

DISSERTATION

Effects of Subliminal Visual Stimuli on the Awareness of an Urge
to Move in Adults with Chronic Primary Tic Disorders

Einfluss von unterschweligen visuellen Reizen auf das
Bewusstsein über einen Bewegungsdrang bei Erwachsenen mit
chronischen primären Tic-Störungen

zur Erlangung des akademischen Grades
Doctor rerum medicinalium (Dr. rer. medic.)

vorgelegt der Medizinischen Fakultät
Charité – Universitätsmedizin Berlin

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Datum der Promotion: 15. September 2025

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Abbreviations

| | |
|--------|---|
| ADC | Analogue-to-Digital Converter |
| ADD | Attention Deficit Disorder |
| ADHD | Attention-Deficit-Hyperactivity Disorder |
| APA | American Psychological Association |
| BDI-II | Becks Depression Inventory-II |
| CAARS | Conners' Adult ADHD Rating Scale |
| CPTSD | Complex Post-Traumatic Stress Disorder |
| DSM-5 | Fifth edition of the Diagnostic and Statistical Manual of Mental Disorders |
| EHI | Edinburgh Handedness Inventory |
| ER | Error rates |
| F | False alarms |
| FIR | Finite Impulse Response |
| GSS | Global Severity Score |
| GTS | Gilles de la Tourette syndrome |
| H | Hits |
| ICD-11 | International Classification of Diseases-11 |
| Inf | Infinity (or real number smaller/larger than can be represented) |
| L | Left |
| LQ | Laterality Quotient |
| mRT | Median Reaction Time |
| ms | Milliseconds |
| NaN | Not a Number (undefined/unrepresented results from mathematical operations) |
| OCD | Obsessive-Compulsive Disorder |

| | |
|--------|---------------------------------------|
| PTD | Primary Tic Disorders |
| PU | Premonitory Urge |
| PUTS | Premonitory Urge for Tic Scale |
| R | Right |
| RT | Reaction time |
| SD | Standard Deviation |
| SDT | Signal Detection Theory |
| sEMG | Surface Electromyography |
| SOA | Stimulus Onset Asynchrony |
| TKEO | Teager-Kaiser Energy Operator |
| TTS | Total Tic Score |
| WHO | World Health Organisation |
| Y-BOCS | Yale-Brown Obsessive-Compulsive Scale |
| YGTSS | Yale Global Tic Severity Scale |

Zusammenfassung

Einleitung: Bei primären Tic-Störungen (PTD), wie dem Gilles de la Tourette Syndrom (GTS), werden Tics häufig mit einer somatosensorischen Empfindung, dem Vorgefühl (premonitory urge) assoziiert. Es ist unklar, ob Tics unwillentlich sind oder ob sie willentliche Reaktionen auf unwillentliche Vorgefühle darstellen. Unklar ist auch, ob dies auch das Bewusstsein für willentliche Handlungen beeinflusst. Eine Möglichkeit, das Bewusstsein über willentliche Handlungen zu erforschen, ist das Libet Experiment. Frühere Studien auf diesem Forschungsgebiet erzielten jedoch gemischte Ergebnisse. Eine Limitation des Libet-Paradigmas wird darin gesehen, dass keine experimentelle Kontrolle über die Bewegungsvorbereitung und -absicht vorliegt. In dieser Studie verwenden wir einen neuen experimentellen Ansatz, um zu untersuchen, ob Erwachsene mit PTD ein verändertes Bewusstsein für Bewegungsdränge im Vergleich zu gesunden Kontrollpersonen haben. Wir vermuten, dass Erwachsene mit PTD ein reduziertes Bewusstsein für Bewegungsdränge aufgrund eines erhöhten neuronalen Rauschens haben könnten.

Methoden: Um motorische Reaktionen experimentell zu modulieren, wurde sublimales visuelles Priming in einen Go/NoGo-Test integriert. Sublimale Primes induzierten eine vorübergehende Bewegungsvorbereitung (urge to move), selbst wenn diese Vorbereitung nicht zu einer tatsächlichen motorischen Reaktion in NoGo trials führte. Zusätzlich wurde ein Drang-Erkennungstest in NoGo-Trials durchgeführt, bei dem die Probanden berichteten, ob sie einen durch den sublimalen Prime induzierten Bewegungsdrang wahrnahmen.

Ergebnisse: Die Ergebnisse zeigen, dass der Priming-Effekt, als Voraussetzung für die Drangwahrnehmung, in beiden Gruppen vorhanden war, jedoch ohne Unterschiede zwischen den Gruppen. Die Kontrollgruppe wies signifikant höhere d-prime-Werte für die Drang-Erkennung als für die Prime-Erkennung auf. Dies deutet darauf hin, dass die Kontrollprobanden einen durch den Prime induzierte Bewegungsvorbereitung nach Ausschluss von Muskelaktivität und Prime-Erkennung wahrnehmen konnten. In der PTD-Gruppe erreichte derselbe Effekt keine statistische Signifikanz, war jedoch numerisch ähnlich. Es wurden keine Unterschiede im Bewusstsein für Bewegungsdränge zwischen Erwachsenen mit PTD und gesunden Kontrollpersonen in dem verwendeten neuen experimentellen Ansatz gefunden.

Implikationen: Die vorliegende Arbeit ist die erste Studie, die eine objektive experimentelle Kontrolle über die Bewegungsplanung bei Erwachsenen mit PTD bietet. Diese Machbarkeitsstudie zeigt, dass die Induktion subliminaler visueller Primes in einer klinischen Population wie Erwachsenen mit PTD möglich ist. Höchstwahrscheinlich ist eine größere Stichprobe erforderlich, um mögliche Unterschiede zwischen Erwachsenen mit PTD und gesunden Kontrollpersonen zu festzustellen.

Abstract

Introduction: In primary tic disorders (PTD), such as Gilles de la Tourette Syndrome (GTS), tics are the predominant feature and are often associated with prior somatosensory phenomena like premonitory urges (PUs). It remains unclear whether tics are truly involuntary or are voluntary responses to involuntary sensory experiences, and whether this also impacts awareness of voluntary actions. One way to explore volition over voluntary actions is the Libet paradigm. Previous studies using this paradigm to assess volition in adults with GTS yielded mixed results. However, the Libet paradigm lacks control over movement preparation and intention. Here, we employ a novel experimental approach to investigate whether adults with PTD have altered awareness of an urge to move compared to healthy controls. We hypothesize that adults with PTD may have reduced awareness of an urge to move due to increased neuromotor noise levels.

Methods: To experimentally modulate motor responses, we applied subliminal visual priming to a modified Go/NoGo task. Specifically, subliminal primes induced a transient movement preparation (urge to move), even when this preparation did not lead to eventual motor output in NoGo trials. Additionally, a concurrent urge detection task was performed in NoGo trials to investigate urge sensitivity. Here, participants reported whether they perceived a transient urge to move, induced by the subliminal prime.

Results: Our results show that the priming effect, as a prerequisite for urge detection, was present in both groups, but without any differences between groups. In the urge detection task, the control group showed significantly higher dprime scores for urge detection than for prime recognition. This indicates that they could discern whether they have transiently prepared a motor response induced by the prime, even in the absence of prior muscle activity and conscious prime discrimination. In the PTD group, the same effect did not reach statistical significance but was numerically similar. Most important, no differences regarding the awareness of an urge to move in this task were found between adults with PTD and healthy controls.

Implications: The present work is the first study which provides objective experimental control over movement planning in adults with PTD. This proof of principle study shows that the induction of subliminal primes is feasible in a clinical population like in adults with PTD. It is possible that a larger sample is required to address differences between adults with PTD and healthy controls.

1 Introduction

1.1 Primary Tic Disorders

Primary tic disorders (PTDs) are a group of neurodevelopmental disorders consisting of motor and/or phonic (vocal) tics (WHO, 2022). According to the International Classification of Diseases-11 (ICD-11, 2018) (WHO, 2022), the PTD class (8A05.0) includes:

- 8A05.00 Gilles de la Tourette syndrome
- 8A05.01 Chronic motor tic disorder
- 8A05.02 Chronic phonic tic disorder
- 8A05.03 Transient motor tics
- 8A05.0Y Other specified primary tics or tic disorders
- 8A05.0Z Tic disorders, unspecified

In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5, 2013), three primary categories of tic disorders are identified: transient tic disorder, chronic motor or vocal tic disorder, and Gilles de la Tourette syndrome (APA, 2013). As chronic motor or vocal tic disorder is defined by tics being present for more than one year, transient tic disorder applies to tics being present for less than a year (APA, 2013). In all three PTDs, tic onset must occur before the age of 18 to be recognised as a primary tic disorder (APA, 2013). Neither the ICD-11 nor the DSM-5 require the presence of subjective impairment for the diagnosis of a tic disorder.

In contrast to PTDs, secondary tic disorders are less common and linked to a wide spectrum of other medical conditions. Examples include neurodevelopmental disorders (e.g., autism spectrum disorders), neurodegenerative disorders (e.g., Huntington's disease), drug-induced tics (e.g., induced by amphetamines or cocaine) and rare conditions, such as lesion-induced tics (Ganos et al., 2022; Kumar & Lang, 1997). Among secondary tic disorders, functional tics, also known as tic-like behaviours, constitute the most common differential diagnosis (Ganos et al., 2021). Distinguishing between primary and functional tics can be challenging (Rigas et al., 2023); however, recently established consensus criteria offer diagnostic guidance (Pringsheim et al., 2023).

1.2 Gilles de la Tourette syndrome (GTS)

Gilles de la Tourette syndrome (GTS) is the most common PTD seen in movement disorders clinics (Arbuzova et al., 2022). The condition is defined by the presence of motor and phonic tics for more than one year, although they do not need to manifest consistently (WHO, 2022). For a GTS diagnosis, tic symptoms must appear before the age of 18 (WHO, 2022). The first tic symptoms in GTS occur in early childhood (Nilles et al., 2023) at about six years (Freeman et al., 2000). GTS typically first manifests with the occurrence of simple motor tics, such as excessive eye blinking. Phonic tics typically exhibit one to two years after the first motor tic (Hassan & Cavanna, 2012). Despite fluctuations in tic frequency and severity (Efron & Dale, 2018; Robertson, 2015), tic symptoms often peak between 11 and 14 years (Hassan & Cavanna, 2012). In most cases, tic symptoms improve in late adolescence and early adulthood (Leckman et al., 1998; Specht et al., 2011). However, they may persist during adulthood, although they are less prominent (Bloch & Leckman, 2009; Pappert et al., 2003).

Gilles de la Tourette syndrome is prevalent worldwide in all cultures and ethnicities (Singer, 2011). The prevalence of GTS in children aged between 6 and 15 years is estimated at 0.77% (95% CI: 0.39-1.51%) (Knight et al., 2012). Due to variations in study populations, differing study methods and challenges with the diagnosis of GTS, prevalence data for children aged between 5 and 18 years ranges widely between 0.4% and 3.8% across studies (Robertson, 2008). In childhood, males are about four times more likely to be affected by GTS than females (Knight et al., 2012). Data on GTS prevalence among adults is limited and ranges (Cubo et al., 2011; Scahill et al., 2014), but the overall prevalence among GTS in adults is estimated at 0.05% (Knight et al., 2012). A recent meta-analysis suggests that GTS affects around 118 in every million adults (0.000118%) (Levine et al., 2019).

People with GTS are often diagnosed with additional neuropsychiatric conditions, including attention-deficit-hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), depression, anxiety disorder (Hirschtritt et al., 2015), and self-injurious behaviours (Fischer et al., 2020). Hirschtritt et al. (2015) found that 72.1% of children with GTS had comorbid ADHD or OCD, and around one-third of GTS-diagnosed children showed combined comorbid ADHD and OCD. Young males with GTS are more likely to have comorbid ADHD than females, but females are more likely to have OCD when diagnosed with GTS (Hirschtritt et al., 2015). Individuals diagnosed with GTS

and comorbid ADHD typically show impulse control difficulties, inattentiveness, restlessness and distractibility, which often affect daily living (decreased school performance, sleep and behavioural disturbances). Furthermore, GTS combined with comorbid ADHD is associated with poorer social adaptation than GTS alone (Gill & Kompoliti, 2020; Robertson, 2006). Individuals with GTS and OCD often experience more intense obsessions related to violence, symmetry, and compulsions such as excessive touching, blinking, or self-harm compared to those with OCD alone (George et al., 1993). The range and severity of these comorbid conditions are often reported to be more disabling than the motor and/or vocal tics (Bernard et al., 2009).

1.3 Clinical Characteristics of Tics in GTS

The cardinal diagnostic feature in GTS is the presence of tics. Tics are described as sudden, brief and nonrhythmic movements and sounds that occur repetitively (Leckman et al., 2022). They are categorised based on the type of output (motor/phonic), complexity (simple/complex), and somatotopic location (face/trunk/extremities) (Leckman, 2017) (see Table 1).

Table 1: Specifications of Tics (modified after Leckman, 2017).

| Type | Complexity | Examples |
|--------|--|--|
| motor | simple <i>(rapid, darting, meaningless)</i> | Eye blinking Facial movements (eye, nose, mouth) Movements with extremities (hand, arm, leg, foot) |
| | Complex <i>(slower, purposeful)</i> | Facial expressions and gestures Bending, rotating, blocking Copropraxia |
| phonic | simple <i>(fast, meaningless sounds)</i> | Coughing, sniffing, grunting Throat clearing, whistling |
| | complex <i>(more meaningful utterances)</i> | Syllables, words, phrases Coprolalia, echolalia, palilalia |

The temporal evolution of motor tics involves a rostrocaudal spread of symptoms (Leckman et al., 1998), first affecting facial muscles and then spreading to lower regions, such as the trunk, abdomen and limbs (Ganos, Bongert, et al., 2015). Categorised by complexity, simple motor

tics are described as abrupt, fast, and non-directive (meaningless) movements. They are usually present for one to two seconds and predominantly involve one muscle group (Leckman et al., 2022). Based on the duration of motor output, simple motor tics can also be categorised as clonic, dystonic, and tonic (Jankovic, 1997). Clonic tics include brief, jerking movements faster than 100 milliseconds (ms), such as eye blinking or nose twitching. Tics lasting more than 500 ms and isometric abdominal contractions are described as tonic tics. Tics that lead to prolonged (lasting several seconds) abnormal postures or twisting movements are referred to as dystonic (Jankovic, 1997).

Complex motor tics are slower, purposeful-appearing movements or gestures, such as brushing hair back (Leckman et al., 2022). They encompass a diverse range of muscle jerks and contractions in different muscle groups (Berardelli et al., 2003) and typically occur in later stages of GTS (Leckman et al., 2022). Individuals with GTS occasionally exhibit sudden episodes where they briefly stop all physical movements without any change in their awareness. These episodes are referred to as “blocking tics” (Jankovic, 1997) or as “blocking phenomena” (Ganos, Müller-Vahl & Bhatia, 2015). Although their pathophysiology remains unclear, two types of blocking phenomena can be observed in the context of tics. Some people experience a momentary break in their voluntary movements during prolonged and severe tonic and dystonic tics (Jankovic, 1997). This interruption may occur because involuntary motor behaviours predominate voluntary movements (Ganos, Müller-Vahl, & Bhatia, 2015). Others might exhibit a sudden halt in all motor activity or have difficulty initiating movements, particularly if maintaining posture against gravity is part of their tic behaviour (Ganos, Müller-Vahl, & Bhatia, 2015).

Phonic tics are also part of the tic spectrum. In the context of GTS, phonic tics are typically brief, simple sounds such as throat clearing or coughing, and they usually appear after the onset of motor tics (Leckman et al., 1998). Complex phonic tics involve syllables, words, and phrases but also coprolalia (socially inappropriate verbal expressions), echolalia (involuntary repetition of words spoken by another person) (Ganos et al., 2012), palilalia (involuntary repetition of utterances or phrases during speech) (Eapen & Robertson, 2015). Complex tics such as copropraxia (motor) and coprolalia (phonic) are less frequent and observed in more severe cases of GTS (Leckman et al., 2022). Tic frequency and severity fluctuate over time, and various contextual and behavioural factors may influence tic output. For instance, stress, anxiety, fatigue, and boredom are associated with increased tic severity, whereas heightened concentration – for example, when playing instruments or engaging in physical activity – attenuates tics in many individuals with GTS (Conelea & Woods, 2008).

1.4 Suppressibility of Tics in GTS

In addition to behavioural factors modulating tic expression, such as concentrating on a specific act or distractibility, the ability to voluntarily suppress tics for a period is a notable clinical characteristic of people with GTS. The capacity of voluntary tic suppression is a clinical criterion to distinguish tics from other hyperkinesia, such as myoclonus or chorea (Zapparoli et al., 2019). In GTS, the suppressibility of tics varies across different body parts. Tics involving body parts that are prominently represented in the brain's somatotopic map, such as hands or the face, may be harder to suppress compared to tics involving less prominently represented body parts, like the feet or the trunk (Ganos, Bongert, et al., 2015). Research indicates that tic suppression involves a selective voluntary inhibitory mechanism in GTS, whereby individuals with GTS can inhibit specific tics while others persist (Ganos, Bongert, et al., 2015). For example, in situations perceived as unpleasant or socially challenging, where expressing tics may draw attention, individuals with GTS may suppress vocal tics while allowing motor tics that may attract less attention in that particular context (Ganos, Bongert et al., 2015). Many people with GTS report that successful tic suppression positively impacts their quality of life and provides satisfaction in social interactions and daily activities (Matsuda et al., 2016). In this situation, tic suppression is a psychosocial compensatory mechanism in GTS, as the expression of tics may draw unwanted attention and adversely affect the individuals' social functioning and psychological well-being (Eapen et al., 2016; Lund et al., 2023). However, voluntary tic suppression requires considerable effort and typically lasts from several seconds to a few minutes. Tic suppression usually engenders internal discomfort or an urge to tic that can intensify to the point where it surpasses the patient's ability to control it (Cohen et al., 2013). In clinical interviews, many adults with GTS describe voluntary tic suppression as exhausting, necessitating heightened concentration, and ultimately giving way to a temporary surge in tics due to an escalating urge to tic (Müller-Vahl, 2010).

1.5 Premonitory Urges (PUs) in GTS

Like the increasing discomfort experienced during voluntary tic suppression, premonitory urges (PUs) are a fundamental aspect of tics (Kwak et al., 2003). These subjective sensory experiences often

precede tics and are typically characterised by vague descriptions such as pressure, tension, a sense of incompleteness or a feeling of not being “just right” (Kwak et al., 2003).

The reported prevalence of PUs varies among adolescents and adults but is estimated to affect approximately 77% of individuals with GTS over 13 and around 90% of those over 18 (Bliss, 1980; Leckman et al., 1993). The experience of PUs in childhood typically increases with age (Banaschewski et al., 2003). In a prevalence study by Sambrani et al. (2016) involving 1,032 children with GTS, the experience of PUs was reported as 46.7% among children under 10, 61.3% among those aged 10 to 12, and 79.9% among those over 12. The age-dependent increase of reporting PUs is believed to correspond to the natural development of introspective abilities in childhood, such as bodily awareness (Banaschewski et al., 2003).

Premonitory urges are typically experienced in the same body area or close to where tics occur (Essing et al., 2022; Leckman et al., 1993). Explorative studies of tic localization and PU frequency revealed that PUs more frequently precede complex tics than simple tics (Cavanna et al., 2017; Essing et al., 2022). However, data on affected body parts is limited and yielded varied outcomes. Cavanna et al. (2017) showed that tics involving the head, upper trunk, and midline abdomen are more commonly preceded by PUs, whereas tics such as blinking or mouth movements exhibit lower rates of preceding PUs. Conversely, a recent study indicates that PUs most often occur in the facial region and head without discernible differences between motor and phonic tics (Essing et al., 2022).

Despite considerable interest in the role of PUs from scientific and clinical perspectives (Cavanna et al., 2017; van de Griendt et al., 2013), the origins of PUs in GTS remain elusive (Ganos, Garrido, et al., 2015; Smith et al., 2022). Early clinical investigations into PUs in GTS suggested that tics may represent voluntary responses to involuntary urges (Bliss, 1980; Faul et al., 2009; Lang, 1991). However, not every tic is preceded by a PU, and some tics occur without the presence of PUs (Martino et al., 2017). Additionally, some people with GTS may not be aware of their tics – blinking tics, for example – and thus may not perceive PUs (Pappert et al., 2003). One perspective posits that PUs may resemble normal human urges. Here, the urge to blink may serve as a suitable model for describing PUs in GTS. Individuals can temporarily suppress blinking at the expense of increasing discomfort akin to PUs in GTS (Hallett, 2015). Notably, PUs appear to be more distressing than the tic itself, with tic expression often relieving and temporarily alleviating the PU afterwards (Cohen & Leckman, 1992; Jackson et al., 2020). Considering the suppressibility of tics

and the phenomenology of PUs, a closer investigation of the perceptual aspects of PU preceding tics may contribute to a better understanding of tic pathogenesis.

1.6 Exteroceptive and Interoceptive Sources of PU

The perceptual sources of PUs remain unclear. Specifically, it is unresolved whether alterations in the processing of exteroceptive or interoceptive signals are involved in the pathophysiology of PUs (Ganos, 2016). It is widely recognised that individuals with GTS report heightened sensitivity to external sensory stimuli (e.g., touch, sight, sound, or smell) (Belluscio, Jin, et al., 2011), pointing towards an association of PUs and exteroception (Ganos, 2016). Schunke et al. (2016) assessed sensory perception thresholds across 13 sensory parameters – including thermal and mechanical/tactile – and pain in 14 people with GTS. They investigated the relationship between these sensory thresholds and PUs, reporting no group differences in any of the tested sensory parameters and no correlation between the sensory parameters and the perceived intensity of PUs in individuals with GTS. Consistent with these findings, other studies have reported no correlation between the severity of this hypersensitivity to external stimuli and PUs (Sutherland Owens et al., 2011; Weisman et al., 2018). Arbuzova et al. (2022) used a different paradigm to examine tactile and visual metacognition and PUs in 25 individuals with GTS using a forced-choice discrimination paradigm and post-trial self-ratings of confidence in their choices. The authors did not observe impaired tactile or visual metacognition in the GTS group, nor did they find correlations between tactile metacognition and subjective reports of PUs or tic severity. These findings indicate that altered processing of external stimuli at the peripheral and central levels may not be the source of PUs in GTS.

Instead, it is suggested that PUs in GTS may stem from altered perceptual processing at the central level and perturbed awareness of internal bodily signals (Farb et al., 2015; Ganos, Garrido, et al., 2015). Individuals with GTS may exhibit increased sensitivity to and awareness of their internal bodily processes (interoception), leading to a heightened perception of PUs. Ganos, Garrido et al. (2015) investigated the relationship between PUs and interoceptive awareness in 19 individuals with GTS using a heartbeat-tracking test to assess interoception (Schandry, 1981). They found that the GTS group had less accuracy than controls in detecting interoceptive signals, indicating decreased interoceptive awareness in GTS. This finding appears to contradict the hypothesis that individuals

with GTS have increased awareness of internal bodily processes. Furthermore, the authors observed that the level of interoceptive awareness strongly predicts PUs, even more than overall tic severity (Ganos, Garrido, et al., 2015). The latter finding is supported by a recent study demonstrating that interoceptive accuracy explains additional variance in PUs (Schütteler et al., 2023). Based on these findings, decreased interoceptive awareness may be associated with higher levels of neural noise for detecting internal signals (Ganos, Asmuss et al., 2015; Münchau et al., 2021). Hence, individuals with GTS may have difficulty detecting internal signals in the presence of ongoing neuromotor noise (Ganos, Asmuss et al., 2015).

Rae et al. (2019) studied 21 adults with GTS who underwent a heartbeat-tracking test alongside a discrimination task. Their results showed that interoceptive accuracy in individuals with GTS was not reduced, but interoceptive sensibility, the subjective sensitivity to bodily sensations, was a predictor of PU severity. Notably, they discovered a disparity in individuals with GTS, showing lower interoceptive accuracy but heightened interoceptive sensibility compared to the control group. This discrepancy, termed interoceptive prediction error, reflects a contrast between the subjective perception of internal bodily signals (interoceptive sensitivity) and the objective measured capacity to detect these signals (interoceptive awareness). Individuals with GTS appear more sensitive to internal bodily signals but exhibit less accuracy in detecting them (Rae et al., 2019). These findings indicate that altered interoceptive processing may contribute to the generation of PUs in GTS.

1.7 Volition and Tics in GTS

The volitional nature of tics remains a subject of ongoing debate in the literature (Singer & Augustine, 2019). It remains unclear whether tics are truly involuntary movements or rather reflect a voluntary response to unwanted sensory experiences (Bliss, 1980; Ganos, Asmuss, et al., 2015). In this regard, tics have been termed “involuntary” (Belluscio, Tinaz, & Hallett, 2011) or “nonvoluntary” (Ganos, Garrido et al., 2015).

Supporting the notion that tics are involuntary movements, some research has demonstrated differences between tics and comparable voluntary movements regarding their cortical preparatory activity (Virameteekul & Bhidayasiri, 2022). Unlike voluntary movements, which typically exhibit distinct event-related motor potentials (Morera Maiquez et al., 2022), such patterns were not observed

during tics (Obeso et al., 1981; Zapparoli et al., 2019). Recent findings have shown that movement-related oscillations in the mu- and beta-band frequencies, commonly observed before voluntary movements, are absent prior to tics in individuals with GTS (Morera Maiquez et al., 2022). Additionally, some tics occur without prior PUs, and some people with GTS are unaware of their tics and do not experience PUs (Martino et al., 2017; Pappert et al., 2003). These details indicate that tics may not solely be a voluntary reaction to unwanted sensory experiences, as suggested by Leckman and colleagues (1993).

However, there is evidence supporting the consideration of tics as voluntary movements. Voluntary movements are generated through conscious activity in brain motor areas, and tics are at least partially generated through voluntary motor pathways (Bohlhalter et al., 2006). Additionally, voluntary movements are often accompanied by specific subjective experiences, such as a sense of agency, a feeling of controlling one's actions, and the conscious intention to act. This subjective experience of intending to do something serves as a predictor prior to the neural preparation of voluntary actions (Haggard, 2005). Individuals with GTS often report that voluntarily expressing tics in response to PUs leads to a temporary sense of relief (Lang, 1991). In a study by Leckman and colleagues (1993) involving 135 people with GTS, 92% reported that their tics were fully or partially a voluntary response to involuntary PUs. Furthermore, individuals with GTS can consciously suppress their tics, although PUs are temporarily alleviated only through tic expression (Cohen & Leckman, 1992; Jackson et al., 2020). The conscious intention to express or suppress tics, along with the neural correlates of tic generation, suggests that tics may possess characteristics of both voluntary and involuntary movements (Ganos, Asmuss et al., 2015).

One classic method to explore the volitional aspects of voluntary movements is the Libet paradigm (Libet et al., 1983) (see Figure 1). In the Libet paradigm, participants are instructed to observe a quickly rotating clock hand and to perform a spontaneous hand movement at any time during the clock's rotation (Libet et al., 1983). After the clock stops at a randomly determined time interval, participants are asked to report the moment they first felt the urge to move their hand (Haggard, 2008). During this process, scalp electrodes record activity from prefrontal motor areas involved in movement preparation (readiness potential; see Figure 1). Participants are instructed to report the moment they first experienced the intention to move (W-Judgement) or the time of the actual movement (M-Judgement). Libet et al. (1983) found that, on average, participants reported the conscious intention to perform the finger movement (W-Judgement) 206 ms before muscle activity

began (M-Judgement). Cortical activity to prepare movements could start one second or more before the onset of the movement, suggesting that the brain prepares the movement before participants are aware of their intention to move (Haggard, 2008).

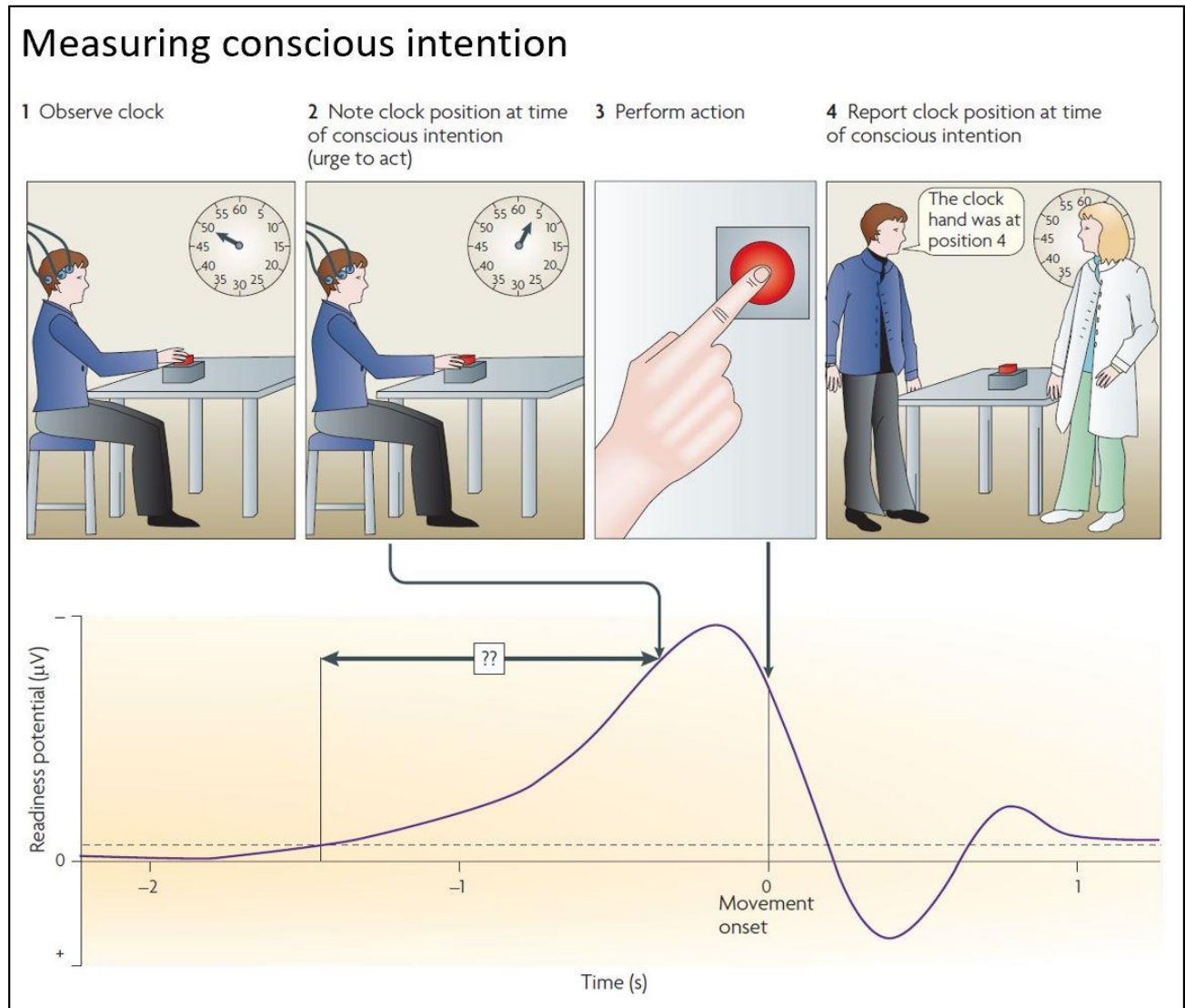


Figure 1: The Libet Experiment: measuring conscious intention (Haggard, 2008, used with permission).

To better understand the reciprocal interactions between volition, tics and PUs, the Libet experiment has been applied to study the awareness of voluntary actions in individuals with GTS. Moretto et al. (2011) demonstrated that adults with GTS become aware of their intention to move only after a delay compared to healthy controls. Similarly, Ganos, Asmuss et al. (2015) found that GTS-

diagnosed people with stronger subjective PUs showed delayed perception of the intention of voluntary actions compared to those with weaker perceived PUs.

Although the Libet paradigm was one of the first attempts to study the intention of voluntary actions, it has been subject to controversy and criticism for various reasons. One limitation of this method is the lack of experimental control over the intention to move. In the Libet paradigm, the timing of movement onset is self-paced and voluntarily chosen by the subject, thus lacking objective control over the subjective report of the first intention to move (Haggard, 2008).

The phenomenology of tics, like tic suppressibility, and the observation that some people are unaware of their tics indicate a complex interplay between voluntary and involuntary aspects of tics. The presence of PUs further complicates this interplay, as individuals with GTS often report performing tics in response to unwanted, uncomfortable PUs (Bliss, 1980; Ganos, Asmuss, et al., 2015). To gain more insights into the awareness of tics and PUs in PTD, a novel experimental paradigm has been developed providing experimental control for both movement planning and subjective reports over the awareness to initiate a movement (Chambon & Haggard, 2012; Stenner et al., 2014). In this paradigm, subliminal visual priming (Eimer & Schlaghecken, 2002) is used in a Go/NoGo task to modulate self-intended voluntary movements by external visual stimuli (Parkinson & Haggard, 2014). A recent study by Altas and Stenner (2024, unpublished data) explores the awareness of an urge to move in healthy individuals using this modified experimental approach. The authors demonstrated that participants could identify whether they had transiently prepared a motor response induced by the subliminal visual prime, even though this preparation did not lead to eventual motor output. Healthy subjects could detect this transient bias towards movement preparation even when there was no muscle activity in the surface electromyography (sEMG). These results indicate that healthy individuals can be aware of their intention to initiate a voluntary movement.

2 Research Question and Hypothesis

This study employs a previously established novel experimental approach (Altas & Stenner, 2024, unpublished data) to explore the awareness of an urge to initiate a voluntary action in individuals with PTD. Specifically, the following research question is addressed:

- Do adults with PTSD have altered awareness of the urge to initiate a voluntary movement, triggered by subliminal motor priming, compared to age- and sex-matched healthy controls?

Based on the literature discussed above, this study makes the following hypothesis: The awareness of an urge to initiate a movement is reduced in adults with PTSD because of increased sensorimotor noise levels. The awareness of an urge to move – quantified as urge sensitivity – was considered the primary outcome parameter in the present study.

3 Materials and Methods

To assess the awareness of an urge to move in individuals with PTSD, the experimental set-up comprised two parts: a questionnaire- and interview-based clinical evaluation and a behavioural experimental task. The following sections provide information on the study population and the study protocol.

3.1 Participants

The new experimental paradigm to assess the awareness of an urge to move in healthy controls was previously investigated at the Leibniz Institute of Neurobiology in Magdeburg (Altas & Stenner, 2024, unpublished data). As this study explores the awareness of an urge to move in adults with PTSD, the experimental setup was transferred from the Leibniz Institute for Neurobiology, Magdeburg, to the Charité University Hospital, Berlin. To ensure that the transferred experimental set-up (Altas & Stenner, 2024, unpublished data) replicated previous results obtained in Magdeburg, a pilot experiment was conducted prior to the main study. For this, 11 healthy participants (female = 6, male = 5) with a mean age of 29.18 (standard deviation \pm 5.87 years) were recruited. The local ethics committee in Magdeburg (120/22) approved the experimental protocol, and adjustments regarding trial numbers and provided instructions were made based on a planned interim analysis following the pilot experiment.

Based on the pilot experiment and the results of a previous study by Altas and Stenner (2024, unpublished data), a power analysis was performed with G*Power (Faul et al., 2009) to

determine the required study sample size. According to this analysis, 20 participants per group (healthy controls and individuals with PTD) were required to achieve 80% power and an effect size of $d = 0.7$ for the primary outcome parameter, namely urge sensitivity, as found in the previous study by Altas & Stenner (2024, unpublished data). Twenty-two adults diagnosed with PTD and 20 age- and gender-matched healthy controls were recruited for the main study. In the PTD group, two participants were excluded after the experiment due to excessive tic activity and inability to complete the task. Hence, the overall recruited sample size of the PTD group was 22 rather than 20, however, 20 participants for each group were included in the subsequent analysis. Existing evidence indicates persistent motor and vocal tic disorders, along with GTS, are probably part of a clinical and possibly pathophysiological continuum (Claudio-Campos et al., 2021). For this, participants with GTS and other tic disorders were recruited for the PTD group. For the PTD group, participants were recruited from the PTD outpatient clinic of the Department of Neurology of the Charité University Medicine Berlin and were contacted via email and telephone.

Controls were recruited via family and friends and via the internet. A reimbursement of €10 per hour was provided for all participants. The study followed the principles outlined in the Declaration of Helsinki and received approval from the local ethics committee (EA2/082/18; Charité University Medicine Berlin, Germany). For the PTD group, participants diagnosed with PTD were included. For the control group, participants with neither diagnosed PTD nor other neurodevelopmental disorders were included. Participants with disorders affecting sensory perception, such as deafness or blindness, were excluded. Other neurological or psychiatric conditions did not constitute an exclusion criterion and were assessed during the study using diverse questionnaires (see section 4.1). All participants, except one control, were right-handed, as evaluated by the Edinburgh Handedness Inventory (EHI; Oldfield, 1971).

Data analysis included 20 adults with PTD (female = 6, male = 14) and 20 healthy controls (female = 6, male = 14) (see results, Table 3). When assessing the awareness of an urge to move, quantified as urge sensitivity, induced by subliminal motor priming, other sources of information (e.g., muscle activity and conscious prime discrimination) may play a confounding role. A planned control analysis was conducted to minimise the influence of muscle activity and conscious prime discrimination on the assessment of urge detection, which involved excluding trials with detectable electromyographic activity and subjects whose conscious prime recognition was above chance level.

For the urge detection analysis, 10 participants per group remained. Figure 2 illustrates the study recruitment process.

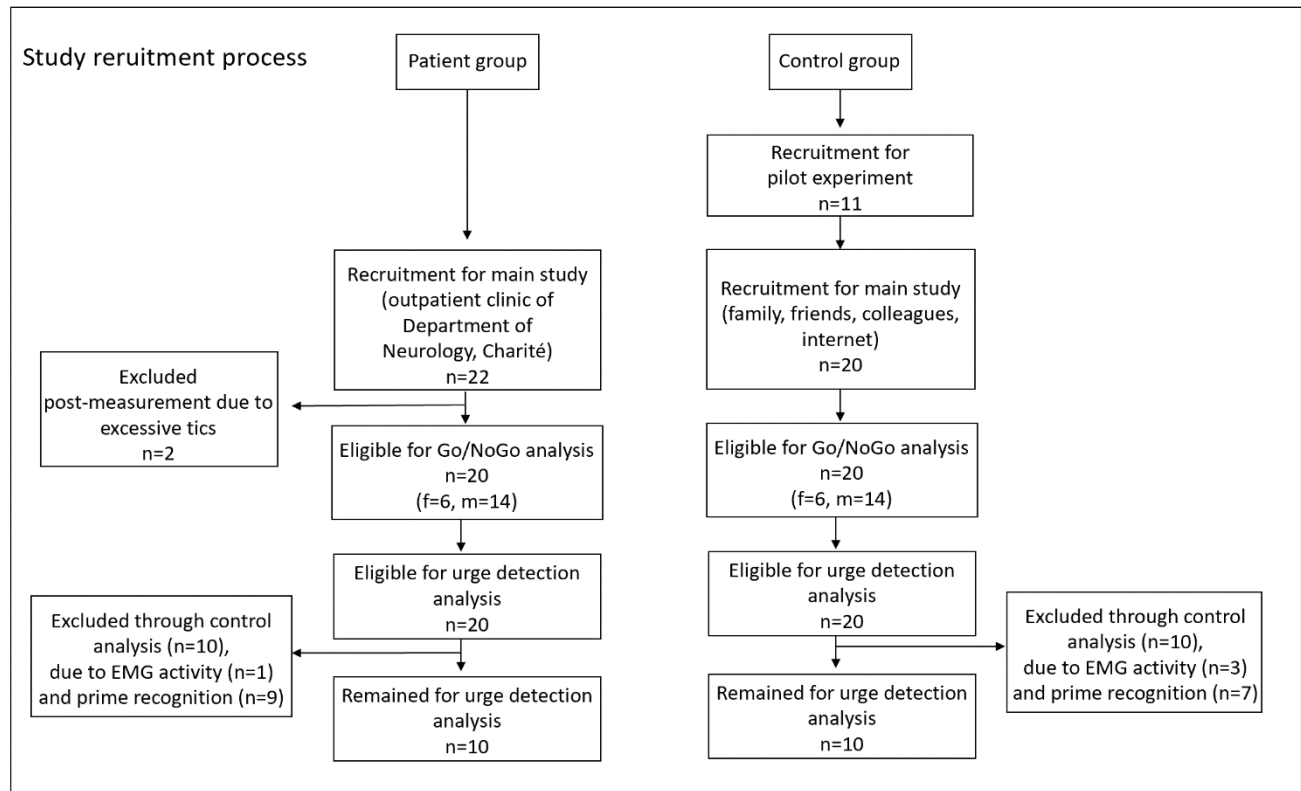


Figure 2: Study recruitment process.

3.2 Clinical Assessment

Upon arrival in the laboratory, participants were introduced to the study procedure, and general information about the study was provided. After clarifying any open questions, participants signed the declaration of consent for participation. Data was acquired pseudonymised, with each participant being assigned to an individual code for the study to guarantee pseudonymity.

All participants underwent a thorough clinical assessment based on questionnaires and semi-structured interviews. The assessment covered demographic information (gender, age, impairment of vision and hearing, drug consumption, comorbidities, and medication) and handedness, which was evaluated using the Edinburgh handedness inventory (EHI; Oldfield, 1971). Additionally, depression was assessed by the Becks depression inventory-II (BDI-II; Beck et al., 2011), ADHD by the Conner's adult ADHD rating scales (CAARS; Conners et al., 1999), and OCD by the Yale-Brown obsessive-

compulsive scale (Y-BOCS; Goodman et al., 1989). In addition, for the PTD group, current tic severity was determined by a semi-structured clinical interview using the Yale global tic severity score (YGTSS; Leckman et al., 1989) and severity of premonitory urges was captured by the self-report premonitory urge for tics scale (PUTS; Rössner et al., 2010).

3.2.1 The Edinburgh Handedness Inventory (EHI)

The EHI is a widely used scale for evaluating hand preference (Robinson, 2021). The short version of the inventory comprises 10 daily living tasks, such as writing, drawing, and using a toothbrush. Participants indicate their hand preference for each of the listed tasks as left (L), right (R), or both (Oldfield, 1971). Responses are recorded with symbols (+) in a particular column. Strong preferences with one hand are indicated with “+ +”, whereas indifference is marked with a “+” in both columns. For scoring, a laterality quotient (LQ) is built to indicate hand preference. A preference for using the left hand is suggested when the LQ is below 40, and a preference for using the right hand is suggested when the LQ is higher than 40 (Oldfield, 1971). Hand preference is considered neutral when the LQ is between -40 and 40, indicating indifference towards left or right-handedness.

3.2.2 The Beck Depression Inventory (BDI-II)

The BDI-II is an adapted version of the Beck depression inventory (BDI; Beck et al., 1961) and is commonly applied to indicate individual depression severity (1996). This screening measure comprises 21 items assessing affective, cognitive, somatic, and vegetative symptoms of depression (Hubley, 2020), with participants rating statements according to their current level of agreement on a scale of 0 to 3. For scoring, the total number of self-evaluated statements is summed and interpreted across four severity clusters: scores between 0 and 13 indicate minimal depression, scores between 14 and 19 indicate mild depression, scores between 20 and 28 indicate moderate depression, and scores between 29 and 63 indicate severe depression (Hubley, 2020).

3.2.3 The Conners' Adult ADHD Rating Scale (CAARS)

The CAARS is frequently used to evaluate ADHD symptoms in adults and is available as a self-rated (CAARS-S) or observer-rated (CAARS-O) tool (Christiansen et al., 2011). The long version (CAARS-S:L) consists of 66 items assessing six dimensions of ADHD (Conners et al., 1998):

- A: Inattention/memory problems
- B: Hyperactivity/restlessness
- C: Impulsivity/emotional lability
- D: Problems with self-concept
- E: DSM-IV inattentive symptoms
- F: DSM-IV hyperactivity-impulsive symptoms
- G: DSM-IV ADHD symptoms total
- H: ADHD index

Dimensions E and F refer to the Diagnostic and Statistical Manual of Mental Disorders (APA, 1994). To answer the CAARS-S:L, a four-point Likert scale from 0 (not at all/never) to 3 (very much/very frequently) is used. Taking the subscales of the CAARS-S:L into account, a total ADHD symptom score (dimension G) regarding the DSM-IV classification of ADHD and an overall ADHD Index (dimension H) is calculated using the gender and age-specific analysis patterns of the CAARS manual (Conners et al., 1998).

3.2.4 The Yale-Brown Obsessive-Compulsive Scale (Y-BOCS)

The Y-BOCS is a clinician-rated interview used to assess obsessive-compulsive symptoms over the past week (Goodman et al., 1989). The Y-BOCS is acknowledged as the gold standard in the clinical diagnosis of OCD (Storch et al., 2015). It consists of 16 items rated on a four-point Likert scale from 0 (not available) to 4 (extremely), covering obsession-related symptoms, such as compulsions (Moritz et al., 2002). Additionally, explorative factors are assessed, such as insight and avoidance, indecisiveness, pathological responsibility, pathological slowness, and pathological doubting (Goodman et al., 1989). The overall OCD score of the Y-BOCS is calculated from the first 10 items (except items 1b and 6b) (Moritz et al., 2002).

3.2.5 The Yale Global Tic-Severity Scale (YGTSS)

The YGTSS is a clinician-rated interview that serves as the gold standard to evaluate tic severity and impairment over the past two weeks in individuals with PTD (Haas et al., 2021; Leckman et al., 1989). The semi-structured interview examines five aspects of present tic symptomatology: number of tics, frequency, intensity, complexity and interference due to motor and phonic tics (Leckman et al., 1989). During the interview, phonic and motor tic subscales are assessed separately with the participant. The domain “overall impairment” refers to the general impact of tics over the last two weeks according to different parts of everyday life (e.g., social relationships, performance in school or at work, self-confidence). The clinician evaluates the subscales during the interview using a six-point Likert-scale from 0 to 5 (a higher score indicates greater disturbance and impact) (Leckman et al., 1989). A total phonic tic score (0–25), motor tic score (0–25) and overall impairment score (0–50) are computed. The Global Severity Score (GSS) is calculated by summing up the three sub-scores of the YGTSS (0-100).

3.2.6 The Premonitory Urge for Tics Scale (PUTS)

The PUTS is a self-rating scale that assesses the intensity of premonitory urges in adults with PTD (Woods et al., 2005). It consists of 10 items rated on a four-point Likert scale from 1 to 4, with higher scores indicating greater intensity of premonitory urges. A total urge score is computed by summing up items 1 to 9, while item 10 refers to tic suppression and the premonitory urge symptom (Woods et al., 2005). For interpretation, a total score of 9 is the lowest score possible. Scores from 9.5–12 indicate low intensity, 12.5–24.5 indicate medium intensity and 25–30.5 indicate high intensity of premonitory urges for tics, which may be associated with moderate impairment. Scores from 31–36 indicate high intensity with probable severe impairment (Woods et al., 2005).

3.3 Experimental Task

Following the clinical assessment, participants performed a computer-based behavioural task designed to probe conscious awareness of an urge to move. The experimental task featured a customised Go/NoGo task applying subliminal visual stimuli to influence motor responses

(Hughes et al., 2009; Schlaghecken, F. & Eimer, M., 1997). These subliminal visual stimuli, called primes, were used to induce a transient movement preparation, even if this preparation did not lead to overt motor output. Concurrently, participants performed an urge detection task to assess their awareness of an urge to move induced by the subliminal primes. Subsection 3.3.1 describes the experimental apparatus and design in detail.

3.3.1 Apparatus

The experiment was conducted in a quiet, dimly lit room. For the Go/NoGo task, a stationary computer equipped with an external LCD monitor (60 Hz, active area 53 x 29.8 cm) was utilised being placed on a stable table with a 70 cm distance from the participants. Two distinct numeric keypads were placed on the table in front of the participants, featuring only the necessary keys for the task to simplify physical reactions. The right keypad featured the horizontally arranged keys numbers 7 and 9 for the Go/NoGo task, while the left keypad included the vertically aligned keys numbers 0 and 1 for the urge detection and discrimination task. The arrangement of the keys on the left keypad was to reduce the influence of prime- or target direction on participants' choices during the Go/NoGo and urge detection tasks. Figure 3 displays the arrangement of the respective keys of the two utilised keyboards.



Figure 3: Numeric keypads for the experimental task.

A table bell was positioned near the left keypad for possible breaks during the experiment. The stimulus delivery and experiment control software Presentation[®] (Neurobehavioral Systems) was employed to execute the experimental task. Additionally, a single-channel ambulatory sEMG (Porti7, TMSi) was utilised to record index finger radial-abduction movements. The measuring electrode was placed on the surface of the right first dorsal interosseus muscle, with the reference electrode on the base of the right thumb and the ground electrode on the right acromion. For sEMG recording, two 30 x 24 mm hydrogel bipolar electrocardiogram electrodes (Kendall[™] and Cardinal Health[™]) were used for the measuring and reference electrodes, and a single 50 x 50 mm self-adhesive TENS electrode (Axion GmbH) for the ground electrode. Surface EMG data was recorded on a separate laptop in an adjacent room. The sEMG recording aimed to identify NoGo trials where participants moved their finger or contracted the muscle without pressing the key (errors of commission). The sEMG device was connected to the recording laptop via a USB cable to facilitate stable and high-speed data transmission during the experiment. Electrical muscle activity was continuously recorded at a 2048 Hz sampling rate using the software bundle TMSi Polybench Data Manager and the TMSi application Quick Recording Application (QRA – PORTI – REV3). A 1 Hz high-pass and 500 Hz low-pass hardware filter were applied during sEMG recording. The task computer and the recording laptop were synchronised via a parallel port interface to ensure synchronous data transmission. When a stimulus was presented on the task monitor, a trigger was sent from the task computer via the parallel port to the EMG laptop to mark the onset of the presented stimulus. Due to technical issues, this procedure was no longer possible from the ninth participant onwards. Instead of automated trigger transmission, a synchronisation procedure was performed from then, as described in subsection 3.3.2.

3.3.2 Task and Procedure

The experimental design comprised four parts: two training sessions consisting of 24 and 48 trials each, lasting between two and four minutes, and a main task. The main task consisted of 672 trials, split into seven blocks (96 trials each), requiring 35 to 40 minutes for completion. There was a subsequent prime discrimination task acting as a control condition for prime recognition. This task

comprised 144 trials divided into two blocks (72 trials each), lasting approximately 10 minutes (see Figure 4).

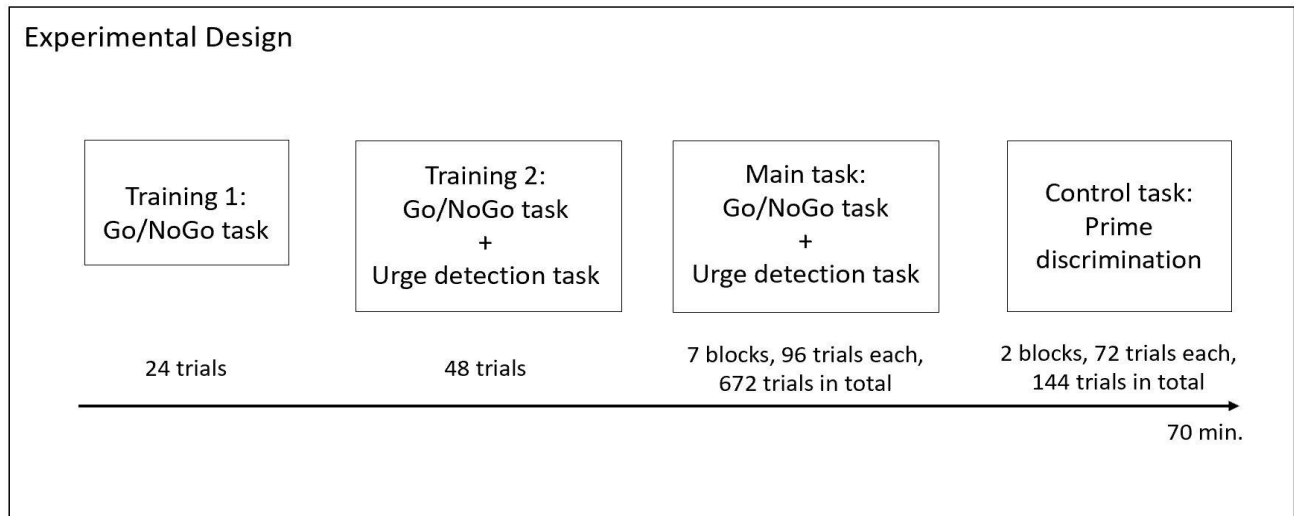


Figure 4: Experimental design of the study.

For the experiment, participants were seated in front of a stationary computer monitor and instructed to adopt a comfortable position to ensure relaxation of all body parts throughout the experiment. Surface electromyography (sEMG) was applied to the right first dorsal interosseus muscle (musculus interosseus dorsalis I) to detect muscle activity induced by the primes as a potential source of information for participants' responses in the urge detection task. Two methods were used to ensure sEMG was synchronised. For the first eight participants, time phase synchronisation of the experimental task and the sEMG recording was achieved via automated trigger transmission during the experiment. Subsequently, due to technical issues that prevented further recording of triggers, a synchronisation procedure was conducted before each experimental stage to mark precise stimuli onset. For the synchronisation, participants rested their right index fingers (with applied sEMG) on the left key (number 7) of the keypad on the right. The experimenter spoke three "Go" signals spaced approximately two seconds apart. Participants briefly pressed the key upon hearing each signal without lifting the index finger before or after each press, ensuring the EMG activity associated with the keypress was largely confined to the time of the keypress. After the synchronisation, participants placed their right index finger on the home key (number 9) of the right keypad (resting position).

Before the main task, two brief training sessions were conducted to familiarise participants with the task. Before each training session, participants received written instructions, which were also

explained to them, and open questions, if any, were addressed. The experimenter was present throughout the training sessions to provide feedback and support, ensuring task comprehension and correct task execution. In the main task, rest periods between blocks were permitted if participants felt fatigued or unfocused. Before the experiment, participants were instructed to maintain a relaxed finger position on the home key, not to press it when at rest, and to focus on the fixation cross in the middle of the monitor (see Figure 5).

For the Go/NoGo task, two types of arrows (target stimuli) pointing right or left were presented in the middle of the screen. When the target pointed to the right (Go trial), participants quickly moved their right index finger from the right home key (number 9) to the left key (number 7), pressed it, and returned to the resting position, with a response time set at 683 ms. Correct and timely responses elicited a sine wave tone (750 Hz, 200 ms, 5 ms linear ramp) for positive feedback, while late but correct responses generated no feedback tone (corresponding to error of omission). When the target pointed left (NoGo trial), participants were required not to react and to refrain from moving their right index finger. Pressing the left key (number 7) in NoGo trials resulted in an error sound for negative feedback, indicating errors of commission. The frequency of Go trials (right-pointing target) and NoGo trials (left-pointing target) was equal, and their order was pseudorandomised in each of the four parts of the experiment.

Additionally, subliminal priming was used in the Go/NoGo task to influence motor responses. Each target stimulus was preceded by an arrow, called a prime, presented under the perception threshold (Elgendi et al., 2018). In this paradigm, the prime could point right (Go prime) or left (NoGo prime) and could thus be either compatible (pointing to the same side as the subsequent target) or incompatible (pointing to the opposite direction as the subsequent target). The frequency of the Go and NoGo primes was also equal, and they were 50% compatible and 50% incompatible in the trials, with the order of Go and NoGo primes pseudorandomised across the experiment (see Figure 5).

In the experiment, the stimuli characteristics of each trial were set up as follows: A black fixation cross appeared in the centre of the monitor. The fixation cross was succeeded by a prime consisting of a solid black arrow ($3.04 \times 1.26^\circ$ visual angle). The prime was displayed for 16.7 ms before being replaced by the fixation cross again. To ensure that prime perception was subliminal, a metacontrast backward mask followed 50 ms after the prime (i.e., 33.3 ms after the fixation cross; stimulus onset asynchrony, SOA). The mask, lasting 117.7 ms, consisted of overlaid negative (solid white) images

of a left- and right-pointing prime arrow encased within a black rectangle. The metacontrast backward mask was shown for 33.3 ms and was then complemented by a combined mask-and-target stimulus. The mask-and-target stimulus was presented for 83.3 ms. Subsequently, the mask vanished, leaving the target stimulus visible in isolation for 33.3 ms. An intertrial interval of 1700 ms to 2000 ms was enforced before each subsequent trial commenced. The font sizes of the fixation cross, primes, mask, and targets subtended 1.1° , $3.04 \times 1.26^\circ$, $3.41 \times 1.78^\circ$, and $5.25 \times 2.1^\circ$ visual angle, respectively. All stimuli were presented in black on a white background, centred on the screen.

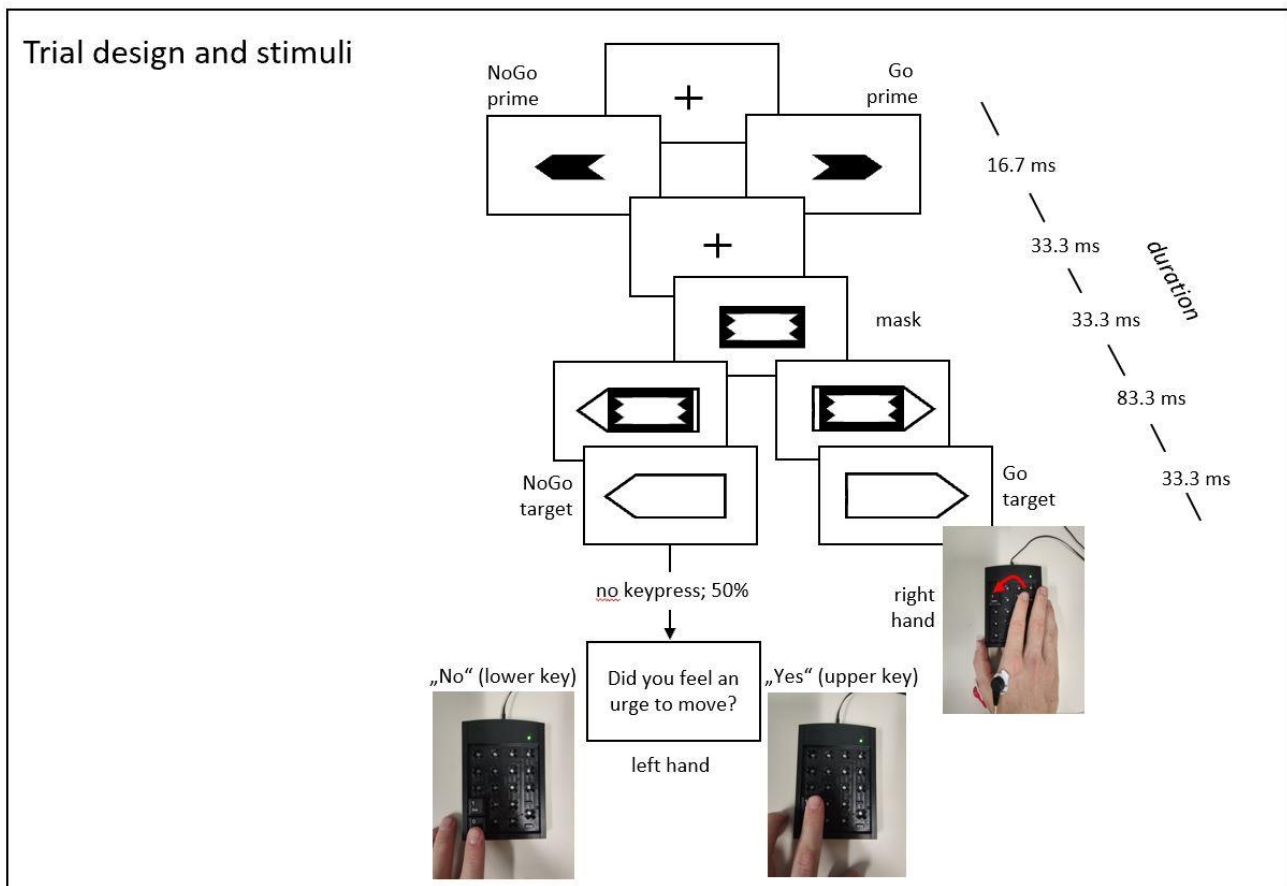


Figure 5: Trial design and stimuli.

During the Go/NoGo task, a concurrent urge detection task assessed the participants' awareness of an urge to move induced by the prime. Specifically, this factor was investigated in NoGo trials during the Go/NoGo task. In NoGo trials, participants were required to withhold their motor response, but Go primes induced a transient movement preparation (at least in most NoGo trials, i.e., in trials without error of commission). The question "Did you feel an urge to move?" was presented in 50%

of the NoGo trials to assess the prime-induced urge to move. A 50% level was chosen to ensure that the participants' focus was on the Go/NoGo task and not the impending question.

In the urge detection task, participants responded using the left numeric keypad with their left index finger, pressing the upper key (number 1) for “yes, I perceived an urge to move” and the lower key (number 0) for “no, I did not perceive an urge to move”. Direct feedback was provided after each trial based on their response and prime direction in that trial. If participants indicated a perceived urge to move (pressed 1) and a Go prime was present in that trial, they received the feedback “Correct! MOVE prime!”. If no urge to move (pressed 0) was indicated and a NoGo prime was presented beforehand, they received the feedback “Correct! No MOVE prime!”. In parallel to the matching responses, there were false positive and false negative feedback options. If participants indicated no urge to move but a Go prime was presented, they received the feedback “Wrong! MOVE prime!” (false positive). If participants confirmed an urge to move but a NoGo prime was presented, they received the feedback, “Wrong! No MOVE prime!” (false negative). The feedback mechanisms allowed participants to calibrate their estimation of an urge to move to the presence of any prime-induced tendency to move.

A prime discrimination task was performed after the main task. This task served as a control measure to identify participants showing above chance-level prime recognition, which might have directly influenced their urge responses in the urge detection task. In the discrimination task, the sequence and the timings of stimuli – including the initial fixation cross, prime, mask, target, and the distribution of primes and targets (left/right and compatible/incompatible) – were identical to those in the main task. However, participants were instructed to refrain from responding to the targets (i.e., they did not perform the Go/NoGo task in the discrimination part). Instead, they had to indicate whether each prime pointed left or right, focusing solely on the prime direction and disregarding the target stimuli. For this, the question “left or right?” was presented after the target, followed by a sine wave tone (800 Hz, 100 ms, 5 ms linear ramp) set at 600 ms after the target. Participants were asked to wait for the tone before indicating whether the prime had pointed left or right. Delaying this perceptual report minimised the effects of any direct motor priming on the perceptual report. Specifically, this response delay was included in the paradigm as motor priming is considered a transient bias to prepare a movement, induced by a prime. As the prime induced a directional effect on the participants' response choice, this tone was set as a time control marker to ensure the effect had been nullified (Stenner et al., 2015). As the prime discrimination task did not focus on timing and thus no control of muscle activity was required, participants responded with their left hand using the left numeric

keypad. In analogy to the urge detection task, responses in the discrimination task were made using the same left-positioned numeric keypad, with orthogonally arranged keys to mitigate any motor priming in this task (i.e., when participants thought the prime was pointing left, they pressed the lower key and vice versa. Left-/rightward pointing primes should, therefore, not induce a preference for either key via motor priming).

If participants perceived the prime as pointing right, they pressed the upper key (number 1), whereas primes perceived as pointing left were indicated by pressing the lower key (number 0). Feedback was provided after each trial following participants' responses. If participants pressed the upper key in alignment with perceiving the prime as pointing to the right, the feedback "pointing right" appeared in green to confirm the accuracy of the response. Similarly, for primes indicating left and the corresponding pressing of the lower key, the feedback "pointing left" was displayed in green. In case of an incorrect response regarding the prime direction, such as pressing key 1 for a right direction when the prime pointed left, the feedback "pointing left" appeared in red to indicate contradiction. Likewise, if the prime pointed right but participants perceived it as left (and confirmed this by pressing key 0), the feedback "pointing right" appeared in red on the screen.

3.4 Data Analysis

The analysis of the behavioural data from the clinical evaluation and the subsequent statistical procedures were performed by M.Sc. Moritz Michael Fuhrmann from the Charité – University Hospital, Berlin. Experimental data was analysed by Dr. med. Max-Philipp Stenner from the Leibniz Institute of Neurobiology, Magdeburg, in MATLAB (the MathWorks Inc.), with custom-written scripts developed for and used in a previous study (Altas & Stenner, 2024, unpublished data), and the FieldTrip Toolbox (Oostenveld et al., 2011). Surface EMG data underwent specific post-recording processing, following an analysis pattern outlined by Altas and Stenner (2024, unpublished data).

The behavioural data from the Go/NoGo and urge detection task was analysed within the framework of signal detection theory (SDT), a psychophysical approach to model perceptual decision-making in forced-choice tasks (Kingdom & Prins, 2016). The following subsections elucidate the fundamental concept of the SDT relevant to this study, followed by a detailed description of the sEMG data analysis procedure.

3.4.1 Signal Detection Theory (SDT)

Various experimental designs assess individuals' ability to discriminate between stimuli, such as between two acoustic or visual stimuli. In a discrimination task, participants distinguish between two distinct stimuli (Macmillan & Creelman, 2005). Performance in such experiments hinges on two key aspects: the degree to which the participant distinguishes the two classes of stimuli (sensitivity) and the degree to which the participants favour a particular response direction (response bias). Signal detection theory offers a comprehensive psychophysical framework for analysing performance in such tasks (Macmillan & Creelman, 2005). The following subsection provides an overview of SDT basics and their application to the present study.

3.4.1.1 Response Characteristics in SDT

As participants' accuracy can vary in psychophysical experiments, it is essential to analyse whether these variations reflect participants' ability to discriminate between stimuli (sensitivity). High sensitivity reflects good discrimination ability, whereas low sensitivity indicates poor ability to discriminate between stimuli (Macmillan & Creelman, 2005). In the present study, participants performed a Go/NoGo task with a concurrent urge detection task. In the Go/NoGo task, two distinct target stimuli were presented on a computer monitor, comprising an arrow pointing either to the right (Go target) or to the left (NoGo target). In Go trials, participants executed a rapid and brief abduction movement with their right index finger but withheld their response in NoGo trials. Moreover, subliminal primes were applied to the Go/NoGo task to influence motor responses. Based on this method, the urge detection task was performed concurrently in NoGo trials where participants needed to withhold their response. Specifically, Go primes induced a transient urge to move in NoGo trials, whereas NoGo primes induced no transient urge to move in these trials. Depending on prime directions, different responses in a single trial in the urge detection task based on the SDT framework were possible (see Table 2).

Table 2: SDT-based responses in the urge detection task.

| Stimulus class | Reported urge response in NoGo trials | |
|------------------------|--|------------------------|
| Prime direction | Urge to move | No urge to move |
| Right | Hit | Miss |
| Left | False alarm | Correct rejection |

A *hit* occurred when participants reported a previously perceived urge to move, and the prime pointed right. A *miss* was registered when participants reported no perceived urge to move, but the prime pointed right. A *false alarm* resulted from a reported urge to move despite the prime pointing left. A *correct rejection* was registered when participants reported no urge to move and the prime pointed left. In SDT, high sensitivity, indicative of effective discrimination, is identified by a high hit rate and a low false alarm rate. However, achieving a perfect hit rate often entails a higher false alarm rate (Macmillan & Creelman, 2005).

3.4.1.2 *d*' (*d*' as Measure of Performance Sensitivity

Performance sensitivity, quantified by the hit rate relative to the false alarm rate, is expressed as *d*' (*d*'), a standard index of performance sensitivity in SDT. Mathematically, *d*' is defined as a normal distribution function resulting from the difference between *z*-transformed hit (*H*) and false alarm (*F*) proportions (Macmillan & Creelman, 2005):

$$d' = z(H) - z(F)$$

To calculate *d*', the absolute hit and false alarm proportions are converted into *z*-values (Macmillan & Creelman, 2005). Identical hit and false alarm rates indicate chance-level (*guessing*) performance, i.e., *d*' = 0 (Stanislav & Todorov, 1999). In this case, participants would be unable to discriminate between two present stimuli. In general, higher *d*' scores are associated with better performance, with a *d*' score of 3 reflecting almost perfect performance (APA, 2018).

In the present study, performance at chance would occur if a participant reported a perceived urge to move in an equal proportion of trials with primes pointing right and left. Figure 6 displays two signal-noise distributions: the probability of occurrence of a given internal signal (vertical axis) and the strength of two stimuli or states that participants try to distinguish (horizontal axis). In terms of SDT, signal and noise distribution follow normal distribution, algebraically displayed as the shape of a Gaussian density distribution. The left distribution curve reflects noise, corresponding to a NoGo prime and no subsequently perceived urge to move in a trial (see figure 6). Noise is always present but easier to perceive when no additional signal is present. The right curve represents noise with an added signal. In the present experiment, this curve refers to an urge to move with a previous Go prime. The vertical line reflects a criterion (Green & Swets, 1966) that serves as response bias. The right side

of the criterion reflects “yes” responses regarding perceived urges to move, and the left side refers to “no” responses in terms of perceived urges to move (Macmillan & Creelman, 2005). Hence, the vertical line reflects an individually chosen cut-off point (decision criterion) for the participant to decide whether there was a perceived urge to move, even if noise alone was present. This cut-off criterion differs for each individual and can range across the signal continuum.

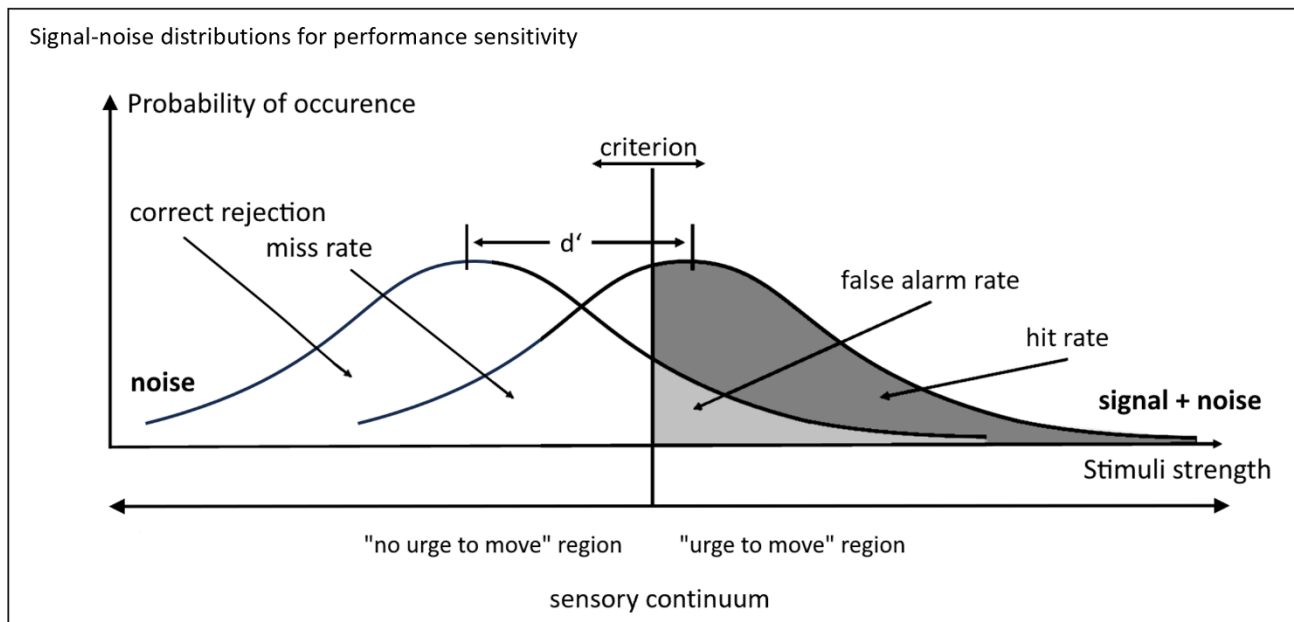


Figure 6: Signal-noise-distributions for performance sensitivity (modified after RIT, n.d.).

The more left a participant sets the criterion, the higher the hit rate will be, at the cost of higher false alarm rates. The values for participants' responses to reporting an urge to move are located on the right side of the decision criterion (vertical line). The hit rate (*hits* reflect participant's reports of an urge to move with prior Go prime) is defined as the area under the curve of the right distribution and to the right of the criterion. The correct rejection rate refers to the area under the curve of the left distribution (noise curve) and to the left side of the decision criterion. The area under the left curve on the right side of the decision criterion reflects the false alarm rate. In the case of a false alarm, participants reported an urge to move (right side of the criterion line) but there has been a previous NoGo prime (noise curve). For the miss rate, participants reported no perceived urge to move but there has been a previous Go prime. This is reflected by the area under the right curve on the left side of the decision criterion. For measuring performance, the sensitivity index d' is obtained as the distance between both

curves measuring participants' sensitivity in perceiving an urge to move in this task (i.e., how “separable” the two distributions are).

3.4.2 Main Analysis

The focus of this study was to investigate whether adults with PTD have a different awareness of an urge to initiate a voluntary action compared to adults without tics. Specifically, the awareness of an urge to initiate a voluntary action was operationalised as urge sensitivity in this experiment. Urge sensitivity was investigated in NoGo trials. In these trials participants successfully withheld their motor response but Go primes induced a transient movement preparation, resulting in the modulation of a transient urge to move. Based on this observation, the priming effect served as a prerequisite for the urge detection task. For evaluating the priming effect, median reaction times (mRT) of Go trials and error rates (ER) over all trials were computed for each subject ($n = 20$ for each group). Error rates encompassed errors of commission (responding to NoGo trials) and errors of omission (withholding a response in Go trials). Furthermore, mRT and ER were compared between groups to ensure uniform priming effects across both groups. This comparison ensured both groups could base their urge detection reports on comparable priming effects.

Assessing the awareness of an urge to move is challenging because other sources of information, such as muscle activity (e.g., induced by Go primes) or prime recognition might influence urge reports in the urge detection task. Given the likelihood that muscle activity and conscious prime recognition affect urge reports, a substantial number of trials were included in the experiment. A planned control analysis was conducted (see subsection 3.4.4) to control for these factors, resulting in a remaining sample size of 10 participants per group for further urge detection analysis. The awareness of an urge to move, quantified as urge sensitivity, was analysed using the SDT framework (Macmillan & Creelman, 2005). Specifically, urge sensitivity was measured via the sensitivity index d' , representing the difference between z-transformed hit and false alarm rates. The hit rate denoted the proportion of trials in the urge detection task in which participants reported an urge to move, and a Go prime implied a motor response. Conversely, the false alarm rate reflected the proportion of trials where participants reported an urge to move, with a prior NoGo prime suggesting no response.

3.4.3 Processing of Surface EMG

To identify muscle activity prior to prime onset in the experimental task, right index finger abduction movements were recorded with sEMG as a control measure. The sEMG data manifests as a continuous bi-dimensional time signal, represented as microvolts over time, sampled at 2048 Hz. Prior to reaching the analogue-to-digital converter (ADC), online analysis included the automatic application of a low-pass filter with a cut-off frequency of 500 Hz. Subsequently, a digital finite impulse response (FIR) filter was automatically applied to the analogue EMG signal with a cut-off frequency of > 500 Hz (TMSi, 2017). Processing of the digital EMG signal commenced with band-pass filtering (30-240 Hz, 4th order Butterworth filter) and application of a band-stop filter (48.5 – 51.5 Hz and harmonics up to 200 Hz, 4th order Butterworth filter). High-frequency amplification was achieved using the Teager-Kaiser Energy Operator (TKEO) transformation (Li et al., 2007) to accurately delineate burst boundaries indicative of muscle activity onset (Solnik et al., 2008). Full wave rectification of the raw EMG data was performed, converting negative values to their positive equivalents to shape the EMG envelope for subsequent analysis (Farina et al., 2014). To further refine the rectified EMG signal, a low-pass filter (6th order Butterworth filter) was applied for smoothing purposes. The data was then epoched between 1500 ms before prime onset and 1500 ms after target onset. NoGo trials exhibiting muscle activity following prime onset were identified for the subsequent control analysis. Through synchronous data transmission via the parallel port during the pilot experiment and the study (until the eighth participant) and the synchronisation procedure (from the ninth participant onwards) to align timelines from the task computer and the EMG laptop, precise determination of the timing of specific target stimuli presentation was achieved.

3.4.4 Control Analysis

In the urge detection task, urge reports could potentially have been based on other sources of information than the awareness of an urge to move. The control analysis addressed two primary factors potentially confounding urge sensitivity: sensory information from prior muscle activity and prime discrimination. Subsection 3.4.4.1 elucidates the specific steps of the control analysis in greater detail.

3.4.4.1 Surface EMG as Control Measure

In the experimental task, participants might interpret their muscle activity from the Go/NoGo task as an urge to move in the urge detection task. It is likely that participants exploited this peripheral source of information because it could reliably result in positive feedback in the urge detection task. Given that Go primes induced a Go response preparation, EMG activity probably differed between Go and NoGo primes, even when subjects eventually did not produce motor output. To address this issue, all NoGo trials with recorded muscle activity prior to prime onset were identified and excluded from the control analysis. Specifically, a trial was excluded if the processed EMG, starting 100 ms after the prime onset and up to 1.5 ms after the target, exceeded 15 times the interquartile range computed across the last second before the prime, above the median computed across the same period. All trials excluded due to EMG activity were further confirmed to be excluded via visual inspection. As a result, four subjects were excluded for further analysis. Three controls had such a low number of remaining trials post-EMG exclusion that chance-based hit or false alarm rates might have occurred. These computed z-scores in the EMG amplitude of 0 and 1 were assessed as values of “infinity (Inf)”. Furthermore, one participant from the PTD group was excluded due to a lack of remaining trials after EMG correction, resulting in a z-score assessed as “Not a Number (NaN)”.

3.4.4.2 Prime Discrimination as Control Measure

It was possible that some participants could recognise prime directions despite backward masking. As a result, even if these participants were unaware of their urge to move, they could respond correctly in the urge detection task by reporting prime direction. In this situation, the discrimination task (control task) was included in the experiment for control purposes.

To mitigate any bias induced by prime recognition, subjects exhibiting a d' score above chance level in the prime discrimination task were excluded from further urge detection analysis. For identifying such participants, the d' score for discriminating prime direction in the prime discrimination task was computed for each participant. Subsequently, a non-parametric within-subject test was employed to assess whether the d' score significantly deviated from a non-parametric distribution of d' values obtained under the null hypothesis (where prime perception is at chance level) of no direction discrimination, with the assumption that, under the null hypothesis, prime perception is at chance level and psychophysical reports are independent of actual prime direction. To create a distribution under

this hypothesis, the original sequence of prime directions across trials can be randomly shuffled while maintaining the original sequence of psychophysical reports. A new d' score was then computed for each of the 10,000 iterations of random shuffling. The resulting p-value was defined as the proportion of iterations where the computed d' score exceeded or fell below the observed d' score, depending on which proportion was smaller (two-sided test).

A two-tailed test was conducted because metacontrast backward masking can induce a negative afterimage of the prime, leading to the impression of the prime pointing in the opposite direction. As a cut-off criterion, participants were excluded from the control analysis if their p-value was less than 0.05. No correction for multiple comparisons was applied in this test to prevent an overly conservative determination of significant prime perception. The aim of this procedure was to ensure that participants with slight prime detection did not bias urge detection analysis. Sixteen participants with prime discrimination above chance level (PTD = 9, controls = 7) were excluded, resulting in 10 remaining participants per group for analysing urge detection after exclusion of EMG activity and prime discrimination.

3.4.5 Statistics

The study's dependent variables included median reaction times (mRT), error rates (ER) and urge sensitivity. Independent variables comprised the factors priming, group, and task. The priming factor varied depending on the dependent variable being analysed. For mRT (analysed only for Go trials), priming levels were represented by Go prime or NoGo prime. For ER (analysed over all experiment trials), priming levels were compatible or incompatible primes. For analysing the ER of each subject in the respective group, errors of commission (responding to NoGo targets) and errors of omission (withholding a response to Go targets) were analysed together. Urge sensitivity was assessed in NoGo trials, where participants successfully withheld their motor response using the sensitivity index d_{prime} (d'). The task factor included the following levels for urge sensitivity: EMG-negative trials (trials with no prior EMG activity) and prime discrimination.

Statistical analyses were conducted using JASP (Version 0.18.00). Data was graphically and descriptively examined for normal distribution using histograms and Q-Q plots to determine appropriate statistical tests. Based on the graphical inspection, the experimental data revealed a lack

of normal distribution in mRT, ER, and urge sensitivity. Due to the control analysis for urge detection, the study had a small sample size ($n = 20$ in each group for Go/NoGo analysis; $n = 10$ for urge detection analysis after the control analysis). Consequently, data was analysed descriptively using box plots, scatter plots, and graphical evaluation. Further, medians and interquartile ranges (IQR, reported Q1-Q3) were calculated, and non-parametric statistical tests were conducted. Wilcoxon signed-rank tests for paired samples were calculated to analyse potential within-group differences. Further, Mann-Whitney-U tests were used to investigate between-group differences in the priming effect and urge sensitivity assessed through the new experimental design. Additionally, the effect size “ r ” for non-parametrical tests was calculated as $r = \left| \frac{z}{\sqrt{N}} \right|$ ($z = z$ -score of the test statistic, $N =$ sample size, Cohen, 1988).

4 Results

4.1 Clinical Characteristics

A summary of the participants’ clinical characteristics is provided below (see Table 3). The study included an equal number of participants with PTD and healthy controls. Mann-Whitney-U tests showed no group differences in demographic domains such as gender ($W = 200.00$, $p = 1.00$), age ($W = 243.50$, $p = 0.244$) and right-handedness ($W = 253.00$, $p = 0.115$), indicating homogeneity along basic demographics in both groups. A significant difference between the PTD group and healthy controls was revealed in the number of participants with comorbidities ($W = 140.00$, $p = 0.02$) and Beck’s depression inventory (BDI-II) ($W = 93.50$, $p = 0.004$). A comparison of ADHD scores did not show a significant difference between both groups ($W = 129.00$, $p = 0.056$).

Table 3: Sample characteristics for the Go/NoGo analysis.

| | Primary Tic Disorders | Controls | P-value |
|---|-----------------------|-----------------|----------------------|
| Number of participants | 20 | 20 | - |
| Gender male (%) | 14 (70) | 14 (70) | 1.00 [^] |
| Age (mean \pm SD) | 28.1 \pm 7.4 | 31.0 \pm 9.0 | 0.244 [^] |
| Right-handedness (%) | 20 (100) | 19 (95) | 0.115 [^] |
| EHI (mean \pm SD) | 87.5 \pm 14.8 | 87.7 \pm 35.8 | 0.115 [^] |
| Antipsychotic medication ^a (%) | 5 (25) | 0 | - |
| Comorbid diagnoses ^b (%) | 7 (35) | 1 (5) | 0.02 ^{*/^} |
| ADHD | 2 | 0 | - |
| ADD | 1 | 0 | - |
| OCD | 1 | 0 | - |
| Depression | 2 | 0 | - |
| Burnout | 1 | 0 | - |
| Anxiety | 1 | 0 | - |
| Borderline | 1 | 0 | - |
| CPTSD | 1 | 0 | - |
| Selective Eating Disorder | 1 | 0 | - |
| Migraine | 0 | 1 | - |
| Y-BOCS (mean \pm SD) | 7.0 \pm 6.7 | 0 | - |
| CAARS (mean \pm SD) | 14.8 \pm 7.2 | 10.0 \pm 5.0 | 0.056 [^] |
| BDI-II (mean \pm SD) | 11.0 \pm 8.2 | 4.4 \pm 3.3 | 0.004 ^{*/^} |
| YGTSS (GSS) (mean \pm SD) | 29.5 \pm 20.0 | - | - |
| YGTSS (TTS) (mean \pm SD) | 16.5 \pm 6.8 | - | - |
| PUTS (mean \pm SD) | 22.7 \pm 4.7 | - | - |

ADD: Attention deficit disorder; *ADHD*: Attention-deficit hyperactivity disorder; *BDI-II*: Beck's depression inventory; *CAARS*: Conners' adult ADHD rating scale; *CPTSD*: Complex post-traumatic stress disorder; *EHI*: Edinburgh handedness inventory; *GSS*: Global severity score; *OCD*: Obsessive-compulsive disorder; *PUTS*: Premonitory urge for tics scale; *SD*: Standard deviation; *TTS*: Total tic score; *Y-BOCS*: Yale-Brown obsessive-compulsive scale; *YGTSS*: Yale global tic severity scale.

^aIncluding data from participants taking multiple medications.

^bFour participants reported having received more than one diagnosis.

*Significance level was $p = 0.05$

[^]Mann-Whitney-U test for unpaired samples

4.2 Go/NoGo Task

The primary analysis of the Go/NoGo task included median reaction times (mRT) and error rates (ER), details of which are presented in the following subsections.

4.2.1 Median Reaction Times

To analyse the priming effect in the Go/NoGo task, mRT were calculated for each subject ($n = 20$ per group) in both groups. Figure 7 illustrates the mRT for Go trials with Go primes and NoGo primes in both groups.

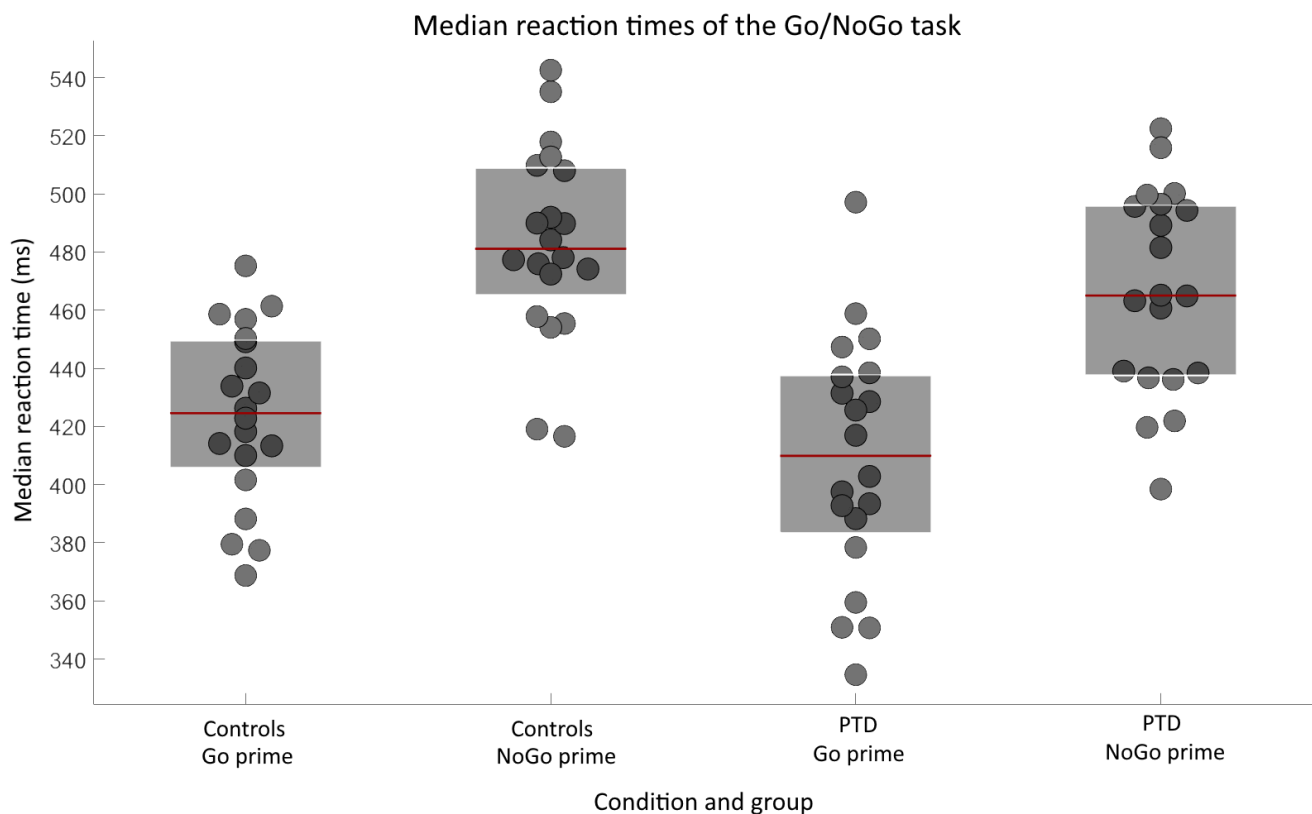


Figure 7: Median reaction times of the Go/NoGo task.

In the PTD and control groups, mRT in Go trials with prior Go primes was significantly lower than that with NoGo primes. The PTD group exhibited lower mRT in Go trials preceded by a Go prime (410 ms, IQR = 386 – 437 ms) compared to NoGo trials with prior Go primes (465 ms, IQR = 438 – 496 ms; $Z = -3.92$, $p < 0.001$, $r = 0.88$). Similarly, controls displayed lower mRT in Go trials with prior Go primes (425 ms, IQR = 408 – 449 ms) compared to Go trials with NoGo primes

(481 ms, IQR = 469 – 508 ms; $Z = -3.92$, $p < 0.001$, $r = 0.88$). The effect size of motor priming in the Go/NoGo task was $r = 0.88$ in both groups reflecting a strong effect according to Cohen (1988). Between-group comparisons showed no differences for mRT in Go trials with Go primes ($W = 244.0$, $p = 0.242$) or with NoGo primes ($W = 242.0$, $p = 0.265$).

4.2.2 Error Rates

Another marker computed for the priming effect in the Go/NoGo task was error rates (ER). Error Rates were analysed regarding compatible primes and incompatible primes. Figure 8 illustrates the descriptives of the median ER percentages in the Go/NoGo task.

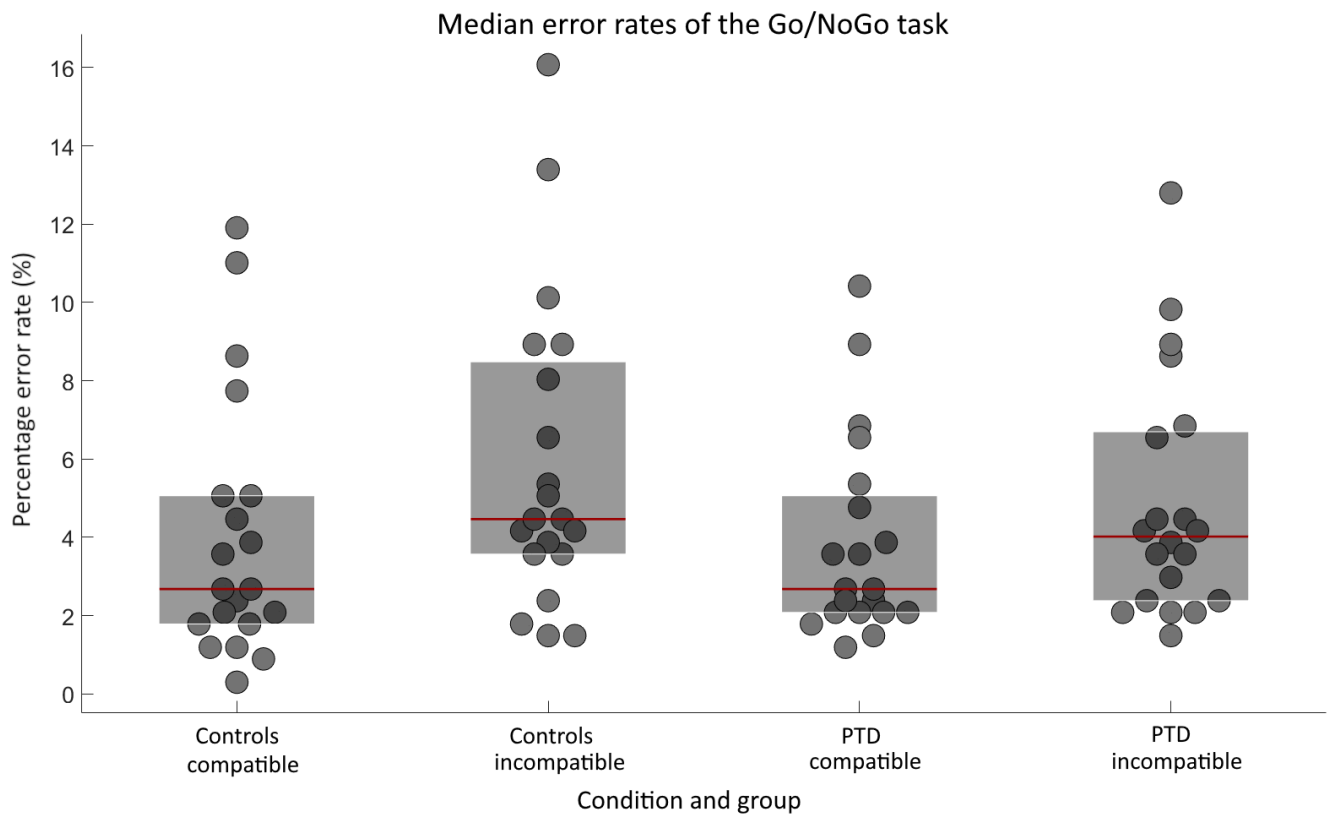


Figure 8: Median error rates of the Go/NoGo task.

Within both groups, the median ER percentage of compatible primes were significantly lower than those of incompatible primes. The PTD group exhibited significantly lower median ER for compatible primes (2.68%, IQR = 2.08 – 4.91%) compared to incompatible primes (4.02%, IQR = 2.38 – 6.62%;

$Z = -1.698$, $p = 0.047$). The effect size was $r = .38$, indicating a medium effect (Cohen, 1988). Controls also had significantly lower median ER for compatible primes (2.68%, IQR = 1.786 – 5.06%) than for incompatible primes (4.46%, IQR = 3.57 – 8.26%; $Z = -2.893$, $p = 0.002$) with an effect size of $r = 0.65$, indicating a strong effect according to Cohen (1988). Furthermore, no group differences were found for ER in trials with compatible primes ($W = 189.5$, $p = 0.786$) or incompatible primes ($W = 233.0$, $p = 0.378$). These results indicate that the priming effect was present in both groups but with no differences between groups.

4.3 Urge Detection Task

To analyse urge sensitivity, median d' scores were calculated for each subject (see Figure 9). All subjects with prime discrimination above chance level were marked for the subsequent control analysis.

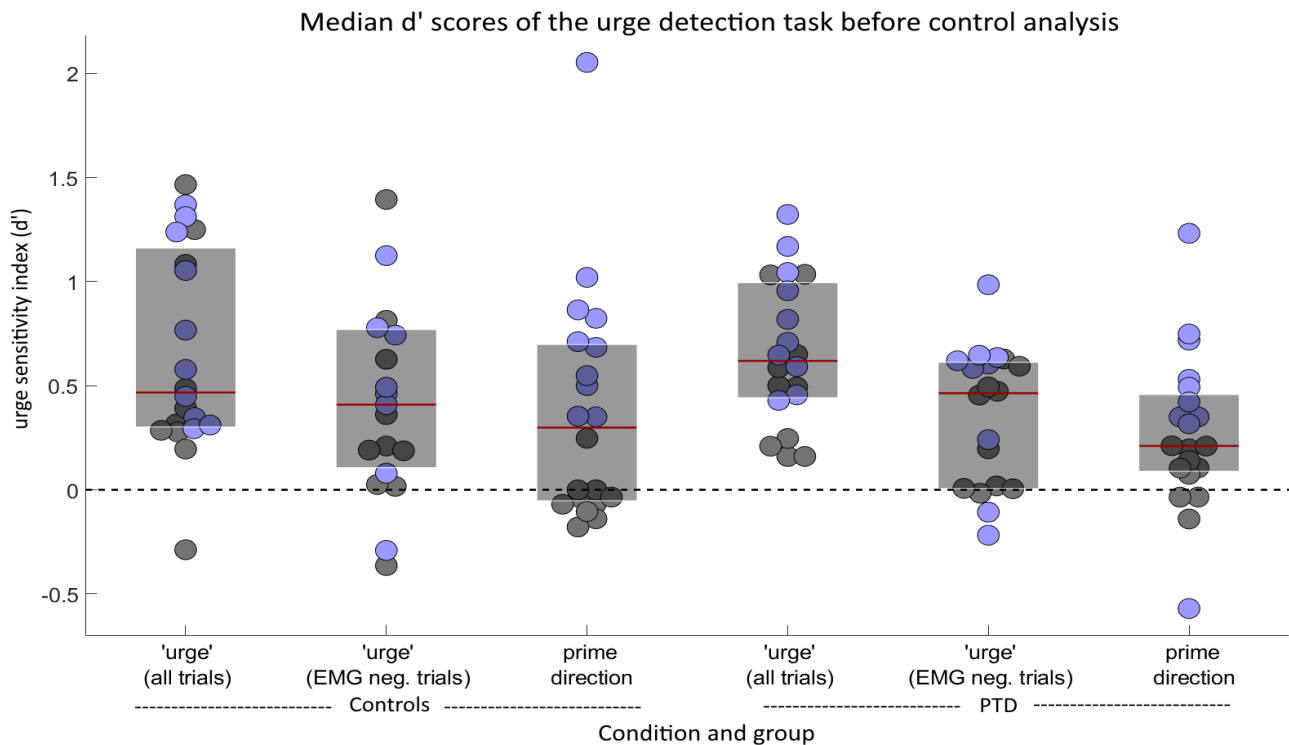


Figure 9: Median d' scores of the urge detection task before control analysis.

Before the control analysis, within-group comparisons showed no significant difference between EMG negative trials ($d' = 0.394$, IQR = 0.1 – 0.5) and prime discrimination ($d' = 0.299$, IQR = 0 – 0.7) in controls ($Z = .734$, $p = 0.487$). In the PTD group, no significant difference was found between EMG negative trials ($d' = 0.488$, IQR = 0 – 0.6) and prime discrimination ($d' = 0.211$, IQR = 0.1 – 0.4, $Z = 1.368$, $p = 0.182$). A between-group comparison showed no difference in median d' scores of EMG negative trials between the PTD group and controls ($W = 151.00$, $p = 0.754$).

After the control analysis, within-group comparisons showed a significant difference between median d' scores of EMG negative trials ($d' = 0.247$, IQR = 0.1 – 0.5) and prime discrimination ($d' = -0.035$, IQR = -0.1 – 0) in controls ($Z = 2.191$, $p = 0.027$). The effect size was $r = 0.69$, indicating a strong effect (Cohen, 1988). In the PTD group, no significant difference was revealed between these two conditions (d' EMG neg. trials = 0.345, IQR = -0.1 – 0.55; d' prime discrimination = 0.105, IQR = 0 – 0.2; $Z = 1.58$, $p = 0.131$). These figures indicate that apart from muscle activity and prime discrimination, controls showed awareness of an urge to move above chance level that reached statistical significance. However, this effect was statistically not significant in the PTD group.

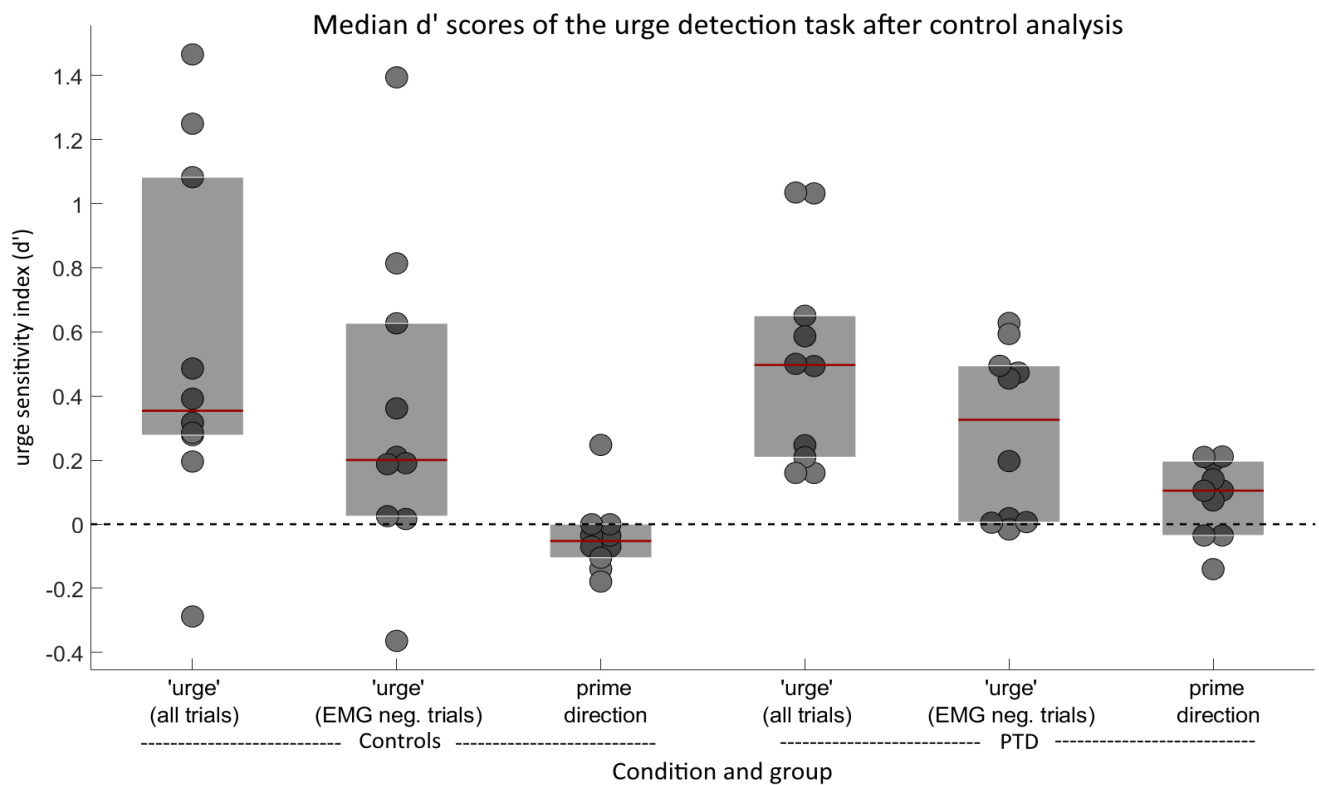


Figure 10: Median d' scores of the urge detection task after control analysis.

A between-group comparison was conducted to address the main research question of whether adults with PTD have altered awareness of the urge to initiate a voluntary movement triggered by subliminal motor priming in this task. The comparison showed no difference in median d' scores of EMG negative trials between the PTD group and controls ($W = 49.00, p = 0.971$), which indicates that both groups were equally able to detect their urges prior to volitional actions.

5 Discussion

In this study, we investigated whether individuals with PTD have altered awareness of an urge to make a voluntary movement compared to individuals without tics. Previous research provides conflicting results regarding the experience of volition as examined by the urge to move in adults with GTS (Ganos, Asmuss, et al., 2015; Mainka et al., 2020; Moretto et al., 2011; Triggiani et al., 2023). For instance, using the Libet paradigm to assess volition, adults with GTS are aware of their intention to move, but only with a delay (Moretto et al., 2011). This finding might be associated with the intensity of perceived urges (Ganos, Asmuss, et al., 2015) or the length of time the individual with GTS has experienced tics (Mainka et al., 2020). The Libet paradigm has been criticised as a measure of assessing volition for various reasons. For instance, the timing of movement initiation in this paradigm is self-paced and voluntarily chosen by the subject, resulting in a lack of objective control over the subjective report of the actual intention to move (Haggard, 2008). This situation may obscure the validity of the results in neuropsychiatric populations, including groups with PTD.

To address this matter, we employed a new approach to provide experimental control over the awareness of an urge to move (Chambon & Haggard, 2012; Stenner et al., 2014). Subliminal motor priming was used in a Go/NoGo task to induce a transient urge to move. Specifically, Go primes transiently induced a movement preparation in NoGo trials, even when this preparation did not lead to subsequent motor output. In half of the NoGo trials, participants performed an urge detection task and reported whether they had previously perceived an urge to move induced by the prime.

Overall, in the Go/NoGo task, mRT of Go trials with prior Go primes were significantly lower than those with prior NoGo primes in both groups. Furthermore, median ER were significantly lower in trials with compatible primes than in those with incompatible primes in both groups. Given that mRT and ER serve as indices for the priming effect, these data confirm that Go primes induced a transient

movement preparation in the Go/NoGo task in this study. There were no group differences in the priming effect on mRT and ER, indicating an equal basis for the urge detection task in both groups. Had this not been the case, it might have influenced urge reports in the key task of urge detection in one of the two groups.

In the urge detection task, the control group showed significantly higher d' scores for urge detection – apart from peripheral information, such as muscle activity – than for prime recognition. This finding indicates that the control group could discern whether they had transiently prepared a motor response induced by the prime, even in the absence of prior muscle activity and conscious prime discrimination. This observation replicates previous findings by Altas and Stenner (2024, unpublished data) demonstrating that healthy people are aware of the urge to initiate voluntary movements, induced by subliminal motor priming. In the PTD group, the same effect did not reach statistical significance but was numerically similar. Most significantly, a between-group comparison of d' scores for urge detection did not show any differences between adults with PTD and healthy controls in this task. This finding indicates that no evidence was found for the primary hypothesis that adults with PTD have a reduced capacity to perceive an urge to initiate voluntary movements. Instead, the findings indicate that the two groups did not differ significantly in their capability to detect their urges prior to voluntary actions.

The influence of subliminal priming on the awareness of an urge to move, as examined in this task, is a relatively subtle effect indicated by the overall very low d' scores in our and a previous study (Altas & Stenner, 2024, unpublished data). As between-group tests compare two distinct groups, each group's variability adds to the total noise in the data. Hence, larger sample sizes are needed to achieve enough power to detect true between-group effects (Cohen, 1988). We focused on excluding all potential information sources that do not reflect the true awareness of an urge to move, induced by a prime. Due to a planned control analysis, only 10 participants per group remained for the final evaluation of urge detection. Consequently, potential differences between the groups may have remained undetected due to the limited sample size following analysis. Furthermore, the small sample size may decrease this study's statistical power. Additionally, it is plausible that the PTD group's data is noisier than the control group's data, possibly due to ongoing antipsychotic treatments or coexisting conditions such as ADHD, ADD, OCD, and depression. These factors potentially reduced the likelihood of detecting statistically significant differences in urge awareness within the PTD group.

Compared to other psychophysical experiments using d' scores as a sensitivity index, the d' scores of this study's participants were numerically low. Priming is probably only one of the factors that influenced movement preparation in the present task. Other possible factors include the subjects' expectation of upcoming targets (e.g., based on the recent history of targets and beliefs about target statistics). Therefore, priming's relatively small impact on the subjective reports, as evident in low d' scores, is consistent with prior expectations. In classic psychophysics, higher d' scores reflect better performance. For instance, a d' score of 3 indicates almost perfect performance, whereas a d' score of 0 indicates chance performance (APA, 2018). In this study, most participants had a d' score clearly below 1, indicating generally poor performance in the urge detection task. Prime discrimination was not as poor before the control analysis, with d' scores for prime recognition being clearly above zero, suggesting that subjects who discerned prime directions in the prime discrimination task also recognised these directions in the main task. Ultimately, the recognition of prime directions potentially influenced urge reports in the urge detection task. However, it cannot be ruled out that the PTD group utilised prime recognition as additional information for their urge reports in this task. Given that the control group showed significantly better urge detection than prime recognition, it is likely that an additional source of information beyond prime recognition was available for urge reports in the control group.

The present study suggests an equal awareness of an urge to initiate voluntary actions in people with PTD and healthy controls. Previous studies found decreased interoceptive awareness in people with tics, suggesting this may be associated with increased neuromotor noise (Ganos, Asmuss, et al., 2015; Ganos, Garrido, et al., 2015). Emerging data supports the suggestion of increased neuromotor noise in individuals with PTD (Ganos, Asmuss, et al., 2015; Ganos, Garrido, et al., 2015; Münchau et al., 2021). The initial hypothesis suggested that people with PTD may be less sensitive to detecting a stimulus-induced urge to move due to increased neuromotor noise levels. Based on this notion, it is possible that people with PTD may have difficulties distinguishing between internal bodily signals and motor noise, making it challenging to detect their urge to move in an experimental context. Ganos et al. (2018) suggested that people with stronger PUs may have higher levels of neuromotor noise, resulting in a reduced capacity to perceive the intention to move. The present study did not investigate this matter, but there is possibly an interplay between neuromotor noise levels and the intensity of PUs, which influences the capacity to detect urges to move in an experimental task.

This study's initial hypothesis suggested that people with tics are less sensitive to detecting an urge to move due to increased neuromotor noise. However, it is plausible that they may be hypersensitive in perceiving urges to move, which may potentially be linked to altered neuromotor noise (Münchau et al., 2021). According to this view, individuals with PTD could have set lower threshold levels for neuromotor signals (Ganos, Asmuss, et al., 2015). Consequently, people with PTD could be more likely to misinterpret neuromotor noise as an urge to tic, as proposed by previous research (Ganos, 2016; Ganos, Garrido, et al., 2015). Furthermore, many people with PTD report PUs before tics (Leckman et al., 1993; Sambrani et al., 2016), suggesting that they might have learned to perceive urges to move over time. Considering the role of noise in PTD, Kurvits et al. (2024) showed that voluntary movements are noisier in individuals with PTD. However, the present study did not find a group effect regarding the capacity to perceive an urge to move induced by a prime. If the neural noise theory (Münchau et al., 2021) holds true for people with PTD, this study's findings indicate that increased neuromotor noise levels do not affect the awareness of an urge to move in this experimental task.

Defining an “urge” in the context of tics and PTD is challenging. Premonitory urges are sensory phenomena experienced by many individuals with GTS. However, individuals with GTS often struggle to precisely describe these sensations (Robertson, 2015). This factor makes it more challenging to precisely define the phenomenon of PUs in GTS. However, defining the context in which PUs are regarded is essential. In this experimental context, the term “urge” refers to a mentally generated process within the central nervous system in which subliminal primes were presented under the perception threshold (Elgendi et al., 2018). These primes induced a transient movement preparation, simulating participants' experiences of an urge to move. However, the operationalised term “urge” in this study may not perfectly align with the phenomenology of PUs in GTS. Understanding the nuances of PU experiences is crucial but challenging, as their subjective reports vary widely (Robertson, 2015). Nonetheless, in demonstrating that individuals with PTD can be aware of the urge to initiate a movement in this study, it may not be essential for them to perceive something identical to their disease pattern.

It is unclear whether tics are involuntary movements or voluntary responses to involuntary bodily sensations, like premonitory urges (Bliss, 1980; Ganos, Asmuss, et al., 2015). Voluntary actions are linked to conscious intention, which is a predictor prior to the neural preparation of voluntary actions (Haggard, 2005). In the present study, subliminal motor priming was used to induce a transient urge

to move by the prime, which may resemble the suggested involuntary nature of PUs in PTD. The underlying processes of PUs combined with tics remain unclear, although some studies have found an interplay between PUs and tics. However, assessing all phenomenological aspects of PUs and tics is challenging. Early studies showed that PUs become more intensive and can be temporarily alleviated through conscious tic suppression (Cohen & Leckman, 1992). However, not every tic is preceded by PUs (Martino et al., 2017), and some people are unaware of their tics and thus may not experience PUs (Pappert et al., 2003). In the present study, participants were allowed to tic freely during the experiment to mitigate potential influences on PUs through voluntary tic suppression. However, participants with PTD who do not experience PUs prior to tics might influence group comparisons regarding urge detection.

Another potential mechanism that may explain the present findings can be seen in reduced tics during moments of concentration. In these situations, individuals with PTD exhibit reduced tics, which resume when they are relaxed (Conelea & Woods, 2008; Nagai et al., 2009). This phenomenon may also account for the employed experimental task. Participants with PTD concentrated throughout the task, which might alleviate tics in a free-ticking state during the experiment, resulting in a temporarily reduced sensitivity to perceiving PUs. This circumstance may serve as a resting mechanism, allowing individuals with PTD to focus on situations requiring concentration; hence, PUs in the background become irrelevant in situations that require concentration.

Using the Libet paradigm, a classical method to assess the volition of voluntary actions, individuals with GTS demonstrated a delay in becoming aware of their initial intention to move (Moretto et al., 2011). As the Libet paradigm lacks experimental control over movement preparation, the new employed paradigm in this study provides an objective baseline for perceiving and urge to move in this task (ground truth) and experimental control over the time when participants should perceive a transient urge to move induced by a subliminal prime (Chambon & Haggard, 2012; Stenner et al., 2014). However, assessing these modulated transient urges to move poses challenges. In everyday life, people rarely encounter questions like “Did you feel an urge to move?”, which makes answering such queries in a controlled setting novel. Participants in both groups were encouraged to utilise any available information to respond to this question within the task. Additionally, they received feedback after each trial, instructing them to consider all relevant information to become aware of their intention of movement preparation. However, subjects possibly relied on other sources of information to report their transient urge to move, such as muscle activity. For instance, a Go prime

could simply result in temporary arousal, more so than a NoGo prime, which people may detect and which, as a result, may influence urge reports in the urge detection task.

6 Limitations

This study represents an early attempt to apply subliminal priming within a Go/NoGo task, combined with a concurrent urge detection task, to assess the awareness of an urge to move in adults with PTD. The urge detection task was administered in half of the NoGo trials where participants withheld their motor response. In contrast, a recent study by Altas and Stenner (2024, unpublished data) utilised a lower percentage of NoGo trials for the urge detection task. In the present study, the urge detection task was performed in 50% of the NoGo trials to shift participants' focus to the Go/NoGo task, thus ensuring a retrospective decision of whether an urge to move was perceived. If the primary focus was on the urge itself, the question would arise whether the prime induced a transient urge to move in the urge detection task. Based on this factor, previous pilot testing on the optimal number of NoGo trials for the urge detection task may be instrumental in refining the study design to enhance efficiency.

The power analysis conducted before the main study indicated a cohort size of 20 participants per group to achieve 80% power and an effect size of $d = 0.7$ for the primary outcome parameter, urge sensitivity, as found by Altas and Stenner (2024, unpublished data). The attempt to exclude all external sources of information resulted in a limited sample size in the present study, making it challenging to detect potential differences between adults with PTD and healthy controls. Before the control analysis, d' scores for urge detection were numerically low, whereas d' scores for prime discrimination were notably above zero. This detail indicates that prime recognition was likely used as additional information for urge reports in the urge detection task. Operationalising the awareness of an urge to move poses significant challenges. This study's experimental design included limited control over transient intentions of movement preparation, which can stem from sources other than the prime. It is crucial to exclude all other information sources to ensure the results' reliability. Participants may have detected their muscle twitches and misinterpreted them as an urge to move when they needed to suppress their response in NoGo trials.

Additionally, it is challenging to show that there was no muscle activity prior to the target onset. Surface EMG was applied to control muscle activity, but it may be necessary to apply an invasive

EMG to provide more control over micro muscle twitches being potentially perceived for urge reports. The analysis protocol of the sEMG to mitigate potential sensory information for urge reports did not rely on hard criteria. EMG negative trials to be excluded were defined based on conservative cut-off procedures. Trials with prior muscle activity in this task can be defined differently, which may influence the results.

Further factors, such as current medication intake and comorbidities along with PTD, might have influenced the findings, possibly resulting in noisier data in the PTD group. The patient group exhibited a range of accompanying conditions, such as ADHD, major depression, and OCD, which might have affected their urge detectability.

Moreover, a change in the methodological procedure during the main study, specifically the inability to automate trigger transmission from the ninth participant onwards, may have affected the accuracy of the muscle activity analysis after target onset. Additionally, expectation bias could have influenced participants' awareness of an urge to move. For instance, if participants expected a Go prime after a series of Go primes, their reaction times would be reduced due to prior response preparation (Misirlisoy & Haggard, 2014). Controlling for such biases in this experimental set-up was challenging.

Finally, PUs are experienced with varying frequency across different body parts, yet studies have yielded conflicting outcomes. Typically, PUs are experienced in the same body area or close to where tics occur (Essing et al., 2022; Leckman et al., 1993). Explorative studies of tic localisation and PU frequency reveal that complex tics are more frequently preceded by PUs than simple tics (Cavanna et al., 2017; Essing et al., 2022). Tics involving the head, upper trunk, and midline abdomen are more commonly preceded by PUs, whereas tics such as blinking or mouth movements exhibit lower rates of preceding PUs (Cavanna et al., 2017). The dependence of PU frequency and tic localization might have impacted the outcome of the present study. We examined a body part, namely the right hand, that was, in many of the participants with PTD, not the part usually associated with their tics. Future studies should consider homogeneous cohorts regarding tic localisation and body parts where PUs are experienced.

7 Conclusion

The present work is the first study involving objective experimental control over movement planning during the assessment of the awareness of an urge to move in adults with PTD. Subliminal visual priming was applied in a modified Go/NoGo task, allowing us to define when participants should feel an urge to move in the urge detection task. This study replicates previous findings that healthy people are aware of the urge to initiate a voluntary movement (Altas & Stenner, 2024, unpublished data). Specifically, this awareness was found even in the absence of other sources of information, such as prior muscle activity and conscious prime discriminability (Altas & Stenner, 2024, unpublished data). This study shows that individuals with PTD do not have altered awareness of the urge to move compared to healthy controls in this experimental task. Furthermore, we demonstrate that adults with PTD can be numerically aware of a transient urge to move during the experiment, even though this effect was not statistically significant in the PTD group in this task.

Future studies should include larger sample sizes to reveal potential differences in the awareness of the urge to move between individuals with PTD and people without tics. More data is needed on the emerging hypothesis that altered neuromotor noise levels contribute to the generation of PUs in PTD. Additionally, homogeneous patient cohorts may provide a better understanding of the role of distinct comorbidities, such as ADHD, OCD, or major depression, in the awareness of urges to move.

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Eidesstattliche Versicherung

„Ich, Moritz Michael Fuhrmann, versichere an Eides statt durch meine eigenhändige Unterschrift, dass ich die vorgelegte Dissertation mit dem Thema: Effects of Subliminal Visual Stimuli on the Awareness of an Urge to Move in Adults with Chronic Primary Tic Disorders / Einfluss von unterschwelligen visuellen Reizen auf das Bewusstsein über einen Bewegungsdrang bei Erwachsenen mit chronischen primären Tic-Störungen selbstständig und ohne nicht offengelegte Hilfe Dritter verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel genutzt habe.

Alle Stellen, die wörtlich oder dem Sinne nach auf Publikationen oder Vorträgen anderer Autoren/innen beruhen, sind als solche in korrekter Zitierung kenntlich gemacht. Die Abschnitte zu Methodik (insbesondere praktische Arbeiten, Laborbestimmungen, statistische Aufarbeitung) und Resultaten (insbesondere Abbildungen, Graphiken und Tabellen) werden von mir verantwortet.

Ich versichere ferner, dass ich die in Zusammenarbeit mit anderen Personen generierten Daten, Datenauswertungen und Schlussfolgerungen korrekt gekennzeichnet und meinen eigenen Beitrag sowie die Beiträge anderer Personen korrekt kenntlich gemacht habe (siehe Anteilserklärung). Texte oder Textteile, die gemeinsam mit anderen erstellt oder verwendet wurden, habe ich korrekt kenntlich gemacht.

Meine Anteile an etwaigen Publikationen zu dieser Dissertation entsprechen denen, die in der untenstehenden gemeinsamen Erklärung mit dem/der Erstbetreuer/in, angegeben sind. Für sämtliche im Rahmen der Dissertation entstandenen Publikationen wurden die Richtlinien des ICMJE (International Committee of Medical Journal Editors; www.icmje.org) zur Autorenschaft eingehalten. Ich erkläre ferner, dass ich mich zur Einhaltung der Satzung der Charité – Universitätsmedizin Berlin zur Sicherung Guter Wissenschaftlicher Praxis verpflichte.

Weiterhin versichere ich, dass ich diese Dissertation weder in gleicher noch in ähnlicher Form bereits an einer anderen Fakultät eingereicht habe.

Die Bedeutung dieser eidesstattlichen Versicherung und die strafrechtlichen Folgen einer unwahren eidesstattlichen Versicherung (§§156, 161 des Strafgesetzbuches) sind mir bekannt und bewusst.“

Dreieich, den 12. November 2024 |

Ort, Datum

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Lebenslauf

Mein Lebenslauf wird aus datenschutzrechtlichen Gründen in der elektronischen Version meiner Arbeit nicht veröffentlicht.

Publikationsliste

- Fuhrmann, M. & Renneberg, S. (2024). Laufen trifft Psychologie: Dein interaktives Workbook für ein starkes Mindset im Lauftraining. Books on Demand.
- Fuhrmann, M. & Renneberg, S. (2024). Laufen trifft Psychologie: Dein interaktives Workbook für ein starkes Mindset im Lauftraining. Books on Demand. Epub.
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Danksagung

An erster Stelle gilt mein Dank meinem Doktorvater Herrn PD Dr. med. Christos Ganos für die freundliche Überlassung des hochinteressanten Themas, die Bereitstellung des Arbeitsplatzes sowie des Labors für die Studiendurchführung. Ich verdanke ihm weiterführend jede hilfreiche Unterstützung und viele hilfreiche Diskussionen während der gesamten Bearbeitungsphase meiner Dissertation. Ich danke ihm für die methodische Freiheit während des gesamten Forschungsprojektes. Seine fachliche Expertise kam mir in zahlreichen Angelegenheiten sehr zugute. Anerkennen möchte ich auch die uneingeschränkte Bereitschaft, seine fachliche und wissenschaftliche Expertise mit mir zu teilen.

Besonders danken möchte ich auch Herrn Dr. med. Max-Philipp Stenner und Doktorand Herrn Arda Altas, die diese Arbeit durch die wissenschaftliche Vorarbeit erst ermöglichten. Herr Dr. Stenner gewährte mir bei der Planung, Durchführung und Auswertung der vorliegenden Arbeit außerordentlich fachliche, erfahrene und wertvolle Unterstützung. Ich danke ihm dafür, dass er mich durch stets zielführende methodische Diskussionen sowie die anhaltende technische Hilfestellung begleitet und unterstützt hat.

Frau Dr. med. Tina Mainka-Frey danke ich ganz herzlich für die fachliche Betreuung, die konstruktiven Ideen sowie fachlichen Impulse, welche mir während der Erstellung der Dissertation stets neue Perspektiven eröffneten. Zudem möchte ich ihre Bereitschaft anerkennen, mich stets freundlich und geduldig durch die vielen nicht-wissenschaftlichen, motivierenden Gespräche sowie Ratschläge zu unterstützen.

Besonders danken möchte ich meinen Studienprobanden, insbesondere den Patientinnen und Patienten, für die sehr gute und zahlreiche Unterstützung und die angenehme Zusammenarbeit.

Allen Mitarbeitenden der AG Bewegungsstörungen der Charité Berlin danke ich für die organisatorische Unterstützung und die Bereitstellung der Messinstrumente. Mein besonderer Dank geht auch an Assistenzarzt Herrn Richard Köhler für den technischen EMG-Support im Rahmen der Studienvorbereitung.

Besonders möchte ich an dieser Stelle auch meinen Eltern, Großeltern und Freunden für die unermüdliche Stärkung und Motivierung danken sowie für das stets offene Ohr für meine Gedanken.