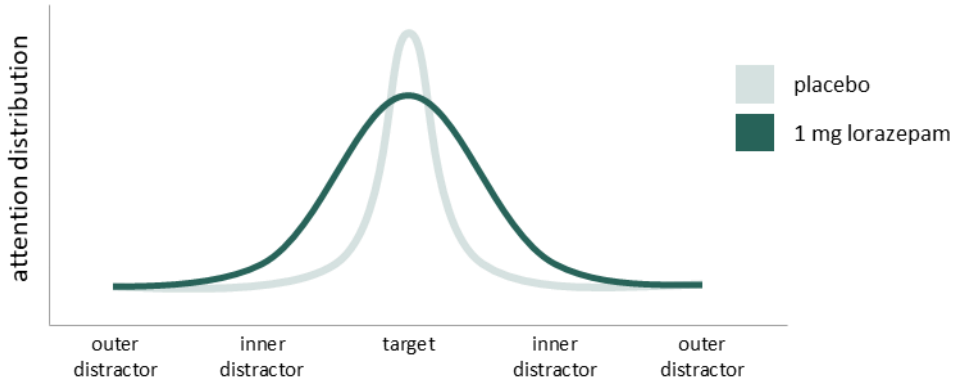


Figure 17. Hypothetical Distribution of Selective Attention in the Eriksen Flanker Task.

This distribution of selective attention may account for the reaction time data under placebo and lorazepam in the modified Eriksen flanker task. Stronger attentional processing is indicated by higher values on the y-axis. Importantly, both lines do not flatten to zero. Adapted from: Faßbender, K., Baumert, P. M., Wintergerst, M. W., Terheyden, J. H., Aslan, B., M Harmening, W., & Ettinger, U. (2023). GABAergic Involvement in Selective Attention. *Journal of Cognitive Neuroscience*, 35(6), 976-989.

In summary, these results suggest that the focus of attention was not only slower to build up but was also built up less effectively and was overall widened under lorazepam, resulting in greater interference. Therefore, it can be concluded that lorazepam-induced increased GABAergic activity worsens distractor interference in Eriksen flanker tasks, not only by slowing the build-up in selectivity as it slows down psychomotor processes in general but by substantially widening the attentional focus.

4 DISCUSSION

Investigating stability and plasticity can provide important insights into processes involved in inhibitory control. This thesis summarises four studies that thoroughly examined the issue of temporal stability of inhibitory control (Study 1) and, for the first time, comprehensively investigated plasticity in inhibitory control following drug administration leading to increased GABAergic signalling (Studies 2 – 4). Furthermore, the results extend our knowledge of a possible unified construct of inhibitory control and highlight sub-processes involved in different inhibitory control tasks. A strength of this thesis is that similar designs

and the same inhibitory control tasks were used in the different studies, allowing conclusions to be drawn across studies.

In the following, findings on the stability and plasticity of inhibitory control will be discussed. Subsequently, implications for inhibition as a unified construct will be addressed, and finally, task-specific results will be discussed in the last section.

4.1 Integration

4.1.1 Stability of Inhibitory Control

Stability is a key element for task selection in various studies, e.g. for investigating clinical samples (Crosbie et al., 2008). When considering stability, studies to date have distinguished between reliable variance and error variance (section 1.2). However, systematic research on separating reliable variance in different inhibitory control tasks into time-stable or situation-specific influences was lacking.

Crucially, in Study 1, we demonstrated for the first time that a large part of the reliable variance in all primary inhibitory variables, except SSRT, was explained by trait influences. Thus, situational influences played only a minor role overall, and our findings confirm the results of Meyhöfer et al. (2016), who found high trait influences in an antisaccade task. Model-based reliabilities and classical reliability coefficients were moderate to excellent for primary inhibitory variables and exclusively excellent for other mean reaction time variables (Studies 1 and 4). A likely explanation of the observed higher reliabilities in variables not primarily measuring inhibitory control (i.e. prosaccades, congruent) might be that these are driven more strongly by automatic processes. It would be possible that automatic processes are more reliable than controlled processes. SERIA modelling (Study 3) revealed a high amount of controlled congruent responses in the Simon task, whereas prosaccades were primarily automatic. Nonetheless, prosaccade latencies did not provide higher reliability than congruent RT in the Simon task, suggesting that the explanation of automatic processes being more reliable than controlled ones is insufficient, and probably, there were other factors influencing reliability. Such task-specific processes are discussed in section 4.1.4.

Taken together, the results substantially add to understanding the stability of inhibitory control tasks measured in standard laboratory settings. Stable underlying traits primarily determined inhibitory control. Therefore, it can be concluded that changes in performance, e.g. in pharmacological or experimental intervention studies, are unlikely to be due to situational influences but to the manipulation itself. Moreover, inhibitory control tasks thus fulfil the important validity criterion of time stability in endophenotype research (Gottesman & Gould, 2003).

4.1.2 Plasticity of Inhibitory Control

Current research addresses not only the stability of inhibitory control but also the ability to change and adapt performance. For example, it has been investigated how training can improve inhibitory control (Talanow & Ettinger, 2018), how disease-related deficits can be compensated (McKay et al., 2022) or how pharmacological interventions can influence inhibition (Allman et al., 2012). Consequently, the first step is to understand changes in performance over time that occur without experimental intervention to correctly classify changes that occur beyond simple task repetition, e.g. through interventions, in a second step.

In Study 1, measurements took place three times at weekly intervals, and the separate consideration of trait and state variance revealed information about trait changes over time. Not only did interindividual differences remain stable over time, but intraindividual changes were minimal. If at all, there were slight, non-linear improvements in performance in inhibitory control, mainly evident between measurement occasions 1 and 2. Presumably, there is potential for performance improvements through repetition, especially after tasks are presented the first time. However, trait changes are unlikely to occur beyond these small improvements without further intervention. Interestingly, there were significant individual differences in changes over time for most variables, i.e. not all individuals changed their performance equally, and participants who performed poorly at measurement occasion 1 improved more strongly in go-/no-go and Stroop tasks. This finding has implications for the investigation of clinical samples, where baseline performance is typically worse (e.g. Kertzman et al., 2008; Lipszyc & Schachar, 2010) and could therefore be affected more strongly

by repeated exposure. Baseline-dependent plasticity was also found in other cognitive control tasks (Diamond & Ling, 2016).

In Studies 2 – 4, increased GABAergic signalling from lorazepam administration primarily resulted in slower RTs/latencies in all studies, confirming previous research on benzodiazepine-induced slowing and increased error rates (e.g. Bruijn et al., 2004; Green et al., 1996; Haas et al., 2009; Masson et al., 2000). In addition, performance impairments were dose-dependent (Study 1; Green et al., 2000). In Study 1, lorazepam also increased error rates on antisaccade, Eriksen flanker and Simon tasks, but in Study 3, error rates in the Eriksen flanker task were not modulated by the drug. Likely, the newly added conditions (inner and outer incongruent) in Study 3 led to more cautious response behaviour, which increased RTs overall and thus reduced error rates. Thus, there was possibly a floor effect.

The most striking result from Studies 2 – 4 is that increased GABAergic activity not only slowed psychomotor processes but also impaired the suppression of incorrect responses, increased the influence of distractors by broadened attentional focus, and enhanced processes of conflict adaptation. Specific findings on the individual tasks are discussed in section 4.1.4. Previous studies obtained evidence of narrowed attentional focus in anxiety (Caparos & Linnell, 2012; Wegbreit et al., 2015). Given the anxiolytic effects of lorazepam, the latter findings fit with our result of widened attentional focus under lorazepam (Studies 1 and 3). Furthermore, we found increased conflict adaptation under lorazepam (Study 2), matching with studies that report impaired conflict adaptation in participants with high generalised anxiety (Larson et al., 2013).

Since the relationship between GABAergic pathways and the cortico-subcortical network underlying inhibitory control has not yet been investigated, it remains challenging to determine the exact neural mechanisms contributing to the worsening of inhibition under benzodiazepines. $GABA_A$ receptors are present in the entire cortical cortex (Fonnum, 1987), while there is also a large cortico-subcortical network involved in successful inhibition (Bari & Robbins, 2013), making it difficult to localise target regions of the observed lorazepam effect. TMS and MRS studies suggest that enhanced inhibitory control is associated with increased GABA concentration in the primary motor cortex (Sohn et al., 2002; Wessel et al., 2013;

Wildenberg, Burle et al., 2010), pre-SMA (Hermans et al., 2018) and basal ganglia (Haag et al., 2015; Quetscher et al., 2014). Concerning attentional focus, there seems to be reduced neural activity in the visual cortex for stimuli that are not focused on (Hopf et al., 2006; Müller & Kleinschmidt, 2004). However, these results are difficult to compare with the effect of lorazepam, which does not selectively affect individual brain regions. Nonetheless, they may indicate that increased GABAergic signalling is not purely harmful when controlling behaviour. However, reduced neural activity may also be controlled by active top-down processes (Carrasco, 2011), and overall our studies emphasise that increased neural inhibition via benzodiazepine administration impairs inhibitory control. This conclusion is supported by MRI studies and investigations on the role of excitatory neurotransmitters (section 1.1.4) or by studies suggesting that variations in arousal influence inhibitory control (Hasher et al., 2007). Questionnaire data from Studies 2 and 4 indicate that lorazepam also had sedative, arousal-reducing effects in our experiments. Thus, reduced activity in neural arousal systems may influence inhibitory control. Other authors suggest proactive inhibition constitutes a default state (Criaud et al., 2012; Jaffard et al., 2008) partially overlapping with the so-called default-mode network of brain activity (Raichle, 2015), which would mean that successful behavioural inhibition relies on actively released proactive inhibition.

In summary, inhibitory control improves slightly with repeated measures, emphasising the importance of practice sessions. Most importantly, such changes should be considered in clinical samples with lower baseline performance. Lorazepam administration, leading to increased GABAergic signalling, i.e. more neural inhibition, seems to impair task performance in general, but also inhibitory processes. The role of inhibitory neurotransmitters in behavioural inhibition has been largely neglected and should be investigated in more detail.

4.1.3 Inhibitory Control as a Unitary Construct

> **"Studies using a single laboratory paradigm for assessing or investigating inhibition do not warrant generalization beyond the specific paradigm studied."**
>
> (Rey-Mermet et al., 2018, p. 515)

It is disputed that inhibitory control as an umbrella term comprises several subcomponents (Dempster, 1995). However, it has not been conclusively clarified which components these are in detail and how strongly they are interrelated (Aichert et al., 2012; Hedge et al., 2018; Pettigrew & Martin, 2014). In particular, the close connection between response inhibition and distractor interference, as postulated by Friedman and Miyake (2004), has been questioned (Stahl et al., 2014). One aspect that needs to be considered is that tasks are always presented in a specific context, and situation-specific components could influence correlations between tasks and constructs. However, results from Study 1 show that despite high stability and very little situational influences and even when only considering reliable variance, different tasks measuring inhibition were only very slightly correlated. When investigating relations at the trait level and also when attempting to conceptually replicate the structure provided by Friedman and Miyake (2004) using data from the first measurement occasion only, the majority of explained variance in all tasks was not due to inhibitory control factors but to task-specific variance.

Conceptual replication based on data from measurement occasion one resulted in the expected division of response inhibition and distractor interference. However, neither the factor loadings on the tasks nor the correlation between the two constructs were significant. Given that we used different tasks than Friedman and Miyake (2004), the comparability of our findings may be reduced. However, the explanatory power of the proposed factor structure would be reduced if only the exact replication using identical task versions would reproduce it because various tasks are used and supposed to measure inhibitory control. In addition, other studies failed to replicate the model despite using the same or similar tasks as the original study (Gärtner & Strobel, 2021; Tiego et al., 2018). Furthermore, a closer look at data of Friedman and Miyake (2004) shows that also in their data, a high amount of variance was

explained by task-specific residual variance instead of common variance. Perhaps not only the model's replicability but its interpretation should be reconsidered (van der Sluis et al., 2007).

Analysing relations between tasks at the trait level also did not provide a conclusive structure of inhibition, as a unique assignment of the tasks to the two constructs, response inhibition and distractor interference, was not possible. However, a model not accounting for correlations between tasks fitted significantly worse than models that did include correlations. One major conclusion is thus that there are at least some commonalities between stable and situationally independent task aspects, but these relationships are small. Our study substantially extends previous investigations (Gärtner & Strobel, 2021) as from our elegant methodological approach we can conclude that the low correlations found in the past and in our own data are not due to situational influences. The tasks measure stable trait-like abilities but are less strongly related than inhibitory control theories suggest.

The SERIA model uses RT distributions to model controlled, automatic responses and the stopping process separately. Commonalities between different tasks may also be reflected in the fact that this model - originally developed for the antisaccade task - can also be applied to the Simon task (Study 3). However, the only significant correlation between model parameters was between controlled congruent and incongruent RTs or latencies, and model parameters related to inhibitory control were not significantly correlated. Therefore, it is more likely that the SERIA model can capture different processes than that both tasks capture identical processes.

In conclusion, the results on stability and plasticity, both on their own and in combination with modelling results, show that inhibitory control tasks do not measure a unified construct. A precise understanding of the construct of inhibitory control is still missing, despite its high relevance to everyday life. Therefore, in the following, further results are discussed separately according to the respective tasks and the subcomponents they measure.

4.1.4 Task Specific Processes

Task-specific processes will be discussed according to their occurrence in the four studies. Go-/no-go, stop-signal and Stroop tasks will be addressed first (Study 1), next antisaccade and Simon tasks (Study 1, 2, 3) and finally, the Eriksen flanker task (Study 1, 2, 4).

Go-/No-Go, Stop-Signal and Stroop Tasks

The go-/no-go task is often compared to the stop-signal task, and both are used as measures of response inhibition. Previous studies often reported significant correlations between both tasks (Bender et al., 2016; Enge et al., 2014; Hedge et al., 2018; Reynolds et al., 2006; Tiego et al., 2018), a finding that was not replicated in Study 1. However, when examining correlations on trait level, go-/no-go and stop-signal tasks showed a higher correlation. While in the go-/no-go task, only little total variance was impacted by state effects, the stop-signal task revealed a relatively high proportion of state variance. It may therefore be assumed that situational influences differently affect tasks, whereas underlying trait ability is related.

SSRT was also the variable with the highest proportion of unexplained error variance, i.e. with lowest reliability. One problem could be that our task version was not optimally designed according to recent recommendations (Verbruggen et al., 2019), resulting in many excluded participants. For example, SSRT is susceptible to changes in the instruction not to wait (Barch et al., 2009; Sylwan, 2004). Despite repeating the instruction multiple times, it is possible that participants ignored the instruction "do not wait for the stop-signal", especially in later measurements, which might be the reason for increased go RT over time. Thus, participants may have deliberately slowed down to avoid errors. Thus, SSRT may be influenced by processes that cannot strictly be separated from inhibitory control, such as motivation and strategy (Leotti & Wager, 2010). This conclusion also fits with the large impact of situational influences on SSRT. Interestingly, the proportion of trait-based variance was particularly strongly associated with traits from other tasks. If it were possible to reduce situational influences on the SSRT, it could be assumed that the task would be very well suited for measuring inhibitory control.

In the Stroop task, as in Flanker and Simon tasks, inhibitory control is estimated using a difference score. Difference scores revealed lower reliabilities than RT measures, a typical finding in congruency effects (Hedge et al., 2018). Thus, the reliability paradox is also evident in our data: Congruency effects are found in every study (Study 1, 2, 4) but are not necessarily reliable (Study 1). It is argued that errors from different distributions are combined in difference scores, and trial-level variability is not considered, reducing interindividual variance (Crawford et al., 2008; Whitehead et al., 2020). However, regarding the accumulation of errors from different distributions, our results show that this explanation is insufficient as congruent and incongruent RTs, each considered separately, have only small measurement errors, and measurement errors of congruency effects were larger than the sum of the two.

Antisaccade and Simon Tasks

Antisaccade error rate was the only primary inhibitory variable demonstrating excellent reliability in LST models. The task was also the only one based on oculomotor instead of manual responses. Previous studies and our data suggest eye movements are well suited to discriminate between individuals (Bargary et al., 2017). Eye movements may be a purer measurement than hand movements (Carpenter, 1994), which would limit comparisons with previous studies that used non-oculomotor versions of the antisaccade task (e.g. Friedman & Miyake, 2004; Gärtner & Strobel, 2021). In the hierarchical LST models, a relatively large proportion of variance in the antisaccade task was explained by trait response inhibition. Importantly, this finding should be interpreted with caution. It is a typical finding that inhibition factors are primarily influenced by one task, often the antisaccade task (Rey-Mermet et al., 2018). However, as long as other task loadings are low, one high loading has little significance in content.

Lorazepam increased antisaccade errors, also when compared to prosaccade errors. This effect has not been adequately addressed in earlier studies (Green & King, 1998; Green et al., 2000; McCartan et al., 2001) but offers insights into possible underlying mechanisms of the task. Parallel programming models (section 1.1.2) assume that antisaccades and prosaccades are programmed in parallel. Incorrect prosaccades result from slow antisaccade generation, and increased antisaccade latencies are accompanied by increased error rates (Massen, 2004).

However, our results show a selective increase in the error rate for antisaccades and therefore do not fit this theory. Instead, the results from Study 1 might support the existence of a separate inhibition unit (Everling & Fischer, 1998) that is influenced by lorazepam. Such an inhibition unit has been postulated in the LATER (Noorani & Carpenter, 2013, 2016) and SERIA (Aponte et al., 2017) models. Accordingly, the SERIA model was well-suited to describe our data (Study 3). However, if increased GABAergic signalling would impair the inhibition unit, lorazepam administration should increase the amount and RT of automatic responses, which was not found. Thus, the model failed to identify the mechanisms behind lorazepam-induced impairments in suppressing incorrect responses in the antisaccade task. In addition, SERIA modelling demonstrated conflict adaptation in the antisaccade task: Controlled prosaccade latencies following an antisaccade trial were slowed down. But again, facilitation in repeated antisaccade trials, conflict adaptation (Study 3), as well as delta plots (Study 2), did not appear to be affected by lorazepam. Thus, in summary, although increased GABAergic activity is shown to impair the suppression of incorrect responses (Study 2), the SERIA model does not reveal the exact mechanism contributing to the deterioration. Further research is therefore needed.

In the Simon task, there is still a lack of clarity about underlying inhibitory processes (Stahl et al., 2014), which was also reflected in our studies. In Study 1 at measurement occasion one, the best fitting model categorised the task as a measure of the distractor interference. However, in Study 3, the task was successfully fitted in the SERIA model, designed to describe response inhibition processes. However, since connections found to other tasks were small overall, also based on SERIA modelling, it can be assumed that the task primarily covers unique processes. In agreement with this unique role, the congruency effect for RT in the Simon task was the only variable that LST models could not successfully explain (Study 1), indicating that within and between different measurements, no consistent construct was measured. Thus, the conflicts may not affect performance consistently, or there are other processes additionally influencing performance. Such an additional process could be conflict adaptation. Study 3 showed that controlled congruent responses slowed down in the Simon task, and incongruent responses were facilitated due to conflict in the previous trial, fitting with the consideration that the task does not measure a single stable construct over time.

The Simon task is the only inhibitory control task consistently showing negative delta plots (Burle et al., 2005; Hommel, 2011; Wildenberg, Wylie et al., 2010), which was also the case in our results (Study 2). Thus, when reacting slowly, incongruent RTs became faster than congruent ones, demonstrating that the effect of the conflict differs depending on whether the response is fast or slow. A reason might be that there is a large temporal gap between relevant and irrelevant response activation in the Simon task (Pratte et al., 2010). The stimulus position is processed faster than the feature colour. In the Eriksen flanker task, irrelevant and relevant stimuli are processed on a similar time course, which is also consistent with the overall smaller Simon effect compared to other congruency effects (Study 1 and Study 2). SERIA analyses also revealed another possible explanation for negative delta plots. In the model parameters, congruent controlled responses were found to have more variability than incongruent controlled responses. Negative delta plots were seen for both the antisaccade task and the Simon task when only considering controlled responses. Automatic responses have shorter latencies and less variability. The more automatic responses, the more the negative delta plots are masked, which was the case in the antisaccade task but not in the Simon task, where there was a higher proportion of controlled responses.

GABAergic effects in the Simon task were similar to those of the antisaccade task, where lorazepam also impaired the suppression of incorrect responses (Study 2). Furthermore, there was a significant correlation between lorazepam-induced changes in the congruency effects for error rate between the two tasks. Apparently, GABAergic influences similarly affected inhibitory processes in error rate. However, results from Study 3, which provide a more detailed examination of the processes using SERIA models, also revealed differences in the effect of lorazepam on the two tasks. Although in both tasks, controlled congruent responses were slower following a high conflict trial, only in the Simon task was this effect additionally enhanced by lorazepam. Thus, conflict adaptation in the Simon, but not in the antisaccade task, is at least partially controlled by GABAergic signalling.

Eriksen Flanker Task

In the Eriksen flanker task, in contrast to antisaccade and Simon tasks, lorazepam additionally increased the congruency effect for RT (Study 2). Thus, GABAergic signalling may be

involved in resolving the conflict resulting from the incongruent flankers. LST model results showed commonalities between response inhibition and distractor interference measured by the Eriksen flanker task (Study 1). However, both modelling and the drug effects show that task-specific abilities largely impact the Eriksen flanker task.

The Eriksen flanker task is not only used as a measure of inhibitory control, but also in the study of the closely related construct of selective attention (Treisman, 1969; van Moorselaar & Slagter, 2020). Regarding GABAergic influences on selective attention, it was shown in previous studies that lorazepam might increase the processing of irrelevant task aspects and limit the ability to focus on relevant details (Duka et al., 1995; Giersch & Herzog, 2004; Michael et al., 2007). Our studies imply that under lorazepam, flankers closer to the target impair performance more strongly than flankers that are more distant (Study 4), which could be explained by a widened attentional focus. If this finding would, on the contrary, simply result from a slowed narrowing of attention, deficits should have disappeared in slow responses. However, delta plots show that lorazepam effects in RT persisted across the entire RT distribution. In addition, the congruency effect for error rate under lorazepam increased at very slow RTs (Study 4). That is, when responding slowly, lorazepam increased the error rate. It is possible that selectivity of attention was initially built up, but this state could not be maintained for long under lorazepam resulting in additional impairments in slow responses.

4.2 Limitations

The studies summarised in this thesis have some limitations. First, only young, healthy participants with relatively high levels of education were studied. This poses a limitation to the generalisability of the findings, as reliability is sample dependent and not an inherent task property (Parsons et al., 2018; Streiner et al., 2015). Studies with homogeneous samples reduce between-subject variance, which makes it more difficult to find reliable interindividual differences and may also have lowered our reliability. In addition, ceiling effects (Liu & Wang, 2021) might have influenced the results. Furthermore, measurement conditions were tightly controlled, and situational influences might play a more significant role in other settings. Regarding GABAergic effects, benzodiazepine administration in healthy individuals is not comparable to administration in clinical samples (e.g. anxiety patients). For example, despite

its known anxiolytic effects (Baldwin et al., 2013), lorazepam did not reduce anxiety in our samples, probably due to low baseline anxiety levels.

Second, the selected variables and analyses did not capture all relevant processes reflected in task performance. In Study 1, only variables based on either RT or error rate were analysed. Since there is an inverse relationship between RT and error rate, the so-called speed-accuracy trade-off (Bogacz et al., 2010; Wickelgren, 1977), the independent interpretations of the variables may be limited. Several alternative measures and variables, e.g. post-error slowing (Draheim et al., 2019), were not considered in Study 1 to keep the analysis straightforward and focussed on the most commonly used variables. For a complete understanding of inhibitory control processes, it would be essential to consider alternative measures or, as in Studies 2 - 4, to consider entire response distributions.

Finally, there are limitations in the explanatory power resulting from task selection. Since the Simon task could not be evaluated using LST models, only the Eriksen flanker task was uniquely assigned to distractor interference, making it difficult to draw conclusions about this construct. Compared to previous studies, a key strength of the summarised studies is that lorazepam effects were not only investigated in a single task. However, assessing three tasks with different underlying cognitive processes is still insufficient to make conclusive statements about inhibitory neurotransmitter effects of inhibitory control.

4.3 Future Research

"The eyes have it!"

(Gegenfurtner, 1999)

In addition to the specific suggestions for future research already mentioned in the previous sections, the following ideas could help enhance our understanding of inhibitory control.

Study 1 showed that most inhibitory control tasks measure stable, trait-like abilities. However, the precise understanding of underlying processes and relationships between tasks is still incomplete. In the future, tasks should be studied more systematically (Chan et al., 2008), and,

for example, multiple versions of the same task should be compared. Even small changes in task design can significantly affect measured processes (White et al., 2011). Guidelines should be developed, and standardised test batteries should be used, simplifying the combination of data from different studies (Karr et al., 2018). For example, consensus guidelines have been developed for the stop-signal task (Verbruggen et al., 2019) and the antisaccade task (Antoniades et al., 2013). Unfortunately, they were not fully implemented in Study 1. In the future, it could be examined whether complete adherence to guidelines in task design would reduce state influences in the stop-signal task.

The next step could also be to develop new paradigms to capture inhibitory control. Our results suggest that tasks using oculomotor measures might be particularly suitable, while using difference scores should be treated cautiously. There are already first promising attempts (Draheim et al., 2021) to develop new tasks that use staircase paradigms instead of difference scores, suggesting the existence of a common factor across tasks.

Furthermore, it would be important to consider not only inhibition but the entire construct of cognitive control, especially since it has yet to be clarified whether inhibition is a distinct construct within cognitive control (Friedman et al., 2008). In this context, tasks for measuring shifting and updating should also be analysed with the help of LST models in order to subsequently be able to establish connections between the three domains at the trait level.

Finally, due to the global non-specific effect of lorazepam on GABAergic processes, it was only possible to draw limited conclusions about the neural basis of the effects found. In order to better elucidate effects at the individual level, blood concentration should also be measured. In addition, functional neuroimaging techniques could contribute to understanding the role of neural inhibition in behavioural inhibitory control.

4.4 Conclusion

"Will we ever know if there is inhibition in cognitive control and does it matter?"

(Aron, 2007, p. 219)

Overall, inhibitory control tasks were found to be mainly determined by stable underlying traits. In addition, the results also suggest plasticity of inhibitory control as indicated by slight improvements after repeated measurement and impairments following increased neural inhibition. In the ongoing debate about whether there is a meaningful construct of inhibitory control and what mechanisms and modulations contribute to this ability, this thesis represents an important extension of previous research by pointing out that inhibitory control tasks do not measure a unified construct, either in terms of the role of neural inhibition or at trait level.

Altogether, this thesis has highlighted the importance of better understanding the complex underlying mechanisms of inhibitory control. Whether we end up calling these mechanisms inhibitory control or conclude that the construct is based on other abilities, whether more general or specific, may not matter. Therefore, while agreeing that it is time to "stop thinking about inhibition as a general cognitive construct" (Rey-Mermet et al., 2018, p. 516), I would like to emphasise that we should not stop addressing inhibitory control in research.

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APPENDIX A [List of Figures and Tables]

Figures

Tables

APPENDIX B [List of Abbreviations]

ACC	anterior cingulate cortex
Ach	acetylcholine
ADHD	attention deficit hyperactivity disorder
BOLD	blood oxygen level-dependent
DA	dopamine
DLPFC	dorsolateral prefrontal cortex
EEG	electroencephalography and
EF	executive function
FEF	frontal eye fields
fMRI	functional magnetic resonance imaging
GABA	γ-aminobutyric acid
ICC	intra-class correlation
LATER	linear approach to threshold with ergodic rate
LGC	latent growth-curve
LST	latent state-trait
MEG	magneto-encephalography
MRS	magnet resonance spectroscopy
nAChR	nonselective acetylcholine receptor
NE	norepinephrine
OCD	obsessive-compulsive disorder
PET	positron emission tomography
PFC	prefrontal cortex
pre-SMA	pre-supplementary motor area
rIFC	right inferior frontal cortex
RT	reaction time
SEF	supplementary eye fields
SEM	structural equation modelling
SERIA	stochastic early reaction, inhibition, and late action
SMA	supplementary motor area
SMG	supramarginal gyrus
SSD	stop-signal delay
SSRT	stop-signal reaction time
STN	subthalamic nucleus
TMS	and transcranial magnetic stimulation
VCPCR	video-based combined pupil and corneal reflection
VLPFC	ventrolateral prefrontal cortex
5-HT	serotonin

APPENDIX C [Publication Study 1]

Faßbender, K., Meyhöfer, I., & Ettinger, U. (2023). Latent State-Trait and Latent Growth Curve Modelling of Inhibitory Control. *Journal of Experimental Psychology: General*, 152(5), 1396–1419. https://doi.org/10.1037/xge0001344

Journal of Experimental Psychology: General

ISSN: 0096-3445

2023, Vol. 152, No. 5, 1396–1419
https://doi.org/10.1037/xge0001344

Latent State–Trait and Latent Growth Curve Modeling of Inhibitory Control

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The reliability of inhibitory control task performance as well as the existence of an underlying unitary inhibitory construct have been questioned. The present study is the first to use a trait and state decomposition approach to formally quantify the reliability of inhibitory control and to examine its hierarchical structure. $N = 150$ participants carried out antisaccade, Eriksen flanker, go/nogo, Simon, stop-signal, and Stroop tasks on three occasions. By applying latent state–trait modeling and latent growth-curve modeling, reliability was estimated and divided into the amount of variance explained by trait effects and trait changes (consistency) and the amount of variance explained by situational effects and effects of Situation × Person interaction (occasion specificity). Mean reaction times for all tasks revealed excellent reliabilities (.89–.99). Importantly, on average, 82% of variance was accounted for by consistency while specificity was rather small. Although primary inhibitory variables revealed lower reliabilities (.51–.85), the majority of explained variance was again trait determined. Trait changes were observed for most variables and were strongest when comparing the first occasion to later ones. In addition, in some variables, those improvements were particularly high in initially underperforming subjects. An analysis of the construct of inhibition on trait level showed that communality between tasks was low. We conclude that most variables in inhibitory control tasks are mainly affected by stable trait effects, but there is only little evidence of a common, underlying inhibitory control construct at trait level.

Keywords: response inhibition, interference control, latent state–trait, latent growth curve, reliability

Supplemental materials: https://doi.org/10.1037/xge0001344.supp

Inhibitory control, the ability to suppress prepotent or conflicting responses or thoughts, plays a critical role in navigating various aspects of daily life (Baumeister, 2014; Moffitt et al., 2011). Inhibitory control tasks have been used not only to measure cognitive processes (e.g., Hutton, 2008), but also to identify impairments in psychiatric and neurological patient populations (e.g., Aron & Poldrack, 2005; Crawford et al., 2002). In this study, we address two important questions in research on inhibitory control. First, we provide a formal investigation of the reliability, stability, and trait and state components of inhibitory control. Second, we use trait-based measures to contribute to the theoretical debate on the unity or diversity of inhibitory control (e.g., Friedman & Miyake, 2004; Gärtner & Strobel, 2021; Rey-Mermet et al., 2018).

To do so, we focus on the inhibitory control dimensions of response inhibition, that is, the ability to suppress prepotent but inappropriate responses (Friedman & Miyake, 2004), and resistance to distractor interference, that is, the ability to suppress processing of irrelevant stimuli or stimulus features (Friedman & Miyake, 2004). We measure these dimensions using the following, frequently implemented paradigms: the antisaccade task (Hallett, 1978), Eriksen flanker task (Eriksen & Eriksen, 1974), go/nogo task (e.g., van der Meere et al., 1995), Simon task (Simon & Rudell, 1967), stop-signal task (Logan & Cowan, 1984), and Stroop task (Stroop, 1935). Typically, the antisaccade, go/nogo, and stop-signal tasks are assigned to response inhibition (Friedman & Miyake, 2004; Gomez et al., 2007; Stahl et al., 2014). The Eriksen flanker and Simon tasks are considered as measures of distractor interference (Friedman & Miyake, 2004; Proctor, 2011). The Stroop task is typically assumed to capture response inhibition (Aichert et al., 2012; Friedman & Miyake, 2004); nonetheless, others highlight the similarity in interference between Eriksen flanker and Stroop tasks (Stahl et al., 2014).

Response inhibition in those tasks is commonly measured using the antisaccade error rate, nogo error rate, and stop-signal reaction time (SSRT). Measurement of distractor interference usually focusses on congruency effects, that is, the difference in mean reaction time (RT) between congruent and incongruent trials. Together, we

This article was published Online First March 13, 2023.
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Data, material and analysis scripts can be found online in R Markdown format (https://osf.io/9sq2g/). We have no known conflict of interest to disclose.
Some of the data were presented at DPPD 2021, TeaP 2021, and DGPs 2022 conferences.
We would like to thank the following people for their great help in data collection: Philine Baumert, Matthias Brandi, Lauren Frantz, Jana Hagen, Alina Hansen, Hannah Heinrichs, Jule Lammers, Sharon Sahler, and Judith Wamser.
Kaja Faßbender served as lead for data curation, formal analysis, project administration, visualization, writing–original draft, writing–review and editing. Inga Meyhöfer served as lead for software and contributed equally to conceptualization, methodology, and served in a supporting role for writing–original draft, writing–review and editing. Ulrich Ettinger served as lead for conceptualization, resources, supervision and served in a supporting role for project administration, writing–original draft, writing–review and editing.
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refer to those variables as *primary inhibitory variables*. In addition, pure RTs and error rates derived from the inhibitory conditions (e.g., RT in the incongruent condition of the Simon task) are also often reported and here labeled as *secondary variables*. Last, we include *control condition variables*; these are RTs and error rates derived from the control conditions (e.g., RT in the congruent condition of the Simon task).

Regarding the first research question of this study, assessing temporal stability and other forms of reliability is crucial (Parsons et al., 2018), especially when performance is assessed repeatedly, as is common in pharmacological studies (Shaffer, 1979), or when individual differences approaches are applied (Aichert et al., 2012; Rey-Mermet et al., 2018; Stahl et al., 2014). However, so far, the temporal stability and reliability of inhibitory control task performance are controversial (Hedge et al., 2018; Paap & Sawi, 2016; Wöstmann et al., 2013). Reliability is frequently measured as temporal stability (e.g., test–retest or intra-class correlations [ICC]) or internal consistency (e.g., split-half correlation or Cronbach's α). Values are interpreted as indicating excellent (≥.80), good (≥.60), or moderate (≥.40; Hedge et al., 2018) reliability.

A summary of previously reported reliabilities of inhibitory control measures is in Table 1. For primary inhibitory variables, highest temporal stability and internal consistency have been reported for antisaccade and go/nogo tasks. RT congruency effects were less temporally stable and internally consistent. Lowest temporal stability was shown for SSRT. For RTs in secondary and control condition variables, good to excellent temporal stability over at least one week and good to excellent internal consistency were observed for all tasks, except for the stop-signal task. Regarding the stop-signal go RT, recent studies showed lower and less consistent temporal stability. For error rates in secondary and control condition variables, only poor to good temporal stability and poor to excellent internal consistency were reported, likely due to low error rates in these conditions.

An issue related to the measurement of test–retest reliability is that even when temporal stability is high, that is, there are few interindividual changes, performance may change intraindividually over time, for example, due to practice, adaptation to the environment or changes in strategy use, thereby reflecting plasticity of underlying processes (Dyckman & McDowell, 2005; Wöstmann et al., 2013). For most tasks and variables, there are both findings of within-subject improvement after repeated performance and those that do not indicate such plasticity (Ettinger et al., 2003; Klein & Berg, 2001; Meyhöfer et al., 2016; Paap & Sawi, 2016; Wöstmann et al., 2013; N.White et al., 2019). The latter include studies using very short test–retest intervals (1 week; e.g., Paap & Sawi, 2016) as well as those with considerably longer ones (approx. 2 months; e.g., Wöstmann et al., 2013). Plasticity effects seem to be most consistent for the Stroop task (Beglinger et al., 2005; Davidson et al., 2003; Martínez-Loredo et al., 2017; Wöstmann et al., 2013). In addition, for antisaccade, go/nogo and Stroop tasks, it was shown that systematic training may improve performance (Dyckman & McDowell, 2005; Talanow & Ettinger, 2018; Wilkinson & Yang, 2012; Zhao et al., 2018).

An important gap in the reliability literature concerns the decomposition of reliable variance into trait and state components. Such a decomposition goes beyond the classical calculations of stability and consistency and provides important information for the interpretation of individual performance. Trait components may be primarily due to genetic and environmental influences, whereas state components can stem from a variety of sources, such as motivation (Botvinick & Braver, 2015), emotion (Dreisbach, 2006), level of arousal/awareness (Lo et al., 2016), background noise (Szalma & Hancock, 2011), or stress (Shields et al., 2016). However, a detailed investigation of trait and state influences on inhibitory control is lacking.

Parameter estimation in so-called latent state–trait (LST) or latent growth curve (LGC) models can be done using structural equation modeling (SEM; Geiser et al., 2015; Steyer et al., 1992, 1999, 2015). LST and LGC models are an extension of classical test theory and decompose the measured value into true score and measurement error. The true score in turn is decomposed into latent trait and latent state residuals. The latent state residuals characterize the effects of the situation and Person × Situation interaction. When analyzing

Table 1
Summary of Previously Reported Reliabilities

Dependent variable	ICC	$r_{test-retest}$	α	$r_{split-half}$	References
Primary inhibitory variables					
AS error rate, nogo error rate in the go/nogo task	.69–.92	.44–.92	.81–.94	.86–.97	c,e,f,g,h,i,k,n,o,s,t,x
RT cong.eff. in Eriksen flanker, Simon, and Stroop tasks†	−.51–.91	.43–.94	.53–.89	.14–.91	a,e,f,g,l,m,o,r,s,v,w,x
SSRT*	.03–.71	.03	.29–.61	.72–.76	b,d,e,g,o,x
Latencies/RTs in secondary and control condition variables					
AS and PS, Eriksen flanker con. and incon., go/nogo go, Simon con. and incon., Stroop con. and incon.	.58–.93	.65–.93	.84–.97	.72–.97	a,c,g,h,i,j,k,l,m,n
Stop-signal go RT	.35–.60	.60–.83	.92–.93		g,q,x
Error rates in secondary and control condition variables					
Prosaccade, Eriksen flanker con. and incon., Simon con. and incon., Stroop con. and incon.	.36–.78	.22–.78	−.18–.86		d,g,j,n,t,x

Note. AS = antisaccade; con. = congruent; ICC = interclass correlation coefficient; incon. = incongruent; PS = prosaccade; cong.eff. = congruency effect; RT = mean reaction time; SSRT = stop-signal reaction time; α = Cronbach's α.
[a] Borgmann et al. (2007). [b] Congdon et al. (2012). [c] Ettinger et al. (2003). [d] Franzen (1987). [e] Friedman et al. (2008). [f] Friedman and Miyake (2004). [g] Hedge et al. (2018). [h] Klein and Berg (2001). [i] Klein and Fischer (2005). [j] Martínez-Loredo et al. (2017). [k] Meyhöfer et al. (2016). [l] Miyake et al. (2000). [m] Paap and Sawi (2016). [n] Płomecka et al. (2020). [o] Rey-Mermet et al. (2018). [p] Roy-Byrne et al. (1995). [q] Saville et al. (2011). [r] Siegrist (1995). [s] Stahl et al. (2014). [t] Talanow and Ettinger (2018). [u] Versino et al. (1993). [v] N. White et al. (2019). [w] Whitehead et al. (2020). [x] Wöstmann et al. (2013).
†Negative ICCs were only reported by N. White et al. (2019), using no more than 40 trials per task. All other studies reported ICCs above .40.
*All except one study (Congdon et al., 2012) reported ICCs below .49.

data taking into account trait and state components, a person's performance is not considered in a situational vacuum, but is always affected by an interindividually varying situation (Geiser et al., 2015; Steyer et al., 1992, 1999, 2015). LGC models additionally include a component accounting for systematic trait changes over time, reflecting plasticity processes such as learning.

The LST approach has mostly been applied to data from psychometric questionnaires (e.g., Schmitt & Steyer, 1993; Schmukle & Egloff, 2005; Schuler et al., 2014), but also from cognitive (Bonnefon et al., 2007; Danner et al., 2011) and oculomotor tasks (Meyhöfer et al., 2016). The latter study reported antisaccade (and prosaccade control task) measures to be highly reliable and mainly influenced by stable traits.

However, to our knowledge, there are no studies reporting results from LST models on any other inhibitory control task and none on LGC models or on the trait-based structure of inhibitory control. Therefore, the first aim of the present study is to fill this important research gap by applying, in preregistered analyses, LST models and, in exploratory analyses, LGC models to data derived from inhibitory control tasks and by analyzing the trait-based structure of inhibitory control. Based on previous studies reporting the classical measures of stability and plasticity and evidence of high heritability in inhibitory control tasks (Friedman et al., 2008), we expected to find high reliability for RTs in secondary and control condition variables and lower reliability in primary inhibitory variables. Overall, we only expected slight improvements over time for all tasks.

The second research question addressed in this study concerns the structure of inhibitory control. Using SEM, Friedman and Miyake (2004) showed that inhibitory control is not homogeneous or unitary, but can be structured into the related yet separable dimensions of response inhibition, interference control, and proactive interference. However, both this specific division and the existence of a general factor underlying inhibitory control have been questioned (Friedman et al., 2008; Gignac & Kretzschmar, 2017; Jewsbury et al., 2016; Klauer et al., 2010; Krumm et al., 2009). Instead it was suggested that tasks commonly applied to measure inhibitory control capture highly task specific demands (Rey-Mermet et al., 2018). A shortcoming of previous studies examining relations among inhibitory control tasks to identify one or more underlying inhibition factors is their (implicit) assumption that commonality between tasks is due to a stable, trait-like ability. However, no study has yet investigated the structure of inhibitory control considering states and traits separately. Thus, it is the second aim of our study to analyze the trait-based structure of inhibitory control. These analyses were not included in the preregistration and are therefore considered as exploratory. Nevertheless, the rationale for including these analyses is that we expect at least some variance in tasks to be explained by an underlying temporally stable inhibitory control factor.

Method

Sample

Healthy participants aged 18–30 were recruited via ads placed around the campus and online. We aimed for $N = 150$ complete datasets including equal numbers of males and females. Exclusion criteria were any current or history of mental disorder, current medication (except for contraceptives, vitamin products and thyroid medicines), and color blindness. Additionally, participants were required to have normal or corrected-to-normal sight and to be right-handed. Participants provided written informed consent and were compensated with 40€ or course credits. The study was approved by the ethics committee of the Department of Psychology at the University of Bonn and is preregistered at https://aspredicted.org/J7V_RSH.

Design and Procedure

The study consisted of an online questionnaire and three laboratory sessions. The online questionnaire (SoSci Survey; Leiner, 2019) comprised items on exclusion criteria, demographic data, and handedness (Edinburgh Handedness Inventory; Oldfield, 1971). Suitable participants were invited to the three laboratory sessions. These took place in three subsequent weeks, with weekday and time of day kept the same within each participant ($\pm$1 hr). In the first session, the exclusion criteria were verified verbally and the Ishihara test (Ishihara, 1917) was presented to test for color deficiencies. Next, participants performed a set of cognitive tasks. Every session started with a smooth pursuit eye movement task, which is not part of the present paper, followed by the antisaccade, Eriksen flanker, go/nogo, Simon, stop-signal, and Stroop tasks. Task order for the inhibitory paradigms was randomized but kept constant for each participant over the three measurement occasions. Each task in every session included 20 practice trials and participants had to verbally reproduce all instructions to optimally ensure comprehension. In the stop-signal task, the practice block was automatically repeated, if the accuracy in this block was less than 50%. Total duration of a session was about 80 min.

Inhibitory Control Tasks

Task Presentation

The antisaccade task was written using SR Research Experiment Builder software (SR Research Ltd., Ontario, Canada; version 1.10) and presented on a flat screen monitor (BenQ, 24″, height: 29.9 cm, width: 53.1 cm, resolution: 1,920 × 1,080 px, 144 Hz refresh rate). Before the task, a horizontal–vertical 5-point calibration and a central drift correction procedure were carried out. During the task, a desktop-mounted video-based combined pupil and corneal reflection eye-tracker (EyeLink 1000, SR Research Ltd., Canada) registered movements of the right eye at a sampling rate of 1,000 Hz and a chinrest stabilized the head to reduce movements. The system had a minimal spatial resolution of 0.01, and an average accuracy of 0.25° to 0.5°. Centroid pupil-tracking algorithms were used to detect pupil and corneal reflection.

All other tasks were written in Presentation (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA) and presented on a separate monitor (Samsung, 19″, height: 30.1 cm, width: 37.6 cm, resolution: 1,280 × 1,024 px, 60 Hz refresh rate) located in the same room without using a chinrest. The distance from eye to monitor was approx. 70 cm throughout all tasks.

Instructions and stimuli were shown on a black (0, 0, 0) background, and trials were presented in random order. In all tasks, the stimulus remained on the screen for a fixed period and did not disappear after a participant's reaction.

Antisaccade Task

In the antisaccade task (Figure 1 in the online supplemental material), each trial started with a fixation stimulus in either yellow (225, 225, 0) or blue (0, 150, 255) presented for 1,000–2,000 ms (random duration) in the center of the screen (0°, 0°). Subsequently, a white (255, 255, 255) peripheral stimulus appeared at 10.32° to the left or right for 1,000 ms. All stimuli were circles of approx. 0.34° in diameter and stroke width of 0.12°. Participants were instructed to look at the peripheral stimulus as precisely as possible (prosaccade) or to look exactly in the opposite direction (antisaccade) depending on the color of the fixation stimulus. The color instruction mapping was counterbalanced across participants but kept constant within a participant across occasions. There were 100 prosaccade and 100 antisaccade trials, and within each condition, each stimulus direction was used 50 times.

Eriksen Flanker Task

In the Eriksen flanker task (Figure 2 in the online supplemental material), each trial started with a central fixation cross (horizontal size approx. 3.21°, vertical size approx. 3.03°) presented for 500 ms. Subsequently, five white (255, 255, 255) arrows were shown (total horizontal size approx. 17.23°, vertical size approx. 3.51°) for 1,000 ms followed by a black screen inter-trial interval (ITI) of 500 ms. Participants were instructed to respond to the direction (right ">" or left "<") of the middle arrow by pressing the "," or "X" key using their left and right index fingers on a QWERTZ keyboard. The four flankers were either congruent (e.g., "<<<<<") or incongruent (e.g., "<<>><<"). There were 100 congruent and 100 incongruent trials, and within each condition, each direction of the middle arrow was used 50 times.

Go/Nogo Task

In the go/nogo task (Figure 3 in the online supplemental material), each trial started with the presentation of a white (255, 255, 255) letter (vertical size approx. 3.65°) for 200 ms in the center of the screen (0°) followed by a black screen ITI of 1,000 ms. Participants were instructed to press the space key as fast as possible on go trials ("H") and oddball trials and not to react on nogo trials. The letter instruction mapping for oddball and nogo trials ("L"/"F") was counterbalanced across participants but kept constant within each participant. There were 160 go trials (80%), 20 oddball trials (10%), and 20 nogo trials (10%).

Simon Task

In the Simon task (Figure 4 in the online supplemental material), each trial started with a fixation cross (horizontal size approx. 3.21°, vertical size approx. 3.03°) presented for 500 ms in the center of the screen (0°). Subsequently, a green (0, 255, 150) or blue (0, 150, 255) circular stimulus of approx. 3.03° in diameter was shown on the right or left side of the screen at 8.99° amplitude from center for 1,500 ms. Each color was assigned to either the "," or "X" keys on a QWERTZ keyboard. Participants were instructed to press the key corresponding to the color, regardless of stimulus position. The stimulus position and the position of the assigned key on the keyboard were either congruent (e.g., stimulus on the left, key located on the left side) or incongruent (e.g., stimulus on the right, key located on the left side). The color instruction mapping was counterbalanced across participants but kept constant within each participant. There were 100 congruent and 100 incongruent trials, and within each condition, each direction was used 50 times.

Stop-Signal Task

The stop-signal task (Figure 5 in the online supplemental material) was adapted from the stop-signal task provided in the Cognitive Experiment III v3 pack provided by Neurobehavioral Systems (https://www.neurobs.com). Each trial started with a fixation cross (font size: 7.5% of screen height) presented for 500 ms in the center of the screen (0°). Subsequently, a white (255, 255, 255) arrow (font size: 10% of screen height) pointing left or right was shown for 100 ms at the same position followed by a black screen. The duration of its presentation (stop-signal delay; SSD) was dynamically adjusted over the task using a tracking procedure. Next, either a white (255, 255, 255) arrow (font size: 12.5% of screen height) pointing up (stop trial) or another black screen (go trial) was presented for 500 ms followed by a black screen ITI of 1,000 ms. Participants were instructed to respond to the direction (right ">" or left "<") of the white arrow by pressing the "," or "X" key on a QWERTZ keyboard and to stop, that is, not to react when the stop-signal appeared. The initial SSD of 400 ms was prolonged by 16 ms after every unsuccessful stop trial or reduced by 16 ms after every successful stop trial. This procedure aimed to ensure that participants successfully stop their response on approx. 50% of stop trials. There were 150 go trials and 50 stop trials, and within each condition, each direction was used equally often.

Stroop Task

In the Stroop task (Figure 6 in the online supplemental material), each trial started with a central fixation cross (horizontal size approx. 3.21°, vertical size approx. 3.03°) presented for 500 ms. Subsequently, the German word for the colors blue ("blau"), green ("grün"), red ("rot"), or yellow ("gelb") was shown (vertical size approx. 2.17°) for 1,000 ms followed by a black screen ITI of 500 ms. The words were either printed in blue (0, 0, 255), green (0, 255, 0), red (255, 0, 0), or yellow (255, 255, 0). On the QWERTZ keyboard the "C" was covered with a green sticker, the "V" with a yellow sticker, the "N" with a red sticker, and the "M" with a blue sticker. Participants were instructed to press the button stickered with the same color as the word was printed in and not to react to the meaning of the word. In congruent trials, coloring and meaning were identical (e.g., the word "red" printed in red) in incongruent trials they differed (e.g., the word "blue" printed in red). There were 100 congruent and 100 incongruent trials. In the congruent condition, every word was used 25 times; in the incongruent condition, every word-color combination was used 8 or 9 times.

Data Processing

In the antisaccade task, saccade detection was based on criteria of amplitude ($\geq 1°$) and starting point ($\leq \pm 100$ px horizontally from central stimulus position). Trials in which no saccade could be detected, as well as responses with latencies to stimulus onset of <80 ms or $>1{,}000$ ms were counted as invalid and were excluded. In the Eriksen flanker, go/nogo (only for the go condition), Simon, Stroop and tasks, missing trials as well as responses with

RT <150 ms or >1,200 ms were counted as invalid and excluded. Latency was defined as the time (ms) between the onset of the peripheral stimulus and the initiation of a directionally correct saccade. RT (ms) was only computed for correct trials, and error rate was defined as the percentage of incorrect (%) responses. Incorrect responses comprised a directionally wrong saccade or an incorrect button press in Eriksen flanker, Simon, and Stroop tasks. Estimation of the SSRT was based on the integration method with replacement of the go omissions by the maximum RT (Verbruggen et al., 2019).

We defined the following dependent variables as *primary inhibitory variables*: antisaccade error rate, RT congruency effect in the Eriksen flanker task, nogo error rate, RT congruency effect in the Simon task, SSRT and RT congruency effect in the Stroop task. *Secondary variables* derived from the inhibitory condition were: antisaccade latency, incongruent RT, and error rate in Eriksen flanker, Simon, and Stroop tasks. *Control condition variables* were: prosaccade latency and error rate, congruent RT and error rate in the Eriksen flanker task, go RT in the go/nogo task, congruent RT and error rate in the Simon task, go RT in the stop-signal task, and congruent RT and error rate in the Stroop task.

The pre-registration includes further variables that are not reported here in order to keep the paper concise. The present selection includes the variables most commonly used in previous literature and was settled before model calculation.

Participants not completing all three sessions were excluded from all analyses. Participants were excluded from a particular task if they did not have complete data for that task in one or more sessions. For each task and each dependent variable, outliers were excluded separately. Outlier detection for the dependent variables took place including the following within-subjects factors: occasion (1, 2, and 3) and task condition (congruent and incongruent for Eriksen flanker, Simon, Stroop; prosaccades and antisaccades for the antisaccade task; not included for go/nogo and stop-signal). An outlier was defined as a participant having a mean value at least four times below or above the interquartile range in a particular variable. This deviates from our pre-registration, as the originally envisaged criterium of three times below or above the interquartile range, as rightly noted in the review process, led to very strict exclusions (e.g., participants with approx. 10% error rate in prosaccades). Importantly, this criterion did not lead to any exclusions of participants who performed better than the average sample. Additionally, participants having fewer than 9 available trials in a particular variable and test set (odd and even; only for SEM analyses) were excluded. For the go/nogo task, we adjusted the criterion to "fewer than five available trials," deviating from our pre-registration, as there are only 10 nogo trials per occasion and test set. For the SSRT, exclusion criteria were based on Verbruggen et al. (2019). Mean RT on unsuccessful stop trials had to be lower than mean RT on all go trials, error rate in stop trials had to be between 25% and 75%, and SSRT had to be positive. A detailed list of all outliers and remaining sample sizes can be found in Table 1 in the online supplemental material.

All data were processed using Matlab 2017b (The MathWorks, Natick, USA). Calculation of dependent variables, outlier detection, as well as all further analyses, including SEM, were carried out in R (R Core Team, 2018), using the packages *apaTables* (Stanley, 2021), *dplyr* (Wickham et al., 2022), *ez* (Lawrence, 2016), *ggplot2* (Wickham, 2016), *lavaan* (Rosseel, 2012), *lsr* (Navarro, 2015), *MVN* (Korkmaz et al., 2014), *papaja* (Aust & Barth, 2022), *rel* (LoMartire, 2020), *rstatix* (Kassambara, 2021), and *splithalf* (Parsons, 2021). Scripts, data, and mores details on excluded participants are available online (https://osf.io/9sq2g/; Faßbender, 2023).

Statistical Analyses

SEM Analyses

LST models (Figure 1A) explain variance by situational, dispositional, and error influences. Therefore, different measurement occasions and different experimental conditions measuring the same construct are required (Kelava & Schermelleh-Engel, 2012). In the present study, different conditions were realized by separating data into two test sets by odd–even classification. To set up LST models, observed variables (X_{ik}) for the three measurement occasions (k) and two test sets (i) were first dismantled into latent states (S_k) and measurement error variances (ε_{ik}). Next, latent states were decomposed into latent trait (T) and occasion-specific state residuals (SR_k). Variance due to consistent attributes of the person is represented by the trait component whereas the state residuals reflect the influences of the situation and the Situation × Person interaction (Steyer et al., 1999).

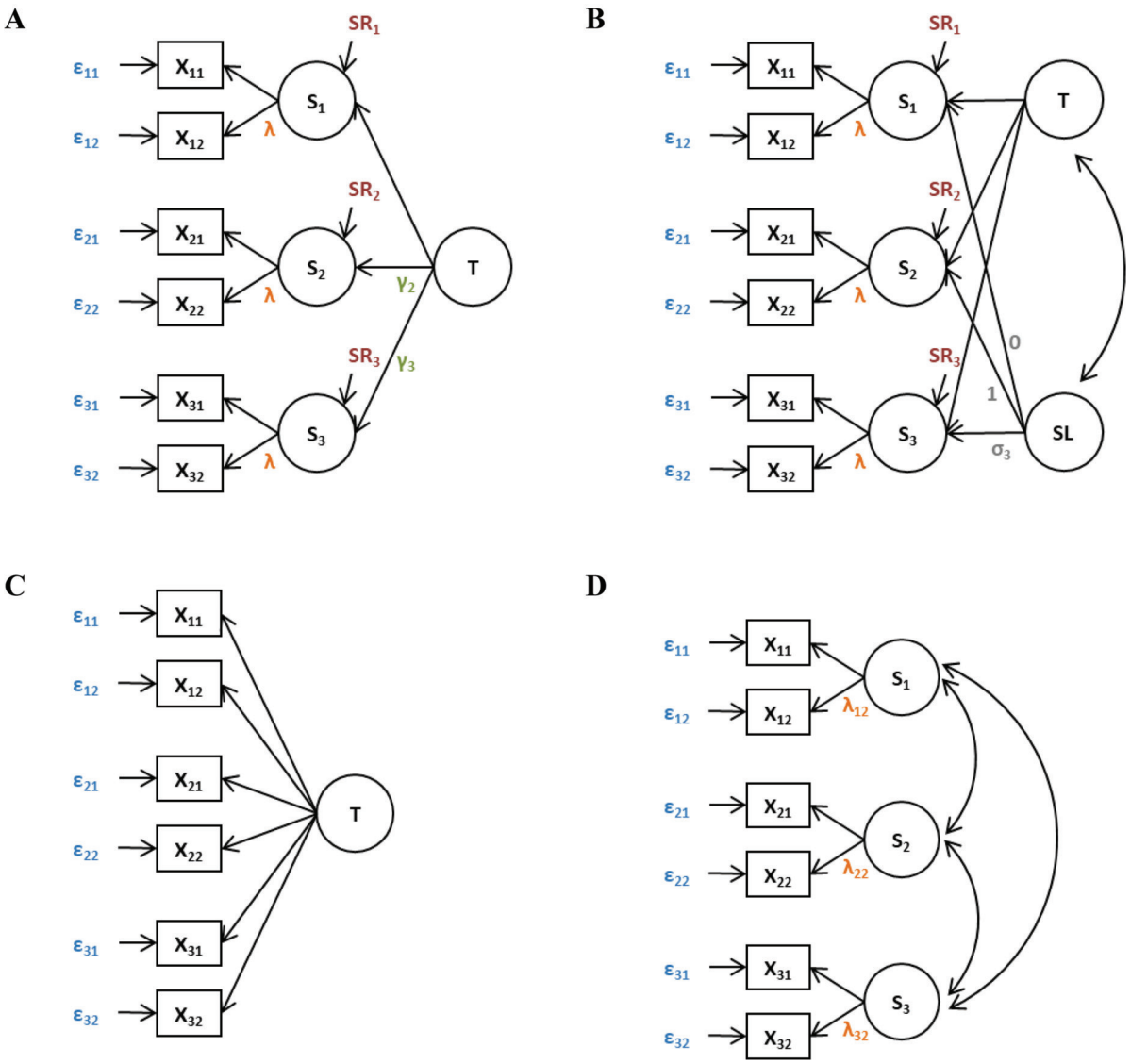
In order to address possible trait changes over time, we performed LST models with freely estimated state intercepts (LST) or with freely estimated trait means (LST_T). The respective other latent variable intercepts were fixed at zero. In addition, second-order LGC models (Figure 1B) were performed. These models again include the latent trait factor, representing true individual differences in trait scores. In addition, latent states are also dismantled into a latent slope factor (SL), representing individual differences in the rate of trait changes.

Next, as we predicted the dependent variables to be mainly influenced by trait effects, we also calculated an LT model (Figure 1C) in which latent states and state residuals were dropped. In this model, observed variables were directly dismantled into measurement error and trait.

Model fits were computed using chi-square statistics (χ^2; should be nonsignificant) and the following indices: root mean square error of approximation (RMSEA; should be approx. $\leq .06$) and its confidence interval; standardized root mean residuals (SRMR; should be approx. ≤ 0.08); and the comparative fit index (CFI; should be approx. $\geq .95$; Beauducel & Wittmann, 2005; Bentler, 2007; Hu & Bentler, 1999). The significance of the individual model parameters was calculated with its critical ratio statistics (C.R. = variance/standard error; Bühner, 2011).

The fitting procedure was based on recommendations by Geiser et al. (2015) and always started with testing for measurement invariance: Our baseline models were LS models (Figure 1D), not including latent trait or slope factors, without any restrictions. This model was tested against an LS model with weak measurement invariance ($\lambda_{12} = \lambda_{22} = \lambda_{32}$), with strong measurement invariance ($\lambda_{12} = \lambda_{22} = \lambda_{32}$; intercepts of manifest variables set to zero; factor means freely estimated) and strict measurement invariance ($\lambda_{12} = \lambda_{22} = \lambda_{32}$; intercepts of manifest variables set to zero; factor means freely estimated; $\varepsilon_{11} = \varepsilon_{12} = \varepsilon_{21} = \varepsilon_{22} = \varepsilon_{31} = \varepsilon_{32}$) using chi-square differences tests. Strict measurement invariance also assumes measures to be τ equivalent. LST, LGC, and LT models, based on those LS models, were only computed if at least strong measurement invariance was given.

Figure 1
Schematic Model Illustrations



Note. Panel A: latent state–trait model, state intercepts (LST) or alternatively trait means (LST_T) were freely estimated. Panel B: latent growth-curve (LGC) model, trait and slope means were freely estimated. Panel C: latent trait (LT) model, trait mean was freely estimated. Panel D: latent state (LS) model, state means were freely estimated. Each model is depicted for three measurement occasions i and two test sets k. Loadings without a label are fixed to 1. Double arrows indicate correlations. Intercepts or means of remaining variables were set to zero. S_k = latent states; SL = latent slope factor; SR_k =latent state residuals; T= latent trait; X_{ik} = manifest dependent variables; γ_k =trait loadings; ε_{ik} = measurement error variances; λ_{ik} = state loadings; σ_k = slope loadings. See the online article for the color version of this figure.

In addition, we tested for homogeneity of indicators. Therefore, we compared the baseline model to a model augmented by an indicator specific factor explaining either variance in odd or even trials. As our indicators are based on an odd–even classification of trials, we did not expect this model to provide a better fit.

When applying LST, LST_T, LGC, and LT models, we aimed at finding the most restrictive best fitting model. Therefore, models were tested against each other using chi-square differences tests, changes in CFI index (should be <.01; Cheung & Rensvold, 2002; Isiordia & Ferrer, 2018) and considering fit indices.

Restrictions to the LST, LST_T, and LGC models were applied and added in the following order: equal measurement error variances ($\varepsilon_{11} = \varepsilon_{12} = \varepsilon_{21} = \varepsilon_{22} = \varepsilon_{31} = \varepsilon_{32}$), equal occasion-specific state residuals and trait loadings on the states set to 1 ($SR_1 = SR_2 = SR_3$; $\gamma_1 = \gamma_2 = \gamma_3 = 1$), assuming measures to be parallel, and the last restriction was setting all state loadings on the observed variables to 1 ($\lambda_{12} = \lambda_{22} = \lambda_{32} = 1$). In the LT model, only the first restriction was applied. In the LGC model, slope loadings on occasions 1 and 2 were fixed ($\sigma_1 = 0$, $\sigma_2 = 1$). Slope loadings on occasion 3 were freely estimated when possible or loadings implying linear trait changes to be linear ($\sigma_3 = 2$), to get smaller over time ($\sigma_3 = 1.5$) or to not change after occasion 2 ($\sigma_3 = 1$) were tested.

SEM analyses were based on covariance matrices of the measurement occasions and separately conducted for each dependent variable. To estimate parameters, maximum likelihood (ML) estimation was chosen. To test the assumption of multivariate normality, Mardia test (1970) for multivariate skewness was deployed. If multivariate normality was not given, ML estimation with robust (Huber-White) standard errors and scaled test statistics (Yuan-Bentler) was used (MLR) and for model comparison scaled chi-square differences tests (Satorra & Bentler, 2001) were used. The detailed procedure of model fitting can be reproduced by following the scripts provided online (https://osf.io/9sq2g/).

Then, common consistency, occasion specificity, and reliability were calculated based on the best fitting model (Geiser et al., 2015; Steyer et al., 1992; Steyer & Schmitt, 1990).

The coefficient of common consistency in LST models is the amount of variance in the manifest variables that can be explained by trait influences:

$$Con(X_{ik}) = \frac{\lambda_{ik}^2 \gamma_{ik}^2 Var(T)}{Var(X_{ik})} \quad (1)$$

In LGC models, common consistency is defined as the amount of variance in the manifest variables that can be explained by both trait and trait change:

$$Con(X_{ik}) = \frac{\lambda_{ik}^2 \gamma_{ik}^2 Var(T) + \lambda_{ik}^2 \sigma_{ik}^2 Var(SL) + 2\lambda_{ik}^2 \gamma_{ik} \sigma_{ik} Cov(T\ SL)}{Var(X_{ik})} \quad (2)$$

High values in common consistency imply measures to be mainly determined by trait influences instead of variable situational influences.

The coefficient of occasion specificity in LST and LGC models is defined as the proportion of variance in the manifest variables that is accounted for by situation and Situation × Person interaction:

$$Spe(X_{ik}) = \frac{\lambda_{ik}^2 Var(S)}{Var(X_{ik})} \quad (3)$$

Common consistency and occasion specificity can be summed up to the reliability coefficient $[\mathrm{Rel}(X_{i,k}) = \mathrm{Con}(X_{i,k}) + \mathrm{Spe}(X_{i,k})]$. A high coefficient indicates high measurement accuracy and low error influences.

Temporal Stability and Internal Consistency

To provide comparability to other studies (Hedge et al., 2018; Meyhöfer et al., 2016; Paap & Sawi, 2016; Wöstmann et al., 2013), internal consistency and temporal stability were analyzed. Internal consistency was realized by calculating Cronbach's α (Cronbach, 1951). As this calculation required equal numbers of complete trials for each variable and participant, which was not always given due to varying numbers of invalid and incorrect trials, we based the calculation on the number of complete trials the participant with the fewest complete trials had. Internal consistency for congruency effects was calculated using a permutation-based split-half approach (Parsons, 2021). Split-half reliability (Spearman-Brown corrected) was calculated for each of 5,000 random splits and then averaged to provide a stable estimate. Next, we randomly selected an equivalent number of trials for each participant. Participants with fewer than 30 complete trials were excluded from the calculations. Temporal stability as a measure of reliability between different measurement occasions was assessed by two-way mixed, single measures ICC coefficients with absolute agreement (Bartko, 1966, 1991; Koo & Li, 2016; McGraw & Wong, 1996).

Analyses of Repeated Measures

Again, for reasons of comparability to previous studies, dependent variables from each task were analyzed using repeated-measures ANOVA with occasion (1, 2, and 3) and task condition (prosaccades/antisaccades or congruent/incongruent) as within-subjects factors. For go/nogo and stop-signal tasks, repeated-measures ANOVA with occasion (1, 2, and 3) as within-subjects factor were analyzed. Partial eta squared was used for calculating effect sizes (Cohen, 1973). For post hoc tests, we report Cohen's *d* (Cohen, 1988).

Mauchly's test of sphericity was performed for each variable, and if the condition of sphericity was violated, Greenhouse–Geisser procedure was applied to correct the *p*-value. We used post hoc tests (Bonferroni-corrected) to further specify the results of the ANOVA. Significance level was set to 5% a priori.

Hierarchical SEM Analyses

In order to address our second research question, the structure of inhibitory control at the trait level was explored based on LST models with varying state intercepts. In a first step, all LST models were combined and correlations between the task-specific traits were allowed. This model was tested against a model with correlations set to zero and against a model with a latent trait inhibition factor. In addition, it was tested whether latent traits could be described by two correlated or uncorrelated factors (e.g., response inhibition and interference control) instead of one.

To provide comparability to previous studies, we also explored the structure of inhibitory control based on data of manifest variables only from occasion 1. We started by analyzing the correlational structure, this time using Pearson correlations. Again, we calculated a model with correlations between tasks set to zero and tested different latent factor structures: a model with one common inhibition factor and models describing data by two correlated or uncorrelated factors.

To obtain clearer information about the model fit in relation to the structure of inhibition and to obtain evidence for a null hypothesis (see also Rey-Mermet et al., 2018), Bayesian hypothesis testing using BIC approximation (Wagenmakers, 2007) was applied in addition to the previously described model comparison process. Bayes factor (BF) > 100 were interpreted as extreme evidence, 30–100 very strong evidence, 10–30 strong evidence, 3–10

moderate evidence, 1–3 anecdotal evidence, and 1 no evidence (Wagenmakers et al., 2018).

Results and Discussion

Sample Description

A sample of $N = 150$ participants (75 female, 75 male) completed the study. Of the original 164 participants, 14 were excluded who had not completed all 3 sessions. Mean age was 22.55 years ($SD = 3.01$). The sample comprised only students, among them 43 (28.67%) studying psychology. The dataset is available online (https://osf.io/9sq2g/). Descriptive results are presented in Table 2 for primary inhibitory variables and Table 3 for secondary and control condition variables.

LST and LGC Models

Variables could not be adequately modeled by LT models. In each case, model fit was not acceptable and LT models explained data was worse than LST and LGC models. Therefore, LT models are not further considered in the results section. Model parameters can, however, be found in Table 2 in the online supplemental material for sake of completeness.

Primary Inhibitory Variables

Model parameters are depicted in Table 4. For the Simon task RT congruency effect, strong measurement invariance was not given. Therefore, LST and LGC models were not computed. All other primary inhibitory variables could be modeled under the assumption of at least strong measurement invariance and thus measurement properties did not change significantly over time.

Model fit was excellent for LST models in all variables. RT congruency effect in the Eriksen flanker task and SSRT could be modeled under the assumption of non-varying state intercepts (LST_T) without significant loss of fit. Describing possible changes over time by a slope factor also resulted in excellent model fit, except for SSRT. Overall, LGC models described the data best for all primary inhibitory variables, again except SSRT. Accordingly, there was no main effect of occasion on SSRT in the repeated-measures ANOVA (Table 3 in the online supplemental material). Bad LCG model fit for SSRT as well as comparable fit of an LST model with and without varying state intercepts indicate that trait changes over time exist for all but this primary inhibitory variable.

However, as shown in Table 5, changes over time were not linear and occurred mainly between occasions 1 and 2. Those changes additionally become apparent in Figures 7 to 12 in the online supplemental material that depict significant interactions between occasion and task condition or main effects of occasion. Slope loadings on state one ($\sigma_1 = 0$) and two ($\sigma_2 = 1$) were fixed, slope loadings on state three (σ_3) were estimated to be 1.5 for antisaccade error rate, RT congruency effect in the Eriksen flanker task and go/nogo error rate and to be 1.1 for RT congruency effect in the Stroop task. In addition, there were significant differences in changes over time for those variables, except for RT congruency effect in the Eriksen flanker task.

An intriguing finding emerged from the analysis of the LGC models on the basis of information about effects of interindividual differences on changes in performance. Specifically, participants with poor performance at occasion 1 improved more than those with high performance on the nogo error rate, $r_{(T,SL)} = -.404$, and the RT congruency effect in the Stroop task, $r_{(T,SL)} = -.567$. For other variables, the correlation between trait and slope was not significant. However, except for antisaccade error rate, the trend was the same: lower trait ability tended to be associated with greater performance improvement.

Latent RT congruency effect in the Simon task did not show strong measurement invariance as the LS model with strong compared to weak measurement invariance provided significantly worse fit, $\chi^2_{diff}(3) = 21.33$, $p < .001$, $CFI_{change} = -.069$. Furthermore, the baseline model could not successfully be applied to the data resulting in non-positive definite covariance matrices of latent variables. Thus, the two test halves did not capture a consistent construct and measurement properties of this variable changed over time. In other words, the impact of the irrelevant stimulus position on RT differed substantially between test halves and over time. Therefore, only the LS model was computed. The correlations between occasions 1 and 2 was $r = .545$, between occasions 1 and 3 $r = .755$, and between occasions 2 and 3 $r = 1.044$. Combining

Table 2
Descriptive Results, Internal Consistency, and Temporal Stability for Primary Inhibitory Variables

Dependent variable	*n*	T1		T2		T3		ICC (95% CI)
		M_1 (SD_1)	α_1	M_2 (SD_2)	α_2	M_3 (SD_3)	α_3	
Antisaccade								
ER AS	134	22.06 (13.42)	.81	19.96 (14.35)	.85	20.03 (15.22)	.88	.76 (.69–.81)
Eriksen flanker								
RT cong.eff.	143	51.52 (19.73)	.67[a]	46.16 (17.24)	.65[a]	42.68 (15.50)	.57[a]	.49 (.37–.59)
Go/nogo								
ER nogo	149	42.37 (19.79)	.66	38.06 (19.59)	.67	37.65 (19.39)	.58	.55 (.46–.64)
Simon								
RT cong.eff.	142	18.00 (22.63)	.54[a]	13.58 (21.19)	.50[a]	9.48 (18.44)	.33[a]	.47 (.37–.57)
Stop-signal								
SSRT	101	143.93 (38.29)		136.99 (39.03)		141.55 (34.74)		.40 (.28–.52)
Stroop								
RT cong.eff.	149	62.22 (30.09)	.56[a]	48.65 (26.17)	.50[a]	45.99 (26.67)	.63[a]	.50 (.37–.61)

Note. Numbers indicate the mean (standard deviation). AS = antisaccade; cong.eff. = congruency effect; ER = error rate; ICC = interclass correlation coefficient; RT = mean reaction time; SSRT = stop-signal reaction time; α = Cronbach's α.
[a] Internal consistency was calculated using a permutation-based split-half approach.

Table 3
Descriptive Results, Internal Consistency, and Temporal Stability for Secondary and Control Condition Variables

Dependent variable	n	T1		T2		T3		
		M_1 (SD_1)	α_1	M_2 (SD_2)	α_2	M_3 (SD_3)	α_3	ICC (95% CI)
Antisaccade								
Latency PS	134	166.04 (18.02)	.89	162.85 (18.82)	.87	161.04 (19.34)	.91	.75 (.67–.81)
Latency AS		240.01 (31.00)	.90	228.98 (27.91)	.91	226.91 (28.59)	.91	.77 (.64–.85)
ER PS		2.34 (2.18)	.36	2.01 (2.30)	.35	2.03 (2.30)	.49	
Eriksen flanker								
RT con.	143	411.76 (44.30)	.97	399.18 (43.57)	.97	396.19 (45.97)	.97	.73 (.65–.80)
RT incon.		463.28 (50.93)	.97	445.34 (48.49)	.96	438.87 (51.34)	.97	.72 (.59–.81)
ER con.	136	0.58 (0.96)	.39	0.56 (0.81)	.14	0.66 (0.95)	.23	
ER incon.		3.25 (3.06)	.64	3.46 (3.49)	.60	4.05 (4.11)	.74	
Go/nogo								
RT go	145	310.45 (37.55)	.97	309.55 (40.12)	.97	308.72 (41.62)	.96	.66 (.58–.73)
Simon								
RT con.	142	469.97 (64.27)	.96	452.44 (65.97)	.97	449.98 (67.64)	.97	.78 (.70–.83)
RT incon.		487.97 (62.47)	.97	466.02 (67.90)	.98	459.46 (67.32)	.98	.75 (.64–.83)
ER con.	137	2.24 (2.51)	.64	2.66 (2.63)	.58	2.84 (2.84)	.64	
ER incon.		4.24 (3.77)	.68	3.49 (2.91)	.59	3.45 (3.29)	.68	
Stop-signal								
RT go	150	437.74 (105.42)	.99	460.35 (116.20)	.99	478.56 (132.28)	1.0	.82 (.74–.87)
Stroop								
RT con.	149	603.04 (70.30)	.96	582.10 (73.80)	.96	574.94 (77.99)	.94	.80 (.71–.86)
RT incon.		665.26 (78.04)	.95	630.75 (74.27)	.94	620.93 (78.49)	.92	.79 (.57–.88)
ER con.	143	3.40 (2.83)	.57	3.15 (2.48)	.38	3.24 (2.78)	.50	
ER incon.		6.11 (5.23)	.77	5.36 (4.03)	.61	5.52 (4.75)	.71	

Note. Numbers indicate the mean (standard deviation). AS = antisaccade; con. = congruent; ER = error rate; ICC = interclass correlation coefficient; incon. = incongruent; PS = prosaccade; RT = mean reaction time; α = Cronbach's α.

Table 4
Evaluation of LST and LGC Model Parameters for Primary Inhibitory Variables

Dependent variable	Model	Restriction	Estimator	$p_{compare}$	$\chi^2(df, p)$	CFI	RMSEA (95% CI, p)	SRMR
Antisaccade task ($n = 134$)								
Error rate AS	LST	A	MLR		19.64 (16, .237)	.99	.04 (.00–.09, .563)	0.03
	LST_T	A		<.001	36.42 (18, .006)	.97	.09 (.05–.13, .057)	0.13
	LGC	**C**		**.312**	**24.40 (20, .226)**	**.99**	**.04 (.00–.09, .588)**	**0.05**
Eriksen flanker task ($n = 144$)								
RT cong.eff.	LST	A	MLR		7.45 (16, .963)	1.0	.00 (.00–.00, .996)	0.03
	LST_T	A		.617	8.41 (18, .972)	1.0	.00 (.00–.00, .997)	0.04
	LGC	**C**		**.335**	**10.59 (19, .937)**	**1.0**	**.00 (.00–.01, .993)**	**0.05**
Go/nogo task ($n = 149$)								
Error rate nogo	LST	A[a]	ML		14.68 (17, .618)	1.0	.00 (.00–.06, .881)	0.05
	LST_T	A		.001	26.61 (18, .087)	.98	.06 (.00–.10, .368)	0.10
	LGC	**C**		**.162**	**19.82 (20, .469)**	**1.0**	**.00 (.00–.07, .818)**	**0.07**
Simon task ($n = 142$)								
RT cong.eff.	LS[b]		MLR		6.75 (8, .564)	1.0	.00 (.00–.08, .792)	0.04
Stop-signal task ($n = 101$)								
SSRT	**LST**	**D**	**MLR**		**9.98 (13, .696)**	**1.0**	**.00 (.00–.07, .869)**	**0.04**
	LST_T				10.17 (13, .680)	1.0	.00 (.00–.07, .859)	0.04
	LGC	C		.004	28.59 (19, .073)	.91	.07 (.00–.12, .234)	0.09
Stroop task ($n = 149$)								
RT cong.eff.	LST	A	MLR		10.69 (16, .828)	1.0	.00 (.00–.04, .973)	0.05
	LST_T	A		.013	18.03 (18, .454)	1.0	.00 (.00–.07, .817)	0.08
	LGC	**B**		**.646**	**11.65 (18, .865)**	**1.0**	**.00 (.00–.03, .983)**	**0.05**

Note. For each variable, the most restrictive best fitting latent state–trait with (LST) and without (LST_T) varying state intercepts and latent state-growth-curve (LGC) models is shown. The LST model was tested against both other models using χ^2 differences tests ($p_{compare}$), and the best fitting model is printed in bold. A = equal measurement errors; AS = antisaccade; B = equal measurement errors, equal occasion-specific state residuals, trait loadings set to 1; C = equal measurement errors, equal occasion-specific state residuals, trait and state loadings set to 1; CFI = comparative fit index; cong.eff. = congruency effect; D = trait loadings set to 1; ML = maximum likelihood estimation; MLR = robust maximum likelihood estimation, scaled test statistics are reported; RMSEA = root-mean-square error of approximation; RT = mean reaction time; SRMR = standardized root mean residual; SSRT = stop-signal reaction time. [a] State variance on occasion 2 was negative and therefore set to 0. [b] Strong measurement was not given; therefore, only the latent state model with weak measurement invariance is depicted.

Table 5
Model Estimates for Primary Inhibitory Variables

Model	S_1 Intercept T_{Mean}	S_2 Intercept	S_3 Intercept	SL_{Mean}	SL_{SD}	$r_{(T,SL)}$
Antisaccade task—error rate antisaccades						
LST	22.42* (1.19)	20.28* (1.28)	20.38* (1.36)			
LGC[a]	**21.89* (1.15)**			**−1.45* (0.64)**	**5.13* (3.14)**	**−.025**
Eriksen flanker task—RT congruency effect						
LST_T	51.27* (1.75)					
LGC[b]	**51.66* (1.63)**			**−5.96* (1.56)**	**6.76 (6.75)**	**−.662**
Go/nogo task—error rate nogo						
LST	41.57* (1.65)	37.33* (1.63)	36.96* (1.61)			
LGC[a]	**42.12* (1.61)**			**−3.31* (1.12)**	**9.08* (4.96)**	**−.404***
Stop-signal task—SSRT						
LST	219.26* (3.66)	200.94* (3.28)	204.27* (3.10)			
LGC[c]	219.45* (3.41)			−18.1* (4.06)	13.11 (16.26)	−.560
Stroop task—RT congruency effect						
LST	59.55* (2.55)	46.58* (2.22)	43.98* (2.24)			
LGC[d]	**59.61* (2.55)**			**−13.49* (2.08)**	**4.64* (9.6)**	**−.567***

Note. Model estimates for best fitting latent state–trait with (LST) or without (LST_T) varying state intercepts and latent state-growth-curve (LGC) models are shown. Numbers in the brackets indicate standard errors. The best fitting model is printed in bold. For all parameters, asterisks indicate $p < .05$. r = correlation; SSRT = stop-signal reaction time; $S_{1–3}$ = latent states; T = latent trait.
[a] Slope loading 3 was set to $\sigma_3 = 1.5$. [b] Slope loading 3 was estimated to be [b] $\sigma_3 = 1.5$, [c] $\sigma_3 = 0.9$, [d] $\sigma_3 = 1.1$.

states 2 and 3 into one common factor still resulted in weak measurement invariance. Thus, the correlation above 1 probably indicates that model fitting was not successful. This is also supported by the low reliability on occasion 3 (Cronbach's $\alpha = .33$). Also, entirely removing occasion 3 did not improve measurement invariance. The detailed model fitting for the RT congruency effect in the Simon task can be found online (https://osf.io/9sq2g/). To rule out the possibility that the poor model fit was due to a random irregularity in the division into odd and even, we reran the models, now based on a completely random allocation of the trials into two test halves. The results of this calculation can be found in Tables 4 and 5 in the online supplemental material. Again, there were problems with the model application, but results give first evidence of low model reliability (.43), only few state influences, and no changes over time. In addition, in Figure 13 in the online supplemental material, individual RT congruency effects are plotted as a function of occasion and odd–even classification for Simon and Eriksen flanker tasks, taken as an example of excellent model fit. This figure clearly illustrates the high intraindividual variance in the RT congruency effect within the test sets and across measurement occasions in the Simon task. However, the interindividual variance was low (see *y*-axis scaling), a common finding regarding difference scores (Whitehead et al., 2020). This resulted in moderate reliability (ICC = .47); thus, the ability to rank individuals according to their performance is limited. Our results are comparable to previous studies, showing only poor to good temporal stability of the Simon task RT congruency effect (ICC = −.19–.69, $r_{test–retest}$ = .43–.71; Paap & Sawi, 2016; N.White et al., 2019; Wöstmann et al., 2013).

Reasons for poor model fit in RT congruency in the Simon task do not seem to be irregularities of the odd–even classification. Also, it was shown that sample and model size do not impact measurement invariance (Putnick & Bornstein, 2016). Instead, it seems more likely that the conflict due to the irrelevant stimulus location was in fact not stable within or between occasions and moreover affected by other parameters. A frequently replicated finding for the Simon task, which is usually not observed in the other tasks, is a positive RT congruency effect for faster RTs that reverses for slower RT. This means that responses to incongruent stimuli then become faster than congruent ones, resulting in negatively sloped delta functions (De Jong et al., 1994; Ridderinkhof, 2002). This clearly shows that the conflict between congruent and incongruent trials is not expressed equally across different trials in the Simon task that differ in RT. A common explanation for this phenomenon is a large temporal gap between relevant and irrelevant response activations, which leads to a passive decrease in response activation and a reduced conflict for slower RTs (Pratte et al., 2010). In addition, there may be an active inhibitory component causing negative congruency effects. An additional, noteworthy finding is that a higher proportion of congruent stimuli within the task reduces levels of proactive inhibition and leads to positive delta plots (Hübner & Töbel, 2019) and increased reliability (Borgmann et al., 2007). We used a version of the Simon task including the same proportion of both conditions and in fact our reliabilities were lower (ICC = .47, $r_{split–half}$ = .33–.54) than for example those reported by Wöstmann et al. (2013; ICC = .69; $r_{test–retest}$ = .71) including more congruent (160) than incongruent (60) trials.

Furthermore, a preceding incongruent trial appears to slow down a subsequent controlled congruent response. Such conflict adaptation does not seem to exist, for example, for the antisaccade task (Aponte et al., 2022). Thus, the conflict also evolves depending on the preceding stimulus. To better understand reasons for the bad model fit, it would be important to apply models to a longer version of the Simon task depending on the congruency of previous trials or separately for slow and fast RTs. Alternatively, it could be investigated whether a higher proportion of congruent trials would improve the model fit. In general, there is no standard procedure to deal with invariant data (Putnick & Bornstein, 2016).

Secondary and Control Condition Variables

As error rates in prosaccades, Eriksen flanker task, Simon task, and Stroop task were very low and had reduced variance (all mean

error rates ≤ 5.85%), SEM results for those variables were excluded from the main analysis but can be found in Tables 6 and 7 in the online supplemental material for the sake of completeness.

Model parameters of secondary and control condition variables are given in Table 6. All variables could be modeled under the assumption of at least strong measurement invariance. Model fits were excellent for LST and LGC models in all variables except for prosaccade latency, go RT in the go/nogo, and incongruent RT in the Stroop tasks, where χ^2 was significant ($p < .001$, $p \leq .009$, and $p \leq .021$, respectively) and RMSEA was >.06. Antisaccade latency and incongruent RT in the Stroop task could be modeled under the assumption of non-varying state intercepts (LST_T) without significant loss of fit.

LGC models described the data best for all variables except antisaccade latency and congruent and incongruent RT in the Simon task. However, only for antisaccade latency data were best described by the LST model without varying state intercepts (LST_T) and this model did not provide poor fit, but simply was more parsimonious. Although the more parsimonious LST models described data best for some secondary and control condition variables, all variables could be described by LGC models with similar good fit.

Thus, there were trait changes over time for most variables. However, as shown in Table 7, except for go RT in the go/nogo and stop-signal tasks, those changes were not linear and occurred mainly between occasions 1 and 2. Slope loadings on states 1 ($\sigma_1 = 0$) and 2 ($\sigma_2 = 1$) were fixed, slope loadings on state 3 (σ_3) were estimated to be ≤1.5, except for go RT in the go/nogo ($\sigma_3 = 2$) and stop signal ($\sigma_3 = 1.8$) tasks that were best described by linear or close to linear trait changes.

Classical analyses of repeated measures confirmed significant changes between all measurement occasions for go RT in the stop-

Table 6
Evaluation of LST and LGC Model Parameters for Secondary and Control Condition Variables

Dependent variable	Model	Restriction	Estimator	$p_{compare}$	$\chi^2(df, p)$	CFI	RMSEA (95% CI, p)	SRMR
Antisaccade task ($n = 134$)								
Latency PS	LST	A[a]	MLR		44.17 (17, <.001)	.96	.11 (.07–.15, .005)	0.03
	LST_T	A		<.001	58.34 (18, <.001)	.95	.13 (.10–.16, <.001)	0.15
	LGC	**B**		**.514**	**44.04 (18, .001)**	**.97**	**.10 (.07–.14, .008)**	**0.03**
Latency AS	LST		MLR		10.27 (11, .506)	1.0	.00 (.00–.08, .788)	0.03
	LST_T			**.799**	**10.83 (13, .625)**	**1.0**	**.00 (.00–.07, .879)**	**0.03**
	LGC				10.27 (11, .506)	1.0	.00 (.00–.08, .788)	0.03
Eriksen flanker task ($n = 143$)								
RT con.	LST	B	MLR	.044[†]	22.35 (20, .322)	1.0	.03 (.00–.07, .733)	0.04
	LST_T	B		<.001	50.55 (22, <.001)	.97	.10 (.07–.13, .008)	0.08
	LGC	**B**			**15.47 (18, .630)**	**1.0**	**.00 (.00–.06, .920)**	**0.02**
RT incon.	LST	B	MLR	.012	28.76 (20, .093)	.99	.06 (.00–.09, .383)	0.04
	LST_T	B		<.001	83.38 (22, <.001)	.94	.14 (.11–.17, <.001)	0.11
	LGC	**B**			**20.77 (19, .350)**	**1.0**	**.03 (.00–.08, .734)**	**0.02**
Go/nogo task ($n = 142$)								
RT go	LST	A	MLR		34.43 (16, .005)	.98	.09 (.05–.12, .035)	0.03
	LST_T	A		.013	43.75 (18, .001)	.97	.10 (.07–.13, .007)	0.10
	LGC	**B**		**.509**	**36.54 (19, .009)**	**.98**	**.08 (.05–.11, .070)**	**0.05**
Simon task ($n = 140$)								
RT con.	**LST**	**B**	**MLR**	**.287**[†]	**17.21 (20, .639)**	**1.0**	**.00 (.00–.05, .937)**	**0.04**
	LST_T	B		<.001	42.24 (22, .006)	.98	.08 (.05–.11, .055)	0.08
	LGC	B			14.26 (18, .712)	1.0	.00 (.00–.05, .950)	0.01
RT incon.	**LST**	**B**	**MLR**	**.240**[†]	**26.92 (20, .138)**	**.99**	**.05 (.00–.08, .481)**	**0.07**
	LST_T	B		<.001	63.95 (22, <.001)	.95	.12 (.09–.14, <.001)	0.11
	LGC	C			25.51 (19, .145)	.99	.05 (.00–.09, .483)	0.04
Stop-signal task ($n = 150$)								
RT go	LST	A	MLR		23.71 (16, .096)	1.0	.06 (.00–.10, .370)	0.01
	LST_T	A		.009	35.87 (18, .007)	.99	.08 (.04–.12, .082)	0.12
	LGC	**C**		**.724**	**25.06 (19, .158)**	**1.0**	**.05 (.00–.09, .514)**	**0.01**
Stroop task ($n = 149$)								
RT con.	LST	A	MLR		22.09 (16, .140)	.99	.05 (.00–.10, .451)	0.01
	LST_T	A		<.001	36.71 (18, .006)	.98	.08 (.04–.12, .077)	0.10
	LGC	**B**		**.516**	**22.8 (18, .198)**	**1.0**	**.04 (.00–.09, .564)**	**0.01**
RT incon.	LST	A	MLR		30.01 (16, .018)	.99	.08 (.03–.12, .140)	0.01
	LST_T	A		.177	33.51 (18, .014)	.99	.08 (.03–.12, .136)	0.04
	LGC	**C**		**.269**	**33.55 (19, .021)**	**.99**	**.07 (.03–.11, .169)**	**0.03**

Note. For each variable, the most restrictive best fitting latent state–trait with (LST) and without (LST_T) varying state intercepts and latent state-growth-curve (LGC) models is shown. The LST model was tested against both other models using χ^2 differences tests ($p_{compare}$), and the best fitting model is printed in bold. Scaled test statistics are reported. A = equal measurement errors; AS = antisaccade; B = equal measurement errors, equal occasion-specific state residuals, trait loadings set to 1; C = equal measurement errors, equal occasion-specific state residuals, trait and state loadings set to 1; CFI = comparative fit index; con. = congruent; incon. = incongruent; MLR = robust maximum likelihood estimation; PS = prosaccade; RMSEA = root-mean-square error of approximation; RT = mean reaction time; SRMR = standardized root mean residual.
[a] State variance on occasion 2 was negative and therefore set to 0.
[†] p value for the comparison between LST and LGC models.

Table 7
Model Estimates for Secondary and Control Condition Variables

Model	$S_{1\ \text{Intercept}}$ T_{Mean}	$S_{2\ \text{Intercept}}$	$S_{3\ \text{Intercept}}$	SL_{Mean}	SL_{SD}	$r_{(\text{T,SL})}$
Antisaccade task—latency prosaccades						
LST	164.53* (1.57)	161.34* (1.62)	159.56* (1.68)			
LGC[c]	**164.60* (1.57)**			**−3.54* (1.02)**	**8.76* (4.70)**	**−.219**
Latency antisaccades						
LST_{T}	**242.00* (2.70)**					
LGC[d]	242.07* (2.70)			−11.17* (1.57)	10.85 (14.44)	−.445
Eriksen flanker task—RT congruent						
LST	409.63* (3.68)	397.11* (3.59)	394.14* (3.81)			
LGC[e]	**409.42* (3.72)**			**−11.53* (2.77)**	**15.31* (10.07)**	**−.204**
RT incongruent						
LST	461.19* (4.27)	443.35* (4.05)	436.9* (4.28)			
LGC[a]	**460.84* (4.23)**			**−16.43* (2.11)**	**16.26* (9.75)**	**−.265**
Go/nogo task—RT go						
LST	309.25* (3.12)	308.35* (3.36)	307.52* (3.48)			
LGC[b]	**309.24* (3.16)**			**−0.87 (1.57)**	**13.54* (8.57)**	**−.242**
Simon task—RT congruent						
LST	**468.00* (5.38)**	**450.5* (5.52)**	**448.07* (5.61)**			
LGC[f]	467.92* (5.38)			−16.95* (3.25)	18.64 (14.82)	−.041
RT incongruent						
LST	**488.87* (5.40)**	**466.87* (5.81)**	**460.33* (5.77)**			
LGC[g]	487.94* (5.26)			−21.92* (3.17)	19.66^{+} (14.94)	.021
Stop-signal task—RT go						
LST	438.01* (8.63)	460.65* (9.51)	478.86* (10.81)			
LGC[h]	**437.82* (8.47)**			**22.36* (4.24)**	**36.31* (19.98)**	**.146**
Stroop task—RT congruent						
LST	606.07* (5.79)	585.02* (6.07)	577.86* (6.39)			
LGC[i]	**605.61* (5.84)**			**−19.20* (4.00)**	**21.59* (12.12)**	**.007**
RT incongruent						
LST_{T}	665.54* (6.46)					
LGC[g]	**665.00* (6.39)**			**−33.35* (3.21)**	**20.98* (11.90)**	**−.226**

Note. Model estimates for best fitting latent state–trait with (LST) or without (LST_{T}) varying state intercepts and latent state-growth-curve (LGC) models are shown. Numbers in the brackets indicate standard errors. The best fitting model is printed in bold.
[a] Slope loading 3 was set to $\sigma_3 = 1.5$. [b] Slope loading 3 was set to $\sigma_3 = 2$. [c] Slope loading 3 was estimated to be [c] $\sigma_3 = 1.1$, [d] $\sigma_3 = 1.2$, [e] $\sigma_3 = 1.4$, [f] $\sigma_3 = 1.2$, [g] $\sigma_3 = 1.3$, [h] $\sigma_3 = 1.8$, [i] $\sigma_3 = 1.5$.
$^{*}p < .05$. $^{+}p = .083$.

signal task, but not for go RT in the go/nogo task (Table 3 in the online supplemental material; Figures 7 to 12 in the online supplemental material). However, LGC models revealed that, in absolute values, changes in this variable were very small (−0.87 ms, compared to 22.36 ms in the stop-signal task). Moreover, go RT in the stop-signal task was the only variable where participants' RTs increased over time, that is, performance deteriorated. Regarding classical analyses of repeated measures (Table 3 in the online supplemental material), we found significant changes from occasion 1 to the later ones for all remaining variables. However, besides go RT in the stop-signal task only incongruent RT in the Stroop task was found to change significantly from occasions 2 to 3. For this variable LGC models also revealed highest changes compared to other variables (T2–T1: −33.35 ms; T3–T2: −11.34 ms) and model fit was not optimal (χ^2 significant, $p = .021$; RMSEA = .07). Previous studies have also shown performance in the Stroop task to improve over time (Davidson et al., 2003; Talanow & Ettinger, 2018; Wilkinson & Yang, 2012).

In addition, there were significant differences in changes over time for all variables (see significant slope SDs in Table 7), that were best described by LGC models. However, there were no significant correlations between trait and slope for any secondary and control condition variable although descriptively lower trait ability was associated with greater performance improvement in all variables except for congruent and incongruent RT in the Simon task and congruent RT in the Stroop task, where correlations were close to zero and go RT in the stop-signal task, where slow RT at occasion 1 tended to be associated with even greater slowing over time.

Summary on Modeling

To obtain interpretable results from the models, good fit indices are crucial. Overall, we observed excellent model fits for LST and LGC models. LT models had to be rejected for all variables. Only SSRT could be best described by an LST model without varying state intercepts, whereas trait changes were present for all other variables and could either be described by an LST model with varying state intercepts or by a slope factor in an LGC model. In addition, in most variables, performance does not change equally for all participants. This can be interpreted as an indication of interindividual differences in plasticity.

Differences in CFI between LST and LGC models were <.01 for all variables except SSRT ($\text{CFI}_{\text{change}} = .04$). Meyhöfer et al. (2016) found prosaccade and antisaccade latencies as well as antisaccade error rates to be best described by LST models. However, they did not test for possible trait changes. Given the small differences in model fit, it is likely that LGC models would have described their data as well. Furthermore, it is striking that Meyhöfer et al. (2016)

could accept LT models for some variables and that in general LT models in their study provided a considerably better fit than in ours. Since Meyhöfer et al. (2016) did not test for measurement invariance, it is possible that trait changes were masked by non-invariant parameters and wrongly interpreted as measurement error or, in LST models, as a state-variability process (Geiser et al., 2015). However, our results also point to highly stable cognitive processes underlying performance in inhibitory control tasks; thus, methodological differences are unlikely to have significantly affected results.

Reliability

Primary Inhibitory Variables

Table 8 contains reliability (Rel), common consistency (Con), and occasion specificity (Spe) for primary inhibitory variables estimated from SEM. Internal consistencies and temporal stabilities are given in Table 2. Model-based reliabilities for primary inhibitory variables were moderate to excellent (Rel = .51–.85).

The only primary inhibitory variable showing excellent reliability was antisaccade error rate (Rel = .85), which was even higher than the values reported by Meyhöfer et al. (2016; Rel = .67–.78). Nogo error rate in the go/nogo task revealed good reliability (Rel = .61). Results on temporal stability and internal consistency for antisaccade and nogo error rate revealed moderate to good reliabilities (ICC = .55–.76; Cronbach's α = .58–.88). This matches earlier findings (ICC = .69–.92, $r_{test-retest}$ = .44–.92, Cronbach's α = .81–.94, $r_{split-half}$ = .86–.97; Ettinger et al., 2003; Friedman et al., 2008; Friedman & Miyake, 2004; Hedge et al., 2018; Klein & Berg, 2001; Klein & Fischer, 2005; Meyhöfer et al., 2016; Płomecka et al., 2020; Rey-Mermet et al., 2018; Stahl et al., 2014; Talanow & Ettinger, 2018; Wöstmann et al., 2013). SEM models also provide information on whether Cronbach's α and ICCs are appropriate estimators of reliability. Cronbach's α is considered an appropriate estimator when parallelism is given. ICCs require at least stability of differences in characteristics over time; otherwise, reliability may be underestimated. As parallelism was given for both variables it is not to assume that reliabilities were underestimated.

Table 8
Reliability, Consistency, and Occasion Specificity for Primary Inhibitory Variables

Dependent variable	*n*	Coefficient	*M*	T1	T2	T3
		Antisaccade task				
ER AS	134	Rel(X)	.85	.83/.83	.85/.85	.87/.87
		Con(X)	.77	.74/.74	.77/.77	.80/.80
		Spe(X)	.08	.09/.09	.08/.08	.07/.07
		Eriksen flanker task				
RT cong.eff.	144	Rel(X)	.65	.71/.71	.63/.63	.61/.61
		Con(X)	.48	.57/.57	.45/.45	.42/.42
		Spe(X)	.17	.14/.14	.18/.18	.19/.19
		Go/nogo				
ER nogo	149	Rel(X)	.61	.62/.62	.58/.58	.62/.62
		Con(X)	.55	.56/.56	.52/.52	.56/.56
		Spe(X)	.06	.06/.06	.06/.06	.05/.05
		Stop-signal				
SSRT	101	Rel(X)	.51	.43/.47	.58/.61	.57/.37
		Con(X)	.28	.22/.25	.32/.34	.34/.22
		Spe(X)	.22	.20/.22	.26/.27	.24/.15
		Stroop				
RT cong.eff.	149	Rel(X)	.52	.56/.60	.47/.51	.47/.52
		Con(X)	.50	.55/.59	.45/.49	.45/.49
		Spe(X)	.02	.02/.02	.02/.02	.02/.02

Note. Values are shown as mean (*M*) and separately for the three measurement occasions and the two test sets. AS = antisaccade; cong.eff. = congruency effect; Con(X) = common consistency; ER = error rate; Rel(X) = reliability; RT = mean reaction time; Spe(X) = occasion specificity; SSRT = stop-signal reaction time.

In line with previous studies that used similar versions of the tasks (ICC = .40–.91; $r_{test-retest}$ = .44–.94; Hedge et al., 2018; Paap & Sawi, 2016; Siegrist, 1995; Wöstmann et al., 2013), RT congruency effects in Eriksen flanker and Stroop tasks in our study showed lower temporal stability (ICC = .49/.50) and internal consistency ($r_{split-half}$ = .50–.67) than pure RT variables. This was also confirmed in model-based analyses (Rel = .65/.52). One problem in calculating difference scores is that error components of congruent and incongruent trials are combined (Whitehead et al., 2020). It is evident, also in our data, that this explanation is incomplete: model-based measurement errors in the Eriksen flanker and Stroop task for RT congruent and incongruent were .04/.04 and .03/.05, whereas for RT congruency effect the amount of unexplained variance was not only slightly but considerably higher (.35/.48). Another problem in the use of difference scores is that trial-level variability is not considered and interindividual variance is reduced when aggregating data (Hedge et al., 2018; Paap & Sawi, 2016), as already mentioned when discussing the RT congruency effect in the Simon task. This leads to reduced reliability or, as Hedge et al. (2018) summarized, the more congruent and incongruent trials are correlated and the more similar their variance, the lower the reliability. From the perspective of experimental psychology, congruency effects are highly reliable if they are observed in almost every case. From a purely mathematical point of view, this impedes a reliable recording of an interindividual ranking (Hedge et al., 2018), which is also evident here, in this differential psychological analysis of classical experimental tasks.

Importantly, lowest reliability and consistency were found for SSRT in the stop-signal task (Rel = .51; Con = .28), and temporal stability was also only moderate (ICC = .40). Low temporal stability for this variable was shown before (ICC = .03–.49, $r_{test-retest}$ = .03; Friedman et al., 2008; Friedman & Miyake, 2004; Hedge et al., 2018; Rey-Mermet et al., 2018; Wöstmann et al., 2013). Congdon et al. (2012) systematically investigated the impact of SSRT calculation methods and outlier criteria on temporal stability. On average, they report good reliabilities (mean ICC = .71). However, applying conservative outlier criteria and thus excluding many participants dramatically reduced reliability (ICC = .32–.57). One problem in our task was the large sample size reduction due to exclusion criteria. We only could include 101 out of 150 participants. The main reason for exclusions was participants having more than 75% or fewer than 25% of successful inhibition in stop trials. The majority of excluded participants (42 of 49) did not fulfil this criterion on all measurement occasions and in both test halves (see online supplemental material). Congdon et al. (2012) used exactly the same criterion, but compared to our data they applied an adaptive tracking procedure that may have been more appropriate than ours (Verbruggen et al., 2019), adapting SDD in 50 ms steps instead of 16 ms. Our smaller step size (or an insufficient number of trials) may be the reason for not reaching approx. 50% inhibition in stop trials (Verbruggen et al., 2019). In all variables except SSRT, model-based reliabilities were shown to

exceed ICC values. One reason for comparable reliability values in SSRT may be that ICC calculations could include more participants than SEM analyses and those differences in sample sizes may have masked differences. In addition, regarding model-based information on appropriateness of Cronbach's α and ICCs, both values may have been underestimated as stability of differences in characteristics over time was not given.

Since go RT in the stop-signal task was highly reliable (ICC = .82; Cronbach's α = .99; Table 3), it was demonstrated that the task itself can capture stable processes and that procedural or technical problems in the measurement may not have been decisive. In addition, SSRT was shown to be an invariant measure. Thus, low reliability cannot be traced back to an ununified construct. Moreover, unknown yet unexplained processes that are not specific to measurement occasion or person seem to influence task performance. This could for example be motivation or different use of strategy (Leotti & Wager, 2010), which corresponds to the fact that go RT in the stop-signal task is the only control condition variable that increased over time. It is also suggested that specific instructions influence SSRT (Barch et al., 2009; Sylwan, 2004). We followed current recommendations (Verbruggen et al., 2019) and explicitly stated not to wait for the stop-signal. Nevertheless, participants may have paid less attention to the instruction, especially on later measurement occasions where the task procedure was already known. Another reason for reduced reliability could be, as explained above, that the SSRT calculation is based on a difference score.

Secondary and Control Condition Variables

Table 9 contains reliability (Rel), common consistency (Con), and occasion specificity (Spe) for secondary and control condition variables estimated from SEM. Cronbach's α and ICCs are given in Table 3.

An interesting observation was that all secondary and control condition variables had excellent reliabilities in our model-based analyses (Rel = .89–1.0). This is again in line with Meyhöfer et al. (2016), reporting excellent but slightly smaller LST-based reliabilities in saccadic latencies (Rel = .83–.89). Our results on internal consistencies for RT variables (Cronbach's α = .87–1.0) confirm previous studies reporting mostly excellent reliability (Cronbach's α = .84–.97; $r_{split-half}$ = .72–.97; Ettinger et al., 2003; Klein & Fischer, 2005; Martínez-Loredo et al., 2017; Meyhöfer et al., 2016; Miyake et al., 2000; Wöstmann et al., 2013). Temporal stability was found to be lower (ICC = .66–.82). Reduced temporal stability given high internal consistency can indicate situational influences. This is also evident in comparison to the model-based reliabilities: ICCs are lower than model-based reliabilities because models separate error variance from reliable but occasion-specific variance. However, since we calculated ICCs considering absolute agreement and not only focusing on relative consistency (McGraw & Wong, 1996), with three measurement occasions it is expectable to find lower values. Again, results are highly comparable to earlier work mostly reporting good to excellent temporal stability (ICC = .56–.93; $r_{test-retest}$ = .65–.93; Ettinger et al., 2003; Hedge et al., 2018; Klein & Berg, 2001; Klein & Fischer, 2005; Meyhöfer et al., 2016; Paap & Sawi, 2016; Płomecka et al., 2020; Roy-Byrne et al., 1995; Saville et al., 2011; Siegrist, 1995; Talanow & Ettinger, 2018; Versino et al., 1993; N. White et al., 2019; Wöstmann et al., 2013) for all variables except stop-signal go RT, where our data imply excellent temporal stability (ICC = .82), whereas previous studies report at most good reliability using ICCs (ICC = .35–.60; $r_{test-retest}$ = .60–83; Hedge et al., 2018; Saville et al., 2011; Wöstmann et al., 2013). Regarding model-based information on the appropriateness of Cronbach's α as estimator of reliability, an underestimation is not to be expected here since excellent reliability was given for all variables. However, for antisaccade latency temporal stability (ICC = .77) may have been underestimated, as there were no equal loadings over time.

Table 9

Reliability, Consistency, and Occasion Specificity for Secondary and Control Condition Variables

Dependent variable	*N*	Coefficient	*M*	T1	T2	T3
		Antisaccade task				
Latency PS	134	Rel(X)	.89	.88/.89	.89/.89	.90/.90
		Con(X)	.82	.81/.81	.82/.82	.84/.84
		Spe(X)	.07	.08/.08	.07/.07	.06/.06
Latency AS	134	Rel(X)	.90	.91/.85	.92/.94	.91/.88
		Con(X)	.78	.72/.67	.85/.87	.78/.76
		Spe(X)	.12	.19/.18	.07/.07	.13/.12
		Eriksen flanker task				
RT con.	143	Rel(X)	.96	.96/.96	.96/.96	.97/.97
		Con(X)	.80	.80/.80	.80/.80	.81/.81
		Spe(X)	.16	.16/.16	.16/.16	.16/.16
RT incon.	143	Rel(X)	.97	.97/.97	.97/.97	.97/.97
		Con(X)	.81	.82/.82	.81/.81	.82/.82
		Spe(X)	.15	.15/.15	.16/.16	.15/.15
		Go/nogo				
RT go	145	Rel(X)	.98	.98/.98	.98/.98	.98/.98
		Con(X)	.77	.76/.76	.75/.75	.80/.80
		Spe(X)	.21	.22/.22	.22/.22	.18/.18
		Simon				
RT con.	142	Rel(X)	.96	.96/.96	.96/.96	.96/.96
		Con(X)	.78	.78/.78	.78/.78	.78/.78
		Spe(X)	.18	.18/.18	.18/.18	.18/.18
RT incon.	142	Rel(X)	.97	.97/.97	.97/.97	.97/.97
		Con(X)	.78	.78/.78	.78/.78	.78/.78
		Spe(X)	.19	.19/.19	.19/.19	.19/.19
		Stop-signal				
RT go	150	Rel(X)	1.0	.99/.99	1.0/1.0	1.0/1.0
		Con(X)	.92	.90/.90	.92/.92	.94/.94
		Spe(X)	.08	.10/.10	.08/.08	.06/.06
		Stroop				
RT con.	149	Rel(X)	.96	.96/.96	.96/.96	.97/.97
		Con(X)	.87	.85/.85	.87/.87	.88/.88
		Spe(X)	.10	.11/.11	.10/.10	.09/.09
RT incon.	149	Rel(X)	.95	.95/.95	.95/.95	.95/.95
		Con(X)	.87	.88/.88	.87/.87	.87/.87
		Spe(X)	.08	.08/.08	.08/.08	.08/.08

Note. Values are shown as mean (*M*) and separately for the three measurement occasions and the two test sets. AS = antisaccade; Con(*X*) = common consistency; con. = congruent; incon. = incongruent; Ind(*X*) = indicator-specific factor; PS = prosaccade; Rel(*X*) = reliability; RT = mean reaction time; Spe(*X*) = occasion specificity.

Consistency and Occasion Specificity

Finally, we showed that the largest part of variance in all variables could be explained by trait influences (Tables 8 and 9). In LGC models, those trait components also included trait changes, but as

previously discussed, those changes were mostly small and occurred mainly from occasion 1 to 2. In secondary and control condition variables, more than 77% of variance was due to trait components (on average 82%). The impact of situation and Situation × Person interaction was considerably lower (on average 13%). Similarly, Meyhöfer et al. (2016) reported a large amount of trait variance in pro- and antisaccade latency (66%–77%) and a smaller amount of occasion specificity (8%–24%).

Since reliability was lower in primary inhibitory variables, the overall proportion of variance explained by traits was naturally also lower than in secondary and control condition variables (on average 52%). When focusing on the proportion of explained variance that was due to traits (Con/Rel × 100), it was observed that variance was also primarily explained by stable, personal processes in all variables (on average 84%) except SSRT (54%). Regarding SSRT, as described earlier, the LST model only accounted for 51% of variance. This variance can be subdivided into 28% variance due to consistency and 22% due to occasion specificity. Thus, compared to other tasks and variables, SSRT is strongly affected by situation and Situation × Person interaction. This fits in very well with the above considerations as to whether, for example, the instruction could have been interpreted differently on different measurement occasions or whether there could be systematic changes in strategy use depending on the point in time.

Hierarchical LST Models

To address our second research question regarding relations between latent traits in different tasks, LST models with varying state intercepts were combined into hierarchical LST models. The results from these models serve to provide an examination of relations between task specific traits in inhibitory control variables. Model constraints are shown in Table 4; however, instead of fixing state variance on occasion 2 to 0 for nogo error rate, trait loadings were set to 1 as for SSRT.

First, a model with all covariances between task-specific traits fixed to zero (variances allowed to vary) was compared to a model with freely estimated correlations between traits. The zero-correlation model provided significantly worse fit (χ^2_{diff} (10) = 27.59, $p = .002$), indicating that traits of different tasks were related. The correlational structure resulting from the model is shown in Table 10. Replacing the freely estimated correlations by one common inhibitory trait factor (i.e., one-factor model; Figure 2) did not significantly reduce model fit (χ^2_{diff} (5) = 5.61, $p = .346$). However, standardized loadings from the common inhibitory factor to task-specific trait factors could not be fixed to 1 without significant reductions in model fit (χ^2_{diff} (5) = 279.68, $p < .001$). Thus, variance in latent traits was not exclusively explained by one common inhibitory ability.

Following traditional classifications of tasks into response inhibition and interference control (Aichert et al., 2012; Friedman & Miyake, 2004; Pettigrew & Martin, 2014), antisaccades, go/nogo, Stop-signal, and Stroop tasks are thought to measure response inhibition, whereas the Eriksen flanker task is considered to measure interference control. As only this task could be assigned to interference control in the hierarchical model, our one-factor model (of all tasks) mathematically corresponded to a model in which the Eriksen flanker trait factor was explained by an interference factor that is correlated with the other trait factors. Therefore, in addition, a response inhibition trait unrelated to the Eriksen flanker task was created (i.e., one-factor model without Eriksen flanker). The comparison between the one-factor model and this model revealed differences in model fit close to significance (χ^2_{diff} (1) = 3.64, $p = .056$; Table 11). BF01 indicates no evidence for the one-factor model excluding the Eriksen flanker task and BF10 indicates only anecdotal evidence for the one-factor model including all tasks. Thus, there was no clear evidence on whether trait interference control (here measured by Eriksen flanker task) was related to trait response inhibition and we cannot make any strong statements about the exact division of the constructs on a trait level, except that the flanker trait could not be separated from response inhibition traits without loss of fit. In other words, even if the Eriksen flanker trait factor captures a different construct than the remaining task, it is still closely related to response inhibition.

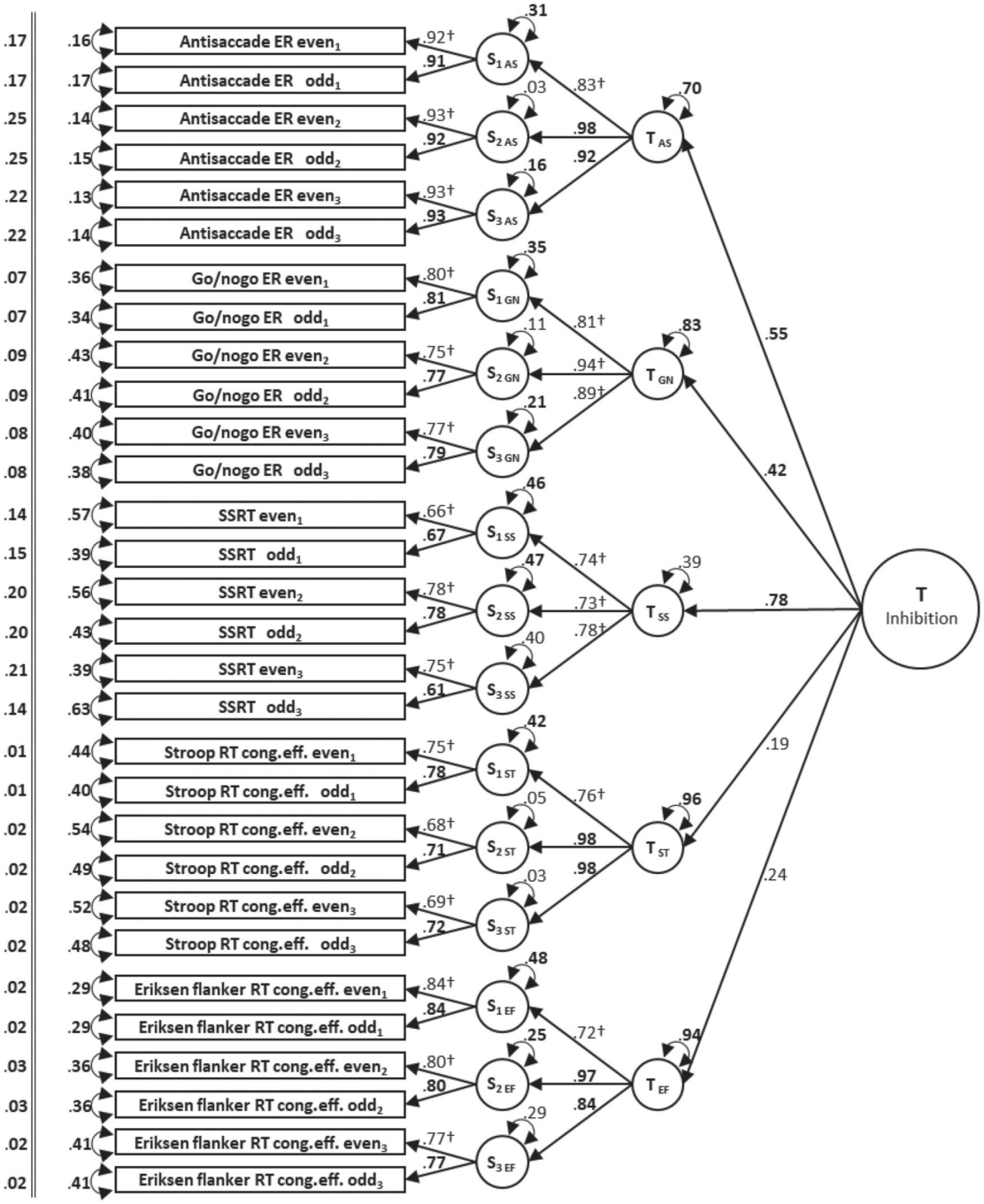
However, others have pointed out that the Stroop task may also be linked to the Eriksen flanker task as in both tasks, conflicts may arise due to stimulus-related and response-related interference (Kornblum et al., 1990; van Veen & Carter, 2005; van Veen et al., 2001; Whitehead et al., 2020). By way of explanation, in both tasks conflict could either be solved by ignoring distracting aspects of stimuli or by controlling responses (Stahl et al., 2014). In agreement with this notion, there was a comparatively high correlation on the trait level between Stroop and Eriksen flanker RT congruency effects in our data ($r = .248$). Therefore, in the two-factor model, there were two hierarchical traits, a latent response inhibition trait loading on antisaccade error rate, go/nogo error rate, and SSRT and a latent interference control trait loading on RT congruency effect in Eriksen flanker and Stroop tasks. In the correlated two-factor model

Table 10
Correlational Structure Based on Traits and Measures on Occasion 1

	Trait based				Occasion 1				
Dependent variable	1	2	3	4	1	2	3	4	5
1 Antisaccade ER AS									
2 Go/nogo ER nogo	.273*				.197*				
3 Stop-signal SSRT	.441*	.271			.026	.029			
4 Stroop RT cong.eff.	.043	.028	.210		−.002	.041	.202*		
5 Eriksen flanker RT cong.eff.	.049	.117	.208	.248	.050	.154	.012	.206*	
6 Simon RT cong.eff.					−.013	.077	−.006	.033	.073

Note. Left: trait-based correlations are derived from a model allowing correlations between task-specific traits in latent state–trait (LST) models. Right: Pearson correlations between primary inhibitory variables on occasion 1. AS = antisaccade; cong.eff. = congruency effect; SSRT = stop-signal reaction time.
*$p < .05$.

Figure 2
One-Factor Model of the Trait Based Structure of Inhibitory Control



Note. One-factor model: trait inhibition loading on all tasks. Numbers next to single-headed arrows are the standardized factor loadings (interpretable as standardized regression coefficients). Numbers next to double-headed arrows are the error variances. Numbers in the column to the left of the model indicate the amount of variance in the dependent variable explained by the latent trait inhibition factor. For all parameters, boldface type indicates $p < .05$. Parameters fixed to one are marked with a cross (†).

Table 11
Model Parameters and Model Comparisons for Hierarchical LST Models

Model	$p_{compare}$	$\chi^2(df, p)$	CFI	RMSEA (95% CI, p)	SRMR	BF01	BF10
Two-factor model correlated[a]		457.31 (431, .184)	.99	.02 (.00–.04, 1.00)	0.08		
Two-factor model uncorrelated	.640	459.12 (434, .195)	.99	.02 (.00–.04, 1.00)	0.08	0	832.99
One-factor model		461.03 (434, .178)	.99	.02 (.00–.04, 1.00)	0.08	2.02	0.5
One-factor model without Eriksen flanker	.056	464.09 (435, .162)	.98	.02 (.00–.04, 1.00)	0.08	0.34	2.91

Note. Two-factor model correlated: latent trait response inhibition loading on antisaccade, go/nogo, and stop-signal tasks, latent trait interference control loading on Stroop and Eriksen flanker tasks; two-factor model uncorrelated: uncorrelated latent trait response inhibition and interference control factor; one-factor model: trait inhibition loading on all tasks; one-factor model without Eriksen flanker: trait inhibition loading on all tasks, except Eriksen flanker. Models were tested against each other row by row using χ^2 differences tests ($p_{compare}$). Factor loadings on task-specific traits were freely estimated without constraining the first loading to 1. BF01 = Bayes factor in favor of the null hypothesis (i.e., the model in the above row); BF10 = Bayes factor in favor of the alternative hypothesis (i.e., the model in the current row); CFI = comparative fit index; RMSEA = root-mean-square error of approximation; SRMR = standardized root mean residual.
[a] Loadings on task-specific traits were constrained to be greater 0, and trait loadings for SSRT were freely estimated in order to avoid the non-identification of the model and negative variances.

(Figure 3) trait response inhibition and trait interference control were correlated; in the uncorrelated two-factor model, the correlation was fixed to 0. However, the correlated two-factor model revealed a non-significant correlation and as shown in Table 11, constraining the correlation to 0 did not significantly reduce fit. Quite on the opposite, BF10 in favor of the uncorrelated two-factor model indicated extreme evidence that in this model response inhibition and interference control were not related on the trait level, which supports the idea (Stahl et al., 2014) that the relationship between response inhibition and interference control may be overestimated by the relation between Stroop and Eriksen flanker tasks when assigning them to different constructs, that is, response inhibition and interference control, respectively. Given the low variance explained in the Stroop task by a response inhibition factor (approx. 2%) in the one-factor model and given the good model fit of the uncorrelated two-factor model, at the trait level the Stroop, like the Eriksen flanker task, could be assigned to an interference control factor that was separate from response inhibition. Taken together, this shows that there appeared to be a stable response inhibition ability and a separate interference control ability across the three measurement points.

The comparison between the uncorrelated two-factor model and the one-factor model using a χ^2 differences test was not possible due to equal degrees of freedom. Model fit was excellent for both models and highly comparable. BF01 indicated only anecdotal evidence for the one-factor model and BF10 indicated no evidence for the uncorrelated two-factor model. Thus, there was no clear evidence on whether trait response inhibition and trait interference control (including the Stroop task) represent the same construct.

In conclusion, when focusing on how traits, that is, stable performance over time in different tasks, are related to each other, our first result is that the Eriksen flanker task was not unrelated to the other tasks, but since we could only include one task typically thought to measure interference control, interpretations of this relation are limited. Our second result is that Eriksen flanker and Stroop tasks may be related, but it was unclear whether this relation was stronger than with the other tasks. And finally, when analyzing how much variance in a task was explained by a stable trait factor across time and tasks at one measurement occasion, it was found that this amount was very small. A general inhibition trait (Figure 2) explained the most variance in the antisaccade error rate at occasion 2 (25%) and the least variance in RT congruency effect in Stroop task at occasion 1 (1%). When divided into two latent traits (Figure 3), the explained variance generally increased slightly, but remained very low (max: antisaccade error rate, occasion 2, 30%, min: RT congruency effect Eriksen flanker task, occasions 1 and 3, 2%). Thus, among the tasks, the proportion of explained variance was highest in the antisaccade task, which is probably the consequence of the higher reliability and consistency of the task itself. Results regarding the variance explained by hierarchical inhibition factors of the other tasks were of course also influenced by the fact that these only showed good and not excellent model reliability.

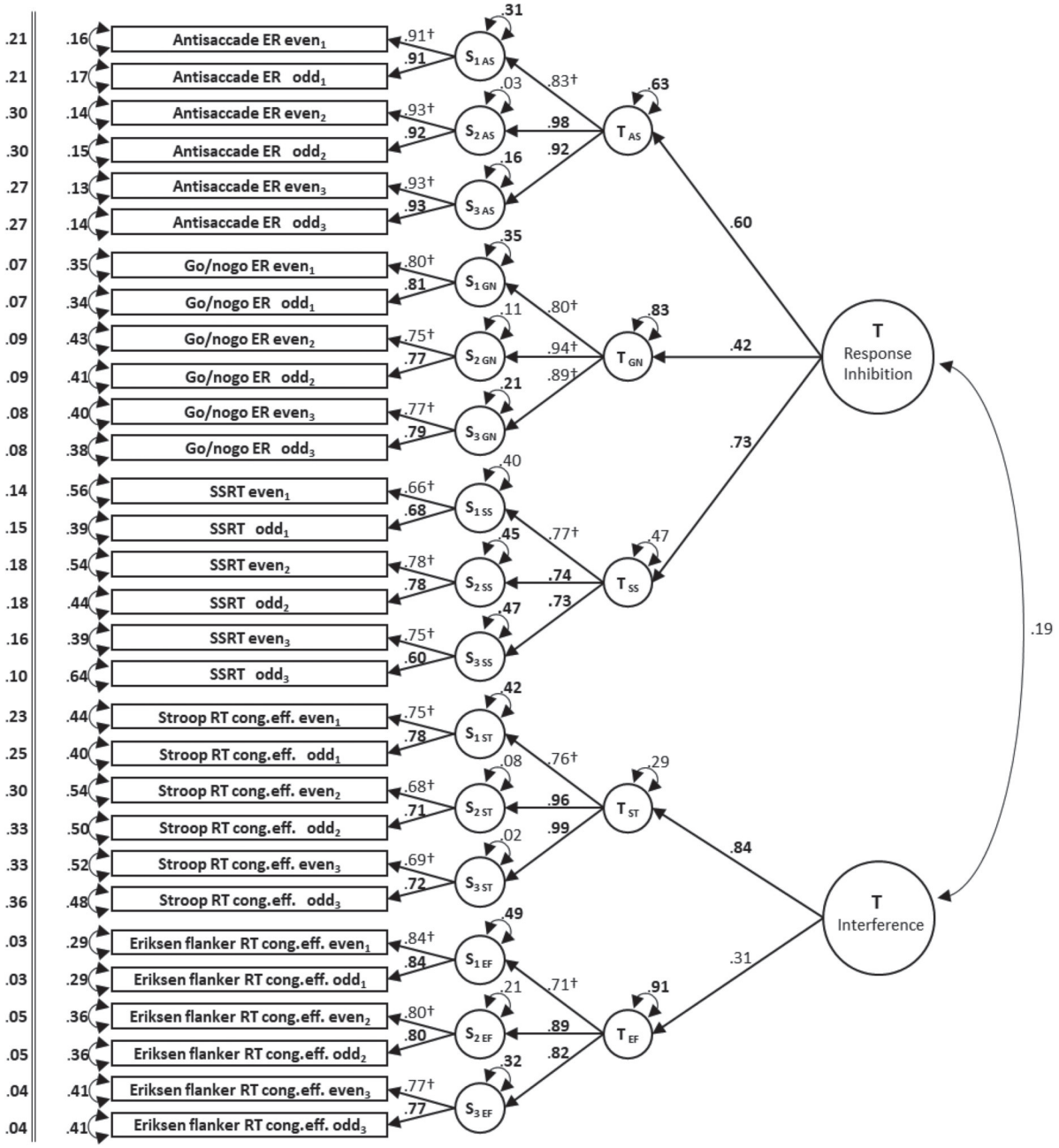
To sum up, the most important finding is that although task-specific traits shared communality, only a very small proportion of variance in tasks was explained by the hierarchical inhibitory control factors and thereby based on cross-task and temporally stable influences.

To facilitate comparison to previous studies (e.g., Friedman & Miyake, 2004; Gärtner & Strobel, 2021; Rey-Mermet et al., 2018), we also identified the latent structure of inhibitory control based on data from occasion 1 without considering state and trait components. Again, Stroop and Eriksen flanker tasks were correlated ($r = .206$), and the only model providing acceptable fit (Table 12) was the correlated two-factor model, with a response inhibition factor loading on antisaccade error rate (loading = 0.27, $p = .181$, explained variance = 7.42%), go/no-go error rate (loading = 0.80, $p = .178$, explained variance = 64.58%), SSRT (loading = 0.04, $p = .815$, explained variance = 0.15%), an interference control factor loading on RT congruency effect in Stroop (loading = 0.28, $p = .102$, explained variance = 7.64%), Eriksen flanker (loading = 0.74, $p = .108$, explained variance = 55.29%), and Simon tasks (loading = 0.11, $p = .415$, explained variance = 1.22%). Contrary to previous findings (Aichert et al., 2012; Friedman & Miyake, 2004; Rey-Mermet et al., 2018; Stahl et al., 2014), neither the correlation between the two factors ($r = .26$, $p = .326$) nor the loading of the factors on the variables was significant. However, a model with all covariances between tasks fixed to zero (variances allowed to vary) provided significantly worse fit than the correlated two-factor model, $\chi^2_{diff}(7) = 15.43$, $p = .031$. Thus, there were relations between tasks but the results suggest that commonality between tasks was rather low. This is also reflected in weak to moderate Person correlations between inhibitory control tasks on occasion 1 (Table 10).

Interestingly, the loading of the response inhibition factor on occasion 1 on the SSRT was close to zero (loading = 0.04), and the stop-signal task correlated mainly with the Stroop task ($r = .202$), which in the model is assigned to the interference control

Figure 3

Two-Factor Model (Correlated) of the Trait Based Structure of Inhibitory Control



Note. Two-factor model correlated: latent trait response inhibition loading on antisaccade, go/nogo, and stop-signal tasks; latent trait interference control loading on Stroop and Eriksen flanker tasks; latent factors are correlated. Numbers next to single-headed arrows are the standardized factor loadings (interpretable as standardized regression coefficients). Numbers next to double-headed arrows are error variances or the correlation between latent factors. Numbers in the column to the left of the model indicate the amount of variance in the dependent variable explained by the latent trait inhibition factor. For all parameters, boldface type indicates $p < .05$. Parameters fixed to one are marked with a cross (†).

Table 12
Model Parameter and Model Comparison for SEM Models on Data From Occasion 1

Model	$p_{compare}$	$\chi^2(df, p)$	CFI	RMSEA [95% CI, p]	SRMR	BF01	BF10
Two-factor model A correlated		3.74 (8, .442)	1.0	.00 [.00–.11, .652]	0.06		
Two-factor model B correlated		3.74 (8, .442)	1.0	.00 [.00–.11, .652]	0.06	7.96	0.13
Two-factor model A uncorrelated	.276	8.81 (9, .117)	.48	.07 [.00–.13, .249]	0.08	1.19	0.84
Two-factor model B uncorrelated		8.81 (9, .117)	.48	.07 [.00–.13, .249]	0.08	1.11	0.9
One-factor model		12.61 (9, .027)	.00	.10 [.01–.19, .124]	0.06	0.06	15.98
One-factor model without Eriksen flanker and Simon	.001	17.72 (11, .007)	.00	.11 [.05–.18, .054]	0.08	0.15	6.51

Note. Two-factor model A correlated, latent response inhibition loading on antisaccade, go/nogo, and stop-signal tasks, latent interference control loading on Stroop, Eriksen flanker, and Simon tasks; two-factor model B correlated, latent response inhibition loading on antisaccade, go/nogo, stop-signal, and Stroop tasks, latent interference control loading on Eriksen flanker and Simon tasks; two-factor model A and B uncorrelated: uncorrelated latent response inhibition and interference control factor; one-factor model: inhibition factor loading on all tasks; one-factor model without Eriksen flanker and Simon: inhibition factor loading on all tasks, except Eriksen flanker and Simon tasks. Models were tested against each other row by row using χ^2 differences tests ($p$compare). Factor loadings on tasks were freely estimated without constraining the first loading to 1. BF01 = Bayes factor in favor of the null hypothesis (i.e., the model in the above row); BF10 = Bayes factor in favor of the alternative hypothesis (i.e., the model in the current row); CFI = comparative fit index; RMSEA = root-mean-square error of approximation; SRMR = standardized root mean residual.

factor. In contrast, SSRT on trait level is the variable showing highest correlations to other tasks overall ($r = .210–.441$). In addition, it is the only variable that did not have significant task specific variance in any hierarchical LST model. Thus, consistency in SSRT is, contrary to the other tasks, mainly impacted by the higher order trait factor. In the initial task-specific LST model, it was found that SSRT was largely impacted by unsystematic error variance (.49) and only about half of the explained variance (Rel = .51) was explained by a stable trait (Con = .28). This trait appeared to be strongly associated with other tasks. In other words, the proportion of performance that remained stable over time in SSRT was rather small overall, but strongly associated with variance that also remained stable in other tasks. In our study, reliability in SSRT was the lowest of all variables, possibly due to methodological constraints, thus our model-based results should be treated with caution.

General Discussion

While temporal stability and plasticity of inhibitory control have previously been studied in separate analyses, a precise examination of trans-situationally stable traits and trait changes over time and state effects was so far missing. In addition, situationally varying and stable components had not been considered when studying the structure of inhibition. Here, we aimed to fill this important research gap by applying LST, LGC, and LT models to six commonly used inhibitory control tasks in a large sample and by focusing on relationships between tasks based on LST models. In addition, we used the results gained from LST modeling to inform the debate on the unity and diversity of inhibitory control by examining trait-based correlations among different inhibitory control variables and factors.

The following main results emerged from the current study. *First*, model-derived reliabilities of primary inhibitory control variables were lower and less consistent than those of secondary and control condition variables. This finding was confirmed by traditional measures of temporal stability and internal consistency. *Second*, a large amount of variance was explained by stable trait components for all variables except SSRT. *Third*, overall the data were precisely described by LST and LGC models but not by LT models. *Fourth*, plasticity effects were evident in the model-based analyses and in the repeated measures analyses, especially from the first to the second occasion. Additionally, for some inhibitory variables, improvement over time was stronger for initially underperforming participants, as indicated by correlations between trait and slope parameters. And *last*, although task-specific traits were related, variance in task performance was determined only to a very small extent by cross-task trait influences. These results thus do not support the idea of individual tasks to be strongly determined by a common inhibitory trait factor.

Overall, our findings with regard to our first research question suggest that measurements of RTs in congruent and incongruent conditions are more reliable than primary inhibitory variables. It is often assumed that inhibitory control tasks elicit both automatic fast and controlled slow processes (e.g., Ridderinkhof, 2002; C. N. White et al., 2011). Since variables of the control conditions are mainly determined by automatic processes, it can be assumed that the measurement of those processes is indeed highly reliable. For RTs on successful inhibition trials (i.e., our secondary variables), we obtained similar evidence of high reliability. However, primary inhibitory variables that measure either the slowing in RT in the case of successful inhibition (congruency effects), the percentage of inhibition failures (antisaccade and nogo error rate) or the RT of the stopping process (SSRT) appear to be less reliable. This could be an indication that controlled processes cannot be measured as reliably as automatic processes.

It is striking that within virtually all dependent variables, the very largest part of explained variance was trait determined. The only variable deviating completely from this pattern of results is SSRT. The SSRT is complex not only in its calculation but likely also in terms of task demands. This variable is the only one where most of the variance remained unexplained, and within the explained variance, mainly state processes seem to have influenced performance.

Among primary inhibitory variables, antisaccade error rate was the most reliable. Eye movement recordings have previously been shown to be very good at differentiating between individuals (Bargary et al., 2017) and may provide purer measures of underlying cognitive processes than manual responses. This notion may also be supported by the relatively large amount of variance in antisaccade error rate that was explained by the latent response inhibition factor.

Regarding our second research question, taken together, both hierarchical LST models and SEM models using data from occasion 1 contradict the existence of inhibitory control as a unitary psychological construct. We are not the first to question this construct (Gärtner & Strobel, 2021; Rey-Mermet et al., 2018; Whitehead

et al., 2020). We are, however, the first to do so under consideration of time-varying and stable task components. Findings inconsistent with a unitary construct have been shown in past research, for example, in non-existent transfer effects from practiced to unpracticed inhibitory control tasks (Talanow & Ettinger, 2018), or in low correlations between inhibitory control tasks (Aichert et al., 2012; Friedman & Miyake, 2004; Hedge et al., 2018; Pettigrew & Martin, 2014; Rey-Mermet et al., 2018). One reason for the low correlations may be task impurity. That is, performance in tasks is not only impacted by inhibitory control ability but also by idiosyncratic task requirements (Friedman & Miyake, 2004). By using SEM, relations between tasks can be assessed with reduced task impurity. Our analyses go one step further and show that task impurity is also present at the trait level. Thus, even if only considering aspects of inhibitory control in different tasks that remain stable over time, low communality is found.

Studies examining inhibition as a part of cognitive control have shown that inhibition can be replaced by a general cognitive control factor (Friedman et al., 2008). At the same time, inhibition is the cognitive control component that is particularly strongly associated with everyday problems and mental illness (Friedman & Miyake, 2017). This suggests that inhibition as a construct should not simply be dropped, but that further research is needed on which aspects determine performance in tasks and relationships to other measures. An important conclusion from our results is also that relationships between manifest inhibitory control task variables and other putatively related constructs should interpreted with caution. When examining such correlations (e.g., between an impulsivity questionnaire score and the error rate on the antisaccade task), it is often implicitly assumed that commonalities are based on a stable cross-task trait rather than on time-varying or task-specific characteristics. Under this assumption, the maximum correlation of these constructs is necessarily constrained by the proportion of explained higher-level trait variance in the task in question.

For example, suppose there is a true correlation between a response inhibition ability underlying performance in an antisaccade task and an impulsivity questionnaire of .80. Assuming that about 25% variance in antisaccades is determined by stable trait inhibition, similar to what we have shown, and assuming that variance in the questionnaire is determined almost exclusively (90%) by this assumed inhibitory ability, the observed correlation could be at most .38 ($.80 \times \sqrt{(.25 \times .90)}$) (Hedge et al., 2018). In our other tasks, however, less variance was captured by an inhibition trait and the assumed reliability and true correlation are estimated unrealistically high at .80. Therefore, correlations between inhibitory control variables and impulsivity questionnaire measures should not be expected to be very high (Cyders & Coskunpinar, 2011). In addition it has been questioned whether experimental tasks and questionnaires capture the same construct at all, as correlations between latent variables and questionnaire measures did not suggest high relations either (Friedman & Gustavson, 2022; Snyder et al., 2021).

Limitations

There are some limitations to this study. First, reliability and thus also trait and state influences are not inherent properties of a task (Parsons et al., 2018). Results strongly depend on sample, task design, and context of the measurement, and generalizations should be made with caution. For example, we assessed a homogeneous sample (young, healthy students). Such homogeneity is likely accompanied by low intraindividual variance and therefore our estimation of reliable trait components can be considered rather conservative. In line with this, ceiling effects in error rates in secondary and control condition variables were observed in our sample. The error rate models of control conditions (Tables 6 and 7 in the online supplemental material) as well as classical measures of reliability (Table 2) show that reliability was very low, especially in the variables that almost all participants completed without error.

Second, we decided to keep task order stable within participants and to vary it between participants. This increases interindividual variance and thus reliability, but also leads to state effects gaining in weight.

Third, we did not have enough measurement occasions and trials to calculate models that leave out the first measurement occasion. Future studies should integrate more measurement occasions and systematically investigate the impact of calculating models with and without occasion 1. In addition, it would be of interest in future research to increase trial number and divide data not only in two test halves but three (Geiser et al., 2015).

Fourth, some variables, which would provide further information about cognitive processes underlying task performance (e.g., RT variability, post error slowing), were not addressed here to focus on the most frequently reported variables and maintain a common thread.

Fifth, in order to investigate similarities and differences between response inhibition and interference control, it would have been useful to include a larger number of tasks. The elimination of the Simon task for modeling reasons led to the fact that only the Eriksen flanker task could be unambiguously assigned to interference control.

Sixth, increasing the number of trials would also be important to improve model application in SSRT in the stop-signal task and in congruency effects. In addition, increasing the step size in the adaptive tracking procedure of the stop-signal task may be important.

Finally, to align the procedure with previous studies of our group, we decided to remove outliers completely and to only include participants who completed all measurement occasions. In future studies, this approach could be reconsidered, as the models would be able to handle missing data.

Implications

Our work has important implications for the application of inhibitory control tasks in the study of interindividual differences, in clinical contexts, and in the study of long-term effects, for example, in psychopharmacology. When aiming to assess individual performance, it seems appropriate to carefully consider the role of potential trait changes over time that might for example reflect learning processes. As there were only few changes from occasion 2 to 3, one could also argue that variance on occasion 1 reflects differences in how fast participants get used to the novel situation. In addition, trait changes over time differ between participants in most variables. Accordingly, hierarchical models show that the amount of variance explained by a cross-task inhibitory trait construct is larger on occasions 2 and 3 compared to occasion 1. Thus, it might in certain cases be useful to include at least one training session. On the other hand, we did include practice trials that were supposed to eliminate the acquaintance with the task and one could also argue that performance on occasions 2 and 3 is impacted by training, which would

make the first occasion particularly suitable in many research domains.

Secondary and control condition variables in antisaccade, Eriksen flanker, go/nogo, Simon, stop-signal, and Stroop tasks were highly reliable, mainly influenced by stable traits and largely unaffected by situational influences. RT congruency effects were less stable and trait improvements were dependent on initial performance. Thus, training sessions might be particularly important for those variables. SSRT in the stop-signal task, as well as RT congruency effect in the Simon task did not show satisfactory reliability or model fit. More research is needed to examine the processes that may have caused these results more closely. Reliability and a large trait component are important criteria for a task's suitability in clinical research, individual differences research or when tasks are presented repeatedly. Among the primary inhibitory variables, antisaccade error rate provided highest reliability and consistency. Importantly, other primary inhibitory variables did not show such high reliability, although the main part of explained variance in all variables, except SSRT and RT congruency effect in the Simon task, was explained by trait influences. We strongly recommend continuing LST and LGC research in clinical samples. This may increase variance and therefore reliability and may shed light onto the effects of psychopathology on intra- and interindividual differences.

Past research has increasingly questioned inhibitory control as a unitary construct. Our results are an important extension of these previous findings, as they clearly show that the lack of correlations between inhibitory control tasks is not due to the fact that temporally varying and temporally stable components of performance have not been taken into account. On the contrary, we show that although inhibitory control task performance is mainly influenced by temporally stable traits, these traits show only very low correlations at the same time.

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Received December 3, 2021
Revision received November 8, 2022
Accepted November 10, 2022 ■

APPENDIX D [Publication Study 2]

Faßbender, K., Bey, K., Lippold, J. V., Aslan, B., Hurlemann, R., & Ettinger, U. (2021). GABAergic modulation of performance in response inhibition and interference control tasks. *Journal of Psychopharmacology*, *35*(12), 1496-1509. https://doi.org/10.1177/02698811211032440

Original Paper

GABAergic modulation of performance in response inhibition and interference control tasks

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Psychopharm

Journal of Psychopharmacology
2021, Vol. 35(12) 1496–1509

DOI: 10.1177/02698811211032440
journals.sagepub.com/home/jop
SAGE

Abstract

Background: Inhibitory control is a crucial executive function with high relevance to mental and physical well-being. However, there are still unanswered questions regarding its neural mechanisms, including the role of the major inhibitory neurotransmitter, γ-aminobutyric acid (GABA).

Aims: This study examined the effects of lorazepam (0.5 mg and 1 mg), a positive allosteric modulator at the $GABA_A$ receptor, on response inhibition and interference control. We also explored the heterogeneity of inhibitory control and calculated delta plots to explore whether lorazepam affects the gradual build-up of inhibition and activation over time.

Methods: $N = 50$ healthy participants performed antisaccade, Eriksen flanker and Simon tasks in a within-subjects, placebo-controlled, double-blind randomized design.

Results: Lorazepam increased reaction time (RT) and error rates dose dependently in all tasks ($p \leqslant 0.005$). In the antisaccade and Simon tasks, lorazepam increased congruency effects for error rate ($p \leqslant 0.029$) but not RT ($p \geqslant 0.587$). In the Eriksen flanker task, both congruency effects were increased by the drug ($p \leqslant 0.031$). Delta plots did not reflect drug-induced changes in inhibition and activation over time. Delta plots for RT in the Simon task were negative-going, as expected, whereas those for the antisaccade and flanker tasks were positive-going.

Conclusions: This study provides evidence for GABAergic involvement in performance on response inhibition and interference control tasks. Furthermore, our findings highlight the diversity of the broader construct of inhibitory control while also pointing out similarities between different inhibitory control tasks. In contrast to RT and error rates, the cognitive processes indexed by delta plots may not be sensitive to GABAergic modulation.

Keywords

Lorazepam, benzodiazepine, response inhibition, interference control, delta functions

Introduction

Inhibitory control, a major dimension of cognitive control, plays an important role in goal-directed behavior. Countless situations require the inhibition of inappropriate reactions, thoughts, impulses, or feelings, and inhibitory impairments that are observed in various neuropsychiatric patient populations (Chamberlain et al., 2006; Ettinger et al., 2018a; Schachar et al., 1993). Inhibitory control is a heterogeneous construct (Aron, 2007; Harnishfeger, 1995) and comprises the ability to suppress the execution of inappropriate responses, termed response inhibition (Friedman and Miyake, 2004), and the capacity to reduce the processing of task-irrelevant stimuli or stimulus features, termed interference control (Friedman and Miyake, 2004).

For this study, we selected three frequently implemented paradigms. The antisaccade task, a measure of response inhibition, requires the inhibition of a prepotent saccade toward a sudden-onset stimulus and the generation, instead, of a saccade in opposite direction (Hutton and Ettinger, 2006). Theoretical models (Aponte et al., 2017; Noorani and Carpenter, 2016) differ with regard to the underlying cognitive processes; some assume a distinct stop unit, whereas others propose that automatic prosaccades and voluntary antisaccades are programmed in parallel, and the inhibition is achieved when the voluntary response is programmed fast enough (Hutton, 2008; Massen, 2004). The Eriksen flanker task requires a reaction to a central stimulus while ignoring peripheral distractors. This task is not only a measure of resistance to distractor interference but also places demands on selective attention (Eriksen and Eriksen, 1974; Friedman and Miyake, 2004; LaBerge et al., 1991). It has been employed in tests of the variable zoom lens theory of attention, where a broader attentional focus is linked to greater difficulty in ignoring the distractors. The Simon task induces conflict between stimulus location and response location in incongruent trials (Hommel, 2011). This task has also been interpreted as a measure of interference control (Proctor, 2011; Simon and Small, 1969).

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Inhibitory control in these tasks is commonly measured as the difference in mean reaction time (RT) or error rate (percent incorrect) between incongruent and congruent trials called congruency effect. Larger congruency effects indicate weaker inhibitory control.

On a neural level, inhibitory control is associated with prefrontal, frontoparietal, and subcortical activation (Aron and Poldrack, 2006; Friedman and Miyake, 2017). Underlying neurotransmitter systems include dopamine, noradrenalin, and acetylcholine (Bari and Robbins, 2013; Ettinger and Kumari, 2019). The role of inhibitory neurotransmitters, however, is less well characterized.

GABA is the primary inhibitory neurotransmitter (Uusi-Oukari and Korpi, 2010). Approximately 10%–40% of cerebral cortex is innervated by GABAergic neurons, which are also widespread in subcortical regions (Fonnum, 1987; Rubenstein and Merzenich, 2003; Uusi-Oukari and Korpi, 2010). There are two classes of GABA receptors, $GABA_A$ and $GABA_B$ (Owens and Kriegstein, 2002). GABAergic influences on human cognition are frequently studied via administration of benzodiazepines. Benzodiazepines are positive allosteric modulators of $GABA_A$ receptors, thus enhancing the agonist's effect (Uusi-Oukari and Korpi, 2010) and decreasing the neuron's excitability. Clinically, benzodiazepines have anxiolytic, arousal-reducing, sleep-promoting, muscle relaxing, and anticonvulsive effects. Negative effects, include sedation, mental slowing, and drowsiness (Baldwin et al., 2013).

In line with these properties, benzodiazepines adversely affect basic sensorimotor functions, including increased RT, reduced saccadic peak velocity, and increased saccadic latency (Ettinger et al., 2018b; Haas et al., 2007; Masson et al., 2000; Visser et al., 2003). Effects on attention include impaired vigilance, choice RT, visual information processing, and encoding mechanisms (Duka et al., 1995; Giersch and Herzog, 2004; Jalava et al., 1995; Wesnes et al., 1997). Furthermore, benzodiazepines may decrease the ability to differentiate between distractor and target (Michael et al., 2007) and impair attentional switching (Post et al., 1997). Effects on attentional processes are relevant in the context of inhibitory control, given the close link between inhibition and attention (Barkley, 1997; Moorselaar and Slagter, 2020; Verbruggen et al., 2008).

However, only little is known about benzodiazepine influences on performance in inhibitory control paradigms. Previous studies have consistently shown increased RT and error rates for both inhibitory and non-inhibitory conditions. Antisaccade latencies and directional error rates are increased by lorazepam, but prosaccade latencies may also be increased (Chen et al., 2015; Ettinger et al., 2018b; Green and King, 1998; Green et al., 2000; Haas et al., 2009; Masson et al., 2000; McCartan et al., 2001). However, specific effects on inhibitory performance, that is, interactions between task (prosaccade vs. antisaccade) and drug conditions, or benzodiazepine effects on the congruency effect, have not been reported.

Regarding flanker tasks, it has been shown that benzodiazepines increase both congruent and incongruent RT dose dependently (Bruijn et al., 2004; Clariá et al., 2011; Riba et al., 2005). Error rates were not affected by lorazepam (Bruijn et al., 2004) or alprazolam (Riba et al., 2005), but alprazolam increased error rates depending on dose (Clariá et al., 2011). However, sample sizes were small ($N \leqslant 12$) and again, benzodiazepine effects on specific measures of inhibitory control were either nonsignificant (Bruijn et al., 2004; Riba et al., 2005) or not reported (Clariá et al., 2011).

To our knowledge, effects of benzodiazepines on Simon task performance have not yet been studied.

Regarding the widely used stop signal and go/no-go response inhibition tasks, some studies failed to observe significant drug effects on stop or go processes (Reynolds et al., 2004; Shadli et al., 2016). Others showed inhibition to stop-signals and estimated time to inhibit the reaction to be impaired under triazolam (Fillmore et al., 2001).

Altogether, these findings do not allow drawing clear conclusions about the impact of benzodiazepines on inhibitory control.

In addition to studying RT and error rates, GABAergic effects on cognitive processes may also be studied by considering how congruency effects change as a function of RT. This approach, called distributional analysis, may reveal distinct patterns not reflected in simple comparisons of RT between congruent and incongruent trials across the entire task (Burle et al., 2005; Pratte et al., 2010). A common tool in distributional analysis is the delta plot, in which trials are binned in quantiles and congruency effects for RT or error rate are plotted against the RT of each quantile.

Applying this approach, Ridderinkhof (2002) proposed a dual-process model, including direct activation and selective inhibition processes. In this model, the build-up of selective inhibition is reflected in delta plots for RT: efficient inhibition leads to a reduction of congruency effects, thus decreasing the delta plot for slower segments. Direct activation is expressed in plots for accuracy (percent correct): stronger direct activation produces a greater congruency effect for faster segments. A common finding is a pattern of negative-going delta plots for RT in the Simon task, where congruency effects at higher RT approach zero or become negative, compared to positive-going delta plots for the Eriksen flanker task, where congruency effects for accuracies grow with increasing RT (Wildenberg et al., 2010b). These patterns may be due to differences in onset and strength of active suppression (Burle et al., 2005; Pratte et al., 2010; Ulrich et al., 2015). Delta plots for the antisaccade task have not been characterized in detail. Including distributional analysis in our study may thus allow characterizing lorazepam effects on specific processes underlying inhibitory control.

Therefore, we comprehensively assessed benzodiazepine effects on response inhibition and interference control task performance using antisaccade, Eriksen flanker, and Simon tasks. Previous studies typically did not use more than one task, thereby failing to provide a systematic characterization of GABAergic effects on inhibitory control. This is an important omission given the heterogeneity of inhibitory control (Aichert et al., 2012; Stahl et al., 2014). Accordingly, we investigated the specificity and generality of lorazepam effects on inhibitory control via systematic investigation of drug effects in congruent and incongruent conditions across tasks. An additional weakness of previous studies is that they often used small ($N < 20$) samples and single drug doses (Visser et al., 2003), thereby suffering from low power and failing to provide estimates of dose–response relations. Therefore, we applied multiple doses (placebo, 0.5 mg lorazepam and 1 mg lorazepam) to a large sample ($N = 50$) in a within-subject design.

We hypothesized increased RT and error rates as a function of dose for all tasks. We also expected incongruent trials to be slower and more error-prone than congruent trials. Due to heterogeneous and insufficient previous studies, analyses concerning

interactions between congruency and drug are labelled exploratory. Nevertheless, since benzodiazepines impair various features of information processing, it is reasonable to assume that inhibitory control is also negatively affected. To further explore the heterogeneity of inhibitory control, we studied correlations between drug-induced changes in congruency effects between tasks. We hypothesized delta plots for response speed to be positive-going for the Eriksen flanker task and negative-going for the Simon task. Analyses of delta plots from the antisaccade task as well as drug effects on delta plots across tasks are exploratory. Finally, we included measures of subjective states, which we expected to reflect lorazepam-induced sedating effects.

Method

Sample

Healthy participants aged 18–35 years were recruited via ads placed around the university campus and online. We aimed for $N=50$ participants to achieve enough power to detect small effects, which may be expected in the lower dose range of lorazepam applied here. We had approximately 99% power to detect an effect of $\eta_p^2=0.10$ ($\alpha=0.05$). Before admission to the study, potential participants were screened for the following exclusion criteria: any current or history of psychiatric, neurological, or physical disorder; any current medication intake (except contraceptives or thyroid medicines); hypertension (blood pressure >140/90) or hypotension (blood pressure <100/60); body mass index (BMI) <18 or >30; current or recent (within last 12 months) consumption of any drugs including nicotine; former intake of any benzodiazepines; and, for women, a positive pregnancy test. Further requirements were that participants had normal or corrected sight, were right-handed and non-smokers. Participants provided written informed consent and were compensated with 90 € or course credits. The study was approved by the ethics committee of the Faculty of Medicine at the University of Bonn (Lfd. Nr. 292/17).

Design and procedure

The design was within-subject, double-blind, and placebo-controlled with counterbalanced order of drug conditions (Latin square design). Participants took part in a screening session and three assessment sessions.

In the screening session, exclusion criteria were checked in a detailed interview and weight, height, and blood pressure were measured. Assessment sessions took place in three subsequent weeks, with day of the week and time of assessment kept the same for each participant as closely as possible (difference between days: mean = 7.12, SD = 0.92, maximum = 14; difference between starting times in minutes: mean = 4.34, SD = 19.85, maximum = 180).

At the beginning of each assessment session, participants' well-being was confirmed and female participants performed a urine pregnancy test (Cleartest® Diagnostik HCG, Wesel, Germany). Then, a capsule containing either placebo (mannitol), 0.5 mg or 1 mg lorazepam (Tavor™, Pfizer, Berlin, Germany) was administered with a glass of still water. After a waiting period of 120 min (Kyriakopoulos et al., 1978), participants completed psychomotor tasks lasting approximately 35 min (not reported here). Subsequently, participants performed the antisaccade, Eriksen flanker, and Simon tasks. Task order was randomized between participants but kept constant for each participant across assessment sessions. After finishing the tasks, participants completed 10 computerized visual analog scale (VAS) (Costa et al., 2013) and the computerized NASA task load index (NASA-TLX) (Hart and Staveland, 1988).

Finally, at the end of each assessment session, participants were asked to guess whether they had received placebo, 0.5 mg lorazepam or 1 mg lorazepam.

Inhibitory control tasks

The antisaccade task (Supplemental Figure S1) was written using the SR Research ExperimentBuilder software (SR Research Ltd., Ottawa, ON, Canada). A chinrest was used to minimize head movements. Each trial started with a central fixation stimulus for 1000–2000 ms (random duration) in either yellow (225, 225, 0) or blue (0, 150, 255). The fixation stimulus was a circle of approximately 0.34° in diameter and stroke width of 0.12°. Subsequent to the fixation stimulus, the peripheral stimulus, a white circle of the same dimensions, was shown for 1000 ms randomly on the left or right side of the screen at 10.32° amplitude from the center. Depending on the color of the central fixation stimulus, participants were instructed to look at the peripheral stimulus (prosaccade) or directly to the exact opposite position of the stimulus (antisaccade). Color-instruction mapping was counterbalanced across participants, but kept the same within each participant. A desktop-mounted video-based, combined pupil and corneal reflection tracker (EyeLink 1000, SR Research Ltd.) registered movements of the right eye at a sampling rate of 1000 Hz. Saccade detection was based on criteria of minimum amplitude (1°), and starting point (±100 pixels horizontally from central stimulus position). Trials in which no saccade could be detected, as well as responses with latencies to stimulus onset of <80 ms or >1000 ms, were counted as invalid and excluded.

The Eriksen flanker task (Supplemental Figure S2) was written in Presentation (Version 18.0, Neurobehavioral Systems, Inc., Berkeley, CA, USA). In each trial, five white (255, 255, 255) arrows (total horizontal size approximately 16.66°, vertical size approximately 3.44°) appeared in the center of the screen. Participants were instructed to respond to the middle arrow, which pointed to the right ">" or to the left "<," by pressing the "," or "X" key, respectively, on a QWERTZ keyboard. The two flankers on each side were either congruent (e.g., "<<<<<") or incongruent (e.g., "<<><<"). Each trial started with a central fixation cross shown for 500 ms. Then the arrows were presented for 1000 ms followed by a black screen interstimulus interval of 1000 ms. Trials in which no response could be recorded as well as responses with RT of <150 ms or >1200 ms were counted as invalid and excluded.

The Simon task (Supplemental Figure S3) also was written in Presentation (Neurobehavioral Systems, Inc.). The target consisted of a green (0, 255, 150) or blue (0, 150, 255) point of approximately 3.03° in diameter appearing on the right or left side of the screen at 8.99° amplitude from the center. Each color was assigned to either the "," or "X" keys on a QWERTZ keyboard. Color-instruction mapping was counterbalanced across participants, but kept the same across assessments within each participant. Participants were instructed to press the key corresponding

to the color, regardless of target position. In congruent trials, the assigned key was on the same side of the keyboard as the target position (e.g., target on the left and key located on the left side); in incongruent trials, the assigned key was on the opposite side of the stimulus (e.g., target on the right and key located on the left side). Each trial started with a central fixation cross shown for 500 ms. Then the stimulus was presented for 1500 ms. Trials, in which no response could be recorded as well as responses with RT of $<$150 ms or $>$1200 ms, were counted as invalid and excluded.

All tasks were presented on a 22-inch LCD monitor (ViewSonic Corp., Brea, CA, USA; height: 29.5 cm; width: 47.5 cm; resolution: 1680 $\times$ 1050 pixels; 60 Hz refresh rate) at a distance of 70 cm from participants' eyes. Stimuli were presented on a black (0, 0, 0) screen and each task consisted of 100 congruent/prosaccade and 100 incongruent/antisaccade trials, presented in randomized order. Eye movement data analysis as well as data preprocessing in all tasks was conducted using the MATLAB 2017b (The MathWorks, Natick, MA, USA).

Dependent variables in the antisaccade task were mean latency of directionally correct saccades (ms) and directional error rate (% incorrect, valid reactions) for antisaccade and prosaccade conditions. Congruency effects for latency and error rate were computed as the difference between antisaccade and prosaccade conditions. Dependent variables in the Eriksen flanker and Simon tasks were RT of correct trials (ms) and error rate (% incorrect, valid reactions) for congruent and incongruent conditions. Congruency effects for RT and error rate were computed as the difference between incongruent and congruent conditions.

Rating scales measuring subjective effects

VAS consisted of 10 continuous horizontal scales with the anchors *not at all* and *very*. A marker could be moved by mouse click to indicate the extent of agreement with each item. Items were "anxious," "attentive," "restless," "tired," "carefree," "my thoughts are racing," "I have self-control," "elevated mood," "energetic," and "irritable" (Supplemental Table S1; Costa et al., 2013). Items were scored from 0 to 100, with higher scores representing stronger expressions of the relevant statement.

The NASA-TLX was used to measure subjective workload (Hart and Staveland, 1988). It consisted of computerized, continuous rating scales that ranged from "very low" to "very high" and related to the expressions "mental demand," "physical demand," "temporal demand," "overall performance," "effort," and "frustration level" (in German language, Supplemental Table S2). Items were scored from 0 to 100, with higher scores representing stronger endorsements of the item. Ratings from NASA-TLX were combined to an overall task load score (Bustamante and Spain, 2008).

Statistical analysis

Statistical analyses were carried out in (R Core Team, 2019), using the packages *ez* (Lawrence, 2016), *e1071* (Meyer et al., 2019), *lsr* (Navarro, 2015), and *pastecs* (Grosjean et al., 2018). Participants were excluded from all variables in a particular task if they failed to follow task instructions in at least one assessment session, indicated by $>$80% error rates or $>$50% missing trials. In the antisaccade task, one participant who produced more than 80% invalid trials in congruent and incongruent conditions (e.g., eyeblinks or artifact) was excluded. In the Eriksen flanker task, two participants with high error rates in the incongruent condition were excluded. In the Simon task, three participants were excluded due to high error rates in congruent and incongruent conditions and one due to a large number of missing trials in both conditions.

Dependent variables from each task were analyzed separately using analysis of variance (ANOVA). For each task and each dependent variable (RT and error rate), the ANOVA comprised the within-subjects factors drug (placebo, 0.5 mg and 1 mg) and task condition (congruent and incongruent for Eriksen flanker and Simon, prosaccades and antisaccades for the antisaccade task). To investigate whether effects of lorazepam on inhibitory processes differ across tasks, we carried out two further ANOVAs with congruency effects for RT and error rate as dependent variables. The ANOVA comprised the within-subject factors drug (placebo, 0.5 mg and 1 mg) and task (antisaccade, Eriksen flanker, and Simon task).

Partial eta-square including its 95% confidence interval (CI) was used for calculating effect sizes of ANOVAs (Cohen, 1973). We used post hoc *t*-tests (Bonferroni-corrected *p*-values) to clarify ANOVA results with Cohen's *d* (Cohen, 1988) as measure of effect size. The Mauchly's test of sphericity was performed for each variable and if the condition of sphericity was violated, the Greenhouse–Geisser procedure was applied. Significance level was set to 5% a priori.

In addition, we examined whether there is a relation between lorazepam-induced deficits in inhibitory control across different tasks. Therefore, change scores were calculated reflecting the difference in the congruency effect (RT and error rate) between placebo and 1 mg lorazepam, the dose at which strongest effects are expected. The Pearson correlations (Bonferroni-corrected) tested for associations between drug-induced changes in congruency effects between different tasks.

Delta plots were constructed following Ridderinkhof et al. (2005). First, individual RT of correct and incorrect responses from all participants were rank ordered separately for congruent and incongruent trials. Next, RT was split into five equal-sized parts (quintiles), and RT and error rate were determined for each quintile. Delta plots were then constructed, plotting the congruency effect for RT or accuracy as a function of RT per quintile (including both congruent and incongruent trials). A comparison between different shapes of delta plots across drug conditions was provided by analyzing the slopes that result when data points between two quintiles are connected. In order to analyze delta plots for RT, ANOVAs were conducted comparing slopes between quintiles 1 and 2, quintiles 2 and 3, quintiles 3 and 4, and quintiles 4 and 5. For error rate, only segments 1 and 2 were analyzed, as direct activation processes are only expected to be seen in the first segments (Ridderinkhof, 2002). All delta plot ANOVAs included the within-subjects factor drug (placebo, 0.5 mg and 1 mg).

VAS and NASA-TLX were analyzed using ANOVA with the within-subject factor drug (placebo, 0.5 mg and 1 mg).

Results

Sample description

A sample of N=50 participants (27 females and 23 males) completed the study. Mean age was 22.4 years (SD=3.68). Dataset and code are available online (https://osf.io/ts5b9/). Descriptive results are in Table 1.

Table 1. Descriptive statistics of inhibitory control variables.

	Placebo	Lorazepam 0.5 mg	Lorazepam 1 mg
Antisaccades (*N*=49)			
Latency PS	165.41 (17.65)	170.17 (21.25)	174.62 (21.24)
Latency AS	236.33 (33.78)	241.21 (37.94)	243.44 (35.35)
Error rate PS (%)	1.30 (1.45)	1.68 (2.01)	1.81 (2.13)
Error rate AS (%)	24.18 (16.32)	26.14 (15.25)	30.01 (14.38)
Flanker (*N*=48)			
RT congruent	433.77 (49.26)	455.36 (55.68)	473.37 (61.39)
RT incongruent	495.13 (53.73)	523.11 (63.89)	547.13 (70.56)
Error rate congruent (%)	0.61 (0.97)	1.21 (1.41)	1.29 (1.62)
Error rate incongruent (%)	5.56 (4.45)	5.72 (3.78)	7.41 (5.05)
Simon (*N*=46)			
RT congruent	455.50 (56.82)	474.09 (66.70)	493.87 (65.59)
RT incongruent	474.07 (56.99)	494.05 (69.44)	512.17 (68.66)
Error rate congruent (%)	1.84 (1.95)	2.73 (3.53)	2.68 (2.08)
Error rate incongruent (%)	2.95 (3.05)	4.77 (4.18)	5.25 (4.08)

Numbers indicate the mean (standard deviation).
AS: antisaccades; PS: prosaccades; RT: reaction time.

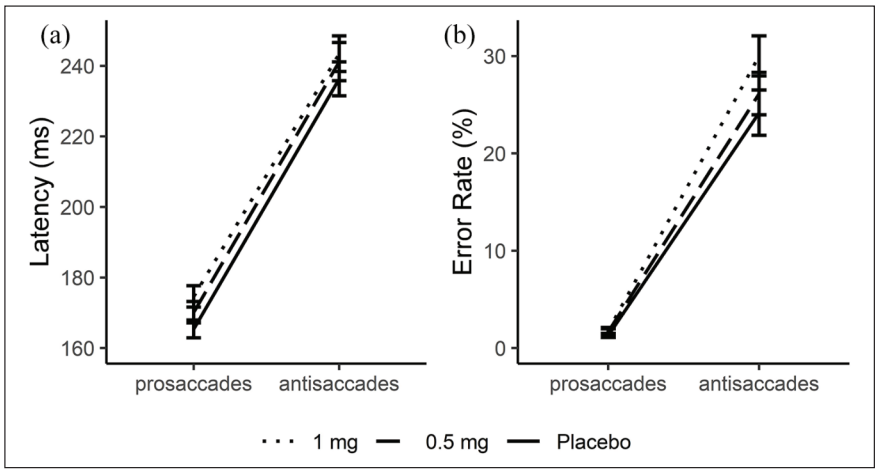

Figure 1. Lorazepam effects on the antisaccade task: (a) effects of lorazepam on prosaccades and antisaccades latency and (b) effects of lorazepam on prosaccades and antisaccades error rate. Error bars indicate the standard error. *N*=49.

Antisaccade task

For latency there were main effects of drug ($F_{(2, 96)}=5.70$, $p=0.005$, $\eta_p^2=0.106$, CI [0.012, 0.219]), indicating longer latencies with increasing drug dose, and task condition ($F_{(1, 48)}=308.40$, $p<0.001$, $\eta_p^2=0.865$, CI [0.785, 0.903]), indicating longer latencies in antisaccades than in prosaccades (Figure 1(a)). The *t*-tests did not reveal significant differences between the three drug conditions (all $p>0.05$) and there was no interaction between drug and task condition ($F_{(2, 96)}=0.54$, $p=0.587$, $\eta_p^2=0.011$, CI [0.0000, 0.068]).

The ANOVA for error rate revealed main effects of drug ($F_{(2, 96)}=6.87$, $p=0.002$, $\eta_p^2=0.125$, CI [0.021, 0.242]), suggesting higher error rate with increasing dose, and task condition ($F_{(1, 48)}=171.22$, $p<0.001$, $\eta_p^2=0.781$, CI [0.657, 0.842]), suggesting fewer errors for prosaccades than for antisaccades (Figure 1(b)). The *t*-tests did not show significant differences between the three drug conditions (all $p>0.05$). In addition, there was an interaction between drug and task condition ($F_{(2, 96)}=6.46$, $p=0.002$, $\eta_p^2=0.119$, CI [0.018, 0.234]). Qualitatively, the interaction suggests that congruency effects increased with increasing drug dose (Figure 1(b)). The *t*-tests revealed that participants made fewer errors in prosaccades than antisaccades at each level of drug (all $p<0.001$). Error rate did not differ significantly between drug conditions in neither of the two task conditions (all $p>0.05$).

Eriksen flanker task

For RT of correct responses, there were main effects of drug ($F_{(2, 94)}=33.95$, $p<0.001$, $\eta_p^2=0.419$, CI [0.262, 0.530]), suggesting higher RT with increasing dose, and task condition

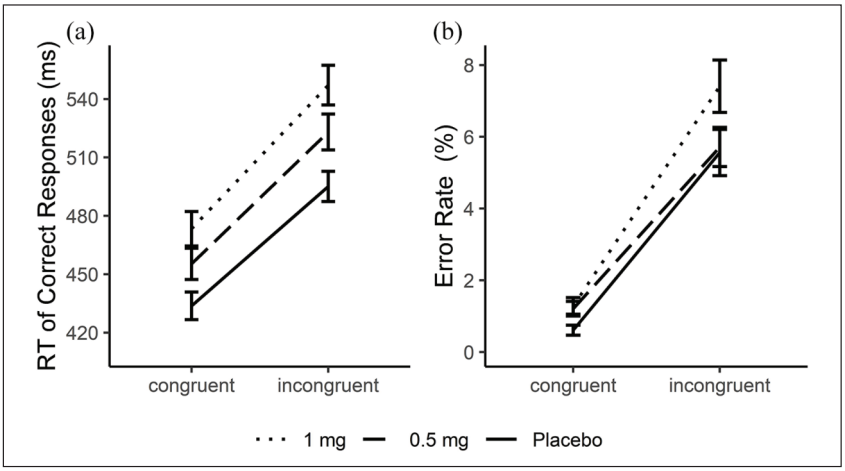

Figure 2. Lorazepam effects on the Eriksen flanker task: (a) effects of lorazepam on congruent and incongruent reaction time (RT) of correct trials and (b) effects of lorazepam on congruent and incongruent error rate. Error bars indicate the standard error. $N = 48$.

($F_{(1, 47)} = 923.69$, $p < 0.001$, $\eta_p^2 = 0.952$, CI [0.921, 0.965]), indicating higher RTs for the incongruent than the congruent condition (Figure 2(a)). The *t*-tests showed that RT was shorter in the placebo condition compared to 0.5 mg lorazepam ($p = 0.037$, $d = 0.723$) and compared to 1 mg lorazepam ($p < 0.001$, $d = 1.028$). RT under 0.5 mg and 1 mg lorazepam was not significantly different ($p = 0.102$, $d = 0.504$). In addition, there was an interaction between drug and task condition ($F_{(2, 94)} = 6.36$, $p = 0.003$, $\eta_p^2 = 0.119$, CI [0.017, 0.236]). Qualitatively, the interaction suggests that congruency effects increased with increasing drug dose (Figure 2(a)). The *t*-tests revealed that RTs were higher in the incongruent than the congruent condition at each level of drug (all $p < 0.001$). In the congruent condition, RTs under placebo were significantly shorter than under 1 mg lorazepam ($p = 0.011$, $d = 1.022$), an effect that was more pronounced in the incongruent condition ($p < 0.001$, $d = 1.054$). Comparing 0.5 mg lorazepam with placebo or 1 mg lorazepam, RT did not differ significantly in neither of the two task conditions (all $p > 0.05$).

The ANOVA for error rate found main effects of drug ($F_{(2, 94)} = 6.96$, $p = 0.002$, $\eta_p^2 = 0.129$, CI [0.022, 0.247]), indicating higher error rates with increasing dose, and task condition ($F_{(1, 47)} = 108.21$, $p < 0.001$, $\eta_p^2 = 0.697$, CI [0.535, 0.782]), indicating higher error rates in the incongruent than the congruent condition (Figure 2(b)). The *t*-tests did not show significant differences between drug conditions (all $p > 0.05$). In addition, there was an interaction between drug and task condition ($F_{(2, 94)} = 3.86$, $p = 0.031$, $\eta_p^2 = 0.076$, CI [0.0000, 0.181], $\varepsilon = 0.84$). Qualitatively, the interaction suggests that congruency effects increased with increasing drug dose (Figure 2(b)). The *t*-tests revealed that participants made more errors in the incongruent compared to the congruent condition at each level of drug (all $p < 0.001$). Error rates did not differ significantly between placebo, 0.5 mg or 1 mg lorazepam in neither of the two task conditions (all $p > 0.05$).

Simon task

For RT of correct responses, there were main effects of task condition ($F_{(1, 45)} = 56.73$, $p < 0.001$, $\eta_p^2 = 0.558$, CI [0.348, 0.680]), indicating higher RTs for the incongruent condition than the congruent condition, and drug ($F_{(2, 90)} = 24.16$, $p < 0.001$, $\eta_p^2 = 0.349$, CI [0.188, 0.470]), indicating increasing RT with increasing drug dose. The *t*-tests revealed that RT was lower in the placebo condition compared to 1 mg lorazepam ($p < 0.001$, $d = 0.999$). For the other comparisons, there were no significant differences (all $p > 0.05$) (Figure 3(a)). There was no significant interaction between drug and task condition ($F_{(2, 90)} = 0.16$, $p = 0.853$, $\eta_p^2 = 0.004$, CI [0.0000, 0.040]).

The ANOVA for error rate revealed main effects of drug ($F_{(2, 90)} = 8.44$, $p < 0.001$, $\eta_p^2 = 0.158$, CI [0.036, 0.282]), suggesting higher error rates with increasing drug dose, and task condition ($F_{(1, 45)} = 24.18$, $p < 0.001$, $\eta_p^2 = 0.350$, CI [0.133, 0.518]), suggesting more errors for the incongruent than the congruent condition (Figure 3(b)). The *t*-tests showed significant differences between placebo and 0.5 mg lorazepam ($p = 0.022$, $d = 0.384$) as well as placebo and 1 mg lorazepam ($p = 0.006$, $d = 0.497$). Error rate did not differ between 0.5 and 1 mg lorazepam ($p > 0.05$). In addition, there was an interaction between drug and task condition ($F_{(2, 90)} = 3.67$, $p = 0.029$, $\eta_p^2 = 0.075$, CI [0.0000, 0.183]). Qualitatively, the interaction suggests that congruency effects increased with increasing drug dose (Figure 3(b)). The *t*-tests revealed that participants made fewer errors in the congruent compared to the incongruent condition under 0.5 mg ($p = 0.027$, $d = 0.554$) and under 1 mg lorazepam ($p = 0.002$, $d = 0.801$) but not under placebo ($p = 0.937$, $d = 0.340$). In the congruent condition, error rate did not differ significantly between placebo, 0.5 mg or 1 mg lorazepam (all $p > 0.05$), whereas in the incongruent condition error rate was significantly higher under 1 mg lorazepam compared to placebo ($p = 0.008$, $d = 0.632$). Comparing 0.5 mg with placebo or 1 mg lorazepam, RT did not differ significantly in neither of the two task conditions (all $p > 0.05$).

Lorazepam effects across tasks

Analyses of the congruency effect for RT/latency across tasks and drug revealed a main effect of task ($F_{(2, 84)} = 107.90$, $p < 0.001$, $\eta_p^2 = 0.720$, CI [0.610, 0.781]). The congruency effect for RT

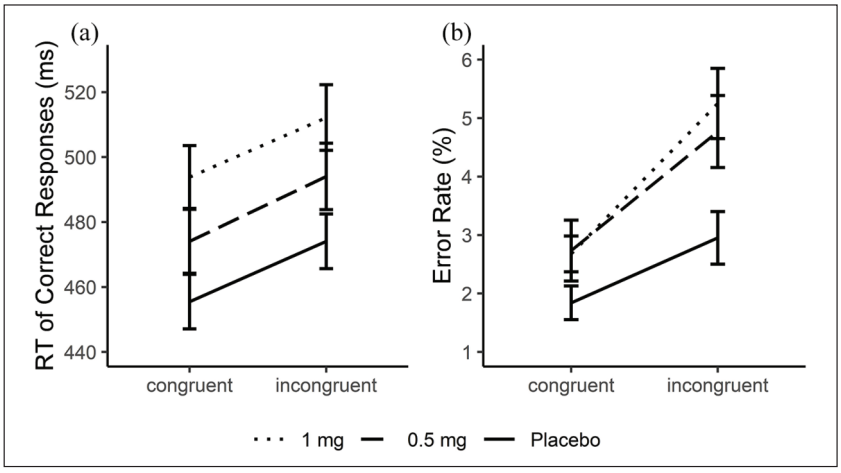

Figure 3. Lorazepam effects on the Simon task: (a) effects of lorazepam on congruent and incongruent reaction time (RT) of correct trials and (b) effects of lorazepam on congruent and incongruent error rate. Error bars indicate the standard error. $N=46$.

differed significantly between the Simon and Eriksen flanker tasks ($p<0.001$, $d=1.774$), between the Simon and antisaccade tasks ($p<0.001$, $d=1.646$) but not between the Eriksen flanker and antisaccade tasks ($p=0.614$, $d=0.121$) (Figure 4(a)). There was no main effect of drug ($F_{(2,\ 84)}=0.41$, $p=0.664$, $\eta_p^2=0.010$, CI [0.0000, 0.068]), but there was an interaction between drug and task ($F_{(4,\ 168)}=2.55$, $p=0.041$, $\eta_p^2=0.057$, CI [0.0000, 0.117]). Qualitatively, the interaction suggests that the congruency effect increased with increasing drug dose only in the Eriksen flanker task (Figure 4(a)). The *t*-tests revealed smaller congruency effects for all drug conditions in the Simon task compared to the Eriksen flanker (all $p<0.001$) and antisaccade tasks (all $p<0.001$). Congruency effects did not differ between the Eriksen flanker and antisaccade tasks for any drug condition (all $p>0.05$). In addition, within each task, *t*-tests did not reveal significant differences in the congruency effect for RT between the three drug conditions (all $p>0.05$).

Analyses of the congruency effect for error rate across tasks and drug revealed a main effect of task ($F_{(2,\ 84)}=110.82$, $p<0.001$, $\eta_p^2=0.725$, CI [0.617, 0.785], $\varepsilon=0.57$), due to greater congruency effects in the antisaccade task compared to the Eriksen flanker ($p<0.001$, $d=1.351$) and Simon tasks ($p<0.001$, $d=1.590$) (Figure 4(b)). Also, the congruency effect for error rate was significantly smaller for the Simon task compared to the Eriksen flanker task ($p=0.033$, $d=0.572$). There was a main effect of drug ($F_{(2,\ 84)}=10.64$, $p<0.001$, $\eta_p^2=0.202$, CI [0.060, 0.333]), which qualitatively suggests increasing error rates with increasing drug dose, but the *t*-tests did not reveal significant differences between the three drug conditions (all $p>0.05$). In addition, there was an interaction between drug and task ($F_{(4,\ 168)}=3.46$, $p=0.020$, $\eta_p^2=0.076$, CI [0.005, 0.144], $\varepsilon=0.67$). Qualitatively, the interaction suggests that the drug-induced increase of the congruency effect is more pronounced in the antisaccade task than the other tasks (Figure 4(b)). The *t*-tests revealed stronger congruency effects for all drug conditions in the antisaccade task compared to the Eriksen flanker task (all $p<0.001$) and the Simon task (all $p<0.001$). Congruency effects did not differ between Eriksen flanker and Simon tasks for any drug condition (all $p>0.05$). Also, within each task, *t*-tests did not reveal significant differences in the congruency effect for error rate between the three drug conditions (all $p>0.05$).

Change score correlations

Change scores between performance under placebo and 1 mg lorazepam for congruency (error rate) were significantly correlated between the antisaccade and Simon tasks ($r=0.407$, $p=0.020$). Other correlations were not significant ($p>0.05$).

Delta plots

For delta plots for RT, there was no significant drug effect for any segment in any of the tasks (all $p>0.05$). Also, delta plots for accuracy in the earliest segment were not significantly influenced by drug in any of the tasks (all $p>0.05$).

Visual inspection shows that delta plots for RT were positive-going for the antisaccade and Eriksen flanker tasks and negative-going for the Simon task (Figure 5). For the Simon task, negative-going delta functions extend even below zero; thus, congruency effects are reversed for higher quintiles.

Subjective effects

Results for subjective measures are in Table 2. For VAS, there were main effects of drug for "attentive" ($F_{(2,\ 98)}=7.82$, $p<0.001$, $\eta_p^2=0.138$, CI [0.028, 0.255]), "tired" ($F_{(2,\ 98)}=5.81$, $p=0.004$, $\eta_p^2=0.106$, CI [0.012, 0.218]) and "I have self-control" ($F_{(2,\ 98)}=9.20$, $p<0.001$, $\eta_p^2=0.158$, CI [0.040, 0.278]), indicating participants were less attentive ($p=0.003$, $d=0.534$), more tired ($p=0.008$, $d=0.441$) and less self-controlled ($p=0.003$, $d=0.602$) under 1 mg lorazepam compared to placebo. The *t*-tests did not show significant differences between 0.5 mg lorazepam and placebo or 1 mg lorazepam (all $p>0.05$). There were no main effects of drug for any other variables (all $p>0.05$).

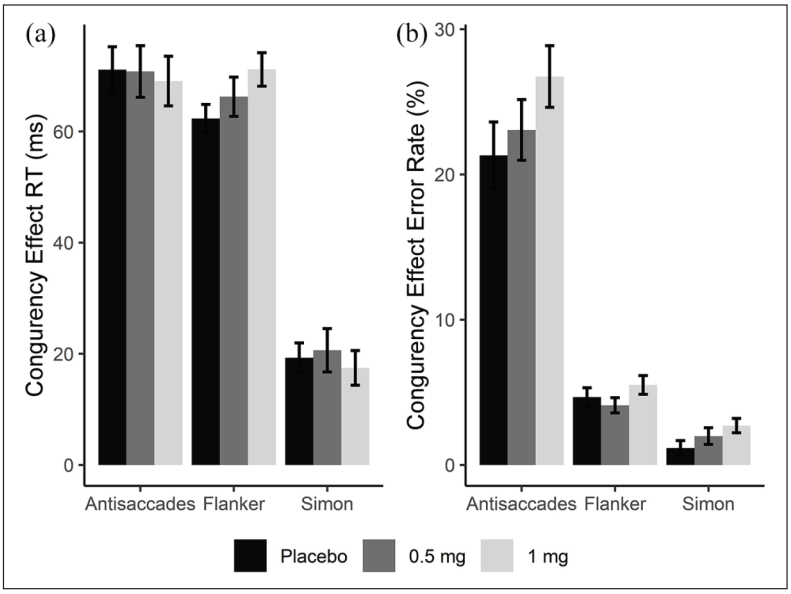

Figure 4. Lorazepam effects on congruency effects in antisaccade task, Eriksen flanker task and Simon task: (a) effects of lorazepam on congruency for reaction time (RT) of correct trials (latency, respectively) and (b) effects of lorazepam on congruency for error rate. Error bars indicate the standard error.

For NASA-TLX, there was no main effect of drug for the overall task load score ($p > 0.05$).

At assessment session 1 and 3, participants could not reliably guess whether they had received placebo, 0.5 mg lorazepam or 1 mg lorazepam (both $p > 0.05$). At assessment session 2, the proportion of participants guessing correctly the drug they had received was significantly above chance level ($p = 0.019$).

Discussion

The key finding is that the benzodiazepine lorazepam reduced performance in all tasks and across task conditions. With regard to inhibitory control measures, however, the drug did not affect performance indices in the same manner across tasks. While lorazepam increased congruency effects in RT and error rate for the Eriksen flanker task, for the antisaccade and Simon tasks the drug increased the congruency effect for error rate but not RT. These differential effects are in agreement with the previously demonstrated heterogeneity of the concept of inhibition (Friedman and Miyake, 2004; Rey-Mermet et al., 2018; Stahl et al., 2014). Generally, it should be noted that main effects of drug were larger than interactions of drug and task condition.

Antisaccade task

In line with previous research, we find negative effects of lorazepam on prosaccade latency (Chen et al., 2015; Ettinger et al., 2018b; Green and King, 1998; Green et al., 2000; Haas et al., 2009; Masson et al., 2000; McCartan et al., 2001) as well as antisaccade latency and error rate (Green and King, 1998; Green et al., 2000; McCartan et al., 2001). The applied doses are lower than those of most previous studies (usually 2 mg). Green et al. (2000) also examined the effect of lorazepam doses below 2 mg on an antisaccade task. Like us, they showed effects to be dose-dependent. Importantly, we also report, for the first time, an interaction between task condition (prosaccade vs. antisaccade) and drug for error rates, but not latencies. This finding, which indicates greater impact of the drug on performance accuracy for antisaccades than prosaccades, might help understanding the precise mechanisms of inhibitory control in this task.

Specifically, there is disagreement in the literature on how to explain successful antisaccade generation (Hutton, 2008). In parallel programming models (Massen, 2004), an erroneous prosaccade is cancelled if the antisaccade response is generated fast enough. Thus, no separate stop or inhibition process is necessary. According to this type of model, comparable increases in both antisaccade and prosaccade latencies should not lead to a selective increase in rate of direction errors in antisaccades compared to prosaccades (Massen, 2004). Thus, our findings of (i) comparable increases in antisaccade and prosaccade latency and (ii) a significantly greater increase in direction errors in the antisaccade than the prosaccade condition question these assumptions. Instead, our findings are in line with the assumption that an additional process may be necessary, as postulated by the LATER (linear approach to threshold with ergodic rate) or SERIA (stochastic, early reaction, inhibition, and late action) models. The Linear approach to threshold with ergodic rate (LATER) model (Noorani and Carpenter, 2013, 2016) involves a go unit for the prosaccade, a go unit for the antisaccade and a stop unit. Transforming the stimulus position to the opposite goal position takes some time and, therefore, the activation of the antisaccade unit is delayed. The stop unit inhibits the erroneous prosaccade. The stochastic early reaction, inhibition, and late action (SERIA)

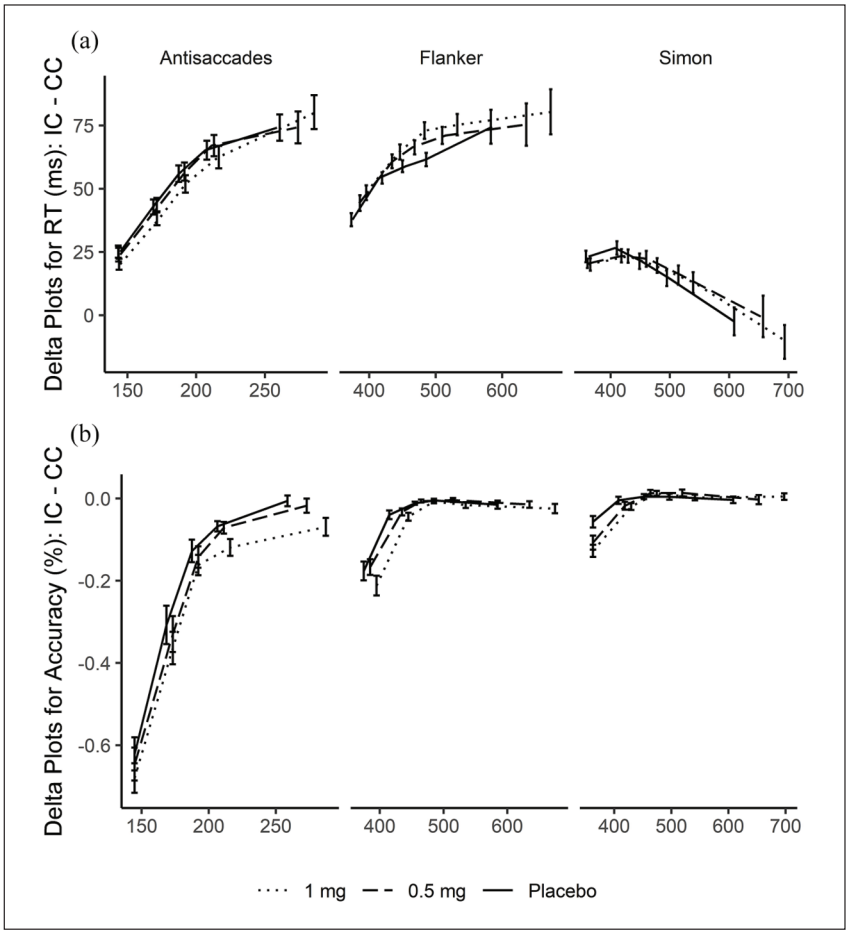

Figure 5. Lorazepam effects in delta plots: (a) delta plots for reaction time (RT) of correct trials (latency, respectively) and (b) delta plots for accuracy (percent correct). In delta plots, congruency effects of each quantile are plotted against the respective RT. Error bars indicate the standard error.
CC: congruent condition; IC: incongruent condition.

Table 2. Descriptive statistics of VAS and NASA-TLX.

	Placebo	Lorazepam 0.5 mg	Lorazepam 1 mg
VAS (*N* = 50)			
Anxious	5.78 (9.89)	2.82 (4.18)	3.94 (6.12)
Attentive	49.4 (25.24)	42.12 (26.83)	31.7 (26.76)
Restless	17.98 (22.54)	12.02 (16.97)	18.24 (24.61)
Tired	52.5 (29.6)	57.48 (27.43)	69.7 (27.04)
Carefree	51.36 (33.49)	60.56 (29.52)	56.36 (30.62)
My thoughts are racing	16.88 (20.52)	13.04 (20.18)	11.24 (13.77)
I have self-control	75.7 (22.2)	64.6 (30.38)	57.14 (29.08)
Elevated mood	46.62 (26.44)	42.46 (25.06)	38.84 (27.17)
Energetic	35.92 (25.47)	32.04 (26.17)	28.42 (25.69)
Irritable	11.88 (18.46)	11.06 (18.1)	12.34 (17.35)
NASA-TLX (*N* = 50)			
Overall task load	39.41 (15.7)	40.89 (15.56)	42.53 (13.75)

Numbers indicate the mean (standard deviation) for each item in arbitrary units from 1 to 100. Higher numbers indicate stronger agreement on the respective scale.
NASA-TLX: NASA task load index; VAS: visual analog scales.

model (Aponte et al., 2017) extends the LATER model by adding a further process that can account for late pro- and antisaccades. Early errors are explained as a failure of inhibition and late errors as the result of a late race between both saccade types. Regarding our data, both models accommodate the interpretation that lorazepam may have had an impact on a dedicated stop process, while also equally affecting saccade generating units of both antisaccades and prosaccades.

Eriksen flanker task

Benzodiazepine effects on RT and error rates in congruent and incongruent flanker task conditions have been shown previously (Bruijn et al., 2004; Clariá et al., 2011; Riba et al., 2005). We replicate this finding and extend it into a lower dose range. In addition, we find an interaction between task condition and drug, both for RT and error rates, suggesting specifically impaired inhibitory control under lorazepam. In previous studies, these interactions were either not significant (Bruijn et al., 2004; Riba et al., 2005) or not reported (Clariá et al., 2011).

The Eriksen flanker task measures the ability to solve the conflict arising between a central target and peripheral distractors. The task is used not only to measure distractor interference, but also for selective visual attention (Eriksen and Eriksen, 1974; LaBerge et al., 1991). Both processes are closely related, since selective attention is required to identify relevant stimuli and to ignore irrelevant distractors (Moorselaar and Slagter, 2020; Treisman, 1969).

Solving conflicts that arise from interference is thought to involve different stages of processing (Kornblum et al., 1990; Stahl et al., 2014). At the early-stage level of response selection, there are influences of both stimulus-related interference and response interference. In the Eriksen flanker task, those are considered to be particularly important (Stahl et al., 2014). At a later processing stage, the initiated response is stopped (response inhibition). This is thought to be particularly relevant, for example, in the antisaccade task.

Other authors highlight similarities between response inhibition and distractor interference tasks, arguing that both processes are related (Friedman and Miyake, 2004). Possible explanations on the one hand are shared requirements of maintaining a task goal facing distracting stimuli or prepotent but inappropriate response tendencies (Friedman and Miyake, 2004). On the other hand, the Eriksen flanker task may require suppressing incorrect responses in incongruent trials, which might be linked to response inhibition (Ridderinkhof et al., 1999; Verbruggen et al., 2005).

As for the antisaccade and Simon tasks, lorazepam increased the congruency effect for error rate in the Eriksen flanker task, showing that lorazepam impairs the cancellation of incorrect responses. However, there was no correlation between lorazepam-induced changes in the Eriksen flanker effect and antisaccade or Simon tasks. Furthermore, lorazepam significantly increased the congruency effect for RT only in the Eriksen flanker task. This indicates that in the flanker task, processes take place that are distinguishable from other inhibitory control tasks and, furthermore, that these processes have a GABAergic basis. As elaborated above, the task places special demands on stimulus interference and selective visual attention. Lorazepam might impair the ability to focus on relevant details, causing irrelevant features to be processed more strongly (Duka et al., 1995; Giersch and Herzog, 2004; Michael et al., 2007). Drawing upon the zoom lens theory of visual attention (Eriksen and St. James, 1986), lorazepam could either slowdown the adjustment or widen the zoom lens. Our results suggest the latter, since otherwise effects on the delta plots for accuracy would be expected.

Generally, the precise inhibitory or attentional effects of lorazepam in the flanker task remain to be investigated further.

Simon task

In the Simon task, RT and error rate were increased under drug compared to placebo and there was an interaction between task condition and drug for error rate but not RT, similar to the results in the antisaccade task.

The Simon task is suggested to be a measure of interference control (Proctor, 2011; Simon and Small, 1969). The requested response is indicated by the relevant stimulus feature, in this case color. The location of the stimulus is an irrelevant stimulus feature, which causes a conflict between stimulus location and response location in the incongruent condition. Assuming that stimulus and response interference take place during response selection (Kornblum et al., 1990; Stahl et al., 2014), differences between the Eriksen flanker and Simon tasks become apparent. In the Simon task, interference is not caused by distracting stimuli but by the irrelevant stimulus feature location. Therefore, it can be assumed that there is, if any, only little stimulus conflict.

This would make the processes that unfold in the Simon task more similar to those that occur in the antisaccade task: an automatically generated response in one direction must be suppressed. This apparent similarity is also reflected in our results. As in the antisaccade task, lorazepam significantly increased the congruency effect for error rate but not RT. Furthermore, the change in congruency effect for error rate from placebo to 1 mg lorazepam correlated between the two tasks. Lorazepam may, therefore, reduce inhibitory control in both tasks in a similar manner. Previous literature also supports the presence of an active inhibition mechanism in the Simon task. Specifically, Verbruggen et al. (2005) observed an interaction between stopping an initiated response in a stop-signal task and resolving interference control in the Simon task.

Overall, the precise cognitive processes that are affected by lorazepam in the Simon task remain to be investigated further.

Delta plot analysis

It might have been expected that lorazepam effects on inhibitory control would also be reflected in the delta plots, extending previous work of dopaminergic influences (Ridderinkhof, 2002). However, this was not the case. Lorazepam did not significantly alter the slopes for RT or accuracy. This indicates that lorazepam had comparable effects on RT and error rates in early and later segments of the response time distribution. Thus, we conclude that delta plots provide measures of cognitive processes that are not sensitive to GABAergic effects, at least not in these tasks and at the studied doses. Assuming that delta plots for RT reflect the gradual build-up of selective inhibition and delta plots for accuracy reflect direct activation, neither of these processes appears to have been selectively impaired by lorazepam or, otherwise, the model does not seem to represent the processes that are impaired. It is important to note that selective inhibition is not identical

with the broader construct of inhibitory control. However, as there were effects of lorazepam on the suppression of incorrect responses in the incongruent conditions of all tasks, it can be hypothesized that inhibitory control under lorazepam is not built up more slowly, but is simply less effective.

Delta plot analysis also provided evidence of differences in the mechanisms underlying performance on the three inhibitory control tasks in this study. Delta plots for RT were positive in slope for the Eriksen flanker and antisaccade tasks. For the Simon task, delta plots for RT were negatively sloped and for later segments congruency effects were even reversed. According to Ridderinkhof (2002), delta functions extending below zero may indicate the build-up of an active suppression mechanism over time. This suppression is stronger for slow responses and can therefore even lead to an overshoot, reflected in negative congruency effects. Generally, a reason for different shapes in delta plots might be the temporal lag between task relevant and irrelevant activations (Hübner and Töbel, 2019; Jong et al., 1994). As stimulus location in the Simon task is processed faster than the relevant feature (color), the temporal overlap of different activations is smaller than in the Eriksen flanker task where target and distractors are processed similarly fast. Overall, these differences lead to a lower conflict in the Simon task, especially for slow responses.

In accordance with these considerations, the Simon effect was significantly smaller overall than both other congruency effects, for RT and accuracy.

Neural mechanisms

The neural mechanisms that mediate the negative impact of lorazepam on inhibitory control remain unknown and should be further investigated.

In rodents, different subtypes of $GABA_A$ receptors were shown to be responsible for sedative effects, anxiolytic effects, and cognitive functions (Chen et al., 2012; Uusi-Oukari and Korpi, 2010). The use of selective $GABA_A$ agonists in future could further clarify whether the drug-induced impairments in inhibitory control observed here are more likely due to cognitive or sedative effects.

A large cortical network is involved in the neural mechanisms of inhibitory control (Aron and Poldrack, 2006; Friedman and Miyake, 2017) and although GABA receptors are distributed throughout the entire brain (Fonnum, 1987), there are only few studies directly investigating the role of GABA in response inhibition and interference control.

Magnetic resonance spectroscopy (MRS) and transcranial magnetic stimulation (TMS) studies suggest higher GABA concentrations in primary motor cortex (Sohn et al., 2002; Wessel et al., 2013; Wildenberg et al., 2010a), pre-supplementary motor area (Hermans et al., 2018), and basal ganglia (Haag et al., 2015; Quetscher et al., 2014) to be associated with better performance in inhibitory control tasks.

However, TMS manipulations do not provide data on natural GABA release, uptake, and concentration (Sumner et al., 2010) and are, therefore, complementary to our approach of direct GABAergic modulation. Likewise, MRS studies are difficult to reconcile with our findings, given that lorazepam does not selectively affect specific areas. Instead, our results implicate that increased GABA activity in many brain areas may be harmful for successful performance.

An often-studied drug, which is associated with GABA release, is alcohol (Kelm et al., 2011). Besides somewhat comparable phenomenology, alcohol has also been shown to have negative effects on inhibitory control (Day et al., 2015), suggesting that direct comparisons between benzodiazepines and alcohol may be of value in this line of research.

A further lead with regard to the neural mechanisms of these effects comes from the hypothesis that variation in levels of arousal may critically modulate inhibitory control (Hasher et al., 2007). The idea that reduced activity in brain arousal systems may be an explanation of reduced inhibitory control is supported both by studies of time-of-day effects (Hasher et al., 2007) and by our own findings of lorazepam, a drug that has sedative, arousal-reducing effects (Brignell et al., 2007).

Subjective effects

Benzodiazepines are used in the treatment of anxious and agitated states and have pronounced and fast-acting effects in relevant patient groups (Ashton, 1994). An expected finding was that our sample of healthy participants reported they were less attentive and more tired with lorazepam, confirming sedative effects of the drug (Baldwin et al., 2013). In addition, participants described themselves as less in control under lorazepam, a self-report that corroborates our findings from the inhibitory control tasks.

Contrary to the clinical use of lorazepam, however, there were no effects on subjectively perceived anxiety. This may be due to the fact that state anxiety levels in this healthy sample in an affectively rather neutral environment were relatively low overall.

Limitations

A general caveat in the interpretation of our findings is that lorazepam induced performance decline across tasks and conditions and impairments on the subjective level. This might indicate general cognitive and physiological effects, limiting our ability to draw conclusions regarding specific effects on inhibitory control.

A further limitation of the study is that we did not measure lorazepam concentrations in blood. These may have been helpful to provide a more comprehensive understanding of the drug's effects and their relation with performance.

Additionally, resulting from a lack of extensive previous studies, most of our analyses were exploratory. Therefore, confirmatory analyses as well as replications are required. Furthermore, the neural mechanisms of the effects reported in this study remain unknown. Accordingly, it would be of considerable interest to apply inhibitory tasks with concurrent measures of brain function in order to obtain a fuller understanding of GABAergic effects. Finally, future work may also elaborate mathematical modeling approaches to data from inhibitory control tasks, such as drift diffusion models (Voss et al., 2013; White et al., 2011).

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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Data availability statement

Data and code can be found online (https://osf.io/ts5b9/).

Supplemental material

Supplemental material for this article is available online.

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APPENDIX E [Publication Study 3]

Aponte, E. A., **Faßbender, K.**, Heinzle, J., & Ettinger, U. (2022). Gabaergic modulation of conflict adaptation and response inhibition. *BioRxiv*, 2022.03.03.482762. https://doi.org/10.1101/2022.03.03.482762

GABAergic modulation of conflict adaptation and response inhibition

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Abstract

Adaptive behavior is only possible by stopping stereotypical actions to generate new plans according to internal goals. It is response inhibition —the ability to stop actions automatically triggered by exogenous cues— that allows for the flexible interplay between bottom-up, stimulus driven behaviors, and top-down strategies. In addition to response inhibition, cognitive control draws on conflict adaptation, the facilitation of top-down actions following high conflict situations. It is currently unclear whether and how response inhibition and conflict adaptation depend on GABAergic signaling, the main inhibitory neurotransmitter in the human brain. Here, we applied a recently developed computational model (SERIA) to data from two studies (N=150 & 50) of healthy volunteers performing Simon and antisaccade tasks. One of these datasets was acquired under placebo-controlled pharmacological enhancement of GABAergic transmission (lorazepam, an allosteric modulator of the GABA-A receptor). Our model-based results suggest that enhanced GABA-A signaling boosts conflict adaptation but impairs response inhibition. More generally, our computational approach establishes a unified account of response inhibition and conflict adaptation in the Simon and antisaccade tasks and provides a novel tool for quantifying specific aspects of cognitive control and their modulation by pharmacology or disease.

Author Summary

Our capacity to prepare for situations that afford conflicting responses (conflict adaptation) and to stop our immediate impulses in these scenarios (response inhibition) are the hallmark of cognitive control. As these abilities require both the *stopping* or *slowing* of response tendencies, a natural question is whether they are mediated by inhibitory neurotransmission in the brain. Here, we combined computational modeling with two experiments to investigate how conflict adaptation and response inhibition interact with each other (experiment 1) and how these are modulated by lorazepam (experiment 2), a positive modulator of the GABA-A receptor, one of the main inhibitory receptors in the human brain. Using our computational model to disentangle conflict adaptation and response inhibition, our results indicate that while lorazepam impaired response inhibition, it improved conflict adaptation. Thus, our results suggests that conflict adaptation is mediated by GABA-A neurotransmission.

Introduction

When confronted with sudden changes in circumstances, cognitive control becomes imperative: this not only involves stopping the previous course of action, but also selecting and executing a new plan tailored to the changing environment (1). In the motor domain, actions are often programmed and executed automatically - for example, turning the eyes to an unexpected visual stimulus - and need to be stopped in time so that an alternative action can be executed. When environmental cues induce such response conflicts, one major challenge is to inhibit reflexive or prepotent behaviors that start without reflection or planning, i.e. exercise *response inhibition* (2,3). Response inhibition is one component of cognitive control in anticipation of upcoming challenges (4). Additionally, cognitive control manifests through the facilitation of strategic or goal-directed actions and typically increases following the experience of response conflicts, a phenomenon called *conflict adaptation* (4–6).

Despite our considerable understanding of the neurobiology of response inhibition (7–11) and conflict adaptation (4,12–15), it remains unclear to which extent stopping automatic behaviors in favor of goal-directed actions relies on GABAergic signaling, the main inhibitory neurotransmitter in the brain. It is also unknown whether the behavioral adjustments that follow high conflict situations are mediated by GABAergic signaling. However, indirect evidence indicates that response inhibition is associated with GABAergic neurotransmission (16–20).

One limitation of previous studies that tried to pin down the role of GABAergic signaling in response inhibition and conflict adaptation is the absence of computational models that statistically formalize the interplay between controlled and automatic behaviors. Indeed, while dual-process models postulate the existence of controlled and automatic actions (21–23), mathematical formalizations of their interaction are still rare (but see (24,25)).

81 Recently, we introduced the *Stochastic Early Response, Inhibition and late*
82 *Action* (SERIA) model for the antisaccade task (Aponte et al., 2017), one of the
83 main paradigms used to measure response inhibition when secondary actions
84 are required (see Fig. 1). SERIA combines the "horse-race" model, used in the
85 stop signal task (27,28), with a linear ballistic accumulation model that
86 decides between controlled actions. The interplay between automatic and
87 controlled behaviors is mediated by a latent inhibitory process that races
88 against the automatic, fast process. In a series of studies (26,29,30) , we have
89 shown that SERIA accurately explains reaction time (RT) distributions and
90 error rates (ER), and predicts several features of the antisaccade task in a
91 variety of conditions.

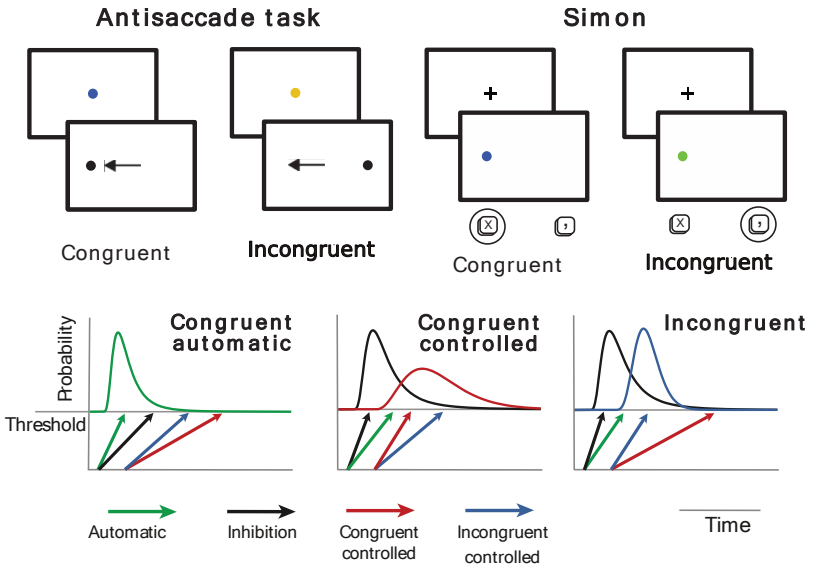

Figure 1: **Antisaccade task.** A central fixation cue was presented for 1000 to 2000ms. Its color (blue or yellow) indicated subjects to saccade to the peripheral stimulus (congruent trial) or to saccade in the opposite direction (incongruent trial). The peripheral stimulus was presented for 1000ms. **Simon task.** Subjects were instructed to press a left ('x') or right (',') key depending on the color (blue or green) of a peripheral cue (display duration 1500ms) following a fixation period of 500ms. On congruent trials, the right-left location of the cue and the correct button matched each other; on incongruent trials, they were in opposite locations. **SERIA model.** Reaction times and actions are assumed to be the outcome of a race to threshold between independent linear accumulators (processes), whose slopes take different, random values on each trial. Initially, the automatic process starts after a short delay from the cue presentation. This process can be stopped by the inhibitory process, if the latter is the first to hit threshold. When this occurs, the outcome of the race between two controlled processes that represent congruent and incongruent responses decides the action. The reaction time on a trial is assumed to be the threshold-hit-time of the corresponding process.

A second paradigm commonly used to measure response inhibition and conflict-induced cognitive control is the Simon task (31). On incongruent trials, an irrelevant spatial feature of the stimulus conflicts with the cued response (for instance, a green colored cue on the right indicating a left key press, when only the color of the cue is relevant). This condition is characterized by slower and more error-prone actions compared to congruent trials, in which the response and the irrelevant spatial location of the stimulus

coincide. The difference in RT and ER between incongruent and congruent trials is called the Simon effect, or, more generally, the congruency effect. The advantage of congruent trials reverses after incongruent trials (i.e., high conflict trials), as conflict induced control slows congruent responses and facilitates incongruent responses (4,32).

In this study, we set out to investigate the role of GABA signaling in response inhibition and conflict adaptation during the antisaccade and Simon tasks. In the first experiment, we confirmed the validity of SERIA in the antisaccade task and demonstrated that the model can be extended to the Simon task. Specifically, SERIA offers a quantitative and comprehensive explanation of the Simon effect, its time course, and its reversal after high conflict trials. To this effect, data from 164 healthy adults performing both tasks were collected and SERIA was applied to trial-by-trial RT.

In the second experiment, we applied the same computational model to a recently published dataset (33) in order to determine the effects of a pro-GABAergic drug on response inhibition and conflict adaptation. Fifty subjects performed the same protocol as in Exp. 1 under placebo, 0.5 and 1.0 mg of the benzodiazepine lorazepam, an unspecific, positive allosteric modulator of the GABA-A receptor. In addition to the expected sedative effect of lorazepam, we found that enhanced GABA-A signaling *boosted* conflict adaptation but *impaired* response inhibition.

Results

The primary goal of Exp. 1 was to verify that response inhibition and conflict adaptation can be explained using SERIA as a single, unified probabilistic model of the antisaccade and Simon tasks. This entails showing that SERIA captures the main qualitative *and* quantitative features of subjects' responses. Thus, we examined if the mean reaction times (RT) and error rates (ER) as well as the RT distributions could be predicted by our model after fitting trial-by-trial responses. Note that the model was never exposed to descriptive statistics (e.g., mean reaction times) or their distributions. Rather, the single input to the model was the list of actions (congruent or incongruent responses) and the corresponding RT of every subject. Therefore, we used the generative nature of the model to *predict* mean statistics and the shape of the RT distributions based on the distribution of the posterior parameters.

The second goal of Experiment 1 was to dissect the explanation that SERIA offers for the congruency effect and for conflict adaptation. Hence, we investigated how different model-parameters change across congruent and incongruent trials, and how these changes interact with the conflict level of previous trials.

Experiment 1

In Exp. 1, from 164 subjects, two were excluded from the analysis of the Simon task because of the elevated number of errors or missing trials (see Methods). The number of excluded subjects increased t o 12 in the antisaccade task, as 11 subjects had 50% or more trials excluded and one subject's ER was higher than 80%.

For clarity, in the following, "conflict level" refers to the *N-1* trial. Congruent trials are considered low conflict trials, and incongruent trials high conflict trials.

Fig. 2 displays the mean RT and ER in all conditions. As expected, in the antisaccade task, subjects were slower ($\Delta = 77$ms; $P < 10^{-5}$) and generated

more errors ($\Delta = 24\%; P < 10^{-5}$) on incongruent trials compared to congruent trials. No conflict adaptation was evident in this task, as the congruency effect *in*creased slightly after high conflict trials (8ms; P=0.023). Regarding ER, we again found no evidence of conflict adaptation as the congruency effect was significantly *higher* after high conflict trials compared to low conflict trials ($\Delta = 9\%; P = 0.004$).

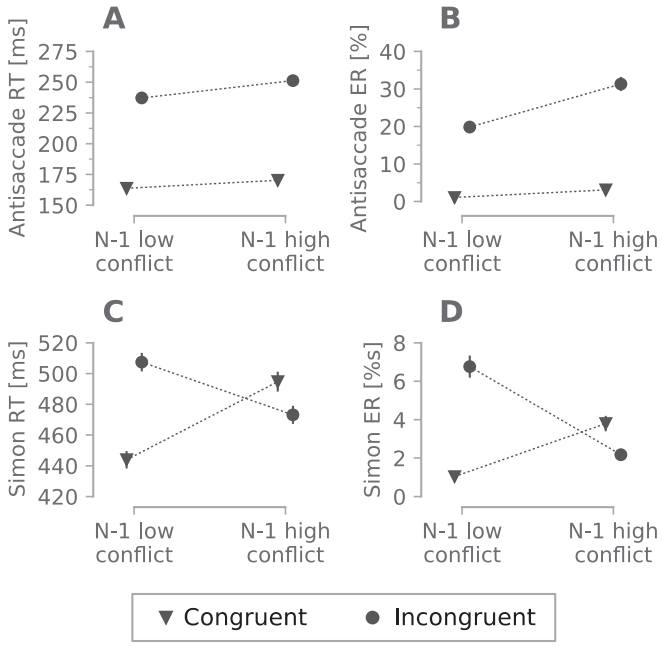

Figure 2: A) Mean RT in the antisaccade task. **B)** Mean ER in the antisaccade task. **C)** Mean RT in the Simon Task. **D)** Mean ER in the Simon task. N-1 refers to the corresponding previous trials. Error bars display the sem.

In the Simon task (Fig. 2C&D), incongruent responses were slower ($\Delta = 21ms, P < 10^{-5}$) and more error prone than congruent responses ($\Delta = 2\%, P < 10^{-5}$). More importantly and in contrast to the antisaccade task, conflict adaptation was observed following high conflict trials. Indeed, the congruency or Simon effect was 63ms after low conflict trials and -22ms after high conflict trials, resulting in a significant interaction between conflict and congruency ($\Delta = 85ms, P < 10^{-5}$). This interaction was driven by two

different factors: congruent responses were slower after high conflict trials ($\Delta = 51ms; P < 10^{-5}$) whereas incongruent responses were faster ($\Delta = -34ms; P < 10^{-5}$). ER followed the same pattern (see Fig. 2D), with a inversion — from positive to negative — of the Simon effect indicated by a significant interaction ($P < 10^{-5}$).

Could SERIA capture the RT distributions of congruent and incongruent trials in both tasks? To answer this question, we fitted SERIA to the RT of each subject in each condition. All group fits displayed here are the weighted average over subjects.

Fig. 3A&D demonstrate that all distributions were fitted with great accuracy. Moreover, the predicted and empirical mean RT and ER closely matched each other (Supp. Fig. 1.) A possible objection here is that congruent responses are not bimodally distributed and consequently there is no evidence that these were generated by two different processes. To answer this objection, we compared SERIA to a simpler model in which all congruent responses originate from a single unimodal distribution. Bayesian model comparison clearly demonstrated that the explanatory power of models (balance between fit and complexity) profited from including a controlled process in the generation of congruent responses (see Supp. Table 1 & 2), even after controlling for the number of parameters. This replicates and extends our previous findings (26,30).

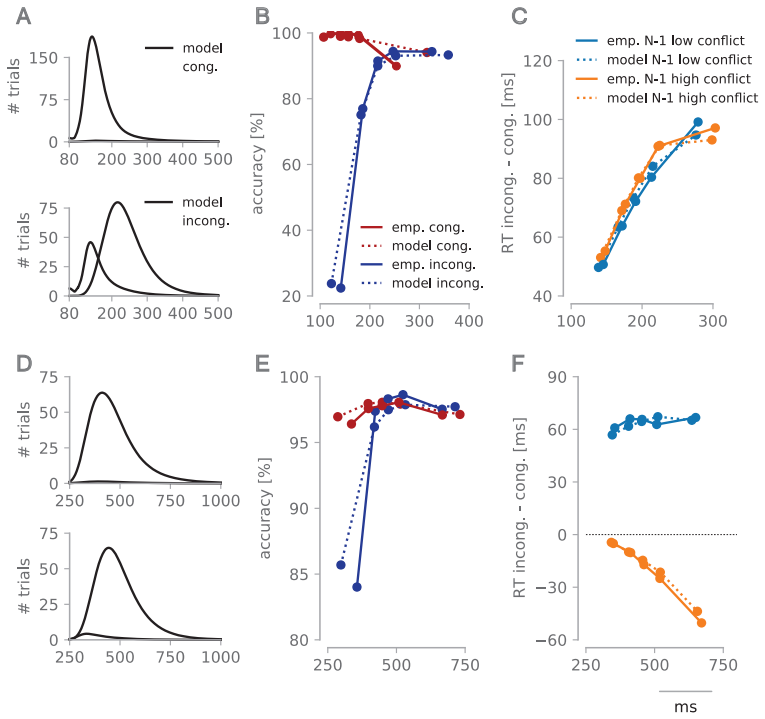

Figure 3: Model fits and distributional analysis. Top row: Antisaccade task. Bottom row: Simon task. **A)** Reaction time (RT) distributions in the antisaccade task. Histograms show empirical data and solid black lines display the model fits. **B)** Accuracy function in the antisaccade task. Accuracy plots were generated by sorting trials in RT percentiles (20, 40, 60, 80 and 100%) and plotting the mean accuracy in each percentile against the corresponding mean RT. **C)** Delta plot in the antisaccade task. As with the accuracy plots, in delta plots trials are binned in RT percentiles and the congruency effect (the difference between mean RT on incongruent and congruent trials) is plotted against the pooled mean RT. **D-F)** RT distribution, accuracy and delta plot in the Simon task, similar to A-C.

Rather than merely predicting the RT histograms, we aimed to reproduce and explain the time course of the congruency effect revealed by delta plots (21). In this analysis, trials are binned in RT quantiles and either the accuracy or the RT congruency effect (i.e., the difference in RT between incongruent and congruent trials) are plotted against the quantile-specific mean RT.

As shown in Fig. 3B&E, the accuracy function followed the same pattern in both tasks, with errors on incongruent trials occurring predominately at low latencies, suggesting that most errors are indeed inhibition failures. Yet, errors

were still possible even at the highest time bins, with similar error rate in congruent and incongruent trials. In general, SERIA could accurately reproduce the accuracy functions.

Despite other qualitative similarities between the two tasks, the Simon effect and the antisaccade cost for RT followed widely different time courses (see Fig. 3C&F). The antisaccade RT cost was always positive and increased with latency in all conditions. By contrast, after high conflict trials, the Simon effect was negative and declined as a function of latency. Yet, after low conflict trials, the Simon effect was positive and changed only minimally across time bins. Qualitatively, the model captured the delta plots with great accuracy in both tasks.

Having shown that indeed SERIA can correctly capture response inhibition and conflict adaptation in the Simon task, we can now ask how the model explains the negative Simon effect after high conflict trials, and why is the slope of the delta plot negative in this condition?

To answer the first question, we note that according to SERIA congruent responses can be generated by either the controlled or the automatic process. Thus, the congruency effect can be approximated by the weighted difference between the RT of incongruent responses and the two types of congruent responses (controlled and automatic):

$$Cong.effect = P_{automatic} * [(incong.RT - automatic\ cong.RT] + (1 - P_{automatic}) * [incong.RT - controlled\ cong.RT],$$

where $P_{automatic}$ is the probability of an automatic response. This probability weights the contribution of the automatic (congruent) process to the overall mean congruent response RT. To understand the congruency effect and how conflict-induced adaptation interacted with it, we examined the contribution of controlled and automatic responses separately.

In the Simon task, after low conflict trials, there was only a small RT difference between controlled congruent and incongruent responses ($\Delta = 9$ms; Fig. 4D). Despite this small difference, the contribution of fast, automatic responses

(approximately 30% of congruent responses, Fig. 4F) led to an overall large Simon effect (predicted by the model to be $\Delta = 60$ms) as automatic responses (Fig. 4E) were on average much faster than controlled incongruent responses ($\Delta = 155$ms). In other words, after low conflict trials, the bulk of the Simon effect was caused by the difference between controlled incongruent and automatic congruent responses.

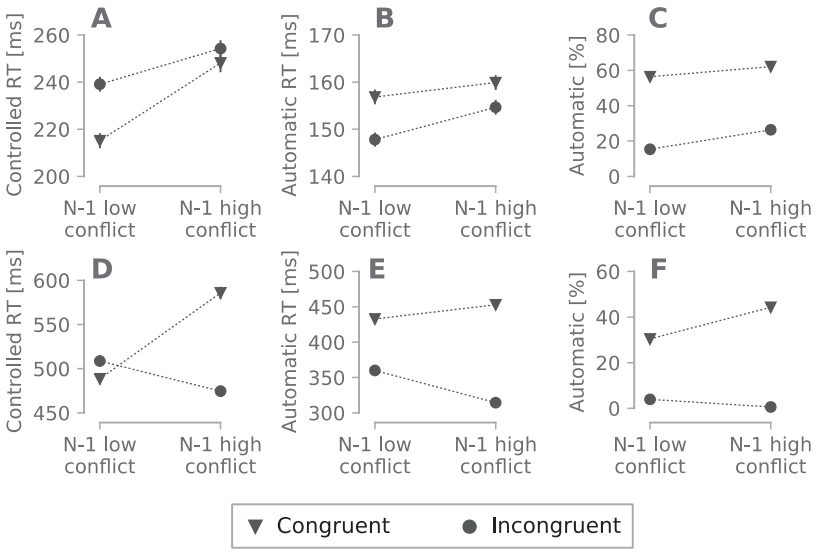

Figure 4: Model based analyses. Top row: Antisaccade task. Bottom row: Simon task. **A)** Reaction time (RT) of *correct* controlled congruent and incongruent responses in the antisaccade task. **B)** RT of automatic responses in congruent and incongruent trials in antisaccade task. **C)** Probability of an automatic response in the antisaccade task. **D-F)** Similar to A-C in the Simon task. Error bars display the standard error of the mean.

By contrast, congruent responses generated by the controlled process were much slower after a high conflict trial than after a low conflict trial ($\Delta = 97ms; P < 10^{-5}$; Fig. 4D). In other words, conflict-induced adaptation specifically slowed controlled congruent responses and this large inhibitory effect explained, to a large extent, the inversion of the Simon effect after high conflict trials. In addition, incongruent responses were facilitated after high conflict trials, as evidenced by reduced RT ($\Delta = 33ms, P < 10^{-5}$; Fig. 4D).

Thus, conflict adaptation in the Simon task was expressed both as inhibition of congruent responses as well as facilitation of incongruent responses.

The antisaccade task displayed an analogous effect. Controlled congruent responses were considerably slower after high conflict trials, compared to low conflict trials ($\Delta = 32ms; P < 10^{-5}$; Fig. 4A). Importantly, this was not directly observable in the empirical mean RT because automatic responses were the dominant component in the congruent condition (61% of all responses; Fig. 4C), masking the contribution of controlled responses. However, in contrast to the Simon task, incongruent responses were also slower after the high conflict condition ($\Delta = 14ms$; $P < 10^{-5}$; Fig. 4A).

The previous analysis explains the congruency effect and conflict adaptation across tasks and conditions but it does not explain its *time course*, i.e., it does not explain the negative slopes in the delta plot in the Simon task. Because the bulk of conflict adaptation was caused by the inhibition of controlled congruent responses, we investigated them in isolation by removing automatic responses from the model predictions. In other words, we used SERIA to predict the distribution of controlled responses in the absence of automatic responses (see Methods). In addition, we plotted the time course of the congruency effect when only the distributions of *controlled* responses were taken into account.

Fig. 5 demonstrates that negative slopes in the delta plots are neither unique to the Simon task nor to trials following high conflict conditions. Instead, the variance of congruent controlled responses was higher than the variance of incongruent responses in all conditions and tasks, leading to negative delta plot *slopes* in this analysis (34). However, this effect was masked by the contribution of automatic responses, especially in the antisaccade task. Hence, conflict adaptation led to negative delta plots in post-conflict trials in the Simon task, but negative *slopes* were a more general effect caused by the high variance of congruent controlled responses.

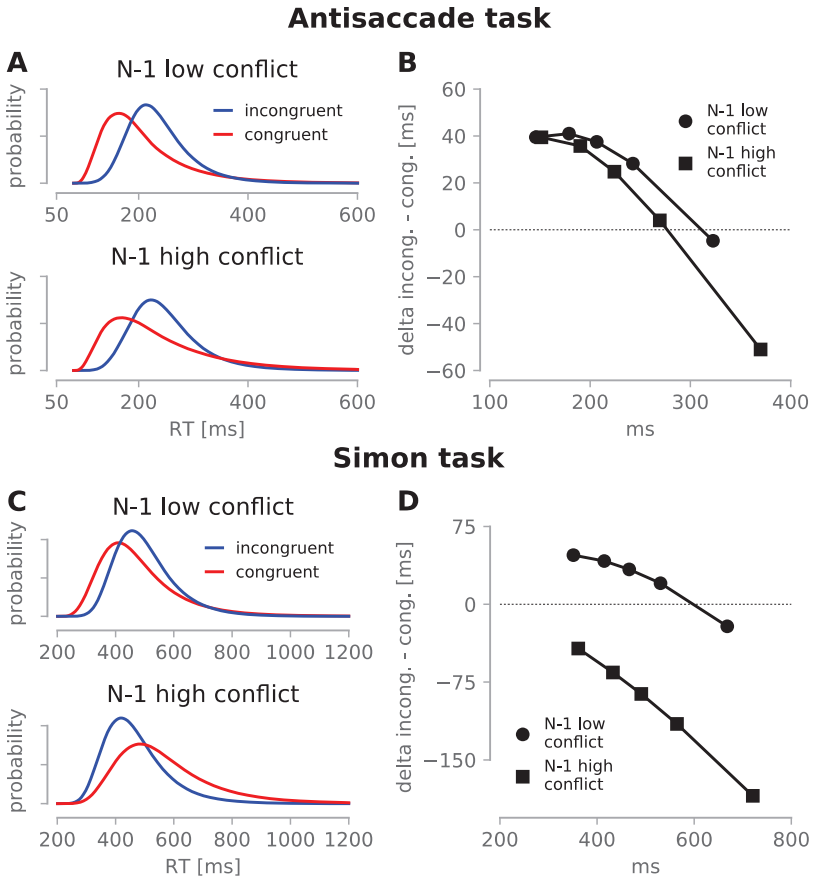

Figure 5: Model based analyses of controlled responses. Top row: Antisaccade task. Bottom row: Simon task. **A)** Normalized reaction time (RT) distribution of controlled responses in the antisaccade task. **B)** Delta plots between the distribution of controlled response in the antisaccade task. **C & D)** Similar to A and B, but for the Simon task. Congruent responses were more variable than incongruent responses in both tasks. This led to delta plots with negative slopes in all conditions. However, only after high conflict trials in the Simon task, the congruency effect was negative in all time bins.

262 However, the main explanation for conflict adaptation in the Simon task was
263 the inhibition of congruent controlled responses across all time bins, which is
264 evidenced by Fig. 5D as negative delta plots. In other words, conflict adaptation
265 in the Simon task manifests as an overall inhibition of congruent controlled
266 responses, which is separable from the negative *slope* of the delta plots. This

267 is absent in the antisaccade task, where no significant conflict adaption was
268 detected.

269 The success of SERIA in fitting the data from these two tasks begs the question
270 whether these paradigms, both considered well validated response inhibition
271 or interference control tasks, measure similar biological functions. If that were
272 the case, we expected that the model-based estimates would correlate across
273 tasks. However, neither the percentage of automatic responses nor their RT,
274 as estimated by SERIA, were significantly correlated after correcting for
275 multiple comparisons (Supp. Table 9). In a purely behavioral analysis, there
276 was a significant but weak correlation between ER on incongruent trials ($r =$
277 $0.208, P < 10^{-3}$ across tasks (Supp. Table 10), but this correlation should be
278 interpreted with caution because subjects rarely made errors in the Simon
279 task (mean ER $< \%5$) and in 30% of cases did not make any at all (Supp. Fig.
280 2).

281 Three main conclusions can be drawn from Exp. 1. First, the same principles
282 can be used to describe and predict behavior in the antisaccade and Simon
283 tasks. Specifically, congruent responses can be generated by a fast but
284 automatic process or by a controlled but slow process. Moreover, response
285 inhibition arbitrates between these two components in a time dependent
286 fashion.

287 The second main conclusion is that after high conflict trials, controlled
288 congruent responses are inhibited as demonstrated by post-conflict slowing.
289 In the Simon task, this led to a negative congruency effect. In the antisaccade
290 task, SERIA also revealed a slowing of congruent responses. However, the delta
291 plot analyses (Fig. 5 B & D) reveals the key difference between tasks: there
292 was generalized slowing in the Simon task but not in antisaccade task, which
293 explains the absence of post-conflict slowing in the latter paradigm.
294 Complementary to the inhibition of congruent responses, incongruent
295 responses were facilitated in the Simon task, but not in the antisaccade task.

296 Finally, our analysis suggests that one of the most remarkable properties of
297 the Simon task — the negative time course of the congruency effect — is likely
298 not specific to this task and not only caused by the inhibition of automatic
299 responses (21–23). Rather, negative slopes are partly caused by the high
300 variability of congruent controlled responses. However, this effect was
301 masked in the antisaccade task, where most congruent responses were
302 automatic. An analogous phenomenon occurred after low conflict trials in the
303 Simon task, but this effect was again hidden by the contribution of automatic
304 responses.

305 These findings set the stage for investigating the role of GABA-A signaling in
306 response inhibition and conflict adaptation using SERIA. The former is
307 reflected by the probability and latency of automatic responses. If response
308 inhibition is facilitated by GABA-A, enhanced GABA-A activity should lead to
309 *fewer* automatic responses with shorter latencies, as the inhibitory process
310 would only fail to stop the fastest automatic actions. This hypothesis can be
311 directly tested using computational modeling, as the effect of GABA-A on
312 voluntary responses can be disentangled from the causes that may lead to
313 decreased performance in the Simon and antisaccade task under
314 benzodiazepines. Increased cognitive control should manifest as higher
315 conflict adaptation expressed by either stronger inhibition of congruent
316 controlled responses or by facilitation of incongruent responses after high
317 conflict trials. In Exp. 2, we investigated the effect of lorazepam (a nonselective
318 positive allosteric modulator of the GABA-A receptor) on the Simon and
319 antisaccade tasks in a new sample.

320 *Experiment 2*

321 Data from Exp. 2 were previously reported in (33). The same tasks were
322 administered in Exp. 1 and 2 but in Exp. 2, each subject (N=50) participated
323 in three sessions, in which either placebo or lorazepam (0.5 or 1.0mg) were
324 administered. We excluded subjects from the final analysis if any of the three
325 sessions would be excluded by the criteria used in Exp. 1. This left 38 valid
326 subjects in the antisaccade task and 46 in the Simon task. As detailed in Supp.

Fig. 1 & 3, we replicated all behavioral and modeling findings from Exp. 1 in this independent sample. Thus, we focus here only on the effects of lorazepam.

We first analyzed RT and ER using classical statistics, recapitulating the findings in (33). RT and ER increased with dose in both tasks (Table 1; see Fig. 6). In terms of RT, lorazepam did not have a significant effect on either the antisaccade cost or the Simon effect (no significant two- or three-way interaction between drug, trial type and conflict; Supp. Table 5 & 6). The effect of lorazepam on ER in the antisaccade and Simon tasks was modulated by trial type and conflict (P=0.019 and P=0.022 respectively; Supp. Table 7 & 8).

Table 1

	Antisaccade task				Simon task		
	Congruent trials						
	Placebo	0.5mg	1.0mg		Placebo	0.5mg	1.0mg
ER [%]	1.0	1.2	1.4		1.6	2.5	2.4
RT [ms]	163	168	172		451	470	489
	Incongruent trials						
	Placebo	0.5mg	1.0mg	P	Placebo	0.5mg	1.0mg
ER [%]	21.7	23.8	27.5		2.6	4.5	4.9
RT [ms]	235	241	243		472	492	509

Lorazepam related behavioral effects. Error rate (ER) and mean reaction time (RT) increased in a dose dependent fashion.

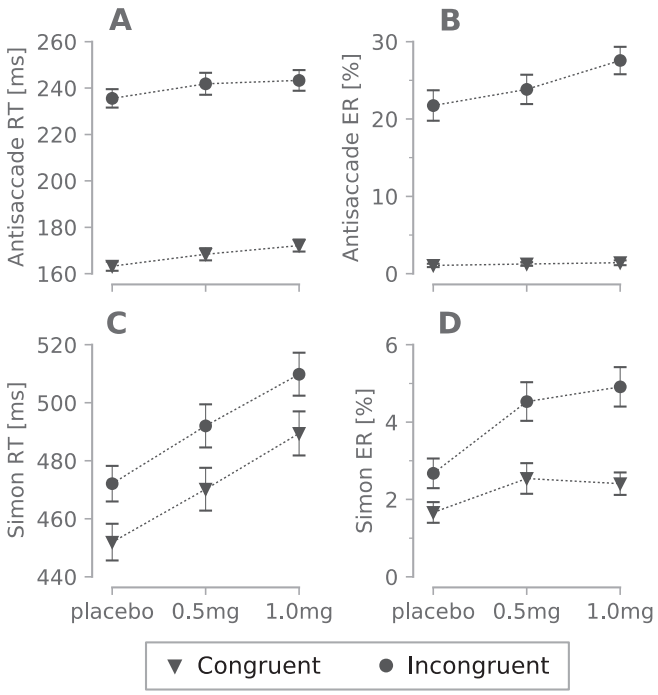

Figure 6: Effect of lorazepam (0.5 or 1.0mg) on reaction times (RT) and error rates (ER) in the antisaccade and Simon tasks. **A)** RT in the antisaccade task. **B)** ER in the antisaccade task. **C)** RT in the Simon task. **D)** ER in the Simon task. Error bars display the standard error of the mean.

337 To better understand the effect of lorazepam on response inhibition and
338 conflict adaptation, we applied SERIA to trial-by-trial RT. Lorazepam impaired
339 controlled responses as reflected by higher RT across tasks and trial types (see
340 Fig. 7 & 8). Supp. Table 13 displays the detailed breakdown and statistical
341 analysis of these effects. The latency of automatic responses increased in a
342 dose dependent fashion in the antisaccade ($P < 10^{-3}$) and Simon tasks (
343 $P = 0.11$). Lorazepam only significantly raised the number of automatic
344 responses at the 0.5mg dose in the Simon task ($P < 10^{-3}$). Thus, rather than
345 enhancing response inhibition, lorazepam impaired it in terms of the RT and
346 the probability of automatic responses in the Simon task.

One of the main findings from Exp. 1 is that the Simon effect turned negative after high conflict trials because congruent controlled responses were inhibited following high conflict trials. Can heightened GABAergic signaling enhance conflict adaptation by improving the inhibition of congruent controlled responses? Indeed, lorazepam led to a dose dependent slowing of controlled congruent responses after high conflict trials (see Fig. 7B) as evidenced by a three-way interaction between the factors drug, previous trial conflict level and trial type ($P = 0.01$). To understand this three-way interaction, we split congruent and incongruent trials and tested for interactions between drug and conflict. Incongruent controlled responses were facilitated after high conflict trials as compared to those following low conflict trials ($\Delta = -29ms; P < 10^{-5}$), but there was no significant interaction between lorazepam and conflict on those trials ($P = 0.992$). By contrast, congruent responses were slower after high conflict trials compared to low conflict trials ($\Delta = 89ms; P < 10^{-5}$), and this effect was modulated by lorazepam ($P = 0.001$). Thus, lorazepam boosted inhibitory conflict adaptation in congruent trials, but did not have a significant impact on incongruent controlled responses.

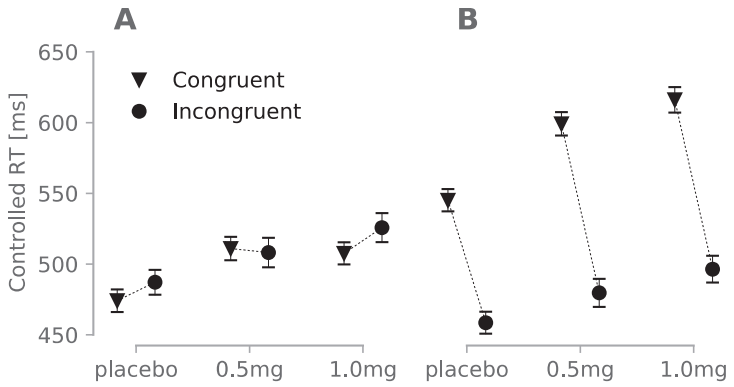

Figure 7: Mean RT of controlled responses in the Simon task. Reaction time (RT) increases as a function of dose. **A)** Trials following the low conflict (congruent) condition. **B)** Trials following the high conflict (incongruent) condition. Response interference was boosted by lorazepam, measured as the difference between controlled congruent and incongruent responses after high conflict trials.

In the antisaccade task (Fig. 8), lorazepam increased the mean RT of controlled responses ($P < 0.001$), but there was no significant three-way interaction between the factors drug, trial type and previous trial conflict ($P = 0.176$). When the effect of conflict level in the previous trial was analyzed separately on congruent and incongruent trials, lorazepam did not significantly interact with conflict level on incongruent ($P = 0.901$) but it did so on congruent trials ($P = 0.046$). Although not strong, the latter effect pointed in the same direction as in the Simon task. As suggested by Fig. 8B, this effect was particularly salient at the highest dose (1mg lorazepam).

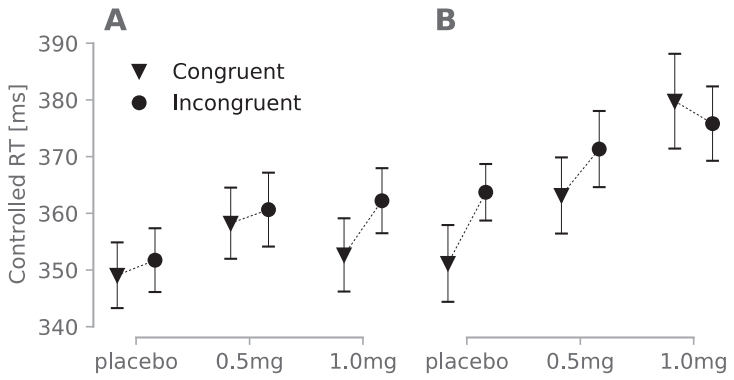

Figure 8: Mean reaction time (RT) of controlled responses in the antisaccade task. A) Trials following the low conflict (congruent) condition. B) Trials following the high conflict (incongruent) condition. Lorazepam increased congruent and incongruent RT ($P < 10^{-5}$).

374

Discussion

The concept of *response inhibition* is a pivotal construct in cognitive neuroscience and psychology. A formal model of this construct should be compatible with two broad observations: (i) some actions can be triggered in an automatic, stimulus driven manner and (ii) a more deliberative, yet slower decision process can generate a larger set of behaviors. The automatic process is tuned to situations that are either stereotypical or that require fast responses. By contrast, the second decision process allows for a richer behavioral repertoire in accordance with goals, feedback, and changes in the environment. While these observations are far from contentious, it is still an open question how these processes interact with each other.

SERIA formalizes the notion that response inhibition is the mechanism that mediates between controlled and automatic responses, and that, in two-alternative force-choice decision tasks, response inhibition is a time dependent process. Our model can be derived from these general premises by adding the assumption that the decision process between controlled actions is also a race to threshold. This is a generalization of the traditional and successful horse-race model (27) of response inhibition used in the context of the stop signal task. Because of its simplicity, SERIA can be formulated in an analytical manner and fitted to trial-by-trial RT and actions. This is in contrast to the common approach of fitting histograms or cumulative density functions (35–37).

Surprisingly, the interplay between conflict adaptation and response inhibition has not been explored in detail so far, even though both functions are seen as components of executive control and have been studied with similar paradigms. As suggested before, one reason for this is the lack of analytical computational models that bring together both functions under a single roof. One of the main results of this study is to show that a single computational model (SERIA) can explain the interplay of response inhibition and conflict adaptation in individual subjects. Specifically, our two data sets

405 demonstrated that SERIA can fully account for RT and ER in the Simon and
406 antisaccade tasks. Indeed, not only was SERIA able to accurately predict RT
407 distributions (Fig. 3A&D), mean RT and ER (Supp. Fig. 1), but it also captured
408 the time course of the congruency effect as visualized in the delta plot analysis
409 (Fig. 3B,C,E,F).

410 SERIA identified how heightened cognitive control and conflict adaptation
411 manifest after a high conflict trial: *controlled congruent responses* are slower
412 after incongruent trials, both in the Simon and antisaccade tasks. This effect
413 was not obvious in the antisaccade task because the large number of automatic
414 responses masked changes in controlled congruent responses. However, our
415 in-depth model-based analysis unveiled this change. In addition, high conflict
416 trials facilitated incongruent responses in the Simon task, while the opposite
417 effect was observed in the antisaccade task.

418 The second experiment allowed us to investigate whether response inhibition
419 and conflict adaptation are mediated by GABA-A signaling using the
420 benzodiazepine lorazepam. Regarding response inhibition, lorazepam
421 increased the latency of fast responses. However, this effect was not specific
422 as it was shared by controlled responses and was to be expected from the
423 sedative effect of benzodiazepines (38,39). Interestingly, we have previously
424 shown (40) that dopamine does not strongly mediate response inhibition in
425 the antisaccade task, whereas cholinergic modulation leads to a dose
426 dependent increase in the number of inhibition failures.

427 Lorazepam had a dose dependent effect on conflict adaptation as shown by the
428 slowing of congruent controlled responses after high conflict trials in the
429 Simon task. In other words, GABAergic signaling boosted cognitive control in
430 the Simon task.

431 Previous studies in other paradigms have suggested that cognitive control
432 manifests as amplification of task relevant information and not inhibition of
433 task irrelevant stimuli (41). While our results are in contrast to this study, it is
434 now clear (6) that findings related to cognitive control are largely domain-

specific and do not easily generalize across paradigms. For example, in our study, incongruent responses were facilitated after high conflict trials in the Simon task, but not in the antisaccade task. Nevertheless, here we offer evidence that cognitive control can be enhanced by conflict-induced GABAergic inhibition.

Our findings invite the question whether conflict adaptation is impaired in generalized anxiety, for which benzodiazepines are a common second-line treatment. Indeed, there is strong evidence that generalized anxiety has a detrimental effect on cognitive control (reviewed in (42)). More specifically, conflict adaptation but not conflict monitoring appears to be blunted in subjects with high generalized anxiety. For example, (43,44) found impaired conflict adaptation using the emotional Stroop task (45). It is worth noting that more recent studies (46,47) have found physiological differences in conflict adaptation between controls and generalized anxiety individuals, but behavioral evidence has not always been positive. However, these studies did not control for medication. Thus, one might hypothesize that benzodiazepines have a positive effect on conflict adaptation thereby normalizing this function in generalized anxiety. Interestingly, anxiety induced by the neuropeptide cholecystokinin-tetrapeptide (CCK4) leads to overactivation of the anterior cingulate cortex, an area critical for conflict adaptation (4,5), and this effect can be prevented by 1mg of the benzodiazepine alprazolam (48). To our knowledge, direct evidence of the role of benzodiazepines in conflict adaptation in anxiety is still lacking.

Other models

SERIA can be seen as a formal version of the activation-suppression model (22,23). It offers a unified conceptual and formal account of response inhibition in the antisaccade and Simon tasks and is compatible with the horse race model of the stop-signal task. However, SERIA and the activation suppression model offer different explanations for the negative slope of the delta plots in the Simon task. The activation suppression model asserts that

negative slopes are caused by the time dependent inhibition of congruent responses, which is weak at short latencies but strengthens over time.

Our computational analysis offers a subtler explanation. According to SERIA, in the antisaccade and Simon tasks, congruent controlled responses are more variable than incongruent (controlled) responses. This leads to negative slopes in the delta plot analysis when the contribution of automatic congruent responses is removed from the distribution of congruent responses (see Fig. 5). The weight of this effect is modulated by the ratio of *controlled* and *automatic* congruent responses, as the latter have shorter latencies and are less variable than controlled responses. In the antisaccade task, automatic responses are dominant, leading to delta plots with positive slopes independently of the conflict level in the previous trial. In the Simon task, automatic responses are less common, leading to directly observable negative slopes after high conflict trials.

In summary, three factors together explain the negative slopes in the Simon task: the larger variability and latency of controlled congruent responses (a factor also present in the antisaccade task), the relatively low number of automatic responses, and conflict adaptation, expressed as faster incongruent responses after high conflict trials.

Other computational models have been proposed for the antisaccade task (discussed in detail in (26,49,50) and the Simon task (24,25). Historically, the main constraint on computational accounts of the Simon effect has been the ability to simulate its negative slope as a function of time because this was initially understood as evidence that controlled and automatic processes were active in the Simon task. While this notion was soon abandoned (34), as radically different models can simulate negative slopes in delta plots (25), this constraint still plays an important role.

Among the models that have been previously proposed, a particularly interesting approach is the extension of the drift-diffusion model (DDM) suggested by (37), which simulates automatic responses through an additive

'bump' in a linear diffusion process. Through this extension, Ulrich and colleagues could simulate the time course of the Simon effect without introducing a third inhibitory process, at the cost of losing analytical tractability and the ability to fit subject-by-subject responses. Currently, it is not possible to formally compare this extension of the DDM with SERIA, as only SERIA has a tractable generative form. Nevertheless, it remains an open question whether an independent stopping process is needed to account for response inhibition.

Is response inhibition a unitary construct?

Despite of the structural similarities between the two tasks captured by SERIA, there were no significant correlations between parameter estimates across them. This negative finding reflects the accumulating evidence that the psychological construct of 'response inhibition' is heterogeneous and does not encompass a single executive function (51–53). Rather, the success of SERIA in capturing behavior under the two distinct tasks implies convergent mechanisms that depend on different biological functions.

Conclusion

This study provides a novel and comprehensive account of the congruency effect in the Simon and antisaccade tasks, its time course, and how this effect interacts with conflict adaptation. Our account is supported by formal model comparison and highly accurate model fits, e.g., of the congruency effect, generated from trial-by-trial fits. We provide evidence that in the Simon task, conflict adaptation manifests both as facilitation of incongruent responses and inhibition of congruent responses after high conflict trial. Importantly, for the first time, we show that conflict induced response inhibition and conflict adaptation are modulated by GABA-A signaling. Our finding that lorazepam differentially impacts on response inhibition and conflict adaptation suggests that positive allosteric modulators of the GABA-A receptor do not affect cognitive control equally but modulate its component processes in different

524 ways: conflict adaptation is facilitated by enhanced GABAergic signaling,
525 whereas response inhibition is impaired in an unspecific manner.

526

527 # Methods

528 *Experimental procedure*

529 The experimental procedure and data from Exp. 2 have been reported
530 previously in detail (33). Thus, we briefly summarize the protocols
531 emphasizing the difference between Exp. 1 and 2. All experimental procedures
532 were approved by the research ethics committees of the Department of
533 Psychology (Exp. 1) and the Faculty of Medicine (Exp. 2) at the University of
534 Bonn and followed the Declaration of Helsinki.

535 *Experiment 1*

536 In Exp. 1, 164 healthy subjects (mean 23 ± 3 years of age; 81 females)
537 performed the antisaccade and Simon tasks. The order in which the tasks were
538 administered was pseudorandomized across subjects. Each task consisted of
539 100 congruent and incongruent trials displayed in random order. Data from
540 Exp. 1 are first reported here.

541 Trials in the antisaccade task started with a central fixation stimulus (random
542 duration of 1000-2000ms) followed by a peripheral cue displayed for 1000ms
543 either on the left or right side of the screen (±10.3°). Subjects were instructed
544 to saccade either to the cue or in the opposite direction, depending on the color
545 of the central fixation (blue or yellow). Eye gaze was measured with an
546 EyeLink 1000 (SR Research, Canada) at 1000 Hz sampling rate. RT was defined
547 as the latency between the presentation of the peripheral cue and the first
548 saccade following this. Saccades with latency lower than 80ms were
549 considered invalid.

550 In the Simon task, subjects were instructed to press a left ('x') or right key (',')
551 on a QWERTZ keyboard depending on the color of a circular cue presented for
552 1500ms on the left or right side of the screen following a 500ms central
553 fixation cross. RT was defined as the latency between cue presentation and the
554 first key press. In both tasks, error rate (ER) was calculated as the ratio

between number of valid incorrect responses and total number of valid responses.

Experiment 2

Exp. 2 (described in (33) consisted of the same tasks as in Exp. 1. A new sample of N = 50 healthy volunteers took part (mean 24 ± 3 years of age; 27 females). However, subjects were administered placebo and lorazepam (0.5 or 1.0 mg) across three different sessions in a within-subject, double-blind, randomized design. The order in which the tasks were administered was randomized across subjects but kept constant across sessions.

Data processing

Details of data preprocessing can be found elsewhere (33). Subjects with fewer than 65% of valid trials or more than 80% ER in any session were excluded from the final analysis.

Modeling

Responses (congruent/incongruent) and their respective RT were modeled with SERIA (26) which posits that actions are the outcome of the competition between four race-to-threshold processes. First, automatic responses are generated by a fast process, which we call the automatic process. In the antisaccade task, this process can only generate saccades toward the cue (prosaccades). In the Simon task, automatic responses are always congruent responses toward the location of the cue (e.g., right button presses for right stimuli, irrespective of the color of the cue). Automatic responses can be stopped by a latent, unobservable inhibitory process, when the latter hits threshold before the automatic process. When this happens, the second race between congruent and incongruent *controlled* responses determines which response is generated. This second decision is modeled with two race-to-threshold processes that compete against each other. The mathematical details of the model can be found in (26). Each of these processes is parametrized by its mean threshold hit time and the corresponding variance.

584 In addition to these 8 parameters (2 per process), SERIA uses three auxiliary
585 parameters: the no-decision time which reflects neuronal transmission delays
586 until the race of the first unit starts, the probability of low latency outliers, i.e.,
587 of reactions whose RT is below the no-decision time, and an extra delay
588 associated with the start of the race between controlled responses. Thus, in its
589 more general version, SERIA has 11 parameters.

590 The antisaccade and Simon tasks were modeled independently. In each task,
591 trials from each session were divided into congruent and incongruent trials.
592 These were split up into those that followed congruent (low-conflict) and
593 incongruent (high-conflict) trials. Hence, each session consisted of 4 different
594 conditions, each of which could be modeled with a potentially different set of
595 parameters, i.e., with 44 different parameters.

596 To constrain the model and to avoid overfitting, the auxiliary parameters were
597 assumed to be constant across the 4 conditions. In addition, the parameters of
598 the automatic process were kept constant across the four conditions.
599 Otherwise, these parameters would be strongly correlated with the
600 parameters of the inhibitory process. Moreover, the parameters of the
601 *incorrect controlled response* were the same across all conditions. In other
602 words, the distribution of the hit times of the incorrect controlled response
603 (e.g., a controlled congruent response on an incongruent trial) was kept
604 constant irrespective of trial type and the conflict level of the previous trial.
605 Finally, the parameters of the inhibitory unit on congruent switch and repeat
606 trials were fixed to the same values. This yielded a total of 20 free parameters,
607 i.e., degrees of freedom, per experimental block comprising the four
608 conditions.

609 We evaluated the possibility that this model overfits the data by comparing it
610 to a simpler model in which congruent responses are always automatic, fast
611 responses but with the same number of parameters. Thus, we could verify if a
612 structurally simpler model, with a comparable number of parameters could
613 parsimoniously explain subjects' performance. As shown in Supp. Table 1 & 2,

SERIA was more parsimonious and accurate than a reference model with equal number of parameters but less structural flexibility.

In Exp. 1, SERIA was fitted using the Metropolis-Hastings algorithm in combination with a hierarchical model. This was used to estimate the prior mean and variance of subject-specific parameters based on the population distribution (i.e., an empirical Bayesian procedure). For Exp. 2, this model was enriched by modeling the effect of lorazepam, i.e., in addition to the population mean and variance, we accounted for the effect of the two doses. Moreover, we modeled subject specific intercepts as random effects. This model provides empirically motivated priors, and we have used it in a variety of previous studies; for details, see (30,40).

The convergence of the Metropolis-Hastings algorithm was evaluated with the $\hat{R}$ statistic (54), such that at most 2% of all the model parameters were allowed to cross the 1.1 threshold ($\hat{R} > 1.1$), commonly used to assert convergence.

Fits and delta plots were generated from the posterior predictive distribution of each subject. In other words, we used the parameter estimates to approximate the conditional density

$$p(A, T|Y)$$

where $A \in \{congruent, incongruent\}$ is the action generated in a trial, $T \in]0,\infty[$ its RT and Y represents the empirical data from a subject.

In practice, the posterior predictive distribution can be estimated by averaging out the likelihood computed from samples collected using MCMC, as

$$p(A, T \mid Y) \approx \sum_{i=1}^{N} p(A,T|\theta_i)$$

where θ_i are samples from the posterior $p(\theta|Y)$.

To analyze the distribution of voluntary congruent and incongruent responses in isolation from congruent responses (see Fig. 5), we use the posterior parameter estimates to compute the distributions:

$$\frac{1}{Z_{cong.}} p(U_{cong.} = t) p(U_{incong.} > t),$$

$$\frac{1}{Z_{incong.}} p(U_{incong.} = t) p(U_{cong.} > t),$$

where

$$Z_{cong.} = \int_0^\infty p(U_{cong.} = t) p(U_{incong.} > t) dt\,,$$

$$Z_{incong.} = \int_0^\infty p(U_{incong.} = t) p(U_{cong.} > t) dt\,.$$

when $U_{cong.}$ and $U_{incong.}$ are the hit time of the controlled congruent and incongruent decision processes. These distributions predict the RT of congruent and incongruent responses in case no automatic response would have taken place.

We also report mean hit time of the controlled congruent and incongruent responses defined as

$$E[T_{cong.}] = \frac{1}{Z_{cong.}} \int_0^\infty t\, p(U_{cong.} = t) p(U_{incong.} > t) dt,$$

$$E[T_{incong.}] = \frac{1}{Z_{incong.}} \int_0^\infty t\, p(U_{incong.} = t) p(U_{cong.} > t) dt\,.$$

The probability of an automatic response (which we have called inhibition failure in previous studies) is defined as the probability that the automatic process hits threshold before any other unit.

$$\int_0^\infty p(U_{uncontrolled} = t)\, p(U_{inhib.} > t)\, p(U_{cong.} > t)\, p(U_{incong.} > t) dt$$

All methods described here are available in the open source TAPAS toolbox. The code used for the analysis is openly available at www.translationalneuromodeling.org/tapas.

Statistical analysis

Behavioral data as well as model parameters were analyzed using generalized linear mixed-effect models (GLME), implemented in the R (3.6.1) statistical package. The independent variables were conflict in the previous trial with levels high (incongruent) and low (congruent), trial type (levels congruent and incongruent) and subject, treated as a random effect. In Exp. 2, we also modeled the effect of lorazepam with levels placebo, 0.5mg, 1.0mg treated as a categorial regressor. For ER, a logistic regression model was used, and significance was assessed with Wald tests. Probabilities estimated using SERIA were analyzed using Beta regression models implemented in the package glmmADMB and significance was again assessed using Wald tests. For RT, F-tests were used in combination with the Satterthwaite approximation to the degrees of freedom.

Acknowledgements

We thank Klaas E. Stephan for his comments on the manuscript.

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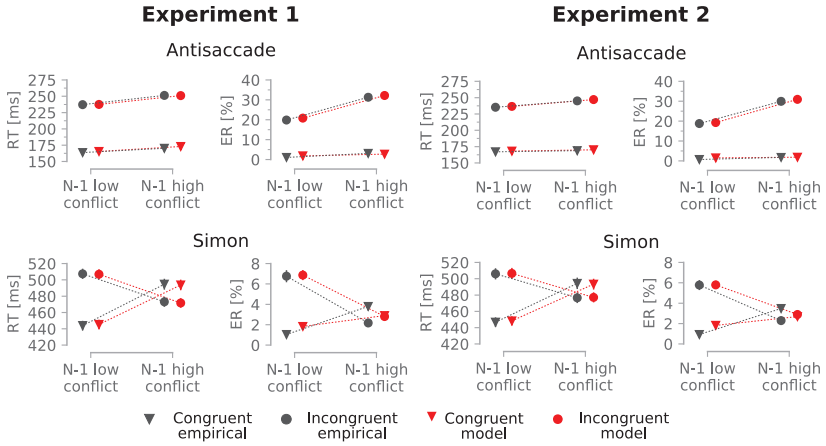
Supporting Information



Supplementary Figure 1: Empirical and predicted reaction time (RT) and error rate (ER) in Exp. 1 and 2. All effects from Exp. 1 were replicated in Exp. 2. The model accurately reproduced the empirical RT and ER. Error bars display the standard error of the mean.

Supplementary material 1 – Model comparison

The key assumption of the SERIA model is that congruent responses can be generated by either a fast, automatic process, or a slow but flexible component. We have shown previously (Aponte et al., 2017) that in some versions of the antisaccade task, RT are bimodally distributed and this constitutes qualitative evidence for the SERIA model. In the versions of the Simon and antisaccade tasks administered here, RT were unimodally distributed, which begs the question whether it is necessary to postulate two decision processes to explain RT and ER on congruent trials.

To answer this question, we compared SERIA to models in which all congruent responses are generated by a single process. Mathematical details for model comparison of different SERIA models can be found in (Aponte al., 2018). We report two metrics: the accuracy (or expected log likelihood), and the Watanabe Akaike information criterion (WAIC) (55), which is equal to the pointwise log likelihood (also called pointwise log predictive density) minus a

866 penalization term that represents complexity. Two variants of each model
867 were tested (see Supp. Table 1-2). In model m_1 and m_2, all congruent
868 responses were generated by an uncontrolled process. In model m_1, we
869 allowed the parameters of controlled responses to be different depending on
870 the four possible conditions (trial type x N-1 conflict level). In model m_2, the
871 parameters of the controlled responses were always equal across conditions.
872 The difference between model m_3 and m_4 is that the variance of the inhibitory
873 unit was kept constant across all conditions, whereas in model m_3 it was
874 different across congruent and incongruent trials. We introduced this model
875 to further simplify model m_3 and improve the convergence of the inference
876 algortihm. All results reported here were obtained with model m_4.

877 In general, SERIA fitted the data from both tasks more accurately and had
878 higher WAIC than single process models with a comparable number of
879 parameters. Thus, the structural flexibility inherent to dual process models
880 explained RT distributions and ER better than single process models.

Supplementary Table 1

	Model	# parameters	Accuracy	WAIC
m_1	Single process	27	-19750	-20655
m_2	Single process	21	-20579	-21200
m_3	Dual process (SERIA)	21	-19117	-19904
m_4	Dual process (SERIA)	20	-19086	**-19871**

Model comparison in the antisaccade task Experiment 1. Four different models were evaluated based on their accuracy (expected log likelihood) and the Watanabe Akaike Information Criterion (WAIC). In model 1 and 2, congruent responses were generated by a single process. In model 2, (automatic) congruent responses were assumed to be identical in all conditions. This model was introduced because in models 3 and 4, all automatic responses (which are always congruent) were identical across conditions. In addition, in model m_4 the variance of the inhibitory unit was not modulated by the conflict level on the previous trial. The highest WAIC is highlighted in bold.

881

Supplementary Table 2

	Model	# parameters	Accuracy	WAIC
m_1	Single process	27	-43083	-43783
m_2	Single process	21	-43940	-44442
m_3	Dual process (SERIA)	21	-42754	**-43379**
m_4	Dual process (SERIA)	20	-42769	-43384

Model comparison in the Simon task Experiment 1. Similar to Supp. Table 1. Bold entry indicates winning models, with almost identical WAIC.

In the Simon task, the two versions of SERIA used were very similar in terms of their accuracy and WAIC, relative to the size of the data set. This and all other results were replicated in Exp. 2 (Supp. Table 3 & 4). All analyses in the manuscript were based on model m_4 as the differences in WAIC were small relative to the set size and it was the model with the fewest parameters). The key pharmacological result in Exp. 2 was significant regardless of the SERIA model used to estimate parameters.

Supplementary Table 3

	Model	# parameters	Accuracy	WAIC
m_1	Single process	27	-13405	-14029
m_2	Single process	21	-14069	-14515
m_3	Dual process (SERIA)	21	-12920	**-13474**
m_4	Dual process (SERIA)	20	-12938	-13498

Model comparison in the antisaccade task Experiment 2. Similar to Supp. Table 1. Bold entry indicates the highest WAIC.

889

Supplementary Table 4

	Model	# parameters	Accuracy	WAIC
m_1	Single process	27	-38730	-39287
m_2	Single process	21	-39371	-39809
m_3	Dual process (SERIA)	21	-38522	**-39016**
m_4	Dual process (SERIA)	20	-38538	**-39016**

Model comparison in the Simon task Experiment 2. Similar to Supp. Table 1. Bold entry indicates winning models.

890 *Supplementary 2 - Experiment 2*

891 Statistical analyses of mean RT and ER in Exp. 2 are displayed in Supp. Table
892 5-8 and summarized below. We do not report standardized effect sizes
893 because these are not well defined for mixed effect models.

Supplementary Table 5

	NumDF	DenDF	F	P
Trial type	1	407	1398.216	< 2.2e-16
Conflict (N-1)	1	407	8.917	0.003
Dose	2	407	6.457	0.002
Trial type * Conflict (N-1)	1	407	4.211	0.041
Trial type * Dose	2	407	0.114	0.893
Conflict (N-1) * Dose	2	407	0.041	0.960
Trial type * Conflict (N-1) * Dose	2	407	0.103	0.902

Antisaccade task Experiment 2 – Mixed effects ANOVA of the mean reaction time.

894

Supplementary Table 6

	Num DF	**Den DF**	**F**	**P**
Trial type	1	495	72.994	$<10^{-5}$
Conflict (N-1)	1	495	13.884	$<10^{-5}$
Dose	2	495	79.528	$<10^{-5}$
Trial type * Conflict (N-1)	1	495	250.079	$<10^{-5}$
Trial type * Dose	2	495	0.046	0.955
Conflict (N-1) * Dose	2	495	1.040	0.354
Trial type * Conflict (N-1) * Dose	2	495	2.534	0.080

Simon task Experiment 2 – Mixed effects ANOVA of the mean reaction time.

895

Supplementary Table 7

	Chisq	Df	P
Trial type	19.6	1	$< 10^{-5}$
Conflict (N-1)	8.7	1	0.003
Dose	37.7	2	$< 10^{-5}$
Trial type * Conflict (N-1)	158.7	1	$< 10^{-5}$
Trial type * Dose	2.7	2	0.264
Conflict (N-1) * Dose	1.3	2	0.531
Trial type * Conflict (N-1) * Dose	7.9	2	0.019

Antisaccade task Experiment 2 – Mixed effects ANOVA of the error rate.

896

Supplementary Table 8

	Chisq	Df	P
Trial type	1298.4	1	$< 10^{-5}$
Conflict (N-1)	202.9	1	$< 10^{-5}$
Dose	40.7	2	$< 10^{-5}$
Trial type * Conflict (N-1)	0.6	1	0.424
Trial type * Dose	0.3	2	0.855
Conflict (N-1) * Dose	4.2	2	0.120
Trial type * Conflict (N-1) * Dose	7.7	2	0.022

Simon task Experiment 2 – Mixed effects ANOVA of the error rate.

Behavioral analysis – Antisaccade task

Antisaccade mean RT (241ms) was higher than prosaccade RT (169ms; $P < 10^{-5}$). The congruency effect (antisaccade cost) was higher after high conflict trials (76ms) compared to trials following low conflict trials (68ms). This yielded a significant interaction between the factor trial type and conflict ($P = 0.042$).

Regarding the mean ER, similar effects were observed as with RT. Antisaccade trials showed higher ER (6%) than prosaccade trials (1%; $p < 10^{-5}$). Again, the congruency effect was higher after high conflict trials (27%) compared to low conflict trials (17%) but this was not reflected in a significant interaction between the factors trial type and conflict ($P = 0.681$).

Behavioral analysis – Simon task

In the Simon task, incongruent trials were on average 20ms slower than congruent trials ($P < 10^{-5}$). In addition, trials that followed the high conflict condition were 10ms faster than trials following the low conflict condition ($P < 10^{-3}$). Importantly, the Simon effect was significantly reduced after high conflict trial ($-18ms$), compared to low conflict trials ($59ms$) which yielded a significant interaction between previous trial conflict level and trial type ($P < 10^{-5}$). We come back to this point in the next section.

The ER on incongruent trials was 1.8% higher than on congruent trials ($P < 10^{-5}$). The congruency effect on trials following the high conflict condition (-1%) was lower compared to trials that followed the low conflict condition (4%) and this interaction was significant ($P < 10^{-5}$).

Supplementary 3 – Correlations across tasks

Supp. Table 9 displays the partial correlation analyses of model-based variables between the antisaccade and Simon task in Exp. 1. Supp. Table 10 displays the same analysis for purely behavioral variables. We applied Holm's method to correct for multiple comparison. Supp. Fig. 2 displays the

925 correlation between the ER on incongruent trials in the antisaccade and Simon
926 tasks.

927

Supplementary Table 9

	Partial correlation coefficient	P	P corrected
Automatic congruent RT	0.029	0.610	0.610
Automatic congruent probability	0.077	0.184	0.368
Congruent controlled RT	0.146	0.011	0.045
Incongruent controlled RT	0.312	$< 10^{-5}$	$< 10^{-5}$
Congruent controlled probability	0.116	0.044	0.132

Correlation between parameter estimates across tasks in Exp. 1. The reaction time of controlled incongruent responses was significantly correlated. No parameter pertaining to inhibitory controlled was correlated across tasks. Multiple comparison correction by Holm's method.

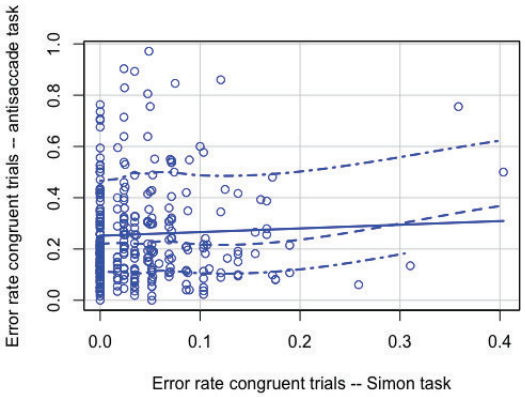
928

Supplementary Table 10

	Partial correlation coefficient	P	P corrected
Error rate incongruent trials	0.208	$< 10^{-3}$	$< 10^{-3}$
Error rate congruent trials	0.081	0.158	0.158
Reaction time incongruent trials	0.309	$< 10^{-3}$	$< 10^{-3}$
Reaction time congruent trials	0.207	$< 10^{-3}$	$< 10^{-3}$

Correlation between behavioral outcomes in Experiment 1. Multiple comparison correction by Holm's method.

929



Supplementary Figure 2: Correlation between the error rates on incongruent trials in the antisaccade and Simon tasks in Exp. 1 Circles represent individual participants. Blue solid line represents the regression slope, and the dotted line the running average of individual participants with its confidence interval displayed as dot-dash lines.

We performed a similar analysis in Exp. 2 (see Supp. Table 11 and 12) except that correlations were computed from estimates from a hierarchical SERIA model that controlled for i) conflict in the previous trial, ii) drug dose, and iii) subject entered as random effect. The subject specific intercepts (random effects) were used as random variables in the correlation analysis, because these represent the mean value of each subject after removing all other confounds.

Supplementary Table 11

	Partial correlation coefficient	P	P corrected
Automatic congruent RT	0.367	0.025	0.075
Automatic congruent probability	0.028	0.864	0.864
Congruent controlled RT	0.470	0.003	0.013
Incongruent controlled RT	0.478	0.002	0.013
Congruent controlled probability	0.277	0.095	0.191

Correlation between model-based variables across tasks in Exp. 2. There was a significant correlation between the reaction time of controlled responses across tasks. Multiple comparison correction by Holm's method.

937

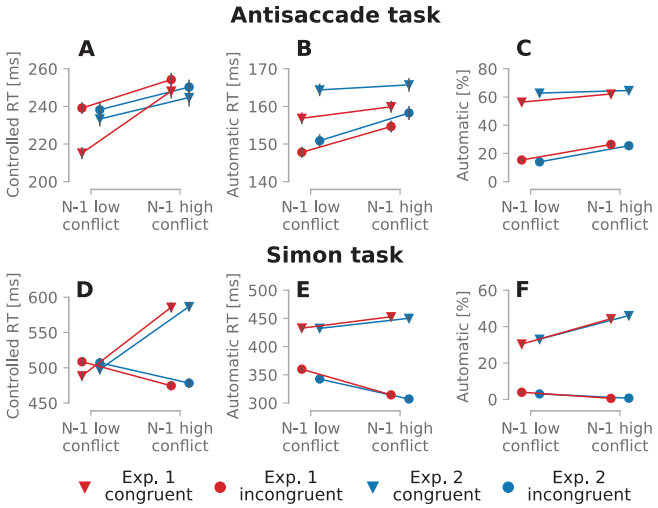
Supplementary Table 12

	Partial correlation coefficient	P	P corrected
Error rate incongruent trials	0.422	0.009	0.027
Error rate congruent trials	0.314	0.058	0.065
Reaction time incongruent trials	0.457	0.004	0.017
Reaction time congruent trials	0.352	0.032	0.065

Correlation between behavioral outcomes in Exp. 2. Multiple comparison correction by Holm's method.

938 *Supplementary material 4*

939



Supplementary Figure 3: Model estimates of controlled and automatic RT as well as the percentage of automatic in Exp 1. and 2. A) Controlled RT in the antisaccade task, B) Automatic RT in the antisaccade task, C) Percentage of automatic responses in the antisaccade task, D-F) Similar to A-C in the Simon task. All parameter findings were replicated across experiments.

940

Supplementary Table 13

	Antisaccade task			
	Placebo	0.5mg	1.0mg	P
Percent automatic responses	41	40	42	0.28
Automatic RT [ms]	155	159	163	$< 10^{-5}$
Controlled congruent RT [ms]	230	240	246	0.012
Controlled incongruent RT [ms]	237	245	249	0.001
	Simon task			
	Placebo	0.5mg	1.0mg	P
Percent automatic responses	19	23	19	$< 10^{-5}$
Automatic RT [ms]	373	382	392	$<10^{-5}$
Controlled congruent RT [ms]	509	555	561	$<10^{-5}$
Controlled incongruent RT [ms]	472	493	511	$<10^{-5}$

Mean model parameters as a function of drug. P values of the marginal effect of lorazepam.

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APPENDIX F [Publication Study 4]

Faßbender, K., Baumert, P. M., Wintergerst, M. W., Terheyden, J. H., Aslan, B., M Harmening, W., & Ettinger, U. (2023). GABAergic Involvement in Selective Attention. *Journal of Cognitive Neuroscience*, *35*(6), 976-989. https://doi.org/10.1162/jocn_a_01989

GABAergic Involvement in Selective Attention

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Abstract

■ Animals need to cope with abundant sensory information, and one strategy is to selectively direct attention to only the most relevant part of the environment. Although the cortical networks of selective attention have been studied extensively, its underlying neurotransmitter systems, especially the role of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA), remain less well understood. Increased $GABA_A$ receptor activity because of administration of benzodiazepines such as lorazepam is known to slow reactions in cognitive tasks. However, there is limited knowledge about GABAergic involvement in selective attention. Particularly, it is unknown whether increased $GABA_A$ receptor activity slows the build-up of selectivity or generally widens attentional focus. To address this question, participants (n = 29) received 1 mg lorazepam and placebo (within-subjects, double-blind) and performed an extended version of the flanker task. The spatial distribution of selective attention was studied by systematically manipulating number and position of incongruent flankers; the temporal build-up was characterized using delta plots. An online task version was presented to an independent, unmedicated sample (n = 25) to verify task effects. Under placebo and in the unmedicated sample, only the number of incongruent flankers, but not their position, influenced RTs. Incongruent flankers impaired RTs more strongly under lorazepam than placebo, especially when adjacent to the target. Delta plot analyses of RT showed that this effect persisted even when participants reacted slowly, indicating that lorazepam-induced impairments in selective attention do not result from simply slowed down build-up of selectivity. Instead, our data indicate that increased $GABA_A$ receptor activity widens the attentional focus. ■

INTRODUCTION

Selective visual attention, the ability to favor goal-relevant stimuli and responses, is often characterized as a zoom lens with its focus sharpening over time (e.g., LaBerge, Brown, Carter, Bash, & Hartley, 1991; Eriksen & St. James, 1986). Despite its high relevance in daily life and its known impairments in neuropsychiatric disorders (Pattij & Schoffelmeer, 2015), the neurotransmitter mechanisms underlying selective attention are not fully characterized.

Understanding the neurotransmitter systems involved in selective attention is important not only for cognitive neuroscience research in healthy populations (Bari & Robbins, 2013), but also for better understanding deficits in neuropsychiatric disorders (e.g., Nigg, 2001) and developing possible treatments (e.g., Yang & Tsai, 2017). From neuroimaging and lesion studies, it is known that selective attention is mediated chiefly by fronto-posterior cortical networks (Corbetta & Shulman, 2002). Neurochemically, the excitatory neurotransmitter acetylcholine (ACh) enhances selective attention (Moore & Zirnsak, 2017; Noudoost & Moore, 2011; Coull, 1998). However, regarding inhibitory neurotransmitters, there is insufficient knowledge. Initial evidence suggests interactions between ACh and the most widespread human inhibitory neurotransmitter, γ-aminobutyric acid (GABA; Granger, Mulder, Saunders, & Sabatini, 2016). In addition, inhibitory neurotransmitters reduce ACh release in rats, thereby impairing attention (Burk, Blumenthal, & Maness, 2018). Importantly, the relationship between GABA and selective attention remains unclear.

One approach to studying GABAergic effects on attention is the administration of benzodiazepines such as lorazepam, which modulate $GABA_A$ receptors by increasing the hyperpolarizing effect of GABA, thus decreasing neuronal excitability (Knoflach & Bertrand, 2021; Uusi-Oukari & Korpi, 2010). Experimentally, benzodiazepines impair performance in simple psychomotor and cognitive tasks, including increased RTs and error rates (e.g., Tannenbaum, Paquette, Hilmer, Holroyd-Leduc, & Carnahan, 2012; de Visser et al., 2003; Wittenborn, 1979). Clinically, benzodiazepines have arousal-reducing, sleep-promoting, muscle-relaxing, antispasmodic and anxiolytic effects (Baldwin et al., 2013). Given the anxiolytic effects of benzodiazepines, studies on anxiety and attention may also provide evidence as to whether benzodiazepines, and thus increased GABAergic activity, might influence attention. Interestingly, both state and trait anxiety have been found to narrow the central attentional focus (Wegbreit, Franconeri, & Beeman, 2015; Caparos

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Journal of Cognitive Neuroscience 35:6, pp. 976–989
https://doi.org/10.1162/jocn_a_01989

& Linnell, 2012), suggesting that GABAergic-induced reductions of anxiety may widen the attentional focus.

Selective attention can be studied using flanker tasks (Eriksen & Eriksen, 1974). In such tasks, participants are typically instructed to react to a central target (e.g., an arrow symbol such as > or <), ignoring peripheral flankers associated with the correct (congruent, e.g., > > > > >) or incorrect response (incongruent, e.g., < < > < <). RTs and error rates are higher in incongruent than congruent conditions, termed *congruency effect*.

We recently studied lorazepam effects on performance in flanker, antisaccade, and Simon tasks (Faßbender et al., 2021). In all tasks, lorazepam increased the rate of erroneous responses, particularly in incongruent conditions, suggesting that the drug impaired the ability to resolve response conflicts. Notably, the flanker task was the only one that additionally revealed an increased congruency effect for RT under lorazepam, thereby implying GABAergic involvement in selective attention. Specifically, a widened attentional focus with lorazepam may increase the impact of incongruent flankers on RTs of responses to the target, and as incongruency in the flanker task delays the production of a correct response (Ridderinkhof, Wylie, van den Wildenberg, Bashore, & van der Molen, 2021), an increased congruency effect for RT could imply a widened attentional focus with lorazepam. One aim of the present study is to address this assumption.

A more fine-grained assessment of selective attention in the flanker task was put forward by White, Ratcliff, and Starns (2011). Their task considers both the number and the position of the flankers by additionally including outer incongruent (only the two outer flankers point in the opposite direction to the target, e.g., < > > > <) and inner incongruent conditions (only the two flankers next to the target point in the opposite direction to the target, e.g., > < > < >). In general, flankers that are more distant to the target are less in the focus of attention and have less influence on RT than flankers closer to the target (Eriksen & Eriksen, 1974). Under an optimal, very narrow attentional focus on the target, outer and inner flankers should only slightly influence responses to the target. Under a somewhat wider attentional focus, however, the influence of flankers should be increased, especially for inner conditions, which should be reflected in a stronger RT congruence effect for inner than outer incongruent conditions. Importantly, the effects of benzodiazepines on attentional mechanisms in this task have not yet been studied.

In addition, only considering mean RT dismisses that the narrowing of attentional focus is also subject to temporal dynamics (Eriksen & Eriksen, 1974). Generally, selective attention is low at stimulus onset, with responses strongly determined by both target and flankers (Ridderinkhof, 2002). Over time, controlled processes increase, and the influence of irrelevant flankers decreases. This build-up of selectivity is illustrated in delta plots where congruency effects are displayed as a function of RT quintiles. These delta plot analyses typically reveal large congruency effects for accuracy (percent correct) in quintiles with short RTs, indicating strong direct activation by irrelevant flankers before build-up of selectivity. For later quintiles, there are typically no differences in accuracy between congruent and incongruent conditions. Thus, participants are able to inhibit incorrect responses when reacting slowly. Delta plots for RT, on the other hand, reflect the build-up of selectivity over time. Fast compared with slow build-up of selectivity reduces the influence of irrelevant flankers and thus congruency effects for RT in later quintiles (Ridderinkhof, 2002).

Using delta plots in combination with the extended task version by White et al. (2011), it is possible to further characterize the build-up of selectivity over time. Specifically, a smaller difference between outer and inner incongruent RT on trials in which participants respond slowly may indicate that the influence of outer flankers decreased over time. Regarding possible lorazepam effects on selective attention, it is thus possible to investigate not only whether there is a general widening of selective attention but also whether such an effect is subject to temporal dynamics. For example, a compensation of potential impairments under lorazepam in slow RT trials could indicate that temporal build-up of selectivity was merely slowed-down by the drug. If, on the other hand, differences persist for slow RT trials, this would suggest that the attentional focus is generally widened, regardless of temporal dynamics.

Here, for the first time, we studied GABAergic influences on selective attention taking into account these issues. In a preregistered Experiment 1, participants performed the extended flanker task after 1 mg lorazepam and placebo (within-subject). Following previous findings, our preregistered hypotheses were that lorazepam would increase RT and error rates (1). In addition, we expected impaired selective attention under lorazepam, which should be reflected in higher congruency effects for RT under lorazepam compared with placebo. On the basis our previous study (Faßbender et al., 2021), we also expected an increased congruency effect in error rate with lorazepam (2). Regarding the extended version of the flanker task, we hypothesized that RT and error rate would increase from congruent to outer, inner, and incongruent conditions (3). Furthermore, we explored the influence of lorazepam on the spatial distribution of attention by comparing drug effects on the outer and inner incongruent conditions. In addition, we included delta plot analyses to investigate whether possible impairments under lorazepam reflect a slowing-down of the build-up of selectivity or a fundamental widening of the attentional focus independent of temporal dynamics. In Experiment 2, we applied the flanker task in an online setting to an independent sample without drug administration, to replicate placebo task effects from Experiment 1 and to provide comparative data for this task version.

EXPERIMENT 1

Methods

Sample

Thirty healthy students aged 18–40 years completed the study. Sample size was determined a priori to obtain ≈85% power with an effect size of $d = 0.5$ and an alpha level of .05 using G*Power (V 3.1).

Participants were recruited through online and local advertisements. After completing an online screening questionnaire, suitable participants were invited to an in-person screening. Participants meeting all inclusion criteria and none of the exclusion criteria were invited to the experimental sessions. Inclusion criteria were: right-handedness, normal or corrected-to-normal vision. Exclusion criteria were: medication consumption (except oral contraceptives in women); any current or history of psychiatric, neurological, or physical disorder; blood pressure below 100/60 or above 140/90; resting pulse < 60 or > 100 beats per minute; body mass index <18 or > 29 kg/m^2 for men or < 19 or > 30 kg/m^2 for women; a history of nicotine consumption (more than 10 cigarettes in lifetime); positive drug or alcohol test; earlier consumption of lorazepam or other benzodiazepines (lifetime); known allergic reactions to medications; and, for women, a positive pregnancy test (Cleartest Diagnostik HCG), breastfeeding, or not using effective contraceptives for the duration of at least one cycle.

All participants gave written informed consent. After completion of experimental sessions, participants were compensated with 100€ or course credits. The study was approved by the ethics committee of the Faculty of Medicine at the University of Bonn (Lfd. Nr. 240/19) and preregistered on OSF (Open Science Framework; https://osf.io/uhrjf/).

Design and Procedure

The study design was within-subject, double-blind, placebo-controlled, with counterbalanced order of drug administration. Participants completed two experimental sessions on separate occasions, 7 days apart, at the same time of day (difference between starting times in minutes: mean = 2.59, *SD* = 2.88, maximum = 10.00).

After confirming participants' well-being and performing a urine pregnancy test (Cleartest Diagnostik HCG) for women, participants received either placebo (mannitol) or 1 mg lorazepam (Tavor, Pfizer). Drugs were encapsulated identically; thus, they were visually indistinguishable and had no odor. Administration was oral, and capsules were served with a glass of water. After administration, there was a waiting period of 1:45 hr (Kyriakopoulos, Greenblatt, & Shader, 1978).

First, participants carried out other oculomotor tasks, which are not described in this study, lasting about 70 min. Subsequently, the flanker task was performed (approx. 3 hr after drug administration). Lastly, participants filled in an online questionnaire containing visual analogue rating scales (Bond & Lader, 1974), the NASA-Task Load Index (NASA-TLX) to assess subjective effects of drug administration and an item asking whether participants thought they received lorazepam or placebo that day. Because of the COVID-19 pandemic, participants wore facemasks during assessments.

Flanker Task

The visual stimulus and task procedure (Figure 1) was written in Presentation software (Version 19.0, Neurobehavioral Systems, Inc.) and presented on a flat-screen monitor (Sony 55XE8505, 55-in., height: 68 cm, width: 121 cm,

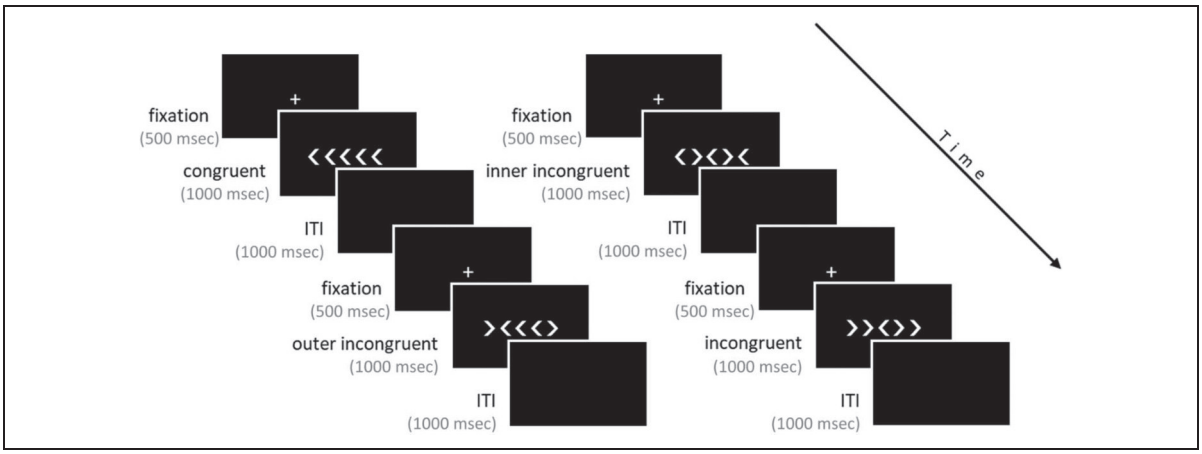

Figure 1. Flowchart of the flanker task. The figure shows four example trials of the flanker task used in Experiments 1 and 2. In all task conditions shown here, the left button should be pressed to indicate the correct response to the central target arrow. During the experiment, each condition also existed with mirror-inverted arrows that had to be reacted to by pressing the right button. Presentation order was randomized. ITI = intertrial interval.

resolution: 3840 × 2160 px, 59-Hz refresh rate). Eye-to-screen distance was about 220 cm. Stimuli were white (r, g, b: 255, 255, 255) on black (0, 0, 0) background. In each trial, a central fixation cross was shown for 500 msec, followed by five arrows (total horizontal size approx. 16.66° of visual angle, vertical size approx. 3.44°) shown for 1000 msec, and an intertrial interval (ITI) of 1000 msec before the next trial began.

Participants were instructed to respond quickly and accurately to the direction of the middle arrow (the target) by pressing a corresponding key on a QWERTZ keyboard, ignoring the flankers. The factor Task Condition comprised four conditions: congruent (all arrows in the same direction, e.g., "< < < < <"), incongruent (all flankers in opposite direction to target, e.g., "> > < > >"), outer (both outer flankers in opposite direction to target, e.g., "> < < < >"), and inner (both inner flankers in opposite direction to target, e.g., "< > < > <"). Participants did not receive feedback on their performance. For each condition, 100 trials (50 right, 50 left) were presented in pseudorandomized order, resulting in 400 trials for each participant. In the beginning, 20 practice trials were presented.

Raw data from all participants were combined and organized on trial level using MATLAB 2017b (The MathWorks). Data sets for statistical analyses on subject level were prepared in R (R Core Team, 2021). Outcome variables were RT for correct trials (msec) and error rate (%).

Subjective Effects

Computerized visual analogue rating scales (VAS; Bond & Lader, 1974) were applied in German to measure subjective effects after completing the flanker test. Participants submitted ratings on 16 continuous scales, each comprising two anchors and scored 0–100. Responses were made by moving a marker using mouse clicks. Variables were *alertness*, comprising "Alert/Drowsy" (1), "Strong/Feeble" (3), "Muzzy/Clear-headed" (4, R), "Well-coordinated/Clumsy" (5), "Lethargic/Energetic" (6, R), "Mentally slow/Quick-witted" (11, R), "Attentive/Dreamy" (13), "Interested/Bored" (14), "Incompetent/Proficient" (16, R); *contentedness*, comprising "Contented/Discontented" (7), "Troubled/Tranquil" (8, R), "Happy/Sad" (9), "Antagonistic/Amicable" (10, R), "Gregarious/Withdrawn (15, R)"; and *calmness*, comprising "Calm/Excited" (2), "Tense/Relaxed (12, R)." Numbers indicate questionnaire positions, and "R" indicates item recoding. Higher scores indicate less alertness, less contentedness, and less calmness.

The computerized NASA-TLX measured subjective workload (Hart & Staveland, 1988). Participants submitted ratings on six continuous scales ranging from "very low" to "very high" and scored 0–100. Items were "mental demand," "physical demand," "temporal demand," "overall performance," "effort," and "frustration level" (in German). All ratings were combined to the *overall task load score* (Bustamante & Spain, 2008).

Statistical Analyses

Statistical analyses were carried out in R (R Core Team, 2021) using the packages *apaTables* (Stanley, 2021), *dplyr* (Wickham, François, Henry, & Müller, 2021), *ez* (Lawrence, 2016), *ggplot2* (Wickham, 2016), and *rstatix* (Kassambara, 2021). Trials were counted as invalid when RT was < 150 msec or > 1200 msec. Participants with > 50% missing/invalid trials or > 80% incorrect in one condition were excluded.

Within-subject ANOVA with the factors Drug (placebo, lorazepam) and Task Condition (congruent, outer incongruent, inner incongruent, incongruent) was carried out for RT and error rate. Effect sizes were reported using partial eta-square and its 95% confidence interval (CI; Cohen, 1973). Significant effects were further explained using post hoc Bonferroni-corrected t tests and effect size d_{AV} (Lakens, 2013). If Mauchly's test indicated violation of sphericity, Greenhouse–Geisser correction was applied. We used a $p < .05$ significance criterion.

For delta plots, RTs of valid trials were rank-ordered separately for congruent, outer incongruent, inner incongruent, and incongruent conditions at subject level and each divided into five equal parts. For each quintile, RT for correct trials and accuracy (% correct) were determined. Delta plots show either the difference between congruent and incongruent conditions or between outer and inner incongruent conditions in RT and accuracy as a function of mean RT of both conditions per quintile. Within-subject ANOVAs, including the factor Drug (placebo, lorazepam), were performed to compare slopes between Quintiles 1 and 2, Quintiles 2 and 3, Quintiles 3 and 4, and Quintiles 4 and 5.

Finally, within-subject ANOVAs with the factor Drug (placebo, lorazepam) were carried out for VAS and NASA-TLX.

Results

Sample Description

The final sample consisted of $n = 29$ (14 female, 15 male) participants. According to preregistered exclusion criteria, none of the initially recruited 30 participants had to be excluded. However, we decided to exclude one participant with an average 69.95% error rate under placebo as outlier. The participant showing the next highest values had an error rate of 4.50%. Percentages of trials excluded as invalid were low (0.01% of all trials for RT < 150 msec; 3.37% of all trials for RT > 1200 msec). Mean age was 22.76 years ($SD = 3.35$ years). Table 1 contains descriptive results and internal consistencies of flanker task data.

Table 1. Descriptive Statistics and Internal Consistencies in Experiment 1

	Placebo		*Lorazepam*	
	M (SD)	*α [95% CI]*	*M (SD)*	*α [95% CI]*
RT con.	524.02 (41.17)	.97 [.95, .98]	577.49 (55.34)	.97 [.94, .98]
RT outer	546.39 (47.40)	.97 [.95, .98]	608.56 (67.98)	.97 [.95, .98]
RT inner	553.13 (49.70)	.97 [.96, .99]	623.49 (73.15)	.97 [.95, .98]
RT incon.	582.98 (46.64)	.97 [.95, .98]	648.59 (61.18)	.96 [.94, .98]
ER con.	0.41 (0.63)	−.05 [−.72, .44]	0.46 (0.89)	.44 [.09, .70]
ER outer	0.86 (1.16)	.37 [−.01, .66]	1.23 (1.88)	.65 [.44, .81]
ER inner	0.83 (1.29)	.51 [.22, .74]	1.50 (1.79)	.50 [.20, .73]
ER incon.	3.18 (3.16)	.70 [.52, .84]	3.56 (3.66)	.74 [.59, .86]

Numbers indicate the mean (standard deviation). RT = mean reaction time; con. = congruent; outer = outer incongruent; inner = inner incongruent; incon. = incongruent; ER = error rate in %; α = Cronbach's α; CI = confidence interval (Feldt procedure), n = 29.

Data sets, code, material, as well as all analyses with complete data sets, are provided on OSF (https://osf.io/y49a3/).

Flanker Task

In line with previous studies, we find that lorazepam slowed down RT across all participants in all task conditions. Interestingly, RT for outer and inner incongruent conditions decreased at different rates, offering insights into the mechanisms of selective attention. Specifically, for RT (Figure 2A), there was a main effect of Drug, $F(1, 28) = 63.34$, $p < .001$, $\eta_p^2 = .693$, CI [.462, .795], indicating longer RT under lorazepam than placebo, and a main effect of Task Condition, $F(3, 84) = 104.34$, $p < .001$, $\eta_p^2 = .788$, CI [.699, .833], $\epsilon = .78$. The main effect of Task Condition was because of an increase in RT from congruent via outer and inner incongruent to incongruent conditions. Importantly, there was also an interaction between Drug and Task Condition, $F(3, 84) = 5.52$, $p = .004$, $\eta_p^2 = .165$, CI [.029, .284], $\epsilon = .77$. This interaction arose because of significant differences in RT between outer and inner incongruent conditions under lorazepam, $t(28) = -3.74$, $p = .014$, $d = -0.053$, that did not exist under placebo, $t(28) = -2.63$, $p = .22$, $d = -0.035$. On the other hand, all other task conditions differed significantly within drug each condition (all $p < .001$), and RT was always higher under lorazepam than placebo within each task condition (all $p < .001$). Thus, the interaction essentially showed that although there was a significant linear trend from congruent, outer incongruent, inner incongruent, to incongruent under lorazepam ($t = 4.24$, $p < .001$) and placebo ($t = 4.77$, $p < .001$), there was a significant RT difference between outer and inner incongruent conditions only under lorazepam, but not placebo.

For error rate (Figure 2B), there was no main effect of Drug, $F(1, 28) = 2.36$, $p = .14$, $\eta_p^2 = .078$, CI [.000, .293], and no interaction between Drug and Task Condition, $F(3, 84) = 0.45$, $p = .64$, $\eta_p^2 = .016$, CI [.000, .067], $\epsilon = .67$. However, there was a main effect of Task Condition, $F(3, 84) = 25.24$, $p < .001$, $\eta_p^2 = .474$, CI [.303, .576], $\epsilon = .43$. t Tests following up that main effect revealed

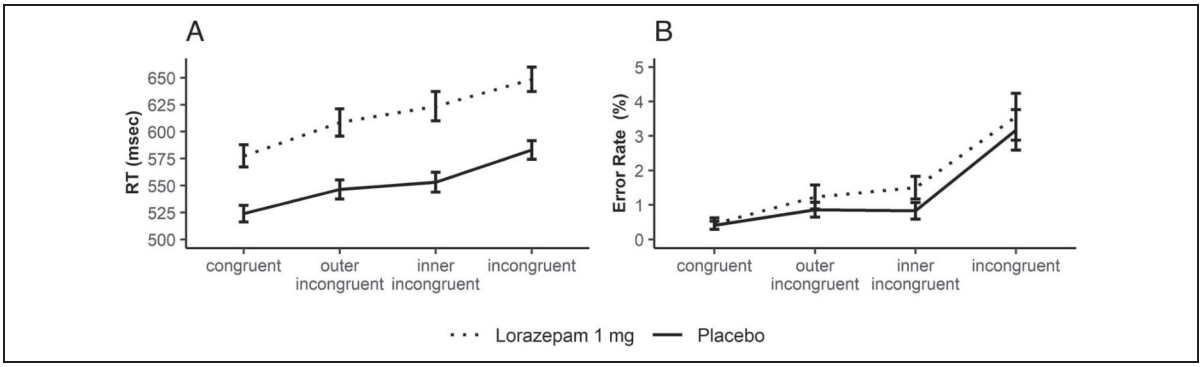

Figure 2. RT and error rate in Experiment 1. The figure illustrates the effects of lorazepam (1 mg) compared with placebo administration on (A) mean RT of correct trials and (B) mean error rate in Experiment 1. Error bars indicate the standard error of the mean, n = 29.

that there were significant differences in error rate between all conditions (all $p < .005$) except between outer and inner incongruent conditions, $t(57) = -0.47$, $p = 1.00$, $d = -0.019$, and a linear trend from congruent to incongruent conditions ($t = 7.35$, $p < .001$). Thus, error rate was unimpaired by drug, but increased from congruent to incongruent conditions, whereas there was no significant difference between outer and inner incongruent conditions.

To provide comparability with our previous study (Faßbender et al., 2021), we repeated the analyses excluding outer and inner incongruent conditions, that is, reducing the data set only to include fully congruent and incongruent conditions. Results replicate our previous findings for RT, with significant main effects of Drug and Task Condition as well as a significant interaction effect (Table 2).

Delta Plots

To examine whether lorazepam effects on flanker task performance may be because of effects on build-up of selectivity or direct activation (Ridderinkhof, 2002), we calculated delta plots for RT and accuracy, respectively.

Delta plots (Figure 3) for RT did not reveal significant drug effects for slopes of any quintile, neither when comparing outer and inner incongruent conditions nor when comparing congruent and incongruent conditions (all $p > .05$). Thus, the increased RT congruency effect under lorazepam was independent of mean RT and was sustained even in trials with higher RT. As expected from previous studies (Pratte, 2021), delta plots for RT were positive-going and visual inspection confirmed slower RT under lorazepam compared with placebo in all quintiles.

Delta plots of slopes for accuracy between Quintiles 4 and 5 revealed significant drug effects when comparing outer and inner incongruent, $F(1, 28) = 4.36$, $p = .046$, $\eta_p^2 = .135$, CI [.000, .360], and congruent and incongruent conditions, $F(1, 28) = 5.77$, $p = .023$, $\eta_p^2 = .171$, CI [.001, .397]. This is illustrated in the fact that there were negative slopes for accuracy under lorazepam for later quintiles, whereas they were positive for placebo. Importantly, those effects were because of lower accuracy in inner incongruent and incongruent conditions (Figure 4) and did not result from higher accuracy for congruent or outer incongruent conditions in later quintiles. This finding suggests that lorazepam lowers the accuracy of responding particularly for slow reactions, especially when inner or both flankers are incongruent.

Subjective Effects

Participants scored significantly higher on VAS alertness and contentedness with lorazepam than placebo. As higher scores indicate less alertness and contentedness, this result indicates that participants were less alert and less content under drug (Table 3). VAS calmness and NASA-TLX task load score were unaffected by lorazepam.

At assessment Session 1, participants could not reliably guess whether they had received placebo or lorazepam ($p > .05$). At assessment Session 2, the proportion of participants guessing correctly was significantly above chance level ($p = .002$).

Order Effects

In an exploratory analysis, the factor Order (placebo–lorazepam, lorazepam–placebo) was included in the ANOVA for RT to test whether drug effects depended on administration order. Main effects for Drug, $F(1, 27) = 95.73$, $p < .001$, $\eta_p^2 = .780$, CI [.593, .854], and Task Condition, $F(3, 81) = 104.38$, $p < .001$, $\eta_p^2 = .794$, CI [.705, .838], $\epsilon = .78$, as well as the interaction between Drug and Task Condition, $F(3, 81) = 7.42$, $p < .001$, $\eta_p^2 = .216$, CI [.059, .340], were confirmed.

In addition, there was an interaction between Drug and Order, $F(1, 27) = 12.62$, $p = .001$, $\eta_p^2 = .319$, CI [.059, .528], indicating that when lorazepam was given in Session 1, RT was significantly higher than when lorazepam was given in Session 2 ($p = .038$). RT under placebo did not differ as a

Table 2. Repeated-Measures ANOVA for Congruent and Incongruent Conditions Only

	Effect	df_n	df_d	F	p	η_p^2 [95% CI]
RT	Drug	1	28	71.97	< .001	.720 [.502, .813]
	Task Condition	1	28	338.20	< .001	.924 [.853, .949]
	Drug × Task Condition	1	28	8.24	.008	.227 [.018, .449]
Error rate	Drug	1	28	0.37	.545	.013 [.000, .179]
	Task Condition	1	28	32.89	< .001	.540 [.259, .690]
	Drug × Task Condition	1	28	0.41	.526	.015 [.000, .183]

Data from outer and inner incongruent conditions were excluded before the analysis to provide comparability with our previous study (Faßbender et al., 2021).

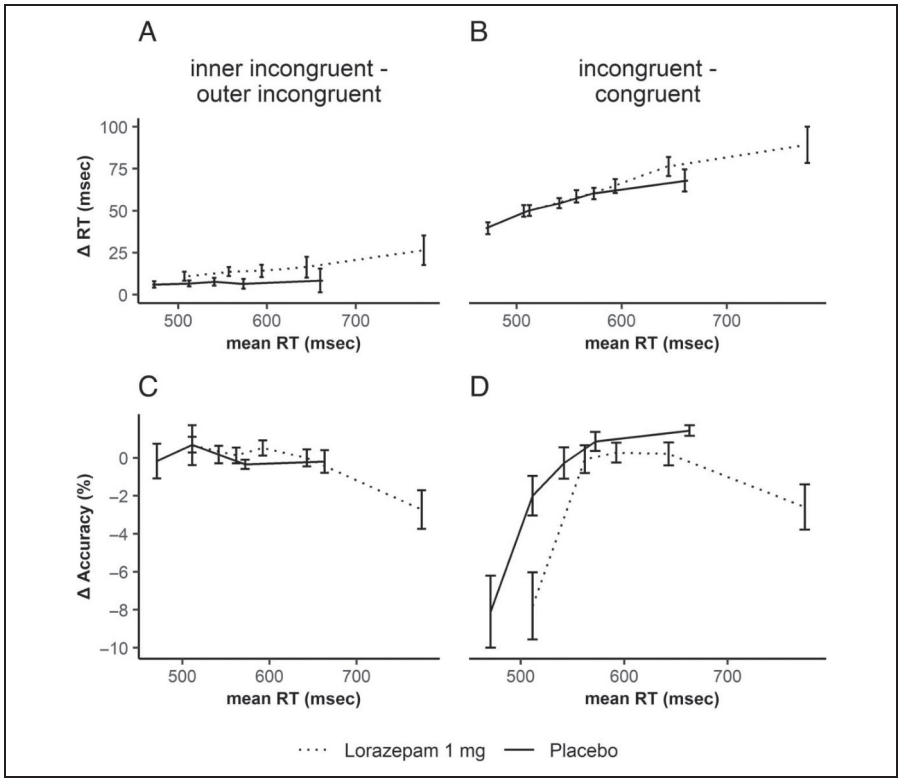

Figure 3. Delta plots in Experiment 1. The figure shows lorazepam effects compared with placebo in delta plots for mean RT of correct trials (A, B) and accuracy (percent correct) (C, D). In delta plots, RTs are rank-ordered and separated into quintiles. For each quintile, the difference (Δ) in RT or accuracy between outer and inner incongruent conditions (A, C) and between congruent and incongruent conditions (B, D) are plotted against the mean RT of both conditions in the respective quintile. Error bars indicate the standard error of the mean, $n = 29$.

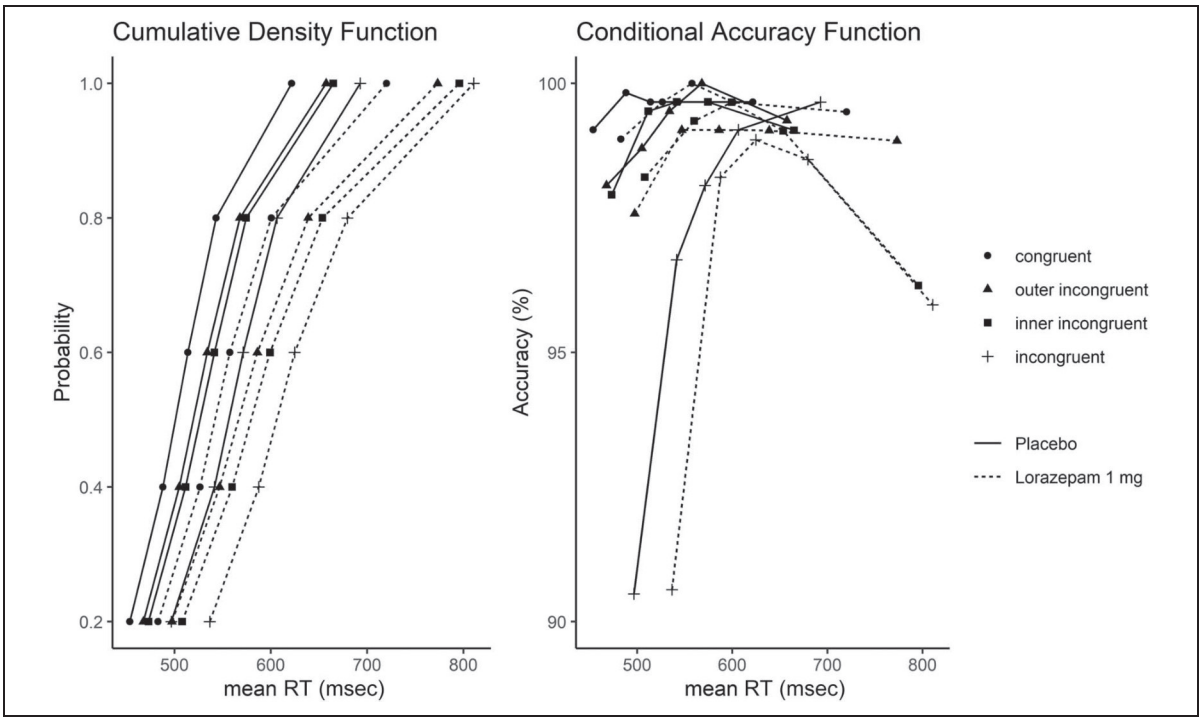

Figure 4. Cumulative density and conditional accuracy functions. Lorazepam effects across task conditions in comparison to placebo expressed in cumulative density function (CDF) and conditional accuracy function (CAF). RTs were first rank-ordered and separated into quintiles. In CDFs, for each condition separately, the cumulative RT probability is plotted against the mean RT for each quintile. In CAFs, for each condition separately, the accuracy is plotted against the mean RT for each quintile, $n = 29$.

Table 3. Descriptive Statistics and Lorazepam Effects on Visual Analogue Scales and NASA-TLX

	Placebo	*Lorazepam 1 mg*	*df*	*t*	*p*	*d*
VAS						
Alertness	37.33 (16.76)	55.36 (15.51)	28	−6.19	< .001	−.279
Contentedness	29.92 (10.87)	37.41 (13.02)	28	−3.66	< .001	−.157
Calmness	26.62 (14.09)	23.00 (13.60)	28	1.13	.27	.065
NASA-TLX						
Overall task load	39.76 (8.79)	42.13 (9.85)	28	−1.21	.24	−.064

The table includes descriptive statistics of the subjective scales under placebo and lorazepam (1 mg), where numbers indicate the mean (standard deviation) for each item in units from 1 to 100, as well as *t* test results testing for differences between both drug conditions. Higher numbers in visual analogue scales (VASs) indicate lower alertness, lower contentedness, and lower calmness. Higher numbers in NASA-TLX indicate a higher reported task load, $n = 29$.

function of administration order ($p = .51$). In addition, RT was higher for lorazepam than placebo in bother order groups (both $p < .001$). Thus, in our data, the overall increase in RT with lorazepam compared with placebo was more pronounced in participants who received lorazepam first.

Furthermore, there was a significant three-way interaction between Drug, Task Condition, and Order, $F(3, 81) = 5.24$, $p = .002$, $\eta_p^2 = .162$, CI [.025, .284], reflecting that the above described interaction between drug and task condition, which was the basis for our interpretation of lorazepam effects on in selective attention, was more pronounced when lorazepam was administered first ($p = .001$), than when placebo was given in Session 1 ($p = .272$). A possible explanation is that, in the second session of the placebo-first group, when the task was well practiced, inner flankers no longer had a stronger influence than outer flankers under lorazepam, as participants had practiced to narrow their attentional focus in this task under optimal conditions, that is, placebo, in the first session.

To ensure that the above reported interaction between Drug and Task Condition was not an artifact of order effects, we used data from Session 1 only and evaluated Drug as a between-subjects factor. Importantly, the interaction was still significant, $F(3, 81) = 4.16$, $p = .019$, $\eta_p^2 = .133$, CI [.010, .250], $\epsilon = .71$. Thus, we conclude that our key findings regarding the impairment of selective attention with lorazepam did not result from order effects.

For error rate, there was no significant main effect of Order, $F(1, 27) = 0.43$, $p = .52$, $\eta_p^2 = .016$, CI [.0000, .190]; no interaction between Drug and Order, $F(1, 27) = 0.64$, $p = .43$, $\eta_p^2 = .023$, CI [.0000, .208]; or between Task Condition and Order, $F(3, 81) = 0.02$, $p = .93$, $\eta_p^2 = .001$, CI [.0000, 1.000], $\epsilon = .43$; and no three-way interaction between Drug, Task Condition, and Order, $F(3, 81) = 2.37$, $p = .10$, $\eta_p^2 = .081$, CI [.0000, .184], $\epsilon = .68$.

EXPERIMENT 2

As this version of the flanker task had not been studied before and as we intended to substantiate our conclusions about lorazepam effects in comparison to the placebo condition, we applied the task in an independent sample without pharmacological manipulation.

Methods

Sample and Procedure

Twenty-seven healthy students aged 18–30 years were recruited by online and local advertisements. Inclusion criteria were: right-handed, normal or corrected-to-normal vision, no medication (except oral contraceptives in women), and no current diagnosis of physical, neurological, or psychiatric condition.

The online assessment started with a short demographic and screening questionnaire. Subsequently, all participants performed the experiment. However, only data from suitable participants were processed further. Participants carried out the flanker task and a Simon task, which is not part of this article. Task order was randomized between participants.

Participants provided informed consent by mouse click. After completion, participants were compensated with psychology course credits.

Flanker Task

The task (Figure 1) was implemented online using PsyToolkit (Stoet, 2010, 2017). Participants were instructed to carry out the experiment undisturbed in a quiet room, sitting comfortably and upright at a table. Mobile phones or tablets were disabled to ensure a sufficient screen resolution.

Task procedure was as in Experiment 1, except for the following variations owing to the online setting. First, participants were instructed to respond by pressing the right or left arrow key on their keyboard. Second, the size of the arrows was specified in pixels (total horizontal size = 720 px, vertical size = 154 px) instead of visual angle, as eye-to-screen distance likely varied. Third, during practice trials, immediate feedback was given after every trial to ensure participants understood the instructions.

Table 4. Descriptive Statistics and Internal Consistencies in Experiment 2

	M (SD)	*α [95% CI]*
RT con.	442.17 (63.38)	.99 [.98, .99]
RT outer	468.01 (69.62)	.99 [.98, .99]
RT inner	469.61 (67.23)	.98 [.97, .99]
RT incon.	503.37 (67.49)	.98 [.96, .99]
ER con.	0.36 (0.76)	.43 [.02, .71]
ER outer	1.81 (1.98)	.56 [.28, .78]
ER inner	2.82 (3.25)	.74 [.57, .87]
ER incon.	7.60 (6.95)	.86 [.77, .93]

Numbers indicate the mean (standard deviation). RT = mean reaction time; con. = congruent; outer = outer incongruent; inner = inner incongruent; incon. = incongruent; ER = error rate in %; α = Cronbach's α; CI = confidence interval (Feldt procedure), $n = 25$.

Data were preprocessed using R (R Core Team, 2021). Outcome variables were RT for correct trials (msec) and error rate (%).

Statistical Analyses

Statistical analyses of task data were as in Experiment 1, except that the within-subject ANOVA included only the factor Task Condition (congruent, outer, inner, incongruent).

Results

Sample Description

The final sample comprised $n = 25$ (17 female, 8 male) participants. Two of the initially 27 participants were excluded because of exclusion criteria (see Experiment 1). Percentages of trials excluded as invalid were low (0.08% of all trials for RT > 1200 msec). Mean age was 22.04 years ($SD = 2.98$ years). Table 4 contains descriptive results and internal consistencies of task performance data. Data sets, code, and material are provided on OSF (https://osf.io/y49a3).

Flanker Task

For RT (Figure 5A), there was a main effect of Task Condition, $F(3, 72) = 127.17, p < .001, \eta_p^2 = .841$, CI [.765, .876]. *t* Tests revealed significant differences between all conditions (all $p < .001$), except between outer and inner incongruent conditions, $t(24) = -0.55$, $p = 1.00$, $d = -0.006$, Similar to the pattern in Experiment 1, this indicates that RT was lowest in the congruent condition and highest in the incongruent condition, whereas RTs in outer and inner incongruent conditions were in between and comparable. Accordingly, the linear trend from congruent to incongruent condition was significant ($t = 3.09$, $p = .002$).

For error rate (Figure 5B), there was also a main effect of Task Condition, $F(3, 72) = 24.67, p < .001, \eta_p^2 = .507$, CI [.323, .610], $\epsilon = .46$. *t* Tests revealed significant differences between all conditions (all $p < .002$) except between outer and inner incongruent conditions, $t(24) = -2.13, p = .26, d = -0.097$. This pattern again indicates that error rate was lowest in the congruent condition and highest in the incongruent condition, whereas error rates in outer and inner incongruent conditions were in between. This finding was also reflected in a significant linear trend from congruent to incongruent condition ($t = 6.39, p < .001$).

Delta Plots

Based on visual inspection, delta plots (Figure 6) strongly resembled those from the placebo condition in Experiment 1 (Figure 3). As expected, there were no noticeable differences in RT and accuracy between outer and inner incongruent conditions for earlier or later quintiles. The difference in RT between congruent and incongruent

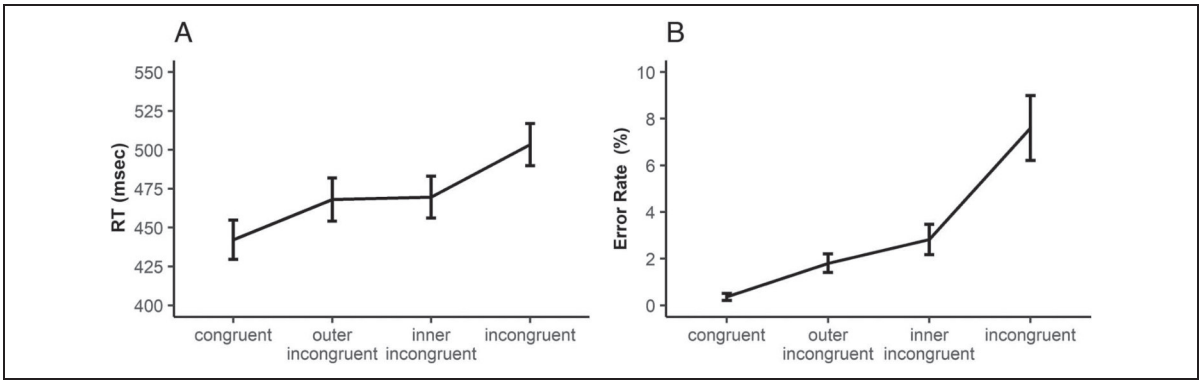

Figure 5. RT and error rate in Experiment 2. The figure illustrates the mean RTs of correct trials (A) and error rates (B) in the online version of the flanker task. Error bars indicate the standard error of the mean, $n = 25$.

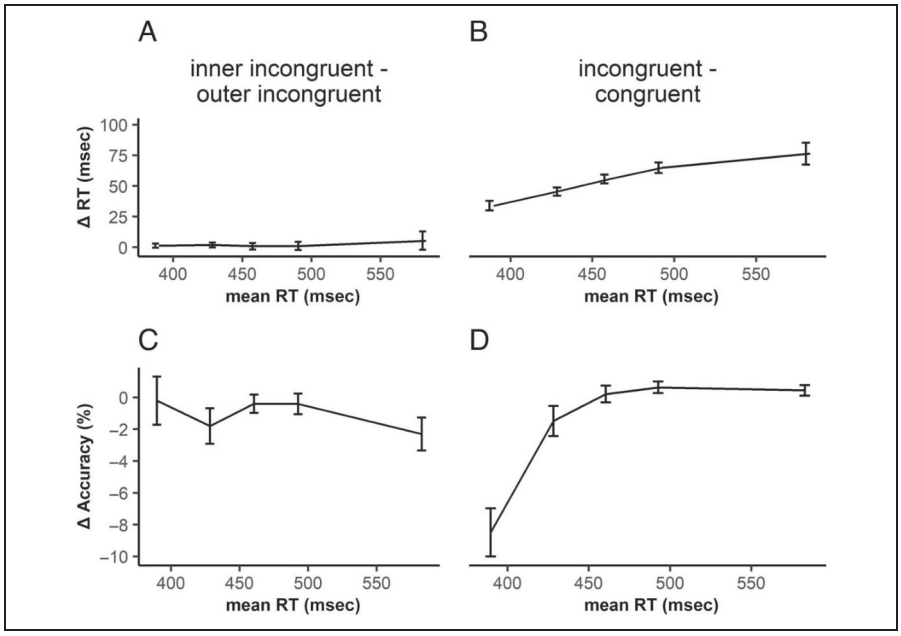

Figure 6. Delta plots in Experiment 2. The figure shows delta plots for the online version of the flanker task for mean RT of correct trials (A, B) and accuracy (percent correct) (C, D). In delta plots, RTs are rank-ordered and separated into quintiles. For each quintile, the difference (Δ) in RT or accuracy between outer and inner incongruent conditions (A, C) and the difference between congruent and incongruent conditions (B, D) are plotted against the mean RT of both conditions in the respective quintile. Error bars indicate the standard error of the mean, $n = 25$.

conditions increased over time, resulting in a positively sloped delta plot. The difference in accuracy decreased over time.

DISCUSSION

Lorazepam Effects on the Flanker Task (Experiment 1)

The present study significantly extends our knowledge of GABAergic involvement in cognition by demonstrating that benzodiazepine-induced increased GABAergic activity widens the attentional focus in a visual attention task. In the following, we first discuss the general worsening of selective attention under lorazepam and then further elaborate on the build-up of selectivity that emerged from delta plot analyses.

The statistically most pronounced effect of lorazepam in this study was an overall increase in RT with large effects size, confirming our hypothesis and previous research (Faßbender et al., 2021; Clariá et al., 2011; Riba, Rodríguez-Fornells, Münte, & Barbanoj, 2005; de Bruijn, Hulstijn, Verkes, Ruigt, & Sabbe, 2004), although there were no drug effects on error rates (Faßbender et al., 2021). Importantly, in addition to these general effects on response slowing under lorazepam that are likely not because of specific impairments in selective attention, there was a significant interaction between drug and task conditions. Thus, lorazepam did not increase RTs equally across task conditions.[1]

Crucially, we showed that the interaction was because of significantly higher RT with outer than inner incongruent flankers under lorazepam, a difference that did not exist under placebo. This critical comparison thus showed that under placebo (and in the absence of a pharmacological manipulation, Experiment 2), only the number of incongruent flankers impacts RT, whereas under lorazepam, their position is additionally relevant. A possible explanation of this result is a hypothetical distribution of selective attention and its modulation by lorazepam as suggested in Figure 7. Under placebo, the overall influence of inner and outer flankers was small but comparable. Under lorazepam, however, inner flankers had a stronger adverse influence on RT than outer flankers. Thus, when focusing on mean RT, it may be concluded that benzodiazepines broaden the spread of selective visual attention by flattening its distribution.

However, these results and their hypothetical model in Figure 7 do not explicate whether increased $GABA_A$ receptor activation simply slows down the build-up of selectivity over time, as it slows down other processes (cf. increased RT overall), or whether the spatial focus of attention is generally widened under lorazepam, reflecting a deficit that is not compensated in trials with high RT. Therefore, we drew upon delta plot analyses to further characterize the process of focusing on the central target over time (Ridderinkhof, 2002; Eriksen & St. James, 1986). Delta plots for RT increased over time in both drug conditions (cf. Ulrich, Schröter, Leuthold, & Birngruber, 2015; Ridderinkhof, Scheres, Oosterlaan, & Sergeant, 2005). The shift of the lorazepam data to the right (Figure 3) indicated the general slowing of responses under drug.

Crucially, if the increase in selective attention over time was simply slowed-down by lorazepam, the difference in RT between lorazepam and placebo should become smaller in later quintiles (Hübner & Töbel, 2012) as slower responses should provide more time for building

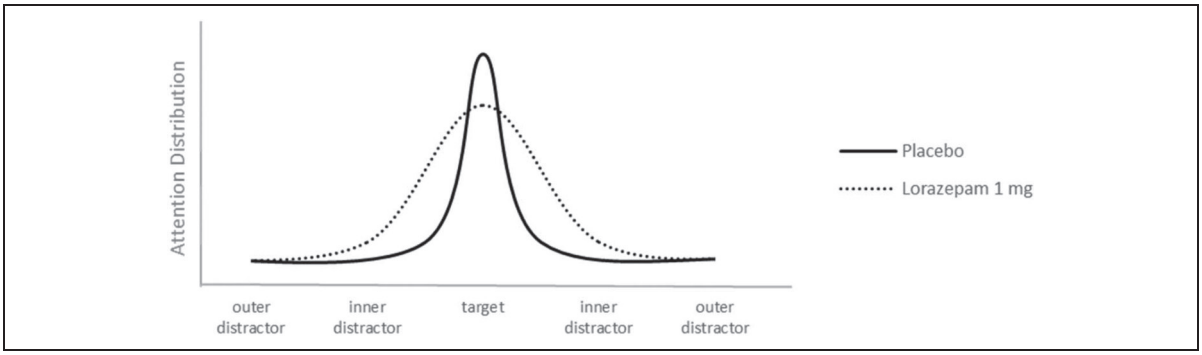

Figure 7. Model representation of a hypothetical distribution of selective attention in the flanker task. Representation of a hypothetical distribution of selective attention to account for the flanker task RT data from Experiment 1 under placebo and lorazepam (1 mg). Higher values on the *y* axis indicate stronger attentional processing. It should be noted that both lines do not flatten to zero.

up selectivity and thereby reducing impairments. White et al. (2011) reported significantly higher RT in inner compared with outer incongruent conditions when participants were instructed to respond quickly, that is, when there was little time to build up selectivity. Without this instruction, thus, at higher RT, there was enough time to build selectivity, and the difference was no longer present. However, delta plot analyses of our data showed that even for late quintiles, in trials with high RT, and despite overall higher RT under lorazepam, the difference in RT between placebo and lorazepam was still observed. Thus, it remained stable over time. Consequently, even slow reactions seemed to have no advantage in attentional focus, which we interpret to indicate that increased $GABA_A$ receptor activation generally widens the attentional focus.

Interestingly, and further disproving the hypothesis of lorazepam induced slowing of build-up of selectivity, delta plots for accuracy indicated even lower accuracy in later quintiles. That is, reacting slowly increased the adverse influence of incongruent flankers on response selection, especially the inner ones, thereby triggering more errors. Specifically, error rate in late quintiles significantly increased for inner compared with outer incongruent conditions and for incongruent compared with congruent conditions, resulting from a decline in inner incongruent and incongruent conditions. This finding was rather unexpected, given that delta plots for accuracy typically do not reveal differences in accuracy between congruent and incongruent conditions for later quintiles (Ridderinkhof, 2002). A possible explanation of this finding is that, with lorazepam, selectivity is initially built up and reduces the influence of the direct activation by irrelevant flankers. However, this suppression apparently cannot be maintained, and after some time, the influence of the irrelevant flankers again increases, and incorrect responses are no longer successfully suppressed. Although this is of course speculative, this pattern of findings further argues against a continuously yet slowed build-up of selectivity under lorazepam. It should be noted that because responses were generally faster under placebo than lorazepam, it is impossible to infer with certainty whether increased error rates in late quintiles is specific to increased $GABA_A$ receptor activity or the result of very slow reactions that did not occur under placebo.

Overall, we conclude that not only simple psychomotor responses and their underlying cognitive processes are slowed down by increased $GABA_A$ receptor activation (e.g., Tannenbaum et al., 2012; de Visser et al., 2003; Wittenborn, 1979), but that the focus of visual attentional is additionally widened.

Further evidence for GABAergic involvement in selective visual attention comes, for example, from research on anxiety. Anxiety has been shown to be associated with narrowed attentional focus (Wegbreit et al., 2015; Caparos & Linnell, 2012). Because lorazepam has known anxiolytic effects, those previous findings are consistent with our interpretation of the drug widening the attentional focus.

Functional neuroimaging studies have identified the neuronal correlates of a gradual decrease in the spatial distribution of attentional focus. For example, BOLD signal in visual cortex is reduced for locations nearby the target compared with the target itself. In higher extrastriate regions, the BOLD signal gradually decreases from the target outward (Hopf et al., 2006; Müller & Kleinschmidt, 2004). This finding indicates stronger neural processing of the target and reduced processing of flankers, the latter suggesting a role of inhibitory local projections using GABA. However, to what extent benzodiazepine-induced alterations in $GABA_A$ receptor activity influence neural processing of targets and flankers remains to be investigated.

Subjective Effects of Lorazepam

As expected, lorazepam reduced self-ratings of alertness. Against our hypotheses, there was no significant effect on calmness, and contentedness even decreased. The latter finding may suggest that participants perceived participation under lorazepam as more negative, perhaps

because of increased fatigue, although there was no effect on perceived workload.

Online Task Assessment (Experiment 2)

The online assessment closely replicated task effects from the placebo condition. Specifically, there were differences in RTs between all conditions except the outer and inner incongruent conditions, as under placebo in Experiment 1. Although this result does not correspond to our previously formulated expectations, it clearly shows that participants were able to direct their selective attention very specifically to the central stimulus in our version of the flanker task. With an increasing number of incongruent flankers, RTs and error rates increased, but the position of the incongruent flankers did not seem to be decisive.

Previous studies have typically manipulated either the proportion of incongruent flankers or the distance from flankers to target. It has been shown that larger distances between target and incongruent flankers reduce RT and error rate (Danielmeier, Wessel, Steinhauser, & Ullsperger, 2009; Eriksen & Eriksen, 1974) and, consistent with our results, a larger proportion of incongruent flankers increases RT and error rate (Forster, Carter, Cohen, & Cho, 2011). To our knowledge, simultaneous manipulation of distance and proportion of incongruent stimuli to the target has only been reported by White and colleagues (2011). In contrast to our results, they found a significant difference between outer and inner incongruent conditions. However, that difference only existed when participants were given feedback to respond more quickly after slow reactions. That instruction, like a short response stimulus interval (RSI), may have led to a lack of preparation for the next response and, thus, comparable to the lorazepam-induced impairments, may have influenced the narrowing of attention in unmedicated participants as well.

Compared with Experiment 1, RTs were faster overall, and error rates were slightly higher, which may be because of the online assessment where we were not able to control the type of device or interruptions during the assessment. This interpretation also fits with the fact that the standard deviations in the online assessment were consistently higher compared with the placebo condition in the laboratory.

Limitations

A number of limitations should be raised.

First, for Experiment 1, it should be noted that the specific effect of lorazepam on selective attention was rather small compared with the general drug-induced increase in RT.

Furthermore, in our task design, presentation times and ITIs were fixed. Therefore, the RSI varied depending on RT and the later the response in the current trial, the less time there was between response and the appearance of the next stimulus. A short RSI may not have provided enough time to sufficiently prepare for the next response resulting in a refractory phase (Hübner & Töbel, 2012). The general lorazepam-induced slowing may thus have affected the build-up of selectivity in the subsequent trial. To ensure that slowing in the previous trial does not affect performance in the current one, future studies could start the ITI immediately after the response by stopping the presentation of the stimuli.

An additional limitation relates to effects of repeated exposure to the tasks and measures in this study. Specifically, participants were better than chance at guessing the drug administered only in assessment Session 2, and there were effects of order of drug administration on RT suggesting that the two-way interaction between task condition and drug was weakened when lorazepam was given second.

Next, in Experiment 1, the flanker task was performed after a series of oculomotor tasks, which may have resulted in fatigue. However, the drug effect should not have been affected as the peak plasma concentration of lorazepam is reached after 1–4 hr. The main metabolite of lorazepam, glucuronide, also reaches its peak concentration after about 4 hr (Elliott, 1976). However, because it has low pharmacological activity (Greenblatt, 1981), we do not assume it influenced the results.

A final limitation is that Experiment 2 was not preregistered. However, assessments took place parallel to Experiment 1 without knowledge of any results.

Conclusion

The present study makes an important contribution to our understanding of the role of the GABAergic system in cognition. Although it was previously known that increased $GABA_A$ receptor activity slows down responses, we now showed that it also causes a generally widened attentional focus. Because benzodiazepine-induced neuronal inhibition occurs across a variety of brain areas, it would next be important to investigate in more detail in which areas neuronal inhibition contributes to widening the focus of attention.

Acknowledgments

We thank Lisa Urfei, Anna Schippers, and Johanne Wiepking for their valuable support in data collection.

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Data Availability Statement

Data sets, code, and material are provided on OSF (https://osf.io/y49a3/).

Author Contributions

Kaja Faßbender: Data curation; Formal analysis; Investigation; Methodology; Software; Visualization; Writing—

Original draft. Philine M. Baumert: Investigation; Validation; Writing—Review & editing. Maximilian W. M. Wintergerst: Investigation; Writing—Review & editing. Jan H. Terheyden: Investigation; Writing—Review & editing. Behrem Aslan: Investigation; Writing—Review & editing. Wolf M. Harmening: Conceptualization; Project administration; Resources; Supervision; Writing—Review & editing. Ulrich Ettinger: Conceptualization; Project administration; Resources; Supervision; Writing—Review & editing.

Funding Information

Wolf M. Harmening, Emmy Noether Program of the German Research Foundation, grant number: Ha5323/5-1.

Diversity in Citation Practices

Retrospective analysis of the citations in every article published in this journal from 2010 to 2021 reveals a persistent pattern of gender imbalance: Although the proportions of authorship teams (categorized by estimated gender identification of first author/last author) publishing in the *Journal of Cognitive Neuroscience* (*JoCN*) during this period were M(an)/M = .407, W(oman)/M = .32, M/W = .115, and W/W = .159, the comparable proportions for the articles that these authorship teams cited were M/M = .549, W/M = .257, M/W = .109, and W/W = .085 (Postle and Fulvio, *JoCN*, 34:1, pp. 1–3). Consequently, *JoCN* encourages all authors to consider gender balance explicitly when selecting which articles to cite and gives them the opportunity to report their article's gender citation balance. The authors of this article report its proportions of citations by gender category to be as follows: M/M = .649, W/M = .243, M/W = .108, and W/W = 0.

Note

1. Note that additional analyses, excluding the newly established outer and inner incongruent conditions to make the data comparable to our previous study, confirmed the previously observed increased congruency effect for RT under lorazepam (Faßbender et al., 2021).

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