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Neural correlates and neural stimulation of temporal recalibration mechanisms in sensorimotor and inter-sensory contexts

Inaugural-Dissertation
zur Erlangung des Doktorgrades der Naturwissenschaften
dem Fachbereich Medizin der Philipps-Universität Marburg

vorgelegt von

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aus Aachen

Marburg, 2024

Angenommen vom Fachbereich Medizin der Philipps-Universität Marburg
am: 28.02.2024

Gedruckt mit Genehmigung des Fachbereichs Medizin.

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Abbreviations

ACC	Anterior Cingulate Cortex
ANOVA	Analysis of Variance
EEG	Electroencephalography
fMRI	functional Magnetic Resonance Imaging
GEE	Generalized Estimating Equations
HC	Healthy Control
ICD-10	International Classification of Diseases and Related Health Problems – 10th Revision
MFG	Medial Frontal Gyrus
SFG	Superior Frontal Gyrus
STG	Superior Temporal Gyrus
SMA	Supplementary Motor Area
SSD	Schizophrenia Spectrum Disorders
tDCS	transcranial Direct Current Stimulation
TMS	Transcranial Magnetic Stimulation
TPJ	Temporo-Parietal Junction
TRE	Temporal Recalibration Effect

Summary

The sensory outcomes of our actions typically follow at a characteristic, predictable time shortly after the action. Predictions about sensory action-outcomes and their timing are believed to be generated by internal forward models based on the actions' motor commands. The comparison between predictions and re-afferent sensory feedback helps distinguish self- from externally generated sensory input. Importantly, in the complex and dynamically changing environment we can be exposed to, and must be able to adapt to, varying delays between our actions and the corresponding sensory outcomes. Therefore, forward models need to be capable of flexibly recalibrating their predictions to account for additional action-outcome delays and thereby maintain our ability of self-other distinction. This process, known as sensorimotor temporal recalibration, has been linked to neural processing in various brain regions, most prominently to the cerebellum. However, until now, it remains unclear whether the neural correlates associated with the adaptation to action-outcome delays can indeed be attributed to the recalibration of forward model predictions, or whether they may partially be explained by the recalibration of the expected inter-sensory timing, such as the timing between the tactile sensations during the movement and a visual or auditory sensory outcome. Moreover, while impairments in self-other distinction in patients with schizophrenia spectrum disorders (SSD) have often been linked to dysfunctional predictive mechanisms of the forward model, it remains elusive whether this could be partly due to the dysfunctional recalibration of these predictions to changing environmental conditions.

In this dissertation, three studies were conducted to fill these knowledge gaps. Firstly, the neural correlates of sensorimotor temporal recalibration were investigated using functional magnetic resonance imaging (fMRI) by controlling for the impact of inter-sensory temporal recalibration mechanisms (**study I**). It was further assessed whether transcranial direct current stimulation (tDCS) applied to the cerebellum can modulate temporal recalibration effects (**study II**). Additionally, this research aimed to investigate whether tDCS can be used to facilitate potentially impaired sensorimotor temporal recalibration mechanisms in SSD (**study III**).

In all studies, a temporal recalibration paradigm was applied which exposed subjects to delayed or undelayed visual or auditory outcomes elicited by actively performed (sensorimotor context) or passively induced (inter-sensory context) button press movements. The effects of this adaptation procedure on subjects' temporal perception were tested in a subsequent delay detection task. This paradigm was applied in healthy subjects during fMRI data acquisition (**study I**) and with different configurations of cerebellar tDCS (**study II**). Furthermore, it was applied in patients with SSD and

matched healthy control subjects while they received anodal tDCS of the bilateral cerebellum, right temporo-parietal junction, or right supplementary motor area (**study III**).

The findings of **study I** demonstrated important contributions of the hippocampus and the cerebellum to temporal recalibration. As both regions were engaged across active and passive movement conditions, they may play a general role in responding to violations of the expected inter-sensory stimulus timing, regardless of the involvement of forward model predictions. Importantly, the availability of forward model predictions also had an influence on neural processing by differentially modulating the activity pattern in frontal, sensory, and posterior cerebellar regions in sensorimotor and inter-sensory contexts. These findings were further supported by **study II**, which showed that anodal stimulation of the cerebellum via tDCS had a faciliatory impact on temporal recalibration, and this effect manifested differently in inter-sensory and sensorimotor contexts. Finally, the results of **study III** demonstrated similar sensorimotor temporal recalibration effects in patients with SSD and healthy control subjects and emphasized again that anodal cerebellar tDCS holds the potential to facilitate temporal recalibration mechanisms, specifically in the sensorimotor context.

This dissertation shows for the first time that, in addition to the cerebellum, the hippocampus plays a critical role in temporal recalibration in both sensorimotor and inter-sensory contexts, potentially by encoding and retrieving the newly learned inter-sensory temporal stimulus associations. It also extends previous research by demonstrating that recalibration-related processes in a range of brain regions, including parts of the cerebellum as well as frontal and sensory processing regions, may depend on whether forward model predictions contribute to recalibration or whether it solely relies on inter-sensory recalibration mechanisms. Finally, the comparable effects of temporal recalibration for both patients and healthy subjects indicate that sensorimotor temporal recalibration mechanisms may be preserved in SSD. The faciliatory impact that cerebellar tDCS had not only on healthy subjects but also on patients further confirms the importance of the cerebellum in temporal recalibration. It also suggests that cerebellar tDCS may be an interesting tool for future research to mitigate known deficits in forward model-based prediction mechanisms in the cerebellum in SSD, even though these deficits may not be explained by the dysfunctional temporal recalibration of these predictions.

Taken together, the findings of this dissertation contribute to a more advanced understanding of the neural correlates of sensorimotor and inter-sensory temporal recalibration mechanisms and provide new insights into the benefits of cerebellar tDCS to promote these mechanisms in healthy subjects and patients with SSD.

Zusammenfassung

Die sensorischen Konsequenzen unserer Handlungen erfolgen in der Regel zu einem charakteristischen und vorhersehbaren Zeitpunkt kurz nach der Handlung. Es wird angenommen, dass Vorhersagen über sensorische Handlungskonsequenzen und den Zeitpunkt ihres Auftretens von internen Vorwärtsmodellen erzeugt werden, basierend auf den motorischen Befehlen der Handlungen. Der Vergleich zwischen diesen Vorhersagen und dem reafferenten sensorischen Feedback trägt dazu bei, selbst erzeugte von externen sensorischen Signalen zu unterscheiden. In der komplexen und sich stetig verändernden Umwelt können wir jedoch verschiedenen Verzögerungen zwischen unseren Handlungen und deren sensorischen Konsequenzen ausgesetzt sein, an die wir uns anpassen müssen. Daher müssen Vorwärtsmodelle in der Lage sein, ihre Vorhersagen flexibel an zusätzliche Verzögerungen anzupassen, um unsere Fähigkeit der Selbst-Fremd-Unterscheidung aufrechtzuerhalten. Dieser Prozess, bekannt als sensomotorische zeitliche Rekalibrierung, wird mit der neuralen Verarbeitung in verschiedenen Hirnregionen in Verbindung gebracht, wobei das Cerebellum besonders prominent ist. Bisher ist jedoch unklar, ob die neuralen Korrelate, die mit der Anpassung an verzögerte Handlungskonsequenzen in Verbindung stehen, tatsächlich der Rekalibrierung von Vorwärtsmodell-Vorhersagen zugeschrieben werden können. Sie könnten teilweise auch mit der Rekalibrierung antizipierter inter-sensorischer zeitlicher Zusammenhänge erklärt werden, wie beispielsweise dem Zusammenhang zwischen den taktilen Signalen während der Bewegung und der visuellen oder auditorischen Handlungskonsequenz. Dazu kommt, dass Beeinträchtigungen in der Selbst-Fremd-Unterscheidung bei Patient*Innen mit Schizophrenie-Spektrum-Störungen (SSD) oft mit dysfunktionalen prädiktiven Mechanismen des Vorwärtsmodells in Verbindung gebracht werden. Bislang bleibt aber unklar, ob dies teilweise auf die dysfunktionale Rekalibrierung der Vorhersagen an sich verändernde Umweltbedingungen zurückzuführen ist.

Um diese Wissenslücken zu schließen, wurden im Rahmen dieser Dissertation drei Studien durchgeführt. Zunächst wurden mittels funktioneller Magnetresonanztomographie (fMRT) die neuralen Korrelate der sensomotorischen zeitlichen Rekalibrierung untersucht, wobei der Einfluss inter-sensorischer zeitlicher Rekalibrierungsmechanismen kontrolliert wurde (**Studie I**). Es wurde weiterhin überprüft, ob durch die Anwendung von transkranieller Gleichstromstimulation (tDCS) des Cerebellums, zeitliche Rekalibrierungseffekte moduliert werden können (**Studie II**). Darüber hinaus hatte diese Forschung das Ziel, den Nutzen von tDCS für die Verbesserung möglicherweise beeinträchtigter sensomotorischer zeitlicher Rekalibrierungsmechanismen bei Patient*Innen mit SSD zu untersuchen (**Studie III**).

In allen Studien wurde ein Paradigma zur Untersuchung zeitlicher Rekalibrierung verwendet. In dessen Rahmen wurden den Proband*Innen visuelle oder auditorische Stimuli präsentiert, die entweder verzögert oder unverzögert auf eine aktiv erzeugte (sensomotorischer Kontext) oder passiv induzierte (inter-sensorischer Kontext) Tastendruckbewegung folgten. Die Auswirkungen dieser Adaptationsphase auf die zeitliche Wahrnehmung der Proband*Innen wurde in einer anschließenden Aufgabe zur Detektion von Verzögerungen getestet. Dieses Paradigma wurde bei gesunden Proband*Innen während der Erhebung von fMRT-Daten (**Studie I**) und mit verschiedenen Konfigurationen von tDCS des Cerebellums (**Studie II**) angewendet. Zudem wurde es bei Patient*Innen mit SSD und gesunden Kontrollproband*Innen angewendet, während diese anodale tDCS des bilateralen Cerebellums, des rechten temporo-parietalen Übergangs oder des rechten supplementär-motorischen Areals erhielten (**Studie III**).

Die Ergebnisse aus **Studie I** zeigten, dass der Hippocampus und das Cerebellum wichtige Beiträge zur zeitlichen Rekalibrierung leisten. Die Tatsache, dass beide Regionen sowohl in aktiven als auch in passiven Bewegungsbedingungen beteiligt waren, spricht dafür, dass diese Regionen auf Abweichungen von antizipierten inter-sensorischen zeitlichen Zusammenhängen reagierten, unabhängig von der Beteiligung von Vorwärtsmodell-Vorhersagen. Der Einfluss von Vorwärtsmodell-Vorhersagen auf die neurale Verarbeitung zeigte sich durch kontextabhängige Modulationen (sensomotorisch vs. inter-sensorisch) des Aktivierungsmusters in frontalen und sensorischen Regionen, sowie in posterioren Bereichen des Cerebellums. Diese Ergebnisse wurden durch **Studie II** weiter gestützt, die zeigte, dass anodale Stimulation des Cerebellums mittels tDCS in der Lage war, zeitliche Rekalibrierungseffekte zu verstärken, und dass sich der Einfluss der Stimulation in sensomotorischen und inter-sensorischen Kontexten unterschiedlich manifestierte. Schließlich zeigten die Ergebnisse aus **Studie III**, dass Patient*Innen mit SSD und gesunde Kontroll-proband*Innen ähnliche sensomotorische zeitliche Rekalibrierungseffekte aufwiesen. Diese Studie wies außerdem erneut darauf hin, dass anodale tDCS des Cerebellums das Potential hat, zeitliche Rekalibrierungsmechanismen zu fördern, insbesondere im sensomotorischen Kontext.

Diese Dissertation zeigt erstmals, dass neben dem Cerebellum auch der Hippocampus eine entscheidende Rolle bei der zeitlichen Rekalibrierung in sensomotorischen und inter-sensorischen Kontexten spielt, möglicherweise durch das Speichern und Abrufen der neu erlernten zeitlichen Assoziation zwischen sensorischen Stimuli verschiedener Modalitäten. Darüber hinaus erweitern die Ergebnisse dieser Dissertation frühere Forschung, indem sie zeigen, dass rekalibrierungsbedingte

Prozesse in verschiedenen Hirnregionen, einschließlich Teilen des Cerebellums sowie frontaler und sensorischer Regionen, davon abhängen, ob Vorwärtsmodell-Vorhersagen zur Rekalibrierung beitragen oder ob sie ausschließlich auf inter-sensorischen Rekalibrierungsmechanismen beruhen. Schließlich weisen die vergleichbaren Effekte zeitlicher Rekalibrierung bei Patient*Innen und bei gesunden Proband*Innen darauf hin, dass die Fähigkeit zur sensomotorischen zeitlichen Rekalibrierung bei SSD erhalten sein könnte. Der verstärkende Effekt, den tDCS des Cerebellums nicht nur bei gesunden Proband*Innen, sondern auch bei Patient*Innen hatte, bestätigt erneut die Bedeutung dieser Region im Rahmen zeitlicher Rekalibrierungsprozesse. Dieser Befund legt außerdem nahe, dass tDCS des Cerebellums ein interessantes Werkzeug in zukünftiger Forschung darstellen könnte, um bekannte Defizite in vorwärtsmodellbasierten prädiktiven Mechanismen im Cerebellum bei SSD zu verringern, selbst wenn diese Defizite nicht durch die gestörte zeitliche Rekalibrierung dieser Vorhersagen erklärt werden können.

Zusammenfassend tragen die Ergebnisse dieser Dissertation zu einem besseren Verständnis der gemeinsamen und differentiellen neuralen Korrelate zeitlicher Rekalibrierungsmechanismen in sensomotorischen und inter-sensorischen Kontexten bei und liefern neue Erkenntnisse über den Nutzen von tDCS des Cerebellums zur Förderung dieser Mechanismen bei gesunden Proband*Innen und Patient*Innen mit SSD.

1. Introduction

1.1. Temporal Recalibration of Action-Outcome Predictions

To be able to interact with the environment in a goal-directed manner, the human sensorimotor system must be capable of identifying causal relationships between sensory stimuli, such as determining which of them have been generated by our own actions. An important cue for the attribution of sensory stimuli as self-generated is provided by their characteristic timing. Typically, the sensory outcomes of our actions are expected to occur instantaneously, without a noticeable delay. For instance, the movement of a cursor on a computer screen is associated with our own action if it occurs smoothly and in close temporal proximity to the hand movement performed with the computer mouse (Haggard, 2005; Moore et al., 2009).

However, we live in a complex and dynamic world in which the environmental conditions we encounter constantly change and confront the sensorimotor system with varying action-outcome delays (Haering & Kiesel, 2015). Fatigue, for example, can cause delays in the processing of sensory outcome signals (Cai et al., 2018), and low-light conditions can delay sensory signals from the retina (Matteson, 1971). Likewise, the response of technical devices can be associated with temporary delays, resulting in delayed feedback of the cursor after moving the computer mouse (Cai et al., 2018). How does the brain adapt to these changes in temporal dynamics to preserve the ability to correctly attribute the delayed sensory outcomes to one's own actions?

The adaptation to action-outcome delays is assumed to crucially depend on predictive mechanisms of the sensorimotor system. A prominent theory of sensorimotor control states that the brain holds internal forward models which take copies of the motor commands (i.e., efference copies) to generate predictions about the sensory outcomes that these motor commands will produce (Blakemore et al., 2000; von Holst & Mittelstaedt, 1950; Wolpert & Flanagan, 2001). These include predictions about the time at which the outcomes can be expected to occur after the action, by accounting for inherent delays in sensory processing and signal transmission (Aliu et al., 2009; Ebert & Wegner, 2010; Haggard et al., 2002; Wen, 2019). If the re-afferent sensory input received when performing the action aligns with the prediction, it is perceived as having been generated by the action itself. Mismatching sensory input, which has been received with an unexpectedly long delay after the action, is attributed to external sources (Wen, 2019). For this distinction of self- from externally generated input to function reliably, forward model predictions must be well-calibrated to the current environmental context. To achieve this, consistently occurring additional delays between action and outcome must be integrated into the prediction-generating process (Cao et al., 2017). When this

is accomplished, forward model predictions again align with the altered action-outcome timing, allowing self-generated sensory signals to remain distinguishable from externally generated ones (Aliu et al., 2009; Cao et al., 2017; Elijah et al., 2016). This process is known as sensorimotor temporal recalibration (Parsons et al., 2013; Stetson et al., 2006).

Empirically, sensorimotor temporal recalibration has been shown to manifest in perceptual changes. After being repeatedly exposed to a constant delay between a simple action (e.g., a button press) and a sensory outcome, the delayed outcome was more likely to be perceived as occurring in synchrony with the action (Cai et al., 2018; Heron et al., 2009; Parsons et al., 2013; Rohde & Ernst, 2013; Stekelenburg et al., 2011; Sugano et al., 2010; Tsujita & Ichikawa, 2012), and smaller action-outcome delays were no longer detected (Arikan et al., 2021; Toida et al., 2014). Furthermore, illusory reversals of the perceived action-outcome relationship could be observed, with undelayed outcomes being perceived as occurring before the action (Heron et al., 2009; Stetson et al., 2006). These perceptual changes are known as the sensorimotor temporal recalibration effect (TRE) and are assumed to result from a shift of the predicted action-outcome timing toward the exposed delay (Arikan et al., 2021; Keetels & Vroomen, 2012; Sugano et al., 2012). A sensorimotor TRE could be observed for both visual action-outcomes, such as light flashes presented on a computer screen, and for auditory ones, such as brief beep sounds (Arikan et al., 2021; Cai et al., 2018; Elijah et al., 2016; Heron et al., 2009; Rohde & Ernst, 2013; Stekelenburg et al., 2011; Stetson et al., 2006; Sugano et al., 2010). Interestingly, the sensorimotor TRE has also been demonstrated to transfer across modalities. For example, after exposure to a visual action-outcome delay, a sensorimotor TRE was also evident in the auditory modality (Arikan et al., 2021; Heron et al., 2009; Sugano et al., 2010, 2012). This phenomenon has been explained by forward model predictions being generated and recalibrated at a supra-modal level rather than in modality-specific circuits, thus affecting the general predicted timing for sensory action-outcomes (Arikan et al., 2021; Heron et al., 2009; Straube et al., 2017; van Kemenade et al., 2016).

1.2. Neural Correlates of Sensorimotor Temporal Recalibration

At the neural level, the generation of forward model predictions and their recalibration in response to environmental changes have been linked to a variety of brain regions.

Firstly, sensorimotor temporal recalibration could be observed to result in activity modulations in sensory systems. Typically, sensory signals that align with the forward model prediction are associated with the suppression of neural activity in various brain regions, including sensory regions. This suppression presumably serves to free processing capacities for external and unpredictable stimuli (Arikan et al., 2019;

Blakemore et al., 1998; Horváth et al., 2012; Ody et al., 2023; Pazen et al., 2020; Schmitter et al., 2021; Straube et al., 2017; Uhlmann et al., 2020). Importantly, after recalibration to auditory action-outcome delays, suppression of neural activation in auditory processing regions could also be observed to occur for the delayed outcomes (Elijah et al., 2016). This suggests that the delayed outcomes now matched the prediction and were perceived as originating from one's own action.

Secondly, it can be assumed that sensorimotor processing regions play a critical role in the process of sensorimotor temporal recalibration. Of particular note is the cerebellum, which has been frequently suggested as the location of internal forward models and thus to be tightly involved in generating predictions about sensory action-outcomes (Blakemore et al., 2001; Cao et al., 2017; Imamizu et al., 2000; Straube et al., 2017; Tanaka et al., 2020; van Kemenade et al., 2018; Welniarz et al., 2021). First evidence for the involvement of cerebellar processes in the temporal recalibration of these predictions has been provided by a magnetoencephalography (MEG) study. In this study, the characteristic suppression of neural activation associated with the processing of self-generated and predictable action-outcomes was shown to also occur for delayed outcomes after temporal recalibration. Importantly, however, this effect was eliminated when the right cerebellum was inhibited using transcranial magnetic stimulation (TMS; Cao et al., 2017). This suggests an important role of the cerebellum, not only in generating forward model predictions but also in recalibrating them in response to changes in temporal action-outcome relationships.

Finally, sensorimotor temporal recalibration has been shown to affect neural processing in brain regions known for error-related processes and conflict detection. Studies using functional magnetic resonance imaging (fMRI) and electro-encephalography (EEG) found that the illusory perception of undelayed action-outcomes as preceding the action after temporal recalibration was linked to activation increases in anterior cingulate cortex (ACC; Stekelenburg et al., 2011; Stetson et al., 2006) and medial frontal gyrus (MFG; Stetson et al., 2006). Since these regions have previously been associated with general conflict detection during information processing (Botvinick et al., 1999; Holroyd et al., 2004; van Veen & Carter, 2002), these findings indicate that recalibration of the expected timing between action and outcome induces changes not only in sensory and sensorimotor regions but also in higher-level cognitive processing systems.

1.3. Neural Stimulation of Sensorimotor Temporal Recalibration Mechanisms

In addition to neuroimaging methods such as fMRI and MEG, non-invasive brain stimulation techniques like transcranial direct current stimulation (tDCS) can be considered an interesting tool for investigating the neural underpinnings of sensorimotor temporal recalibration. While the former methods can only reveal correlations between the activation of a brain region and a given task, targeted stimulation of a specific region has the advantage of providing direct causal evidence for the impact of this region on task-related performance.

The classic tDCS setup consists of two electrodes, an anode and a cathode, which are attached to the scalp and used to apply weak direct current over the underlying brain regions. Conventional stimulation protocols apply currents of around 2mA for a duration of up to 20 minutes in adherence to standard safety guidelines (Bikson et al., 2016). Anodal stimulation is expected to modulate brain activity by increasing cortical excitability through neuronal depolarization, while cathodal stimulation is expected to decrease excitability by hyperpolarizing neurons (Nitsche et al., 2003; Nitsche & Paulus, 2000). Thus, tDCS allows for the investigation of the contribution of the stimulated brain region in a given task by comparing task-related performance during active stimulation to a control condition where only sham stimulation has been administered. Effects induced by a single session of tDCS with standard stimulation parameters have been shown to persist for 60-90 minutes (Nitsche et al., 2003; Nitsche & Paulus, 2000). Side effects of the stimulation are mild and transient and may include itching or tingling sensations, headache, and dizziness (Bikson et al., 2016). To date, various brain functions have already been successfully modulated by tDCS, including perceptual (Costa et al., 2015), motor (Wang et al., 2021), and cognitive processes (Shin et al., 2015).

Initial evidence suggests that sensorimotor temporal recalibration mechanisms can be modulated by tDCS as well. Aytemür et al. (2017) demonstrated that the sensorimotor TRE observed after recalibration to visual action-outcome delays decreased when cathodal tDCS was applied to the visual cortex. Beyond that, numerous studies have successfully employed tDCS on different brain regions to investigate related processes that are also known to be associated with sensorimotor predictive mechanisms (e.g., Haggard & Whitford, 2004; Khalighinejad & Haggard, 2015; Weightman et al., 2021). The stimulation of these regions could, therefore, also be valuable in advancing our understanding of their contribution to sensorimotor temporal recalibration.

Stimulating the angular gyrus with anodal tDCS, for example, modulated the intentional binding effect, which is an implicit measure of the sense of agency, i.e., the subjective feeling of being the source and in control of one's own actions and their corresponding sensory outcomes (Khalighinejad & Haggard, 2015). This finding supports previous studies that linked the posterior parietal cortex, including the angular gyrus, and adjacent temporal regions (known as the temporo-parietal junction, TPJ), to the detection of violations of the sense of agency that arise from mismatches between predicted and perceived sensory action-outcomes (Farrer et al., 2008; Nahab et al., 2011; Sperduti et al., 2011; Zito et al., 2020).

Similarly, the sense of agency could be influenced by anodal or cathodal tDCS of the pre-supplementary motor area (SMA), a region assumed to be closely connected to the process of generating the efference copy signals used by the forward model for prediction generation (Haggard & Whitford, 2004).

Lastly, cerebellar tDCS has demonstrated the potential to enhance the process of sensorimotor adaptation, i.e., the adaptation of goal-directed movements in response to deviations between expected and perceived movement feedback (Doppelmayr et al., 2016; Panico et al., 2018; Weightman et al., 2021; Yavari et al., 2016). The dependence of sensorimotor adaptation on cerebellar processes has been frequently reported and was attributed to the processing of prediction errors and consequently the updating of action-outcome predictions of the forward model in this region (Shadmehr et al., 2010; Synofzik et al., 2008; Tanaka et al., 2020; Tseng et al., 2007). This makes the cerebellum a particularly interesting stimulation target for studying the contribution of this region to sensorimotor temporal recalibration, as this process is similarly assumed to be connected to the updating of forward model predictions.

1.4. Sensorimotor Temporal Recalibration Mechanisms in Schizophrenia Spectrum Disorders

Schizophrenia spectrum disorders (SSD) are severe, chronic mental illnesses with a lifetime prevalence of 0.75% (Moreno-Küstner et al., 2018) and a typical onset in late adolescence or early adulthood (Welham et al., 2004). The disorders have a considerable negative impact on individuals' daily functioning (Harvey et al., 2012) and overall quality of life (Desalegn et al., 2020). Additionally, they carry a significant socioeconomic burden, as they rank among the top 20 causes of disability (in the years between 1990 and 2017; James et al., 2018). In the ICD-10 (International Classification of Diseases and Related Health Problems – 10th Revision) these disorders span the diagnoses F20 – F29. The most prominent diagnosis within this spectrum is schizophrenia, which is defined by the manifestation of characteristic positive and

negative symptoms over a specific duration. Positive symptoms include hallucinations, delusions, disorganized thinking, and motor abnormalities. Negative symptoms can take the form of blunted affect, alogia, avolition, and anhedonia, as well as reduced social and cognitive functioning. The schizophrenia spectrum additionally includes diagnoses that are characterized by a similar profile of symptoms with certain variations. For example, this may involve the co-occurrence of depressive or manic symptoms in schizoaffective disorders or the presence of persistent delusions in the absence of other positive or negative symptoms in delusional disorders.

The emergence of certain positive symptoms in SSD has often been linked to dysfunctional sensorimotor predictive mechanisms. For instance, the suppression of neural activity, typically associated with the processing of predictable, self-generated sensory input in healthy individuals, has been demonstrated to be reduced in patients (Ford et al., 2001; Martinelli et al., 2016; Shergill et al., 2014; Uhlmann et al., 2021). This finding may result from dysfunctional forward models that do not adequately predict the sensory outcomes of self-generated actions, leading to severe impairments in self-other distinction, such as the misattribution of self-generated input as externally produced (Lindner et al., 2005). Such an impairment has been proposed to contribute to the emergence of auditory verbal hallucinations, which may result from one's own inner speech being misperceived as an external voice. Similarly, delusions of control, i.e., the misperception of one's own thoughts or actions as being controlled by an external force or another person, have been explained as arising from impairments in self-other distinction (Pynn & DeSouza, 2013).

Importantly, as of now, it remains unclear to which process within the forward model-based predictive mechanism the dysfunction in patients can be attributed. It may, for example, be based on a failure of computational processes of the forward model itself during prediction generation or on a failure of comparing predicted and re-afferent sensory input. It is also conceivable, however, that it partly relies on a deficit in sensorimotor temporal recalibration, i.e., in flexibly recalibrating forward model predictions to changing temporal dynamics in the environment, such as variations in action-outcome delays. This could result in constantly miscalibrated predictions that do not adequately account for the temporal action-outcome relationships of the current environmental context, thereby failing to generate reliable predictions. However, whether patients with SSD exhibit deficits in sensorimotor temporal recalibration has not been investigated yet.

In this context, the application of tDCS could also be of interest. tDCS has proven to be valuable not only for gaining a better understanding of the role of specific brain regions but has also been successfully applied in a clinical context to ameliorate certain

deficits and, ultimately, symptomatology in patients with psychiatric disorders (Herrera-Melendez et al., 2020). In patients with SSD, tDCS has been used to improve, e.g., auditory hallucinations (Bose et al., 2014; Brunelin et al., 2012), negative symptoms (Aleman et al., 2018; Valiengo et al., 2020), cognitive functioning (Hoy et al., 2014; Smith et al., 2015), and even action-outcome processing (Straube et al., 2020). Therefore, the stimulation of brain regions closely linked to forward model predictions, such as the cerebellum, TPJ, and SMA, may serve as a promising tool for enhancing potentially impaired temporal recalibration mechanisms and alleviating related symptoms in patients with SSD.

1.5. Controlling for the Impact of Inter-Sensory Recalibration Mechanisms

Notably, the ability to recognize causal relationships between sensory stimuli and to adapt to additional delays between them is not only crucial for identifying the sensory outcomes of one's own actions but also plays an important role in a purely perceptual context without the involvement of an action. For example, the characteristic and expected temporal proximity between inputs from different sensory modalities is crucial for identifying those that were caused by the same source (Keetels & Vroomen, 2011). For instance, when listening to a person speak, the corresponding visual signals (e.g., the lip movements) and the auditory signals reach us almost simultaneously (with some constant shift due to differences in inherent transmission and processing times of signals from different sensory modalities; Van der Burg et al., 2015), and can therefore easily be attributed to the same person. But when additional delays between the visual and auditory signals are introduced, for example, when the image of a person is transmitted slightly delayed during an online conference, inter-sensory matching mechanisms need to adjust the expected relative timing between the signals from both sensory modalities to preserve the ability to correctly attribute them to the same source or person (Alais et al., 2017). This is also an important adaptive process, here referred to as inter-sensory temporal recalibration. An inter-sensory TRE manifests similarly to the sensorimotor TRE in terms of changes in the expected relative timing between signals from two different sensory modalities. Thus, after these signals have been repeatedly presented with a constant delay between them, they are perceived as synchronous again (Di Luca et al., 2009; Fujisaki et al., 2004; Harrar & Harris, 2008; Van der Burg et al., 2013; Vroomen et al., 2004). This effect has not only been observed for auditory-visual modality pairs but also for auditory-tactile and visual-tactile pairs. It has even been shown to transfer across different modality pairs (Di Luca et al., 2009). Importantly, in this scenario, the TRE does

not involve the recalibration of forward model predictions due to the absence of a self-generated action.

Consequently, when adapting to an action-outcome delay, it can be assumed that not only forward model predictions about the action-outcome timing recalibrate to the delay. Inter-sensory matching mechanisms are also likely to contribute by recalibrating the expected relative timing between signals of different sensory modalities, such as between the tactile sensations during the movement and a visual or auditory outcome stimulus. Until now, both temporal recalibration mechanisms have mostly been investigated in isolation. It therefore remains unclear which of the neural correlates associated with the adaptation to action-outcome delays can be specifically attributed to the recalibration of forward model predictions, as opposed to the recalibration of inter-sensory matching mechanisms. First studies therefore included a control condition that only induced inter-sensory recalibration to delays between the tactile or proprioceptive sensations on an effector which was moved passively (Arikan et al., 2021) and a corresponding visual or auditory stimulus. The inter-sensory TRE elicited in this condition appeared to be weaker compared to the sensorimotor TRE elicited in a condition where the movement was actively self-generated, suggesting the additional recalibration of forward model predictions in the latter condition (Arikan et al., 2021). The implementation of such a passive control condition is therefore essential to elucidate commonalities and differences in the neural correlates of sensorimotor and inter-sensory temporal recalibration.

1.6. Aims and Research Questions

This dissertation aimed to disentangle the neural correlates of the adaptation to action-outcome delays that can be attributed to sensorimotor temporal recalibration (i.e., the recalibration of forward model predictions) from those due to the recalibration of inter-sensory matching mechanisms (**study I**). Furthermore, it aimed to investigate the potential of tDCS for modulating sensorimotor temporal recalibration (**study II**), and, finally, whether patients with SSD exhibit impairments in this mechanism, and whether this impairment can be alleviated by tDCS applied to relevant brain regions (**study III**).

In all studies, a temporal recalibration paradigm was employed. In this paradigm, subjects went through adaptation phases during which they were exposed to auditory or visual stimuli that followed a button press movement either undelayed or with a constant delay. A subsequent delay detection task assessed whether the exposure to the delayed stimuli elicited a TRE, with smaller delays being less likely to be detected due to a shift in temporal perception. Importantly, the button press movement was either actively performed by the subjects to assess the sensorimotor TRE, or it was passively performed

by a custom-made passive button device to isolate the inter-sensory TRE. For healthy subjects, the sensorimotor TRE was hypothesized to be stronger than the inter-sensory TRE in all studies due to the recalibration of forward model predictions in addition to the recalibration of inter-sensory matching mechanisms (**H1**). Furthermore, the TRE was expected to transfer between modalities and thus also manifests for a sensory modality not used during adaptation. The modality transfer was assumed to be stronger for the sensorimotor compared to the inter-sensory TRE due to the hypothesized generation and recalibration of forward model predictions on a supra-modal level in this condition (**H2**).

In **study I**, the temporal recalibration paradigm was applied during fMRI data acquisition. Brain regions assumed to be closely linked to the generation of forward model predictions, particularly the cerebellum, were hypothesized to be specifically involved during temporal recalibration and its modality transfer in active movement conditions (**H3**).

To investigate the impact of tDCS on sensorimotor temporal recalibration, the same recalibration paradigm was applied in **study II**, while subjects received different configurations of cerebellar tDCS or sham stimulation. Due to the cerebellum being the presumed location of internal forward models, tDCS applied to this region was expected to modulate forward model-based predictive mechanisms and thereby specifically impact the sensorimotor TRE and its modality transfer (**H4**).

Finally, in **study III**, the temporal recalibration paradigm was employed in patients with SSD and healthy control (HC) subjects while anodal tDCS was applied to the bilateral cerebellum, right TPJ, or right SMA, or while subjects received sham stimulation. Patients with SSD were hypothesized to exhibit a reduced sensorimotor TRE and reduced modality transfer of the sensorimotor TRE compared to HC due to a dysfunctional recalibration of forward model predictions (**H5**). Furthermore, compared to sham stimulation, tDCS on the mentioned brain regions was expected to facilitate forward model-based predictive mechanisms and thus the sensorimotor TRE and its modality transfer in both groups, thereby alleviating the hypothesized deficit in patients (**H6**).

2. Aggregation of Study Results

2.1. Study I: Neural Correlates of Sensorimotor and Inter-Sensory Temporal Recalibration

This study has been published as:
Schmitter, C.V., Kufer, K., Steinsträter, O., Sommer, J., Kircher, T., & Straube, B. (2023). Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements. *Human Brain Mapping*, hbm.26508.
https://doi.org/10.1002/hbm.26508 (IF: 4.8)

Previous research has linked sensorimotor temporal recalibration, i.e., the recalibration of forward model predictions in response to changes in action-outcome delays, to processing changes in frontal and anterior cingulate regions (Stekelenburg et al., 2011; Stetson et al., 2006), as well as in regions for early sensory processing (Elijah et al., 2016). Moreover, the cerebellum could be attributed a crucial role in this process, as it has been proposed to be the location of internal forward models and therefore to be strongly involved in the generation and recalibration of forward model predictions about sensory-action outcomes (Blakemore et al., 2001; Cao et al., 2017; Tanaka et al., 2020). Importantly, however, when adapting to action-outcome delays, not only forward model predictions but also inter-sensory matching mechanisms can be assumed to recalibrate in order to account for changes in the expected timing between the tactile sensation during the movement and the corresponding visual or auditory outcomes (Arikan et al., 2021). Thus far, it remains open which of the neural correlates observed during the adaptation to action-outcome delays can be specifically attributed to sensorimotor, as opposed to inter-sensory temporal recalibration. This study aimed to bridge this gap by investigating the neural correlates of the adaptation to delays between movements and a corresponding auditory outcome. The movements were either actively generated (in which case sensorimotor and inter-sensory recalibration mechanisms can be assumed to contribute), or they were passively induced (in which case only inter-sensory recalibration can be assumed to occur due to the absence of motor commands and thus forward model predictions).

During fMRI data acquisition, 25 healthy subjects participated in the temporal recalibration paradigm. In adaptation phases, they were exposed to tones that followed actively elicited or passively performed button press movements, either undelayed (0ms delay) or delayed by 150ms. The effects of this procedure on temporal perception in the

auditory (unimodal condition) and visual modality (modality transfer condition) were assessed in a subsequent delay detection task. Behavioral data were analyzed by fitting psychometric functions to the proportion of detected delays during the delay detection task. The TRE was defined in terms of a shift in psychometric functions, and thus larger delay detection thresholds in conditions with delayed tones compared to undelayed tones during the preceding adaptation phase.

A repeated-measures analysis of variance (ANOVA) performed on the delay detection thresholds revealed that the sensorimotor TRE (active conditions) was stronger than the inter-sensory TRE (passive conditions). This indicates that, in addition to inter-sensory matching mechanisms, forward model predictions recalibrated to the delay in this condition (**H1**). Moreover, the TRE was limited to the auditory modality and did not transfer to vision (**H2**).

At the neural level, across active and passive movements, exposure to delayed vs. undelayed tones during adaptation phases was associated with stronger activity in left hippocampus (150ms > 0ms). During the subsequent delay detection task, across auditory and visual conditions, the same hippocampal cluster, along with anterior and posterior parts of the bilateral cerebellum (lobules IV-VIII), was recruited more strongly when the tones during the previous adaptation phase had been delayed. Importantly, during adaptation, activations in frontal regions (left MFG and superior frontal gyrus, SFG), the bilateral posterior cerebellum (lobules VIII-X), and sensory processing regions (left postcentral gyrus and superior temporal gyrus, STG) were differentially modulated depending on the type of movement.

These findings extend previous research by pointing to an important role of the hippocampus in temporal recalibration. This may be related to the encoding of novel temporal associations between the movement and the corresponding auditory sensory outcome during adaptation, as well as the retrieval of these updated associations during the delay detection task. The results of this study further emphasize the contribution of cerebellar processes to temporal recalibration. Importantly, the involvement of both regions across active and passive movement conditions highlights their general role in responding to violations of the expected stimulus timing (inter-sensory recalibration), independent of the involvement of an active action and forward model predictions (**H3**). This is consistent with previous findings that attributed important roles to both hippocampus (Chen et al., 2011; Duncan et al., 2012) and cerebellum (Kotz et al., 2014; O'Reilly et al., 2008; Roth et al., 2013) for storing expectations about the (temporal) relationship between sensory stimuli and their adaptation to changing environmental conditions, across both sensorimotor and perceptual domains. Finally, the differential activation pattern observed during adaptation with active compared to passive

movements in frontal, sensory, and posterior cerebellar regions supports the notion of a large network of brain regions in sensory, sensorimotor, and higher-level cognitive processing systems associated with temporal recalibration (Cao et al., 2017; Elijah et al., 2016; Stekelenburg et al., 2011; Stetson et al., 2006). Importantly, this result extends previous findings by demonstrating that the exact role of these regions during temporal recalibration differs depending on whether it only relies on changes in inter-sensory timing or whether it involves forward model-based predictive mechanisms (**H3**).

Together, the findings of this study contribute to a more comprehensive understanding of the neural underpinnings of sensorimotor and inter-sensory temporal recalibration. They suggest that certain brain regions previously associated with sensorimotor temporal recalibration, such as parts of the cerebellum, may rather be involved in the recalibration of inter-sensory matching mechanisms. However, they also demonstrate that the availability of forward model predictions influences recalibration-related processes in frontal, sensory, and posterior cerebellar regions.

2.2. Study II: Neural Stimulation of Sensorimotor and Inter-Sensory Temporal Recalibration Mechanisms

This study has been published as:
Schmitter, C.V., & Straube, B. (2022). The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration. *Frontiers in Human Neuroscience, 16,* 998843. https://doi.org/10.3389/fnhum.2022.998843 (IF: 2.9)

The cerebellum is traditionally considered a key brain region for generating forward model predictions and recalibrating them in response to changes in environmental conditions, such as increasing action-outcome delays (Blakemore et al., 2001; Cao et al., 2017; Tanaka et al., 2020). But thus far, it remains unclear to what extent the contribution of the cerebellum in responding to changes in action-outcome delays can indeed be attributed to the recalibration of forward model predictions in this region. It may also be more generally involved in the recalibration of the expected inter-sensory timing between sensory stimuli beyond the sensorimotor domain (Kotz et al., 2014; O'Reilly et al., 2008; Roth et al., 2013). Cerebellar tDCS has already been successfully applied for modulating processes assumed to be closely related to predictive mechanisms based on the forward model. This includes, for example, sensorimotor adaptation, i.e., the adaptation of movements to unexpected action-outcome deviations (Doppelmayr et al., 2016; Panico et al., 2018; Weightman et al., 2021; Yavari et al., 2016). However, the effectiveness of cerebellar tDCS for the modulation of temporal recalibration mechanisms has not been investigated yet. This study aimed to elucidate the impact of different configurations of cerebellar tDCS on sensorimotor and inter-sensory temporal recalibration mechanisms.

Twenty-two healthy subjects participated in the temporal recalibration paradigm in four separate sessions while they received anodal or cathodal tDCS of the bilateral cerebellum, dual-hemisphere cerebellar tDCS (i.e., simultaneous anodal tDCS of the right and cathodal tDCS of the left cerebellar hemisphere), or sham stimulation. Anodal tDCS is known to increase cortical excitability while cathodal tDCS decreases it (Nitsche et al., 2003; Nitsche & Paulus, 2000). Dual-hemisphere tDCS could previously be shown to increase overall stimulation effects (Kwon & Jang, 2012; Vines et al., 2008; Workman et al., 2020) due to the reduction of inhibitory inter-hemispheric influences (Kwon & Jang, 2012). Thus, anodal tDCS was expected to facilitate and cathodal tDCS to decrease the sensorimotor TRE and its modality transfer, while dual-hemisphere stimulation was expected to result in the overall strongest faciliatory stimulation effect. During tDCS (with 2mA for 20 minutes), subjects went through adaptation phases during which they were

exposed to visual stimuli that followed actively elicited or passively performed button press movements, either undelayed (0ms delay) or delayed by 150ms. The effects of this procedure on temporal perception in the visual (unimodal condition) and auditory modality (modality transfer condition) were assessed in a subsequent delay detection task.

Repeated-measures ANOVAs were performed on the TRE, i.e., the difference in delay detection thresholds following exposure to delayed vs. undelayed visual stimuli. According to these analyses, for the visual modality, no sensorimotor TRE (active conditions), inter-sensory TRE (passive conditions) or modulatory effects of tDCS on the TRE could be observed. For the auditory modality, however, anodal cerebellar tDCS facilitated recalibration in passive conditions by inducing an inter-sensory TRE, which was absent with sham stimulation. Importantly, it is also conceivable that temporal recalibration does not manifest in a general shift in delay detection thresholds but elicits changes in the perception of individual delay levels only, e.g., at delays close to the adaptation delay. Therefore, in a secondary analysis, the TRE was computed separately for each delay level used in the delay detection task (0, 83, 167, 250, 333, 417ms), defined as the difference in the percentage of detected delays for conditions following exposure to delayed vs. undelayed visual stimuli. A generalized estimating equations (GEE) analysis, which is specifically well suited for such complex repeated-measures designs (Ma et al., 2012), was then applied to test for stimulation-dependent modulations of the TRE depending on the individual delay levels. This analysis revealed that anodal cerebellar tDCS also induced a sensorimotor TRE in the auditory modality, which was absent with sham stimulation, but specifically at the delay closest to the adaptation delay (167ms). For the inter-sensory TRE, the facilitatory influence of cerebellar tDCS occurred at a larger delay level (333ms).

The findings of this study shed further light on the role of the cerebellum and its relative contributions to sensorimotor and inter-sensory temporal recalibration mechanisms. The faciliatory effect of anodal cerebellar tDCS on the TRE suggests mechanisms for temporal recalibration in the cerebellum that were amplified by the stimulation (**H4**). Importantly, since this effect was overall stronger for passive (i.e., inter-sensory) conditions, these findings provide additional evidence for the importance of the cerebellum in generating and recalibrating predictions, not exclusively in the sensorimotor but also in the perceptual domain, as suggested by previous research and by **study I** (Kotz et al., 2014; O'Reilly et al., 2008; Roth et al., 2013). Nonetheless, the different manifestation of the TRE across the range of tested delays in active and passive conditions suggests differences in the exact underlying recalibration mechanism for inter-sensory and sensorimotor contexts (**H1**). The fact that the facilitation of the

sensorimotor TRE by anodal cerebellar tDCS was precisely tuned to the delay level closest to the adaptation delay may indicate a sensorimotor temporal recalibration mechanism that operates particularly precisely. This may be due to the high predictability of self-generated sensory action-outcomes (Blakemore et al., 2001; Cao et al., 2017), leading to a particularly precise shift in the prediction about the temporal occurrence of the action-outcome. Finally, the manifestation and facilitation of the TRE in the auditory modality after exposure to delayed visual stimuli in this study support the notion that temporal recalibration mechanisms in the cerebellum are not modality-specific but may operate on a supra-modal level (**H2**; Arikan et al., 2021; Heron et al., 2009; Straube et al., 2017; van Kemenade et al., 2016).

Together, the findings of this study open interesting perspectives for future work on psychiatric disorders like SSD, which are believed to be associated with dysfunctions in forward model-based predictive mechanisms and their recalibration. Here, anodal cerebellar tDCS may constitute a tool for supporting the rehabilitation of cerebellar-dependent recalibration mechanisms.

2.3. Study III: Sensorimotor Temporal Recalibration in Schizophrenia Spectrum Disorders

This study has been published as:
Schmitter, C. V., & Straube, B. (2024). Facilitation of sensorimotor temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals. *Scientific Reports*, *14*(1), 2627. https://doi.org/10.1038/s41598-024-53148-3 (IF: 4.6)

The emergence of core positive symptoms in SSD, such as hallucinations or delusions of control, has been linked to dysfunctional forward models which fail to adequately predict the sensory outcomes of self-generated actions. This could result in the misattribution of self-generated sensory input as externally produced (Ford et al., 2001; Lindner et al., 2005; Pynn & DeSouza, 2013; Uhlmann et al., 2021). Thus far, it remains unknown whether these dysfunctions are partly related to deficient sensorimotor temporal recalibration mechanisms, leading to action-outcome predictions being constantly miscalibrated since they do not account for the temporal action-outcome relationships of the current environmental context. tDCS has already demonstrated the potential to reduce certain deficits and improve symptomatology in patients with SSD (Bose et al., 2014; Smith et al., 2015; Valiengo et al., 2020), and has even been shown to exert a positive influence on action-outcome processing (Straube et al., 2020). However, whether tDCS on regions associated with predictive mechanisms based on the forward model, such as the cerebellum (Blakemore et al., 2001; Cao et al., 2017; Tanaka et al., 2020), the TPJ (Farrer et al., 2008; Nahab et al., 2011; Sperduti et al., 2011; Zito et al., 2020), and the SMA (Haggard & Whitford, 2004), can be applied to reduce potential deficits in sensorimotor temporal recalibration in SSD, and thus alleviate associated symptoms, has not been investigated yet.

Therefore, in this study, 22 patients with SSD and 20 HC participated in the temporal recalibration paradigm in four separate sessions while receiving anodal tDCS (with 2mA for 20 minutes) on the bilateral cerebellum, right TPJ, right SMA, or sham stimulation. In the adaptation phases all subjects were exposed to tones that followed actively elicited or passively performed button press movements, either undelayed (0ms delay) or delayed by 200ms. Temporal recalibration effects were assessed for the auditory (unimodal condition) and visual modality (modality transfer condition) in a subsequent delay detection task.

According to a mixed ANOVA, both SSD and HC exhibited similar TREs which were stronger in sensorimotor (active conditions) than in inter-sensory (passive

conditions) contexts (**H1**). Importantly, cerebellar tDCS had a faciliatory impact on the sensorimotor TRE in both groups, specifically for the auditory modality. Across both groups, the TRE transferred to the visual modality (**H2**), but this effect did not differ between active and passive conditions and was not facilitated by tDCS.

The comparable effects for both groups indicate that sensorimotor temporal recalibration mechanisms may be preserved in SSD. Thus, these findings do not provide evidence for the claim that the observed dysfunctions in predictive mechanisms based on the forward model, resulting in deficits in self-other distinction in SSD (Ford et al., 2001; Shergill et al., 2014; Straube et al., 2020; Uhlmann et al., 2021), can be attributed to impairments in recalibrating these predictions to varying action-outcome delays (**H5**). Moreover, the results of this study further corroborate findings of **study I** and **II** and of previous research by demonstrating the importance of the cerebellum for temporal recalibration (Blakemore et al., 2001; Cao et al., 2017; Tanaka et al., 2020). The fact that cerebellar tDCS specifically facilitated the sensorimotor TRE in this study suggests that the stimulation specifically targeted the recalibration of forward model predictions in this region (**H6**). However, since the modality transfer of the TRE appeared similarly for active and passive conditions, the findings do not speak for the presence of supra-modal forward model predictions in the cerebellum (Arikan et al., 2021; Heron et al., 2009; Straube et al., 2017; van Kemenade et al., 2016). Instead, they suggest that the supra-modal recalibration of inter-sensory matching mechanisms can account for the transfer effect, leading to changes in the expected relative timing between tactile, auditory, and visual sensory stimuli.

Together, these results suggest that cerebellar tDCS could be a promising tool for addressing deficits in action-outcome monitoring and related adaptive sensorimotor processes in SSD. This could include processes such as sensorimotor adaptation, which involves the adaptation of movements in response to deviations between expected and perceived movement feedback and has repeatedly been found to be deficient in patients (Bartolomeo et al., 2020; Bigelow et al., 2006; Cornelis et al., 2022; Picard et al., 2012). The fact that the ability to recalibrate forward model predictions is preserved in patients may also indicate that this adaptability constitutes an important resource in SSD that could potentially be utilized for training forward models to generate adequate predictions and thereby eventually improve impairments in self-other distinction.

3. Discussion

Due to the complex and constantly changing sensory environment, the ability to flexibly adapt to varying delays between actions and their sensory outcomes is essential. But so far, it has remained largely unclear which neural correlates of this process can be attributed to sensorimotor temporal recalibration, i.e., the recalibration of forward model predictions about the action-outcome timing, or to the recalibration of inter-sensory matching mechanisms. It has also remained elusive whether tDCS applied to regions associated with predictive mechanisms based on the forward model can modulate sensorimotor temporal recalibration, and whether known deficits in patients with SSD in predicting the sensory outcomes of their own actions can be partly explained by dysfunctions in adequately recalibrating these predictions to the current environmental conditions. The studies of this dissertation demonstrated that contributions of parts of the cerebellum and the hippocampus to the adaptation to action-outcome delays may be explained by inter-sensory temporal recalibration mechanisms. However, the availability of forward model predictions could be shown to influence recalibration-related processes in frontal, sensory, and posterior cerebellar regions (**study I**). Furthermore, it appeared that sensorimotor temporal recalibration mechanisms may be preserved in SSD (**study III**), and that cerebellar tDCS holds the potential to facilitate temporal recalibration mechanisms (**studies II and III**). Together, these findings contribute to a more advanced understanding of the neural correlates of sensorimotor and inter-sensory temporal recalibration mechanisms and provide new insights into the usability of tDCS in facilitating these mechanisms in healthy subjects and patients with SSD.

3.1. Sensorimotor vs. Inter-Sensory Temporal Recalibration Effects

At the behavioral level, the sensorimotor TRE appeared to be stronger compared to the inter-sensory TRE in **study I** in healthy subjects and in **study III** across the HC and SSD groups. These findings support the notion that, in addition to inter-sensory matching mechanisms, forward model predictions contribute to the emergence of the sensorimotor TRE (**H1**). Importantly, the results across the three studies also suggest differences in the manifestation of the TRE depending on the sensory modality used during adaptation. Subjects adapted to delays between the movement and the auditory stimulus in **studies I and III** which revealed the expected advantage of temporal recalibration in the sensorimotor context. In **study II**, however, the adaptation modality was visual. Here, a TRE appeared only after anodal tDCS of the cerebellum and was then overall stronger in the inter-sensory context. This is in line with the previous finding showing that, compared to audition, the TRE after visual adaptation was primarily driven by inter-

sensory recalibration mechanisms (Arikan et al., 2021). These modality-specific findings may be related to the fact that temporal perception and predictability are less precise for visual than for auditory stimuli (Grahn, 2012; Grondin, 2010). Thus, visual action-outcome predictions might have lower temporal resolution, and temporal prediction errors during adaptation could consequently be associated with more noise, resulting in a smaller shift in temporal perception. Alternatively, since the sensorimotor TRE occurred only at the delay level closest to the adaptation delay in **study II**, it may also be assumed that the visual delay adaptation procedure resulted in a particularly precise shift in temporal forward model predictions and, therefore, did not lead to an overall stronger sensorimotor TRE.

While we cannot favor any of these possible explanations based on the present data, the studies of this dissertation collectively suggest that there are differences in the manifestation of the TRE between sensorimotor and inter-sensory contexts, which might be modality dependent. These findings support the claim that forward model predictions contribute to the emergence of the sensorimotor TRE and highlight at the same time the need to further investigate modality differences in temporal recalibration and their underlying mechanisms.

3.2. Modality Transfer of Temporal Recalibration Effects

A modality transfer of the behavioral TRE could be found in both directions in this dissertation, i.e., from vision to audition (**study II**) and from audition to vision (**study III**). This suggests that temporal recalibration mechanisms are not modality-specific (**H2**).

Importantly, however, there was no advantage of the modality transfer in sensorimotor conditions, i.e., no stronger sensorimotor vs. inter-sensory TRE in the transfer modalities. Thus, these results do not support the assumption of the supra-modal recalibration of forward model predictions (Arikan et al., 2021; Heron et al., 2009; Straube et al., 2017; van Kemenade et al., 2016). Instead, they support the notion of supra-modal inter-sensory temporal recalibration mechanisms that recalibrate the expected general timing between sensory signals of multiple modalities. Inter-sensory recalibration did therefore not exclusively affect the temporal relationship between signals of the modality pair used during adaptation (Di Luca et al., 2009).

3.3. Neural Underpinnings of Sensorimotor vs. Inter-Sensory Temporal Recalibration

At the neural level, the results of the studies in this dissertation collectively demonstrate that the involvement of certain brain regions during temporal recalibration (including the hippocampus and parts of the cerebellum) may be associated with the recalibration of

inter-sensory matching mechanisms. However, it also appeared that modulations in recalibration-related processing occurred in frontal, sensory, and posterior cerebellar regions, depending on whether forward model predictions contributed to the recalibration (**H3**).

Firstly, **study I** demonstrated for the first time an important role of the hippocampus in temporal recalibration. The hippocampus has already previously been linked to adaptive processes of the sensorimotor system, such as the acquisition and retrieval of new spatial or temporal mappings between a movement and its sensory feedback during sensorimotor adaptation (Anguera et al., 2007; Scheidt et al., 2011; Standage et al., 2022). Moreover, beyond the sensorimotor domain, this region has been recognized as important for forming associations, for example, regarding the temporal relationship of sensory stimuli, and detecting violations of the learned stimulus associations (Chen et al., 2011; Duncan et al., 2009; Staresina & Davachi, 2009; Wallenstein et al., 1998). Since the involvement of the hippocampus in **study I** was evident across both sensorimotor and inter-sensory contexts, these findings indicate a general role of this region in learning and retrieving new temporal associations between the tactile sensations during the movement and the corresponding sensory outcome stimulus, as well as in detecting mismatches between the expected and the observed inter-sensory stimulus timing.

Furthermore, **study I** demonstrated the importance of the cerebellum for temporal recalibration. Anterior and posterior parts of this region showed increased activation across sensorimotor and inter-sensory contexts during the delay detection task when the stimulus during previous adaptation had been delayed. Along similar lines, **study II** showed that stimulation of the cerebellum with anodal tDCS could facilitate the TRE and its modality transfer (**H4**). Importantly, this faciliatory effect was not limited to the sensorimotor context. This finding thus provides further direct evidence for the essential role of cerebellar processes in temporal recalibration, even in the absence of forward model predictions. While the cerebellum has traditionally been primarily associated with sensorimotor processes and the prediction of sensory action-outcomes (Blakemore et al., 2001; Tanaka et al., 2020), these findings align with a body of research demonstrating the significance of this region in establishing and adjusting internal model predictions, not only in the sensorimotor but also in the perceptual domain (Kotz et al., 2014; O'Reilly et al., 2008). These also include predictions about the temporal relationship of different sensory events (Beudel et al., 2009; Coull et al., 2013; Moberget et al., 2008; Roth et al., 2013). The faciliatory influence of tDCS on the TRE in **study II** and the increased cerebellar activations observed after adaptation in **study I** may therefore indicate that temporal recalibration manifests in the implementation of new

internal models in the cerebellum about the temporal relationship between sensory stimuli, i.e., between the tactile sensation during the movement and the visual or auditory stimulus, respectively.

Importantly, **study I** also demonstrated activity modulations in a set of brain regions depending on the involvement of forward model predictions during temporal recalibration. Among them were frontal and sensory processing regions, which have already been associated with sensorimotor temporal recalibration in previous studies (Elijah et al., 2016; Stekelenburg et al., 2011; Stetson et al., 2006). Interestingly, these activity modulations also extended to lobules of the cerebellum that were more posteriorly located compared to the ones found to be associated with recalibration across both sensorimotor and inter-sensory contexts. This suggests functional differences in cerebellar subregions for temporal recalibration, depending on the presence of forward model predictions. It could also partially explain why, unlike **study II**, the faciliatory impact of anodal cerebellar tDCS was specific to the sensorimotor TRE in **study III**, across HC and SSD groups. This would point towards the specific amplification of recalibration mechanisms of the forward model in this region (Cao et al., 2017). Although the electrode montage for tDCS on the cerebellum was similar in both studies, due to the low spatial resolution of this technique, no definite conclusions about the subregions targeted by the stimulation can be made, particularly as this can also depend heavily on the subjects' individual anatomy (Tzvi et al., 2022). Fine-grained differences in the contribution of cerebellar subregions during temporal recalibration depending on the context could, therefore, partially explain differences in whether the stimulation predominantly facilitated inter-sensory or sensorimotor temporal recalibration mechanisms.

Overall, the results of the three studies contribute to a more advanced understanding of the role of the cerebellum in temporal recalibration. They highlight the importance of considering functional differences between cerebellar subregions for future investigations of temporal recalibration mechanisms in this brain region. Furthermore, these findings imply the need for future research to further examine the mechanism by which these functional differences arise in cerebellar, as well as in frontal and sensory regions, i.e., how forward model predictions influence temporal recalibration processes in these regions.

3.4. Implications for Schizophrenia Spectrum Disorders

In **study III**, patients with SSD exhibited similar temporal recalibration effects as HC, indicating that sensorimotor temporal recalibration mechanisms may be preserved in SSD. These findings suggest that the frequently observed aberrant processing of action-

outcomes in SSD (Ford et al., 2001; Shergill et al., 2014; Straube et al., 2020; Uhlmann et al., 2021) cannot be attributed to dysfunctions of the forward model in flexibly recalibrating action-outcome predictions to changing environmental conditions, such as varying action-outcome delays (**H5**). The results of this study, therefore, imply that the failure in the prediction generation process in SSD originates elsewhere. It could, for instance, be attributed to a more fundamental failure of computational processes of the forward model itself or to dysfunctions in the comparator mechanism for comparing predicted and re-afferent sensory input.

Importantly, although the sensorimotor TRE in patients was not reduced compared to HC, anodal tDCS applied to the cerebellum was able to enhance the TRE in both groups (**H6**). On the one hand, these results confirm the findings of **studies I and II** by contributing to the understanding of the involvement of this region in temporal recalibration. Moreover, the modifiability of this process by tDCS, even in patients, could potentially have further implications in the clinical context. Abnormalities in cerebellar functions have previously been associated with a variety of symptoms in SSD due to the universal role of this region in motor, perceptual, and cognitive functions and its extensive connectivity with various cortical areas (Andreasen & Pierson, 2008; Pinheiro et al., 2021). Therefore, the cerebellum has been considered a particularly promising stimulation target in the clinical context because, due to its widespread connectivity, cerebellar stimulation can indirectly modulate processes in a variety of different cortical regions (Grimaldi et al., 2016; Hua et al., 2022). In this context, it is particularly interesting that sensorimotor processes, which are potentially closely related to temporal recalibration due to their association with the cerebellum and predictive mechanisms of the forward model, have been repeatedly shown to be impaired in SSD. This includes sensorimotor adaptation, where patients showed deficits in the ability to adapt reaching (Bartolomeo et al., 2020; Bigelow et al., 2006; Cornelis et al., 2022) or eye movements (Coesmans et al., 2014; Picard et al., 2012) to shifted or rotated visual feedback. Thus, interesting directions for future research may be derived from the results of **study III**, which suggest that cerebellar tDCS can facilitate adaptive functions of the forward model in patients. For example, it could be conceivable to train sensorimotor adaptation abilities or the general ability of the forward model to generate appropriate action-outcome predictions. Concurrent stimulation of the cerebellum via tDCS could potentially enhance training outcomes, ultimately alleviating symptoms such as impairments in self-other distinction.

3.5. Limitations and Outlook

Some limitations of the studies in this dissertation must be acknowledged, which may constrain the interpretability of the obtained results.

Firstly, it should be noted that the tDCS technique, which was used in two studies of this dissertation, has some limitations. Most importantly, the spatial resolution of tDCS is rather low due to the large electrode size (Woods et al., 2016). Especially for tDCS on the cerebellum, due to the highly complex anatomy of this region, it remains somewhat unclear which parts of the cerebellum are being targeted by the stimulation. It is also conceivable that the stimulation extends to nearby areas depending on the individual anatomy of the subject (Manto et al., 2021). The application of the new and spatially more precise method of high-definition tDCS could, therefore, help in future studies to make more fine-grained statements about the anatomical basis of stimulation effects (Parlikar et al., 2021) and to further disentangle the contribution of different parts of the cerebellum to sensorimotor and inter-sensory temporal recalibration. Alternatively, the electrode montage could be adjusted based on the individual anatomy of a subject, for example, by obtaining an anatomical scan via MRI prior to the stimulation (Vaghefi et al., 2015). Despite these concerns, the converging findings from the tDCS and fMRI studies of this dissertation are promising since both methods identified an important role of the cerebellum in temporal recalibration, supporting the notion that relevant cerebellar regions were also targeted by the stimulation.

Additionally, considering potential applications of tDCS in patients to improve impairments in self-other distinction, it remains unclear how long the effects of the stimulation last. Long-term modulatory effects have been achieved with cerebellar tDCS in the past through the enhancement of cerebellar plasticity (van Dun et al., 2016), and the combination of tDCS and task-specific training procedures has been shown to lead to faster or more robust training outcomes (Bolognini et al., 2009). However, further research would be necessary to determine the factors of an optimal stimulation protocol to achieve maximal effectiveness, including stimulation intensity, duration, or the number of stimulation sessions.

Moreover, the interpretability of findings for temporal recalibration mechanisms in SSD may be limited by characteristics of the patient sample. Most patients were under antipsychotic medication at the time of their participation. This may have mitigated potential deficits because antipsychotics are often found to primarily address positive symptoms like hallucinations and delusions (Egerton et al., 2020), which are thought to be linked to the dysfunctions in predictive mechanisms of the forward model examined in this study (Ford et al., 2001; Frith et al., 2000; Lindner et al., 2005; Uhlmann et al., 2021). This may have partly contributed to the lack of differences in sensorimotor temporal recalibration between patients and HC in this study. For future research, it could thus be interesting to make use of larger samples to determine how current symptom severity may be related to sensorimotor temporal recalibration abilities in SSD.

Furthermore, it must be noted that based on the studies of this dissertation, it remains unclear to what extent the same or different mechanisms underly the adaptation to visual and auditory action-outcome delays. The partially different results on the behavioral level between the studies in this work, along with findings from previous studies (Arikan et al., 2021; Sugano et al., 2016), suggest that the adaptation modality may influence the manifestation of temporal recalibration effects, although the reasons for this remain largely unresolved. To investigate this further, an additional study closely related to this dissertation is currently examining data from an fMRI experiment where the adaptation modality was visual instead of auditory (as in **study I**; see Kufer et al., 2024). Similarly, a related ongoing study is currently investigating the neural correlates of temporal recalibration in SSD and HC using fMRI. This study also involves the adaptation to visual and auditory action-outcome delays. These data will provide additional insights into commonalities and differences in temporal recalibration depending on the adaptation modality. They will also help determine whether the similar behavioral effects in patients and HC are also accompanied by comparable neural processing during recalibration, or whether differences emerge at the neural level between the groups.

Finally, it is important to emphasize that the actual mechanism underlying sensorimotor temporal recalibration and the influence of tDCS on this process are not yet fully understood. The most widely accepted concept in this research field so far are the mentioned forward models, which generate and adapt predictions about the sensory outcomes of actions based on the movement's efference copies (Blakemore et al., 2000; Cao et al., 2017; Wolpert & Flanagan, 2001). However, a recently emerged and ongoing debate has challenged the view that this theoretical model can be applied to all types of action-outcomes. It has been suggested that especially non-body-related, external outcomes of an action, like the abstract visual and auditory stimuli used in the present studies, may be predicted by more general predictive mechanisms that operate across perceptual and motor domains, rather than by predictive mechanisms of forward models based on efference copy signals (Dogge et al., 2019; Jagini, 2021; Press et al., 2020). This reasoning aligns with predictive coding accounts, which assume that the brain holds internal models that generate predictions about all upcoming sensory signals. These internal models are constantly updated to minimize the error between the prediction and the actual sensory input, without the involvement of action-specific processes (Clark, 2013; Rao & Ballard, 1999). However, the difference in temporal recalibration effects between sensorimotor and inter-sensory contexts observed in the present studies, as well as the differences in the predictive processing of actively and passively generated sensory input found in previous studies (Arikan et al., 2019; Blakemore et al., 1998;

Horváth et al., 2012; Ody et al., 2023; Pazen et al., 2020; Schmitter et al., 2021; Straube et al., 2017; Uhlmann et al., 2020), may contradict this view. Since active (sensorimotor context) and passive conditions (inter-sensory context) are assumed to only differ in the presence of motor commands and thus the availability of efference copy signals, these findings collectively suggest that there are distinct features in predictive mechanisms depending on the involvement of an active action, as proposed by the forward model framework. Nevertheless, this debate highlights the existing uncertainty about the exact mechanisms by which action-outcome predictions are generated and adapted and how these processes are represented at the neural level. Investigating this in more detail in the future would not only enhance our understanding of these mechanisms themselves, but also shed light on where dysfunction may occur in patients with SSD.

3.6. Conclusions

The studies of this dissertation examined for the first time the neural correlates of sensorimotor temporal recalibration, i.e., the recalibration of temporal action-outcome predictions generated by internal forward models, by systematically controlling for the influence of inter-sensory temporal recalibration mechanisms. Additionally, this mechanism was investigated for the first time in patients with SSD. Results indicated that the hippocampus contributes to temporal recalibration in both sensorimotor and inter-sensory contexts, possibly by encoding and retrieving the new inter-sensory temporal stimulus associations. Recalibration-related processing in the posterior cerebellum, as well as in frontal and sensory regions was found to depend on the context and thus on the availability of forward model predictions during recalibration. Hence, the studies of this dissertation extend previous research by pointing to context-dependent contributions of these regions to temporal recalibration. This paves the way for future research to further explore the mechanisms through which forward model predictions influence recalibration-related processes in these regions. Furthermore, the results indicated that there may be no fundamental impairment in sensorimotor temporal recalibration in SSD, and that tDCS applied to the cerebellum holds the potential to further enhance recalibration in both healthy subjects and patients. This opens intriguing perspectives on the potential usability of this technique to facilitate related sensorimotor predictive mechanisms in the cerebellum known to be impaired in patients, and, ultimately, to improve self-other distinction and related symptomatology.

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Appendix

I. Reprint of Original Manuscripts

Study I: Publication Schmitter et al., (2023)

Schmitter, C.V., Kufer, K., Steinsträter, O., Sommer, J., Kircher, T., & Straube, B. (2023). Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements. *Human Brain Mapping*, hbm.26508.
https://doi.org/10.1002/hbm.26508

Received: 4 May 2023 | Revised: 18 September 2023 | Accepted: 26 September 2023

DOI: 10.1002/hbm.26508

RESEARCH ARTICLE

WILEY

Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements

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Funding information
Deutsche Forschungsgemeinschaft (DFG, German Research Foundation), Grant/Award Numbers: 286893149, 429442932, 222641018; Cluster project "The Adaptive Mind" funded by the Excellence Program of the Hessian Ministry of Higher Education, Science, Research and Art

Abstract

When we perform an action, its sensory outcomes usually follow shortly after. This characteristic temporal relationship aids in distinguishing self- from externally generated sensory input. To preserve this ability under dynamically changing environmental conditions, our expectation of the timing between action and outcome must be able to recalibrate, for example, when the outcome is consistently delayed. Until now, it remains unclear whether this process, known as sensorimotor temporal recalibration, can be specifically attributed to recalibration of sensorimotor (action-outcome) predictions, or whether it may be partly due to the recalibration of expectations about the intersensory (e.g., audio-tactile) timing. Therefore, we investigated the behavioral and neural correlates of temporal recalibration and differences in sensorimotor and intersensory contexts. During fMRI, subjects were exposed to delayed or undelayed tones elicited by actively or passively generated button presses. While recalibration of the expected intersensory timing (i.e., between the tactile sensation during the button movement and the tones) can be expected to occur during both active and passive movements, recalibration of sensorimotor predictions should be limited to active movement conditions. Effects of this procedure on auditory temporal perception and the modality-transfer to visual perception were tested in a delay detection task. Across both contexts, we found recalibration to be associated with activations in hippocampus and cerebellum. Context-dependent differences emerged in terms of stronger behavioral recalibration effects in sensorimotor conditions and were captured by differential activation pattern in frontal cortices, cerebellum, and sensory processing regions. These findings highlight the role of the hippocampus in encoding and retrieving newly acquired temporal stimulus associations during temporal recalibration. Furthermore, recalibration-related activations in the cerebellum may reflect the retention of multiple representations of temporal stimulus associations across both contexts. Finally, we showed that sensorimotor predictions modulate

recalibration-related processes in frontal, cerebellar, and sensory regions, which potentially account for the perceptual advantage of sensorimotor versus intersensory temporal recalibration.

KEYWORDS
cross-modal temporal recalibration, forward model, functional magnetic resonance imaging, prediction, sensorimotor adaptation, sensorimotor temporal recalibration, temporal recalibration effect

1 | INTRODUCTION

Effective perception of and interaction with the environment greatly depend on the temporal structure of sensory and sensorimotor events. For instance, the characteristic and highly predictable temporal relationship between actions and their sensory outcomes facilitates the discrimination between self-generated sensory inputs and those originating from external sources (Haggard, 2005; Moore et al., 2009). Since the sensory environment is vastly complex and subject to constant change, an essential ability of the nervous system is to sustain this function even under flexibly changing environmental conditions, such as varying action-outcome delays (Haering & Kiesel, 2015). For instance, dimmed light conditions can delay signals from the retina (Matteson, 1971), motor or sensory systems can be delayed due to fatigue, or a mouse click may lead to delayed responses of a computer due to system overload (Cai et al., 2018).

The compensation for variations in action-outcome delays is thought to be achieved by a sensorimotor temporal recalibration mechanism, which updates the perceived relative timing between actions and their sensory outcomes. Experimentally, temporal recalibration can be induced by introducing a constant delay between a subject's action (e.g., a button press) and corresponding sensory outcomes (Arikan et al., 2021; Cai et al., 2018; Cao et al., 2017; Elijah et al., 2016; Heron et al., 2009; Rohde & Ernst, 2013; Stekelenburg et al., 2011; Stetson et al., 2006; Sugano et al., 2010, 2012, 2016, 2017; Tsujita & Ichikawa, 2012). Following repeated exposure to this manipulation, subjects tend to perceive the delayed action-outcome as synchronous with the action (Keetels & Vroomen, 2012; Sugano et al., 2010, 2012, 2016, 2017; Yamamoto & Kawabata, 2014) and shorter delays are detected less frequently (Arikan et al., 2021; Schmitter & Straube, 2022). Moreover, undelayed outcomes are illusory perceived as occurring before the action (Cai et al., 2018; Heron et al., 2009; Rohde & Ernst, 2013; Stekelenburg et al., 2011; Stetson et al., 2006; Sugano et al., 2010; Tsujita & Ichikawa, 2012). These perceptual changes are known as the "temporal recalibration effect" (TRE). They are interpreted in terms of recalibration of sensorimotor predictions about the action-outcome timing, which results in a perceptual shift toward the presented delay.

These sensorimotor predictions, that is, predictions about the sensory outcomes of actions, are traditionally believed to be produced by internal forward models by using copies of the actions´ motor commands (Backasch et al., 2014; Blakemore et al., 1998; Cao et al., 2017; Elijah et al., 2016; Knoblich & Kircher, 2004; Leube, Knoblich, Erb, Grodd, et al., 2003; Leube, Knoblich, Erb, & Kircher, 2003; Straube et al., 2017). When sensations align with the expected action-outcome timing, they are attributed as originating from the own action. A temporal discrepancy, however, like an unexpected long delay, results in a prediction error and the inference that the sensations were caused externally or by another agent (Haggard et al., 2002; Hughes et al., 2013; Imaizumi & Tanno, 2019; Zapparoli et al., 2020). Therefore, it has been proposed that sensorimotor temporal recalibration can be achieved by internal forward models through the updating of sensorimotor predictions (Cao et al., 2017) to maintain adequate agency attribution despite changes in environmental conditions (Cai et al., 2018; Parsons et al., 2013; Stetson et al., 2006). It has even been suggested that the recalibration of sensorimotor predictions occurs on a supra-modal level and thus affects the general predicted timing for sensory outcomes of an action instead of modality-specific processes. Evidence for this claim has been derived from findings that the TRE can transfer to another modality, that is, after recalibration to a sensorimotor delay in one modality, effects of this procedure on temporal perception were also evident in another modality (Arikan et al., 2021; Heron et al., 2009; Sugano et al., 2010, 2012).

Importantly though, in a purely perceptual context, that is, in the absence of actions and sensorimotor predictions, recalibration of the perceived intersensory timing is also known to occur. For example, repeatedly exposing subjects to delays between auditory and visual stimuli shifts their synchrony perception of these stimuli toward that delay (Fujisaki et al., 2004; Harrar & Harris, 2008; Van der Burg et al., 2013; Vroomen et al., 2004). These effects also appeared not to be modality-specific but to transfer to different modality pairs other than the one used during recalibration (Di Luca et al., 2009). Such a flexible intersensory temporal recalibration mechanism aids the attribution of signals from different sensory modalities to the same or different environmental source despite varying delays in signal transmission and sensory processing systems (Chen & Vroomen, 2013). Considering this, the TRE in a sensorimotor context as described above may at least in part be explained by temporal recalibration of these general intersensory matching mechanisms. For example, in terms of recalibration of the tactile sensation during the button press movement and the resulting visual or auditory outcome (Arikan et al., 2021; Stetson et al., 2006). Therefore, without controlling for the impact of intersensory recalibration, the sensorimotor TRE

alone does not provide conclusive evidence for temporal recalibration of sensorimotor predictions.

If the sensorimotor TRE relies on both the recalibration of sensorimotor predictions and intersensory matching mechanisms, it might be expected to be stronger compared to conditions in which only intersensory recalibration can occur. Indeed, the TRE has already been shown to be more pronounced when subjects actively performed the action themselves, as opposed to conditions in which the effector was externally touched (Stetson et al., 2006) or moved passively (Arikan et al., 2021). A TRE observed in passive conditions can be accounted for by intersensory temporal recalibration alone, since there is no motor command and therefore no involvement of sensorimotor predictions. Thus, the less pronounced effect in this condition implies a component in sensorimotor temporal recalibration that is specific to sensorimotor delays and may indeed be related to the recalibration of sensorimotor predictions (Arikan et al., 2021).

The question of the extent to which sensorimotor temporal recalibration can be attributed to intersensory recalibration as opposed to recalibration of sensorimotor predictions also arises with respect to the neural correlates of this process. To date, evidence suggests that neural correlates of sensorimotor temporal recalibration are distributed across a variety of networks, including sensory systems (Cai et al., 2018; Elijah et al., 2016; Stekelenburg et al., 2011), areas involved in sensorimotor processing and prediction generation (Cao et al., 2017; Schmitter & Straube, 2022), and even higher-order brain regions involved in general mismatch or error detection (Stekelenburg et al., 2011; Stetson et al., 2006). However, it remains unresolved whether the involvement of these regions and networks can be attributed specifically to the temporal recalibration of sensorimotor predictions, as opposed to more general mechanisms of intersensory temporal recalibration.

First, sensorimotor temporal recalibration has been associated with processing changes in sensory systems. For instance, after recalibration to audio-motor delays, the auditory N1 ERP component exhibited responses to delayed action-outcomes typically observed for undelayed ones (Elijah et al., 2016). In similar veins, after recalibration to visuo-motor delays, undelayed outcomes led to responses of the visual P1 component typically expected for stimuli deviating from the expected timing (Stekelenburg et al., 2011). These results demonstrate that sensorimotor temporal recalibration affects early sensory processing systems, although their precise role in recalibration remains to be clarified. It also remains unclear if processing changes in these regions reflect recalibration mechanisms specifically related to sensorimotor contexts or whether they may be partly related to the recalibration of more general intersensory matching mechanisms.

Second, another category of brain regions that have been linked to temporal recalibration are those believed to be involved in recalibration by building and updating internal forward models. Most prominent among these is the cerebellum (Arikan et al., 2019; Blakemore et al., 2001; Leube, Knoblich, Erb, Grodd, et al., 2003; Straube et al., 2017; Tanaka et al., 2020; van Kemenade et al., 2018; Welniarz et al., 2021). Critical dependence of recalibration on cerebellar processes could, for instance, be shown by a transcranial magnetic stimulation study. In this study, recalibration-related activity in auditory processing systems was eliminated after inhibition of the right cerebellum (Cao et al., 2017). A recent tDCS study further showed that anodal stimulation of the bilateral cerebellum influenced temporal recalibration. By comparing the TRE resulting from the exposure to delayed outcomes of actively performed versus passively elicited movements, it appeared that this effect was not exclusive to the sensorimotor context (active movements) but extended to the intersensory context (passive movements) where no action and thus no sensorimotor prediction was involved (Schmitter & Straube, 2022). Thus, further clarification is needed as to what extent recalibration-related processes in the cerebellum are truly specific to the sensorimotor context or whether it also serves comparable functions in the recalibration of intersensory timing.

Third, neural correlates of sensorimotor temporal recalibration have been identified in brain regions known for more general error-related processing. For instance, the processing of undelayed outcomes that were illusory perceived as occurring before the action after recalibration has been associated with activation increases in error processing regions, such as in anterior cingulate cortex and medial frontal cortex (Stetson et al., 2006). In the same line, modulations in the N450 component related to error processing in anterior cingulate cortex could be associated with temporal recalibration to visuo-motor delays (Stekelenburg et al., 2011). This indicates that recalibration elicits changes not only in lower-level sensory, but also in higher-level cognitive processing systems.

Finally, evidence for the neural correlates underlying sensorimotor temporal recalibration may also be derived from a wider range of studies investigating potentially related processes. These include, for example, sensorimotor adaptation, that is, the adaptation of movements to temporal (or spatial) action feedback perturbations. Sensorimotor adaptation is partly thought to rely on learning processes based on sensory prediction errors, that is, discrepancies between the predicted and the observed sensory consequence of the motor commands (Morehead et al., 2017; Standage et al., 2022). As described above, sensorimotor temporal recalibration is also assumed to arise due to the updating of predictions about the sensory outcomes of our actions after repeated exposure to sensory prediction errors. Hence, both processes may be associated with partially similar neural correlates. Indeed, it has consistently been reported that regions such as the cerebellum, medial and prefrontal regions, and anterior cingulate cortex are also involved during sensorimotor adaptation (Anguera et al., 2007; Ruitenberg et al., 2018; Standage et al., 2022; Tzvi et al., 2022). In addition, the hippocampus has been implicated in this process by forming and retrieving new sensorimotor mappings, suggesting that memory systems are involved in sensorimotor adaptation (Scheidt et al., 2011; Standage et al., 2022). Similar processes could be assumed to be involved in sensorimotor temporal recalibration, but so far evidence for this claim is missing.

To conclude, a range of different brain regions and networks can be associated with sensorimotor temporal recalibration. But, it remains unresolved whether their contribution can be specifically attributed to the recalibration of sensorimotor predictions or whether

it is partly the result of more general intersensory recalibration mechanisms. Therefore, for the first time, we investigated the neural correlates of temporal recalibration in both sensorimotor and intersensory contexts together, to disentangle common and distinct components underlying recalibration in both contexts. To this end, during fMRI data acquisition, subjects underwent adaptation phases during which they were repeatedly exposed to a fixed delay between actively performed versus passively generated button press actions and an auditory outcome. In a subsequent test phase, they were asked to detect varying delays between button press and outcome to assess to what extent the delay exposure led to temporal recalibration.

We expected the behavioral TRE to be stronger in active versus passive movement conditions due to the hypothesized recalibration of sensorimotor predictions in addition to the expected timing between the senses. Neural correlates for temporal recalibration across both movement types were expected in regions for general error and mismatch detection, such as frontal and anterior cingulate regions, and in regions for early sensory processing. Differences between the neural correlates of temporal recalibration in active and passive conditions were hypothesized to occur in regions known for motor and sensorimotor processes, such as the cerebellum. Finally, we expected that exposure to the delayed auditory stimuli during adaptation would induce a behavioral TRE and recalibration-related brain activation also for visual stimuli during test. We expected this to occur particularly in active conditions, due to the recalibration of sensorimotor predictions on a supra-modal level.

2 | MATERIALS AND METHODS

2.1 | Participants

Twenty-five healthy volunteers participated in the study (10 female; mean age: 24.76 years, SD = 5.13). All reported being right-handed (Edinburgh Handedness Inventory; Oldfield, 1971: mean laterality quotient = 79.6%, SD = 22.888) and had normal or corrected-to-normal vision. No one reported any current or past psychiatric or neurological disorders. Subjects gave written informed consent and received financial reimbursement for their participation. The study was conducted according to the Declaration of Helsinki and was approved by the local ethics commission (Study 141/17) of the medical faculty of University of Marburg, Germany.

2.2 | Equipment and stimuli

Subjects performed button presses with their right index finger using a custom-made MR-compatible pneumatic passive button device (see Figure 1). During the fMRI experiment, the device was placed next to subjects' right leg. In active conditions, they pressed the button actively by themselves, while in passive conditions it was pulled down by compressed air with a force of max. 20 N. As active (sensorimotor context) and passive (intersensory context) movements elicited similar tactile and proprioceptive sensations, this manipulation enabled us to

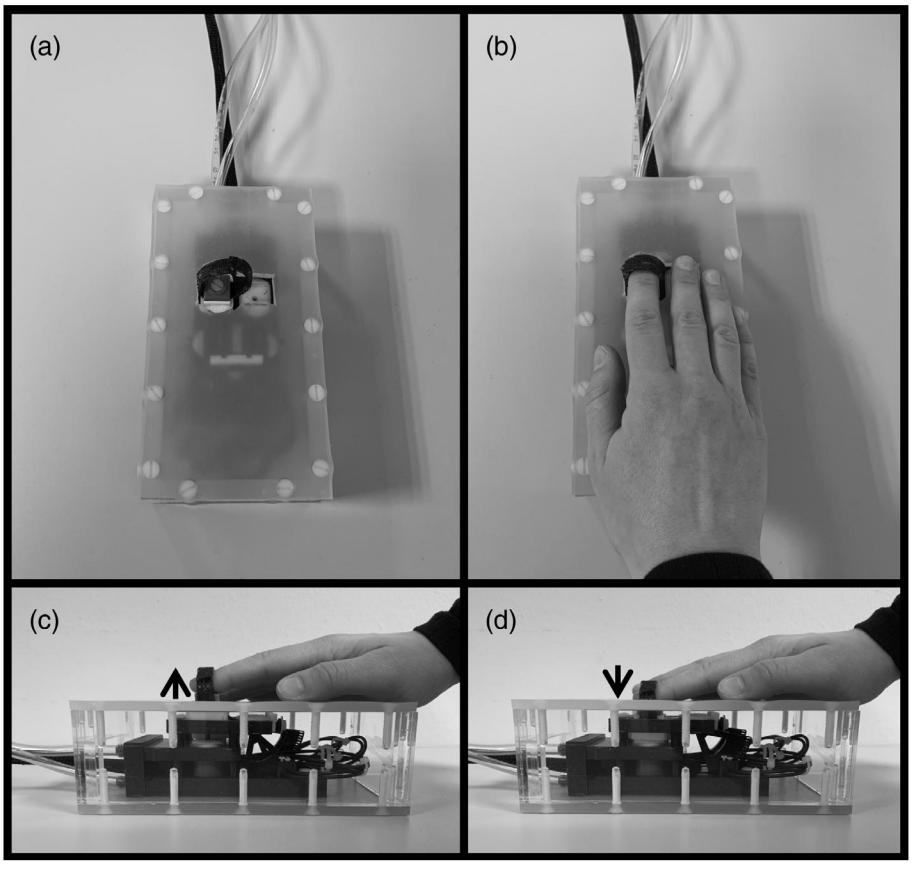

FIGURE 1 Custom-made MR-compatible pneumatic passive button device. (a,b) Subjects placed their right index finger on the button device. During the experiment, the button could be actively pressed by the subjects, or it was pulled down passively by compressed air. (c) A movement started with the button in the upper position. (d) When the button was moved to the lowest position, the stimulus presentation was triggered, either with or without a delay.

disentangle recalibration effects arising due to changes in sensorimotor predictions from those due to changes in intersensory timing. To ensure that subjects' fingers followed the button movement smoothly during passive conditions, they were tied to the button by using an elastic fabric band. During the movements, optic fibers allowed for the tracking of the button position by custom-written software. Thereby, visual or auditory stimuli could be displayed at the end of a button press movement (i.e., when the button reached the lowest position) with high temporal accuracy with or without an additional delay. The visual stimulus was a Gabor patch (1-degree visual angle, spatial frequency: 2 cycles/degree), which appeared at the center of a monitor (refresh rate: 60 Hz). The monitor was located behind the MRI scanner and subjects could see it through a mirror mounted on the head coil. The auditory stimulus was a sine-wave tone (2000 Hz with 2 ms rise and fall) and was presented through MR-compatible headphones (MR-Confon Optime1, Magdeburg, Germany). Visual and auditory stimuli were presented for a duration of 33.4 ms each.

2.3 | Experimental design and task description

Subjects underwent multiple pairs of adaptation and test phases. Adaptation phases consisted of two parts separated by the presentation of a fixation cross. During both parts, consecutive button presses had to be performed, either actively or they were elicited passively (factor "movement type"). Each button press was followed by the presentation of the auditory sensory outcome in form of the tone. Importantly, the tone occurred either immediately after the button press was registered (undelayed, 0 ms delay) or after a constant delay of 150 ms (factor "adaptation delay").

After each adaptation phase, a test phase assessed the impact of the previously presented adaptation delay on perception (the same experimental procedure has already been applied in previous studies, see Arikan et al., 2021 and Schmitter & Straube, 2022). Each test phase comprised six test trials during which the button was pressed once, either actively or passively. The movement type in each of the six test trials always corresponded to the one used in the preceding adaptation phase. In each test trial, the button press elicited the stimulus presentation (visual or auditory, factor "test modality") with one of six different temporal delays (0, 83, 167, 250, 333, and 417 ms). Each of the six delays was used once in each test phase in counterbalanced order. Subjects were instructed to report whether they detected any delay between the button press movement and the visual or auditory stimulus presentation. Responses were made by using one of two buttons on a button pad that was attached to subjects´ left leg. The assignment of the responses (delay, no delay) to the response buttons was counterbalanced across subjects.

The TRE was defined as difference in delay detection performances after an adaptation phase with delayed versus undelayed tones. The undelayed tone was expected to be in line with the natural prediction of undelayed sensory action-outcomes (active conditions), or with the expectation of temporal alignment between the tactile or proprioceptive and the auditory signals (passive conditions). The detection rates after exposure to the undelayed tones were thus expected to reflect baseline performance in the task without the influence of previous temporal recalibration. Conversely, the delayed tones were expected to induce the need for sensorimotor or intersensory temporal recalibration, respectively. Here, lower delay detection rates compared to baseline performance were expected to reflect a shift of the expected stimulus timing toward the adapted delay and thus temporal recalibration. In summary, the factors "adaptation delay" (0 vs. 150 ms), "movement type" (active vs. passive), and "test modality" (visual vs. auditory) were combined to eight different experimental conditions.

2.4 | Procedure

The fMRI experiment was divided into four scanning runs, composed of 16 adaptation-test pairs each. In each run, conditions with the same adaptation delay were blocked. This was done to prevent rapid switches of adaptation delays and thus potential spill-over effects between delayed and undelayed conditions. Whether a run started with the conditions of the 0 or 150 ms adaptation delay was counterbalanced across subjects. Within the block of each adaptation delay, conditions with active and passive movements were also blocked. Which of the movement type was presented first was counterbalanced across runs. In each run, each condition was presented with two consecutive adaptation-test pairs resulting in a total number of eight adaptation-test pairs per condition (see Figure S1 in the supplementary material for an overview of an exemplary experimental run).

An adaptation phase started with an instruction text displayed for 2000 ms on the screen indicating the movement type of the following button presses (see Figure 2). As soon as the instructions disappeared, subjects could start pressing the button or the button started to move passively. Each button press elicited the presentation of the tone, either undelayed or delayed by 150 ms. In passive conditions, nine button presses with a duration of 500 ms and in an interval of 800 ms were performed during the first part of the adaptation phase, followed by the presentation of a fixation cross of jittered length (1000, 1500, 2000, or 2500 ms). After the fixation cross disappeared, a second part of the adaptation phase was executed comprising another nine button presses. In active conditions, subjects had 8000 ms during each of the two parts of the adaptation phase to execute the button presses.

A test phase also started with an instruction text displayed for 2000 ms indicating the movement type and sensory stimulus modality of the following test trials. Before each test trial, the cue "Ready" was presented for 1000 ms. The disappearance of this cue initiated the test trials. In active conditions, subjects had 2000 ms to perform one button press. However, they were instructed to delay their button press by ~700 ms after the cue had disappeared. This was done to ensure that the button press was not reflexive, but a truly self-initiated action (Rohde & Ernst, 2013; Straube et al., 2020; van Kemenade et al., 2016). The onset for the passive button movement was jittered (0, 500, and 1000 ms). Each button press triggered the presentation of the visual or auditory outcome with one of the six test delay levels. Afterwards, the question "Delay?" was presented for a duration of 2000 ms and subjects had to respond via the button pad whether they detected a delay between the button movement and

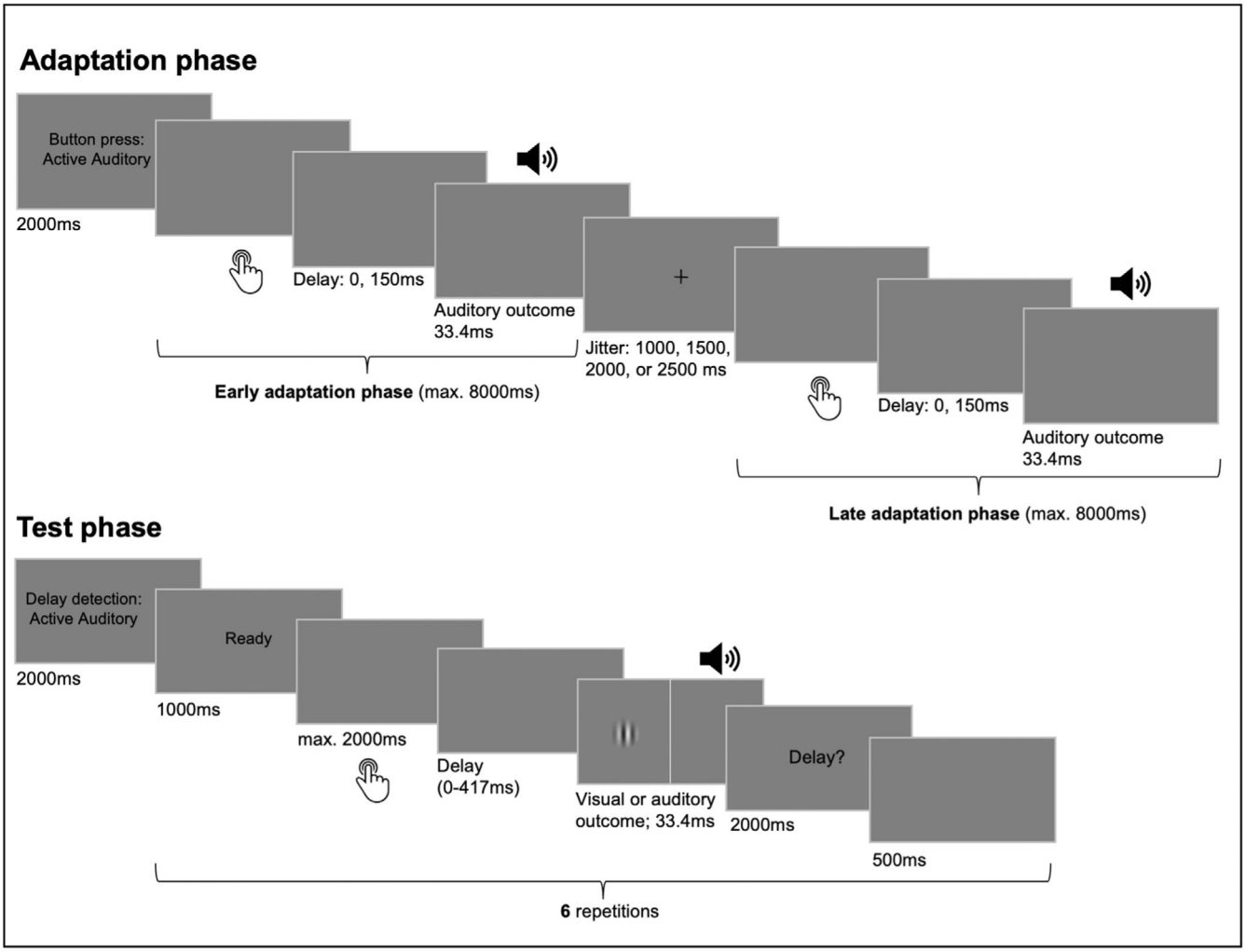

FIGURE 2 Trial structure and timing of events. Subjects went through multiple pairs of adaptation and test phases. During adaptation phases, the button had to be moved actively by the subjects or it was moved passively. After each button press, a tone appeared, either undelayed with respect to the button press or delayed by 150 ms. Adaptation phases were separated into an early and a late part divided by the presentation of a fixation cross of jittered length. In active conditions subjects had 8000 ms to perform the button presses in each part of the adaptation phase. In passive conditions, nine button presses were automatically triggered in each part. In the subsequent test phases, subjects pressed the button once in each test trial, either actively, or the button was moved passively. Here, the outcome was presented after the button press with one of six delay levels (0–417 ms) and subjects had to report whether they detected a delay in each trial. While the outcome modality was auditory during adaptation it could be visual or auditory during test.

the outcome. After a pause of 500 ms, the cue was presented again to initiate the next test trial. The last trial of each test phase was followed by a jittered intertrial interval before the beginning of the next adaptation-test pair (1000, 1500, 2000, and 2500 ms). To ensure that subjects were familiar with the task and performed the button presses correctly, they additionally participated in a training session outside the MRI scanner on a separate day before the fMRI experiment (for details see section 2 in the Supporting Information).

2.5 | MRI data acquisition

MRI data were collected with a 3 Tesla MR Magnetom TIM Trio scanner (Siemens, Erlangen, Germany) with a 12-channel head-coil at the Department of Psychiatry and Psychotherapy in Marburg. Functional images were obtained parallel to the intercommissural line (anterior commissure–posterior commissure) using a T2*-weighted gradient echo-planar imaging sequence (64×64 matrix; repetition time [TR] = 1650 ms; echo time [TE] = 25 ms; flip angle = 70°; slice thickness = 4.0 mm; gap size = 15%; voxel size = $3 \times 3 \times 4.6$ mm; field of view [FoV] = 192 mm). In each run, 560 volumes of 34 slices each were acquired in descending order covering the whole brain. Anatomical images were obtained using a T1-weighted MPRAGE sequence (256×256 matrix; TR = 1900 ms; TE = 2.26 ms; flip angle = 9°; slice thickness = 1.0 mm; gap size = 50%; voxel size = $1 \times 1 \times 1.5$ mm; FoV = 256 mm). To prevent motion artefacts, subjects´ heads were surrounded by foam pads during data acquisition.

2.6 | Data analyses

Test trials for which the movement was not or incorrectly executed (i.e., the button did not reach the lowest position at which the stimulus presentation was triggered; 2.1% of all trials) were excluded from the analyses of behavioral and fMRI data. Additionally, trials for which a subject's response was missing (6.4% of all trials) were excluded from the analysis of behavioral data.

2.6.1 | Analysis of behavioral data

The proportion of detected delays during test phases served as a measure for the subjects' delay detection performance and was calculated separately for each subject and experimental condition. Subsequently, psychometric functions in form of cumulative Gaussian distribution functions were fitted to these data using the Psignifit toolbox version 4 (Schütt et al., 2016) for Python version 3.8.5 (Python Software Foundation, https://www.python.org/). Delay detection thresholds (i.e., the delay that could be detected in 50% of all trials) and slopes (evaluated at the detection thresholds) were derived from the psychometric functions. The detection thresholds were used as measure for the overall delay detection performance (lower values indicate better performance). The slopes represented the increment in detected delays with increasing delay levels, indicating the ability to discriminate between delays.

The detection thresholds and slopes were then forwarded to repeated-measures ANOVAs including the factors "adaptation delay," "movement type," and "test modality." For significant interaction effects including the factor "adaptation delay," Bonferroni-corrected post-hoc one-tailed *t*-tests were performed to test for significant TREs for the different movement types or test modalities. A TRE was defined as larger detection thresholds indicating a shift of psychometric functions to larger delays or flatter slopes indicating worse performance in discriminating between the delay levels after exposure to the delayed versus undelayed tones. Furthermore, post-hoc two-tailed paired-samples *t*-tests were used to test whether the TRE differed significantly between the active and passive movements or between the auditory and visual test modality. All tests were conducted with JASP (Version 0.14.1; JASP Team, 2020).

2.6.2 | Analysis of fMRI data

MRI data were preprocessed and analyzed with the Statistical Parametric Mapping toolbox (SPM12; www.fil.ion.ucl.ac.uk) for MATLAB (Version 2020b, Mathworks, Sherborn, Massachusetts). To correct for head motion, functional images were realigned to the mean image of each run. Anatomical images were co-registered to the functional images, segmented and normalized to the standard Montreal Neurological Institute (MNI) template. Functional images were normalized to the MNI template as well and voxel sizes were resampled to a size of $2 \times 2 \times 2$ mm. Finally, functional images were smoothed with an 8 mm full-width at half maximum kernel.

For the analysis of activity modulations during adaptation and test phases, a General Linear model (GLM) was designed for each subject including the data from both phases. For the adaptation phases, the four experimental conditions composed of the factors "movement type" and "adaptation delay" were each modeled separately for both parts of the adaptation phase (early and late), resulting in eight regressors of interest. Since the focus of our study lies on the fMRI activations related to the stimulus perception and not on activations related to the movement execution per se, for each regressor the button press events during adaptation were included from stimulus onset until stimulus offset. Adaptation phases for which less than three valid button presses were registered in the first (early) or second (late) part were excluded from the analysis as presumably not enough stimulus presentations occurred to allow for recalibration. For the test phases, the eight experimental conditions composed of the factors "movement type," "test modality," and "adaptation delay" were modeled as separate regressors of interest. Test trials were included as the entire 2 s during which the button presses could be performed, and stimuli were presented. If a subject's response to the delay fell already into the period of the test trial (i.e., it was not given while the question was presented, but it was given too early), data from the respective test trial were included from trial onset until response onset. Test trials for which no valid button press was registered were excluded from the analysis. The time during the presentation of the instruction texts, the cue "ready," the jitter (fixation cross) in the middle of the adaptation phase, and the question "delay" were included as separate regressors of no interest, as were the six realignment parameters to account for variance due to head motion. Low frequencies (<0.0078 Hz) were filtered out with a high-pass filter with a cut-off period of 128 s to correct for baseline drifts in the BOLD signal. BOLD responses for all events were modeled with the canonical hemodynamic response function with the onset corresponding to the onset of the respective event. For GLMs at single-subject level, T-maps were obtained by contrasting each of the eight experimental conditions against implicit baseline. This baseline corresponded to the mean activation of all events that were not captured by the regressors in the GLM. For group-level analyses, the resulting contrast estimates for each subject were used in a flexible factorial design.

To correct for multiple comparisons at cluster level, Monte Carlo simulations (Slotnick, 2017; Slotnick et al., 2003) were used to determine the cluster extent beyond which the probability for false-positives does not surpass a threshold of alpha = .05 (considering the estimated smoothness of the data: 7 mm). According to the results after 10.000 simulations, a cluster had to exceed the minimum of 42 activated continuous voxels at $p < .001$ uncorrected to achieve correction for multiple comparisons at $p < .05$ for the data of this study. Activations of the group-level contrasts were anatomically labeled using the Automated Anatomical Labeling toolbox (AAL; Tzourio-Mazoyer et al., 2002) for SPM.

On group level, hypotheses regarding recalibration-related activations in adaptation and test phases were tested by means of

T-contrasts. First, we computed the main effect of the "adaptation delay" separately for adaptation and test phases to assess effects of the exposure to the delayed versus undelayed tones on neural activations. Furthermore, to test for delay-dependent activation differences between movement type (active vs. passive), we assessed the two-way interaction of "adaptation delay" and "movement type" for both phases. Since the impact of the adaptation delay may differ between early and late phases of adaptation, for the investigation of neural activations during adaptation, we further computed the three-way interaction composed of the factors "movement type," "adaptation delay," and "adaptation phase." Finally, to investigate whether delay-dependent activations differed in test phases with the same (auditory) or a different modality (visual) than during previous adaptation, we calculated the interaction of "adaptation delay" and "test modality" as well as the three-way interaction of "adaptation delay," "movement type," and "test modality." Additionally, we used conjunction analyses to test for potential overlapping delay-dependent activations for both sensory modalities. For a sanity check, we further computed the main effect of "movement type" to assess whether stronger motor-related activation was associated with active compared to passive movement conditions.

3 | RESULTS

3.1 | Behavioral results

Behavioral results are displayed in Figure 3. The repeated-measures ANOVA on the delay detection thresholds revealed a significant main effect for the factor "adaptation delay" [$F(1,24) = 13.691$, $p = .001$, $\eta_p^2 = .353$]. Detection thresholds were larger and detection performance thus decreased after exposure to the delayed [$M = 242.528$, $SD = 77.192$] than to undelayed tones [$M = 222.858$, $SD = 88.307$]. This indicates temporal recalibration to the delay and thus a significant TRE. Moreover, the ANOVA revealed significant two-way interactions of the "adaptation delay" with the factors "movement type" [$F(1,24) = 5.596$, $p = .026$, $\eta_p^2 = .189$] and "test modality" [$F(1,24) = 13.213$, $p = .001$, $\eta_p^2 = .355$]. According to post-hoc paired-

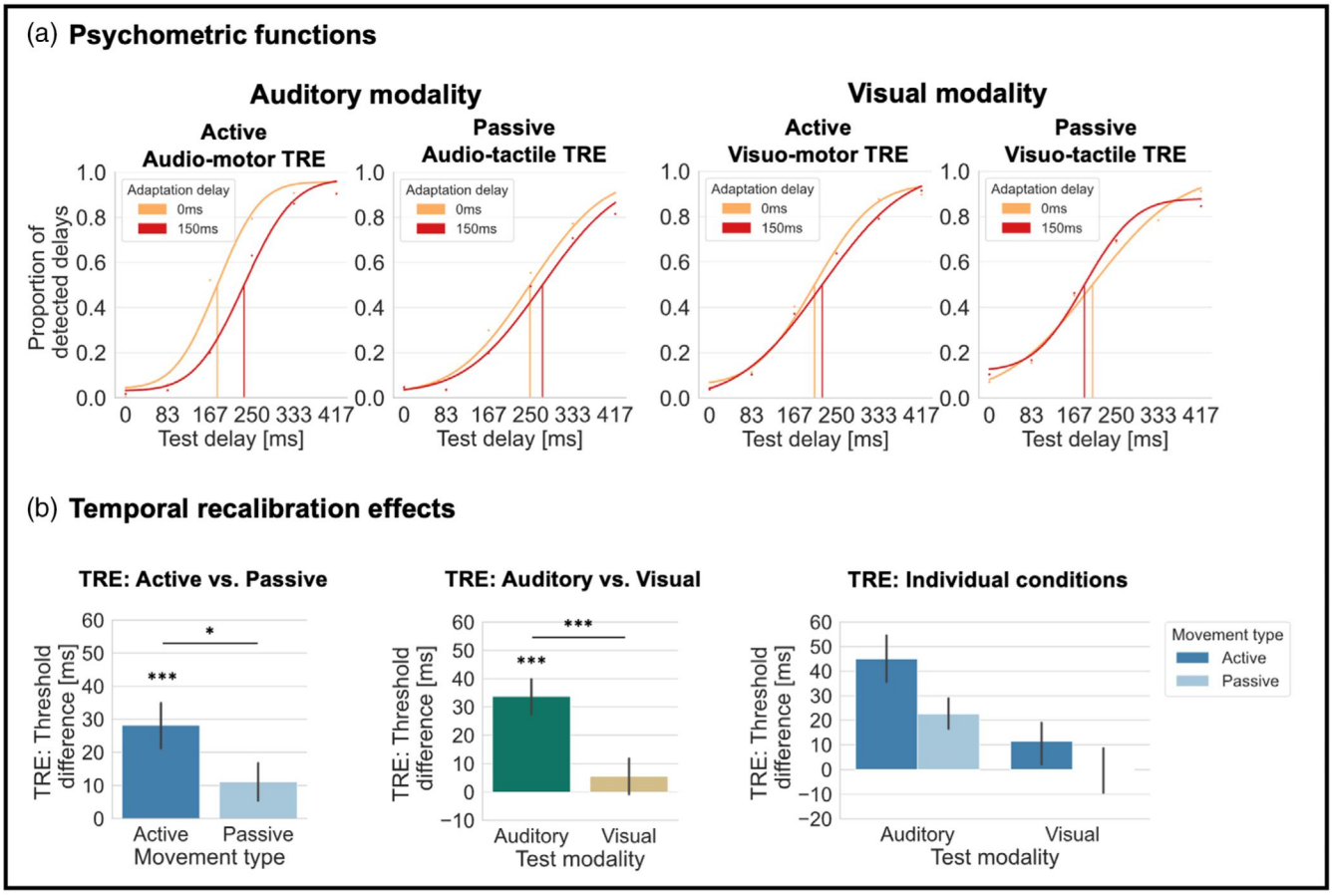

FIGURE 3 Behavioral results. (a) Psychometric functions were fitted to the delay detection data for each experimental condition. The TRE corresponded to a rightward shift of the psychometric functions after exposure to tones delayed by 150 ms (red) compared to undelayed tones (orange) indicating decreased delay detection thresholds and thus temporal recalibration. Psychometric functions are displayed on group level for illustration purposes. For the statistical analyses, the functions were fitted to the subjects´ individual detection rates. (b) The TRE was significant for active and auditory conditions. Furthermore, the TRE was significantly larger in active than in passive and in auditory than in visual conditions. Error bars indicate standard errors of the means. * $p < .05$, *** $p < .001$.

samples tests, the TRE was significant in active [mean sensorimotor TRE = 28.205, SD = 38.839; $t(24) = 3.631$, $p < .001$, $d = .726$] as well as in passive conditions [mean intersensory TRE = 11.135, SD = 23.565; $t(24) = 2.363$, $p = .013$, $d = .473$]. Comparing the TRE in active and passive conditions further revealed that the sensorimotor TRE (active) was significantly larger than the intersensory TRE [passive; $t(24) = 2.366$, $p = .026$, $d = .473$, two-tailed] indicating an advantage of temporal recalibration due to the presence of sensorimotor predictions. Another pair of post-hoc paired-samples tests demonstrated that the TRE was significant for auditory sensory outcomes [mean auditory TRE = 33.764, SD = 29.939; $t(24) = 5.639$, $p < .001$, $d = 1.128$] while the TRE for visual outcomes failed to reach significance [mean visual TRE = 5.576, SD = 35.613; $t(24) = .783$, $p = .221$, $d = .157$]. This suggests that the TRE observed in the auditory modality did not transfer to vision. Additionally, directly comparing the auditory and visual TRE revealed a significantly stronger effect in auditory than in visual conditions [$t(24) = 3.635$, $p = .001$, $d = .727$, two-tailed]. The three-way interaction of all factors did not reach significance [$F(1,24) = .336$, $p = .568$, $\eta_p^2 = .014$].

The repeated-measures ANOVA on the slopes of the psychometric functions did not reveal a significant main effect of the "adaptation delay" [$F(1,24) = 4.082$, $p = .055$, $\eta_p^2 = .145$], indicating that exposure to the delayed versus undelayed tones did not impact the ability to discriminate between the delay levels in the delay detection task. None of the interactions with the factors "movement type" and "test modality" became significant (all $p > .197$).

3.2 | fMRI results

For a sanity check, we tested whether activations in active and passive movement conditions differed in regions for motor-related processes. Active conditions were associated with stronger activation in large clusters, primarily in left precentral gyrus and in the cerebellum (for details see section 5 in the Supporting Information). This supports the argument that sensorimotor predictions based on motor commands of actions should be specific to the active conditions in our study.

3.2.1 | Neural correlates of temporal recalibration during adaptation phases

We tested for differences in brain activation during adaptation phases due to exposure to the delayed versus undelayed tones across movement types. The 150 > 0 ms contrast revealed a cluster in left hippocampus, which showed stronger activations during exposure to the tones that were delayed by 150 ms compared to undelayed tones (see Figure 4a). According a more fine-grained anatomical labeling using the Anatomy Toolbox for SPM (Eickhoff et al., 2005, 2006, 2007), this cluster could be assigned with highest probability to the hippocampal subregion CA1 (35.3.0%) and dentate gyrus (5.9%; Amunts et al., 2005). The reversed contrast (0 > 150 ms) did not reveal significant clusters of activation.

To test whether delay-dependent modulations of neural activations differed between sensorimotor (active) and intersensory contexts (passive), we assessed interaction effects of the factors "adaptation delay" and "movement type." We found no significant activations for the interaction contrast assuming stronger activations during exposure to the delayed versus undelayed tones in active compared to passive movement conditions [(Act150 > Act0) > (Pas150 > Pas0)]. However, the reversed interaction contrast [(Act0 > Act150) > (Pas0 > Pas150)] revealed activations in frontal regions including a cluster in left middle frontal gyrus (MFG) extending

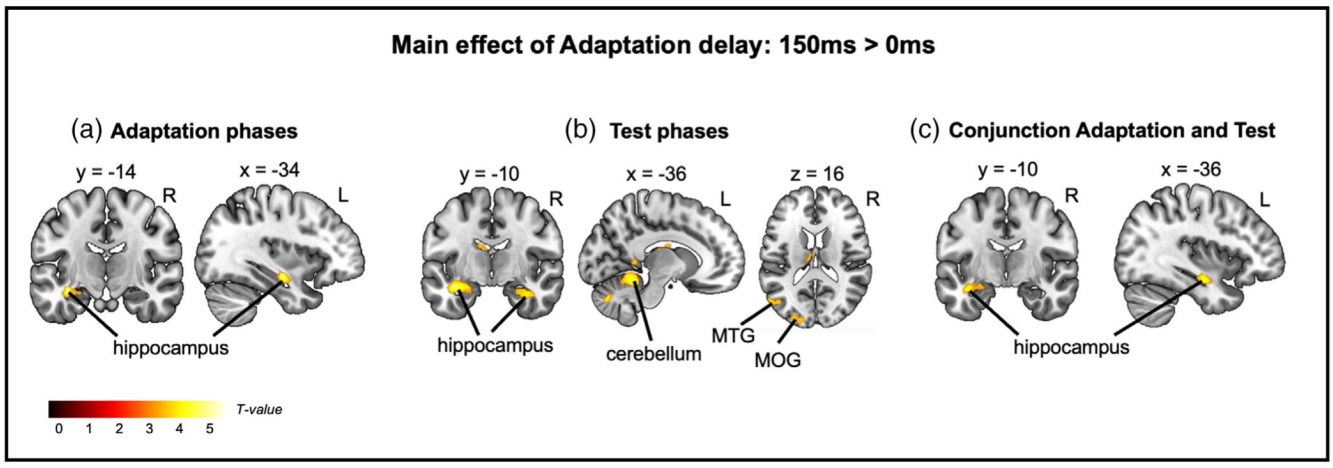

FIGURE 4 fMRI results: Main effect of Adaptation delay in adaptation and test phases. (a) Stronger activations were found in adaptation phases in hippocampus during exposure to the delayed versus undelayed tones. (b) During test phases, previous exposure to delayed versus undelayed tones was associated with increased activations in multiple regions, including hippocampus and cerebellum, as well as occipital and temporal regions. (c) A conjunction of the main effect of the adaptation delay during adaptation and test phases revealed that a cluster in left hippocampus was similarly modulated by the delay in both phases.

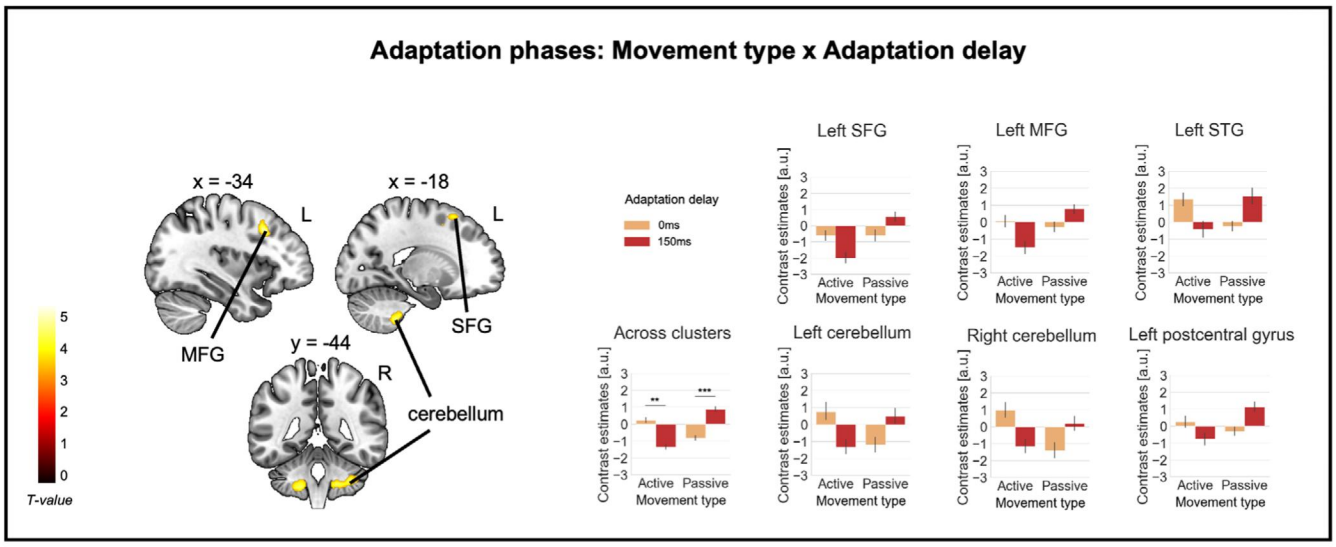

FIGURE 5 fMRI results: Interaction of Movement type and Adaptation delay during adaptation phases. During adaptation phases, clusters including frontal regions, cerebellum, postcentral gyrus, and STG showed significant activations for the "adaptation delay" × "movement type" interaction with a relative activation decrease in active conditions during delay exposure compared to exposure to undelayed tones, while the opposite pattern appeared in passive conditions. Error bars indicate standard errors of the means. ** $p < .01$, *** $p < .001$.

to inferior frontal gyrus, and a cluster in left superior frontal gyrus (SFG) extending to MFG. Further activations emerged in the left posterior cerebellum, spanning lobules VIII, IX, and X, and in the right posterior cerebellum, involving lobules VI, VIII, IX, and X, as well as crus I and II. Finally, significant clusters were found with peaks in left superior temporal gyrus (STG), left postcentral gyrus, and left middle occipital gyrus (MOG; see Figure 5). According to post-hoc paired-samples *t*-tests performed on activations across all clusters identified by this contrast (i.e., eigenvariates extracted with the VOI function of SPM12), in active conditions, activations in these regions were significantly reduced during exposure to the delayed ($M = -1.343$, $SD = 1.165$) versus undelayed tones ($M = .219$, $SD = 1.514$; $t(24) = 3.682$, $p = .001$, $d = .736$, corrected alpha = .025, two-tailed). In passive conditions, the reversed pattern emerged with significantly stronger activations during exposure to the delayed ($M = .884$, $SD = 1.148$) versus undelayed tones ($M = -.822$, $SD = 1.071$; $t(24) = -5.325$, $p < .001$, $d = -1.065$, corrected alpha = .025, two-tailed). The three-way interaction contrast including the factor "adaptation phase" did not reveal significant clusters of activation.

While we expected the delayed tones to be associated with increased error-related activations, the relative activation decrease during delay exposure in active conditions was surprising. To further explore potential reasons for this pattern, we assessed whether the decrease in activations observed in this condition was specific to early phases of adaptation but leveled off in late phases after an extended period of adaptation, or whether this pattern persisted consistently throughout delay exposure in active conditions. This exploratory analysis revealed that the significant difference between adaptation delays in terms of reduced activation during exposure to delayed tones was indeed mainly driven by early phases. The activation difference between the delays vanished during late phases of adaptation due to an activation increase for the delayed tones (for details see section 4 in the Supporting Information).

3.2.2 | Neural correlates of temporal recalibration during test phases

We tested whether exposure to the delayed versus undelayed tones during adaptation had a differential impact on activations during the delay detection task at test. The 150 > 0 ms contrast revealed stronger activations after previous exposure to the delayed tones in a cluster in left hippocampus and a cluster comprising right hippocampus and right parahippocampal gyrus. As during the adaptation phases, according to the anatomy toolbox, the hippocampal clusters were mainly assigned to the subarea CA1 (left: 36.0%, right: 29.4%) and to the dentate gyrus (left: 17.5%, right: 6.0%). Moreover, a cluster in left anterior cerebellum was found, including lobules IV/V, and crus II, which extended to anterior and posterior parts of the right cerebellum, including lobules IV, V, VI, VII, VIII, and crus I and II. This suggests an impact of temporal recalibration to delayed tones on the recruitment of these areas during delay detection (see Figure 4b). Furthermore, the contrast revealed significant activations with peaks in left posterior orbitofrontal cortex, right putamen, left middle temporal gyrus, left thalamus, and left MOG. The reversed contrast (0 > 150 ms) did not reveal significant clusters of activation.

Since partly overlapping regions showed activations for the main effect of the adaptation delay during adaptation and test phases, we further used a conjunction of this contrast for both phases (Adaptation 150 >0 ms ∩ Test 150 >0 ms) to assess whether clusters of the same areas that were modulated by the delay during adaptation were also differentially recruited during test. This analysis revealed

that a cluster in left hippocampus was involved more strongly during exposure to the delayed versus undelayed tones in adaptation phases and was also more strongly activated at test when the tones during previous adaptation had been delayed (see Figure 4c). As during adaptation and test phases separately, the hippocampal cluster of the conjunction was assigned with highest probability to the subregions CA1 (35.3%) and to the dentate gyrus (6.1%).

Exploratorily examining this conjunction analysis separately for both test modalities further revealed that these overlapping hippocampus activations for both phases were specific to the auditory test modality (x, y, $z = -36$, -10, -18, cluster size = 107 voxels, $t = 4.00$), but not present for the visual modality (for details see Supporting Information, section 6). For a detailed summary of all clusters involved in the reported contrasts, see Tables S1 and S2 in the Supporting Information. During test phases, the interaction of "adaptation delay" and "movement type" did not reach significance. Furthermore, the interaction contrasts of "adaptation delay" and "test modality" did not reveal meaningful clusters of activation (except for small clusters, which could not be assigned unambiguously to gray matter volume by the AAL toolbox) and the three-way interaction including all three factors was not significant either. Finally, the conjunction of the 150 > 0 ms contrast for the auditory and visual test modality testing for overlapping delay-dependent brain activations did not reveal any significant activations.

4 | DISCUSSION

We investigated the neural correlates of sensorimotor temporal recalibration that can be attributed to the recalibration of sensorimotor predictions as compared to the recalibration of intersensory matching mechanisms. Our findings imply important roles for the hippocampus and the cerebellum in recalibration across sensorimotor and intersensory contexts, suggesting processes that are more likely to be attributed to the recalibration of intersensory timing. Context-dependent differences emerged in terms of a stronger behavioral TRE in sensorimotor (active) conditions and differential neural activations in frontal cortices, cerebellum, and sensory processing regions. This suggests the influence of sensorimotor predictions in recalibration-related processes in these regions and potentially accounts for the perceptual advantage of sensorimotor compared to intersensory temporal recalibration.

4.1 | Behavioral TRE

At the behavioral level, we found a TRE in both active and passive movement conditions in form of increased delay detection thresholds after exposure to delayed versus undelayed tones. The passive TRE reflects intersensory temporal recalibration in terms of modulations of the perceived relative timing between signals from different sensory modalities (Fujisaki et al., 2004; Harrar & Harris, 2008; Van der Burg et al., 2013; Vroomen et al., 2004). The active TRE reflects sensorimotor temporal recalibration in terms of changes in the expected timing between actions and their sensory outcomes (Arikan et al., 2021; Cai et al., 2018; Cao et al., 2017; Elijah et al., 2016; Heron et al., 2009; Rohde & Ernst, 2013; Stekelenburg et al., 2011; Stetson et al., 2006; Sugano et al., 2010). Importantly, the TRE in active conditions was stronger than the one in passive conditions. Thus, the shift in temporal perception was stronger after recalibration due to sensorimotor delays compared to intersensory delays. These findings are in line with the assumption that recalibration in sensorimotor contexts involves a component beyond the recalibration of the perceived intersensory timing, such as the recalibration of sensorimotor predictions about the timing of a self-generated action-outcome (Arikan et al., 2021).

The comparison between auditory and visual conditions revealed that a TRE manifested only in auditory conditions and did not transfer to the visual modality. Previous studies investigating the modality-transfer of temporal recalibration effects, especially in sensorimotor contexts, reported mixed results. While some found a transfer in both directions, that is, from audition to vision and vice versa (Heron et al., 2009; Sugano et al., 2010), other found this effect to be limited to a transfer from vision to audition (Arikan et al., 2021; Sugano et al., 2012). Generally, the auditory modality has been suggested be more susceptible to temporal recalibration than the visual modality due to a more precise temporal perception and discriminability of auditory stimuli (Grahn, 2012; Grondin, 2010). This also results in a better predictability for the timing of auditory events and predictability is assumed to be important for temporal recalibration effects to occur (Rohde et al., 2014). These inherent differences between the modalities may partly explain why the transfer of recalibration effects to the visual modality was absent in this study. Still, our results do therefore not provide evidence for supra-modal predictive mechanisms in temporal recalibration.

4.2 | The role of the hippocampus in temporal recalibration

At the neural level, comparing activations during exposure to delayed versus undelayed stimuli (adaptation phases), revealed increased activations in the left hippocampus. Similarly, during subsequent test phases, activations in bilateral hippocampus were stronger when the stimuli in the previous adaptation phase were delayed. Interestingly, a conjunction analysis revealed that there was an overlap of the clusters in left hippocampus, which responded more strongly to delayed stimuli during adaptation and was also more strongly recruited during subsequent test phases.

The hippocampus has previously been shown to be involved in the acquisition and retrieval of new sensorimotor mappings during sensorimotor adaptation. For instance, during the adaptation of reaching movements to a rotated visual feedback display, the updating of the expected relationship between the motor programs and the visual feedback has been associated with the hippocampus (Anguera et al., 2007; Scheidt et al., 2011; Standage et al., 2022). Also beyond

the sensorimotor domain, the hippocampus has been recognized as playing a crucial role in associative learning and the associative binding of events that are separated in space or time (Staresina & Davachi, 2009; Wallenstein et al., 1998). It is known to be involved in detecting mismatches that arise due to the comparison of expected and perceived stimulus associations (Chen et al., 2011; Duncan et al., 2009; Kumaran & Maguire, 2006, 2007; Long et al., 2016), and consequentially in updating the stored associations (Duncan et al., 2012). The detection of these mismatches has specifically been related to the hippocampal subarea CA1 (Chen et al., 2011; Duncan et al., 2012).

In our study, activations in hippocampus could also mainly be assigned to the CA1 area, both during adaptation and during test and across both active and passive conditions. During adaptation phases, the activation increases during exposure to the delayed tones may thus be explained by the detection of violations of the learned temporal stimulus associations. And consequently, by the encoding of the novel association between the auditory stimulus and tactile sensations during the button movement. This indicates the importance of the hippocampus in recalibrating the perceived timing between sensory stimuli with and without the involvement of an action. During test phases, a partly overlapping cluster in CA1 was also more strongly involved when subjects were previously exposed to the delayed tones. The detection of the varying delays during test presumably requires the comparison of the learned and therefore expected delay between the button movement and the tone with the actual delay in each trial. Thus, these results suggest that the encoded temporal association of the stimuli must be retrieved during that task, leading to increasing engagement of the hippocampus, especially when these associations have just been updated to account for the additional delay introduced during adaptation. In summary, our findings imply an important role for the hippocampus during temporal recalibration through the acquisition and recall of new temporal stimulus associations. The fact that it was involved during both active and passive conditions suggests a general role of this region in responding to violations of the expected stimulus timing (intersensory recalibration) beyond the sensorimotor domain.

4.3 | The role of the cerebellum in temporal recalibration

Next to the hippocampus, the cerebellum also exhibited stronger activations during the delay detection task after previous exposure to delayed compared to undelayed tones. The cerebellum has frequently been proposed as the location of internal forward models that generate predictions about the sensory outcomes of self-generated actions (Arikan et al., 2019; Blakemore et al., 2001; Leube, Knoblich, Erb, Grodd, et al., 2003; Straube et al., 2017; Tanaka et al., 2020; van Kemenade et al., 2018; Welniarz et al., 2021). In this line, it could also consistently be associated with processes requiring the adjustment of these internal model predictions to environmental changes such as in sensorimotor temporal recalibration (Cao et al., 2017) or sensorimotor adaptation due to action feedback perturbations (Block & Celnik, 2013; Cassady et al., 2017; Galea et al., 2011; Tzvi et al., 2022). However, the role of the cerebellum in implementing and updating internal models does not appear to be not unique to the sensorimotor domain. Similar mechanisms seem to be at play for purely perceptual processes (Kotz et al., 2014; O'Reilly et al., 2008; Schubotz, 2007). In that regard, the cerebellum has been shown to be involved in generating and recalibrating temporal predictions for sensory events also in the absence of actions, and in detecting incongruencies between the predicted and perceived intersensory stimulus timing (Beudel et al., 2009; Coull et al., 2013; Kotz et al., 2014; Moberget et al., 2008; O'Reilly et al., 2008; Roth et al., 2013).

In our study, performing the delay detection task requires the generation of internal model predictions about the expected delay between the stimuli or between action and outcome to judge about the presence of an additional delay in the trial. Considering the significance of the cerebellum in storing and updating these internal models across motor and perceptual domains, the increased engagement of the cerebellum during test phases may be attributed to the storage of multiple internal models or temporal stimulus associations after recalibration. A similar phenomenon has for example been reported for multiple visuo-motor mappings found to be stored in cerebellum after sensorimotor adaptation to different visuo-motor rotations (Kim et al., 2015). Thus, the presence of multiple representations for the temporal stimulus associations in the cerebellum could result in a conflict in the predicted stimulus timing or a broader time window for predictions. Consequently, higher uncertainty or higher processing demands in prediction generation could be associated with our task after exposure to the delayed tones and may account for the increasing engagement of the cerebellum after recalibration. To conclude, our findings suggest that activations in the cerebellum may be related to the retention of multiple internal predictive models during recalibration, which are not specific to sensorimotor predictions about action-outcome relationships. Instead, as the cerebellum contributed to active and passive conditions, our findings highlight the importance of recalibration-related processes in the cerebellum which may rather reflect components of intersensory temporal recalibration across domains of action and perception.

4.4 | Differential neural correlates of sensorimotor versus intersensory temporal recalibration

The recalibration-related activations in the hippocampus and the cerebellum discussed above could be observed across both active and passive conditions, suggesting contributions of these regions to more general intersensory temporal recalibration mechanisms. Opposed to that, differences between active and passive conditions emerged during adaptation phases as revealed by the interaction of "movement type" (active vs. passive) and "adaptation delay" (0 vs. 150 ms), including frontal regions (left SFG and MFG), regions for sensory processing (left STG and postcentral gyrus), and the bilateral cerebellum. In active conditions, this manifested in terms of a relative decrease in

activations during exposure to the delayed versus undelayed tones, while the opposite pattern emerged in passive conditions (i.e., increased activations during exposure to delayed tones).

The activation decreases during exposure to actively elicited delayed tones was surprising at first, since we expected that the delay would deviate from the natural expectation of undelayed action-outcomes, and therefore, would elicit a prediction error signal associated with increasing activations in this condition. Instead, it appeared that the regions involved in the interaction contrast exhibited stronger activation in response to stimuli that occurred in synchrony with the action, resulting in stronger overall activation for the undelayed tones. Consequently, the activation was at least initially suppressed for the delayed tones. A similar activation pattern has been observed in previous studies that aimed at identifying brain regions responding to the feeling of self-control over stimuli or the attribution of self-agency. Action-outcomes presented in synchrony with the action and judged as being self-generated were associated with increased activation in cerebellum, parietal areas (Matsuzawa et al., 2005), and in posterior midline areas, like the precuneus and posterior parietal cortex (Fukushima et al., 2013). In our task this effect appeared in posterior structures of the bilateral cerebellum, and additionally activated frontal regions and areas for somatosensory (postcentral gyrus) and auditory processing (STG). Interestingly though, when exploratorily examining the activation pattern separately for early and late adaptation phases, it appeared that the relative activation decrease during exposure to the actively elicited delayed tones was mainly driven by early phases (see section 4 in the Supporting Information). As the engagement of these regions increased from early to late phases, the difference in activation for delayed and undelayed tones disappeared. A similar phenomenon could be observed earlier, whereby the activation pattern elicited by the processing of delayed stimuli approached the typical pattern observed for the processing of undelayed stimuli after recalibration (Elijah et al., 2016). This may be explained by the delayed tones being perceived as occurring synchronously with the action after a longer period of exposure to the delays. It may even be speculated that initially, the delayed tones were not fully perceived as being generated or controlled by one's own action, but after some exposure time they were and signaled the need for recalibration. Regardless of what the exact explanation for this change is, it appears that after a longer time of exposure to the delay, the delayed tones were similarly processed as the undelayed ones in the regions involved in this contrast. Since the undelayed tones should be naturally in line with sensorimotor predictions, this suggests that after the recalibration of these predictions, the delayed tones were similarly perceived as being in line with them. This is consistent to behavioral findings, where after temporal recalibration, the delayed action-outcome is perceived as occurring in synchrony with the action (Heron et al., 2009; Parsons et al., 2013). However, it is important to note that the explanation of the activation pattern change across adaptation phases is only a post-hoc interpretation, as the three-way interaction of "movement type," "adaptation delay," and "adaptation phase" appeared to have lacked sufficient power to reach statistical significance in our study. Thus, the explanation for the exact reason of the activation pattern remains speculative and should be taken with caution.

A question that remains open is how to reconcile these results with a range of studies that reported the reversed activation pattern. Here, increased activations in response to temporal or spatial action-outcome deviations and violations of the sense of agency indicated prediction error processing (Haggard, 2017; Leube, Knoblich, Erb, & Kircher, 2003; Nahab et al., 2011; Zito et al., 2020). One difference between our study and these previous ones, which may be responsible for the difference in activation pattern, is the nature of the task. Unlike many studies investigating agency-related processing (Haggard, 2017; Moore, 2016), we did not ask subjects to rate their subjective feeling of agency over the action-outcome but asked them to just attentively listen to the tones during adaptation. This might have made the detection of regularities in the action-outcome relationship more important for the task than the explicit detection of prediction errors (Wen & Haggard, 2020). Thus, the increasing activations observed throughout adaptation may correspond to the detection of, or increased confidence in detecting, the novel temporal relationship between action and outcome. In line with this assumption, it may be assumed that recalibration in active conditions in our task was not mediated by prediction-error based learning, but rather by the detection of temporal regularities or the detection of synchrony between action and outcome. Notably though, while the expected pattern of increased activation for the processing the delayed versus undelayed tones did not appear in active conditions in our study, it was evident in passive conditions. Here, the delayed tones were associated with higher activations across all regions of the interaction contrast in both adaptation phases. This is consistent with the notion that temporal mismatches between the tactile sensation during the button movement and the tone were detected and resulted in an intersensory error signal (Bushara et al., 2001; Dhamala et al., 2007; Stevenson et al., 2010).

In conclusion, our findings coincide with previous studies in confirming the importance of regions in frontal cortices (Standage et al., 2022; Stetson et al., 2006) and the cerebellum (Cao et al., 2017; Schmitter & Straube, 2022) during temporal recalibration. Additionally, activations in STG for auditory processing and in postcentral gyrus for somatosensory processing are consistent with previous findings of processing changes due to recalibration in sensory regions associated with the modalities engaged in the task (Aytemür et al., 2017; Elijah et al., 2016; Stekelenburg et al., 2011). Importantly, we extend these findings by showing that the exact contribution of these regions to temporal recalibration may differ depending on whether it relies solely on changes in intersensory timing, or whether sensorimotor predictive mechanisms come into play due to the involvement of an action. The presence of sensorimotor predictions may influence the engagement of these regions during temporal recalibration, potentially facilitating the effects of this process on perception. Hence, they could be responsible for the greater behavioral recalibration effect observed in active compared to passive conditions.

4.5 | Modality-transfer of temporal recalibration effects

Although behavioral effects of temporal recalibration did not transfer from the auditory to the visual modality in our study, no differential brain activations were observed in test phases between the two test modalities. There were also no overlapping activations for the 150 > 0 ms contrast between auditory and visual conditions. Thus, we did not observe a clear signature for neural correlates for the transfer of recalibration effects to the visual modality. However, when exploring the impact of the adaptation delay on activations during visual and auditory test phases separately (see section 6 in the Supporting Information), it appeared that the hippocampal activations were predominantly driven by the auditory modality. Conversely, cerebellar activations were mainly driven by the visual modality. As described above, the cerebellum has been considered as important for hosting and recalibrating internal model predictions about the outcomes of one's own actions (Arikan et al., 2019; Blakemore et al., 2001; Leube, Knoblich, Erb, Grodd, et al., 2003; Straube et al., 2017; Tanaka et al., 2020; van Kemenade et al., 2018; Welniarz et al., 2021). This has even been suggested to occur on a supra-modal level, that is, for the general predicted timing for action-outcomes of different sensory modalities (Straube et al., 2017; van Kemenade et al., 2016, 2017). The fact that the delayed auditory outcome during adaptation led to increased activation of the cerebellum during the visual delay detection task, could thus imply certain cross-modal interactions in temporal recalibration. Nonetheless, due to the absence of behavioral recalibration effects in vision and of clearly common or distinct recalibration-dependent brain activations for both modalities, our findings do not provide direct evidence for modality-transfer in temporal recalibration and thus for the recalibration supra-modal predictive mechanisms.

4.6 | Limitations and directions for future research

Finally, some limitations of the present study and potential directions for future research will be discussed. First, active and passive movement conditions were designed to minimize differences between them, with the only difference being the availability of sensorimotor predictions during active movements. However, it could be argued that unintentional differences occurred, such as differences in the allocation of attentional resources, which have been demonstrated to modulate the magnitude of the sensorimotor TRE (Heron et al., 2010). We explicitly instructed subjects to carefully monitor the stimuli throughout the experiment and close attention to the stimuli during test phases was necessary in all conditions for detecting the delays. Thus, although we cannot rule out the possibility that differences in attention may have emerged, we think it is unlikely that this factor alone can account for the differences between active and passive movement conditions observed in our study.

Second, across the experimental runs, the adaptation delay switched multiple times from 0 to 150 ms and back. It may be argued that this rapid switching of temporal contingencies prevented recalibration effects to consistently manifest in all conditions. However, the occurrence of recalibration effects in both sensorimotor and intersensory contexts, despite these multiple switches, argues against that. It even highlights the flexibility of temporal recalibration mechanisms that can react rapidly to continuously changing environmental conditions. One may also consider that a certain amount of recalibration could have been necessary for the undelayed stimuli during adaptation. It is possible that they did not precisely match the natural expectation for the stimulus timing as we assumed, or that recalibration back to the natural expectation of undelayed stimuli was necessary after being previously recalibrated to the delay. Hence, it could be informative in the future to compare delay detection performance after delay adaptation with a baseline assessment of detection performances without any prior adaptation phases.

Third, the adaptation phases in our experiment were rather short (consisting of a max. of 18 button presses). It may be interesting for future research to study these recalibration mechanisms with a more extended period of adaptation. This may enable the investigation of how differences in neural activation between the contexts manifest when recalibration can be presumed to be well-advanced or even complete. It could also allow us to answer the question of whether context-dependent differences in neural processing can be attributed to differences in how recalibration-related activity dynamically changes over time. It may also be speculated that a longer adaptation period would be necessary for the manifestation of modality-transfer effects of recalibration, which were absent in our study.

Finally, it would be interesting to explore whether the neural correlates of temporal recalibration, and their modulation by sensorimotor predictions, converge across different adaptation modalities. For example, by comparing the correlates of recalibration to delayed auditory and visual stimuli. This could provide insights into whether they share common neural substrates of temporal recalibration or whether they depend on modality-specific circuits.

5 | CONCLUSIONS

The aim of the present study was to disentangle the behavioral and neural correlates of sensorimotor temporal recalibration that can be attributed to the recalibration of sensorimotor predictions from those that may be related to recalibration of intersensory timing. We found that recalibration across sensorimotor and intersensory contexts was associated with activation in hippocampus highlighting its role in encoding and retrieving the novel intersensory temporal associations. Additionally, our findings emphasize the role of the cerebellum in recalibration possibly related to the retention of multiple representations of the temporal stimulus associations. Context-dependent differences emerged in terms of a stronger behavioral recalibration effect in sensorimotor versus intersensory conditions and were at the neural level captured by differential activation pattern in frontal cortices, cerebellum, and sensory processing regions. These findings cannot be explained by intersensory recalibration alone but suggest the

influence of sensorimotor predictions, which modulate recalibration-related processes in these regions, and potentially account for the perceptual advantage of sensorimotor compared to purely intersensory temporal recalibration.

ACKNOWLEDGMENTS

We thank Michelle Achenbach, Trâm Đỗ, Mechthild Wallnig, and Rita Werner for assistance in data collection. Open Access funding enabled and organized by Projekt DEAL.

FUNDING INFORMATION

This research project was supported by the Deutsche Forschungsgemeinschaft (DFG), German Research Foundation: CRC/TRR135, A3 (project number: 222641018), STR1146/15-1 (project number: 429442932), STR1146/9-2 (project number: 286893149) and by "The Adaptive Mind," funded by the Excellence Program of the Hessian Ministry of Higher Education, Science, Research and Art.

CONFLICT OF INTEREST STATEMENT

The authors declare no competing financial interests.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in Zenodo at 10.5281/zenodo.7886438.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Schmitter, C. V., Kufer, K., Steinsträter, O., Sommer, J., Kircher, T., & Straube, B. (2023). Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements. *Human Brain Mapping*, 1–18. https://doi.org/10.1002/hbm.26508

Supplementary material for the research article “Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements”

1. Overview of an exemplary experimental run

The fMRI experiment was divided into four scanning runs, composed of 16 adaptation-test pairs each. See **Supplementary Fig. 1** for an overview of an exemplary order in which the individual experimental conditions were presented in a run.

		ADAPTATION PHASE			TEST PHASE	
		18 adaptation trials (button presses)			1 test trial for each of the 6 test delays	
Condition	**Adaptation-test pair**	**Adapt. modality**	**Movement type**	**Adapt. delay**	**Test modality**	**Movement type**
1: ActAud0	1	Auditory	Active	0ms	Auditory	Active
	2					
2: ActVis0	3	Auditory	Active	0ms	Visual	Active
	4					
3: PasAud0	5	Auditory	Passive	0ms	Auditory	Passive
	6					
4: PasVis0	7	Auditory	Passive	0ms	Visual	Passive
	8					
5: ActAud150	9	Auditory	Active	150ms	Auditory	Active
	10					
6: ActVis150	11	Auditory	Active	150ms	Visual	Active
	12					
7: PasAud150	13	Auditory	Passive	150ms	Auditory	Passive
	14					
8: PasVis150	15	Auditory	Passive	150ms	Visual	Passive
	16					

Supplementary Fig. 1. Overview of an exemplary experimental run. Button press actions were performed either actively or passively (*movement type* factor). During adaptation phases, the button presses elicited auditory outcomes (adaptation modality) that were either delayed by 150ms or undelayed (*adaptation delay* factor). During test phases, button presses were followed by either auditory or visual outcomes (*test modality* factor). Conditions with the same adaptation delay were blocked. Within blocks of the same adaptation delay, conditions with the same movement type were blocked as well. The order of adaptation delay and movement type blocks was counterbalanced across runs and subjects and is presented here in an exemplary order. In each of the four runs, each condition was presented with two consecutive adaptation-test pairs, resulting in a total number of 8 x 2 = 16 adaptation-test pairs per run and of 4 x 2 adaptation-test pairs per condition.

2. Procedure of the training session prior to the fMRI experiment

To ensure familiarity with the experimental procedure and that button presses were correctly executed, subjects also participated in a training session outside the MRI scanner on a separate day before the fMRI experiment. During that session, they were trained not to apply any counter-pressure during passive button movements, but to let their finger be moved by the device. They were trained to execute the button presses with the correct timing, i.e., in intervals of approx. 800ms (during adaptation phases) and for a duration of approx. 500ms (for both adaptation and test phases). The button press duration of 500ms was chosen to ensure that the upward movement of the button did not interfere with the detection of delays for any of the test delay levels (the maximum delay level was 417ms). Additionally, subjects experienced the test phases for each experimental condition, once with no delay and once with the maximum delay level between movement and outcome (417ms) to familiarize with the stimuli and the delays. For training purposes, they received feedback about the actual presence of a delay. Subjects were instructed to respond as accurately, but not as fast as possible. Lastly, they participated in a 10-minute training of the experiment to further familiarize with the procedure. After successfully completing the training, subjects were invited altogether to two fMRI sessions at separate days, one of which comprised the auditory recalibration experiment as described in the present manuscript. During the other session, not described here, subjects went through a similar experimental procedure, but with a visual stimulus during adaptation phases. The order of the two sessions was counterbalanced across subjects. The present manuscript focuses only on the results from the auditory recalibration experiment.

3. Supplementary tables for the main fMRI results

The following Tables provide a detailed overview of all clusters involved in the contrasts reported in the main manuscript. **Table 1** contains results of the main effect of the *adaptation delay* during adaptation and test phases, as well as for the conjunction of both phases. **Table 2** contains the results of the interaction analysis with the factors *adaptation delay* and *movement type* performed for the data of the adaptation phases.

Table 1

Group results for the main effect of the adaptation delay (150ms > 0ms) during adaptation and test phases and for the conjunction of both phases.

Cluster peak	Cluster extent	Local peaks	Hem	Coordinates			T-val.	no. vox.	$p_{FWE\text{-}corr}$ (peak-level)	$p_{FWE\text{-}corr}$ (cluster-level)
				x	y	z				
Adaptation phase: 150ms > 0ms										
Hipp *(67.19%)*			L	-34	-14	-14	4.42	128	.099	.320
		Hipp	L	-24	-12	-16	3.79		.595	
Test phase: 150ms > 0ms										
Hipp *(68.49%; 2mm)*			L	-36	-10	-18	4.68	292	.037	.050
		Hipp	L	-28	-12	-18	4.38		.114	
		Hipp	L	-32	-20	-20	3.76		.634	
ITG *(2mm; 3.50%)*			R	46	-16	-20	4.63	400	.044	.017
	Hipp *(48.00%)*		R							
	Parahipp *(17.50%)*		R							
	FG *(5.25%)*		R							
		Parahipp	R	34	-20	-20	4.24		.181	
		Hipp	R	36	-6	-24	4.18		.220	
Cereb IV/V *(15.09%)*			L	-10	-46	-16	4.35	1716	.125	<.001
	Cereb VI *(14.92%)*		R							
	Cereb crus I *(11.48%)*		R							
	FG *(8.51%)*		R							
	Cereb IV/V *(5.07%)*		R							
	Cereb crus II *(4.72%)*		R							
	LG *(4.08%)*		L							
	Vermis VII *(3.44%)*		.							
	Vermis IV/V *(3.32%)*		.							
	Cereb VIII *(3.09%)*		R							
	Cereb crus II *(3.03%)*		L							
		Cereb VI	R	18	-66	-32	4.08		.299	
		FG	R	28	-46	-18	3.94		.427	
OFCpost *(52.69%)*			L	-34	-68	-20	4.33	93	.133	.480
	IFGorb *(44.09%)*		L							
	OFCant *(3.23%)*		L							
Putamen *(24.59%; 1.41mm)*			R	30	-16	-6	4.03	61	.343	.676
Putamen *(4.35%; 1.41mm)*	Insula *(63.04%)*		R	38	0	-6	3.80	46	.586	.777
			R							
Cereb VI *(25.68%)*			L	-36	-68	-20	3.79	148	.603	.253
	FG *(68.92%)*		L							
	Cereb crus I *(5.41%)*		L							
		FG	L	-34	-60	-14	3.45		.919	
		FG	L	-30	-52	-14	3.39		.949	
MTG *(70.97%)*			L	-54	-70	16	3.74	62	.658	.669
	MOG *(24.19%)*		L							
		MTG	L	-44	-70	14	3.60		.800	

Thal LP			L	-6	-16	18	3.64	61	.762	.676
(13.11%; 2.24mm)	Caudate *(11.48%)*		L							
		Caudate *[2.45mm]*	L	-10	-10	22	3.50		.883	
MOG			L	-24	-90	18	3.58	85	.819	.525
(74.12%)	SOG *(25.88%)*		L							
		MOG	L	-16	-92	16	3.47		.903	
Conjunction Adaptation & Test: 150ms > 0ms										
Hipp			L	-36	-10	-18	4.28	120	.159	.352
(68.83%; 2mm)		Hipp	L	-24	-12	-16	3.79		.595	

N = 25. Coordinates are listed in MNI space. Significance level: p < .001 uncorrected with a minimum cluster extent of 42 voxels (p < .05 Monte Carlo cluster level corrected). Additionally, FWE-corrected p-values at peak and cluster level are displayed. For peak voxels labeled as located outside gray matter the closest anatomical region is displayed with its distance to the peak in parentheses (in mm). The contribution of each anatomical region to the corresponding cluster is indicated in percent after the anatomical label. For better readability, only regions with a contribution > 3% are displayed. Hem = hemisphere, Cereb = cerebellum, FG = fusiform gyrus, Hipp = hippocampus, IFGorb = inferior orbitofrontal gyrus, ITG = inferior temporal gyrus, LG = lingual gyrus, MOG = middle occipital gyrus, MTG = middle temporal gyrus, OFCant = anterior orbitofrontal cortex, OFCpost = posterior orbitofrontal cortex, Parahipp = parahippocampal gyrus, SOG = superior occipital gyrus, Thal LP = lateral posterior thalamus, R = right, L = left.

Table 2

Group results for the interaction effect of *adaptation delay* and *movement type* during adaptation phases.

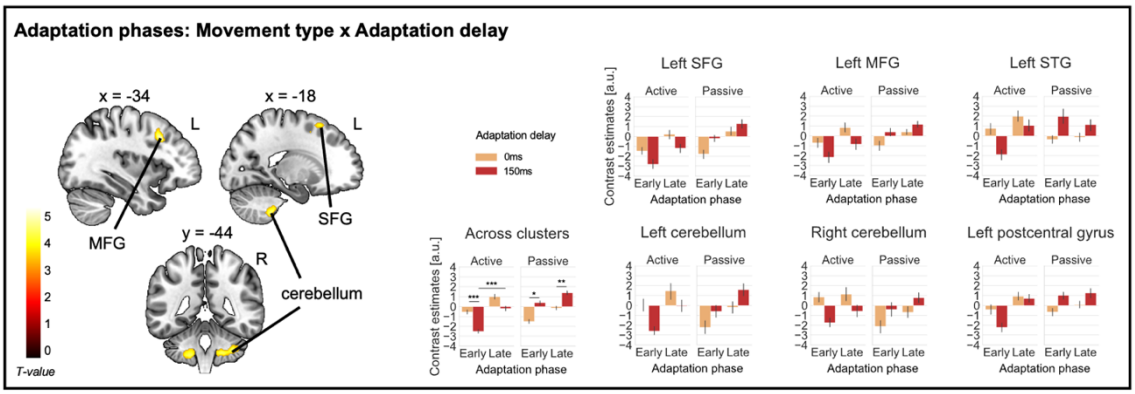
Cluster peak	Cluster extent	Local peaks	Hem	Coordinates			T-val.	no. vox.	$p_{FWE\text{-}corr}$ (peak-level)	$p_{FWE\text{-}corr}$ (cluster-level)
				x	y	z				
MFG *(92.62%)*	IFGoperc *(6.71%)*		L	-34	18	36	4.82	149	.022	.250
STG *(65.38%)*	MTG *(34.62%)*		L	-64	-26	6	4.28	52	.158	.736
Cereb IX *(62.34%)*	Cereb X *(23.38%)*		L	-18	-42	-48	4.11	154	.270	.236
	Cereb VIII *(10.39%)*		L							
Cereb VIII *(37.90%)*	Cereb IX *(36.53%)*		R	32	-44	-44	4.06	219	.317	.112
	Cereb X *(2.74%)*		R							
	Cereb VI *(2.74%)*		R							
	Cereb crus I *(2.74%)*		R							
	Cereb crus II *(2.28%)*		R							
		Cereb IX	R	20	-44	-46	4.03		.341	
Pallidum *(1.41mm, 5.88%)*				16	-4	-8	3.91	51	.467	.743
PostCG *(80.00%)*			L	-46	-16	28	3.82	75	.566	.585
SFG *(85.06%)*	MFG *(13.79%)*		L	-18	18	58	3.68	87	.726	.513
		SFG	L	-20	6	50	3.57		.828	
MOG (64.06%)	AG *(29.69%)*		L	-44	-76	26	3.60	64	.805	.656
	MTG *(6.25%)*									

N = 25. Coordinates are listed in MNI space. Significance level: p < .001 uncorrected with a minimum cluster extent of 42 voxels (p < .05 Monte Carlo cluster level corrected). Additionally, FWE-corrected p-values at peak and cluster level are displayed. For peak voxels labeled as located outside gray matter the closest anatomical region is displayed with its distance to the peak in parentheses (in mm). The contribution of each anatomical region to the corresponding cluster is indicated in percent after the anatomical label. For better

readability, only regions with a contribution > 2% are displayed. Hem. = hemisphere, AG = angular gyrus, Cereb = cerebellum, IFGoperc = inferior frontal gyrus opercular part, MFG = middle frontal gyrus, MOG = middle occipital gyrus, MTG = middle temporal gyrus, PostCG = postcentral gyrus, SFG = superior frontal gyrus, R = right, L = left.

4. Post-hoc comparisons of early vs. late adaptation phases for the interaction contrast *movement type x adaptation delay*

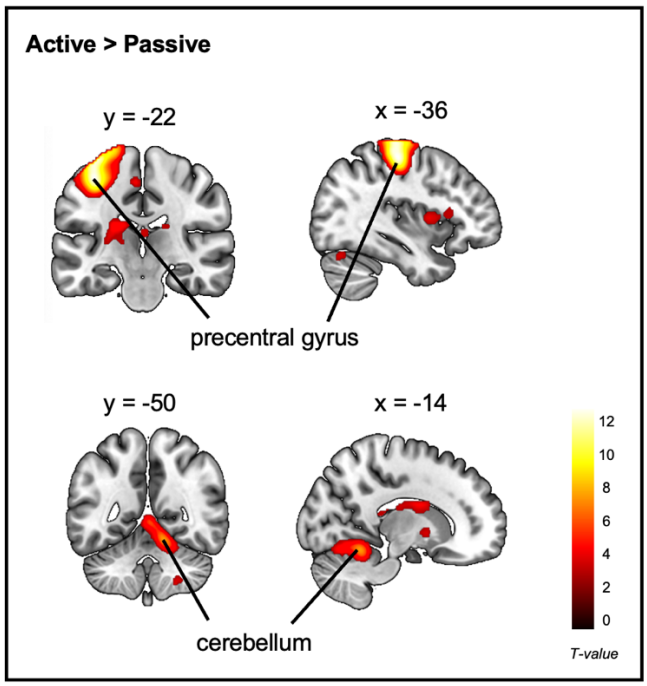
The *movement type x adaptation delay* interaction during adaptation phases revealed that activations for active conditions during exposure to the delayed tones were reduced compared to the undelayed tones. This pattern of activation was surprising since we expected the delayed tones to be associated with increased error-related activations. Although the three-way interaction including the factor *adaptation phase* was not significant, we exploratorily tested whether the decrease in activations observed in this condition was specific to early phases of adaptation but leveled off in late phases after an extended period of adaptation. By means of paired-samples t-tests, we therefore tested for delay-dependent differences in activation in active conditions (i.e., eigenvariates) across clusters separately for early and late adaptation phases. This exploratory analysis revealed that the significant difference between adaptation delays in terms of reduced activation during exposure to delayed tones was indeed mainly driven by early phases (0ms: M = -.160, SD = 1.894; 150ms: M = -2.227, SD = 1.471; $t(24) = 3.741$, $p = .001$, $d = .748$, corrected alpha = .025, two-tailed), but vanished during late phases of adaptation (0ms: M = 1.093, SD = 2.146; 150ms: M = -.147, SD = 2.167; $t(24) = 2.000$, $p = .057$, $d = .400$, corrected alpha = .025, two-tailed). Further exploratory paired-samples t-tests between activations during early vs. late phases, separately for each adaptation delay, revealed that this flattening of delay-dependent activations during late phases can be explained mainly by increasing activations from early to late phases during exposure to the delayed tones ($t(24) = -3.754$, $p < .001$, $d = -.751$, corrected alpha = .025, two-tailed), while activations did not change significantly across phases during exposure to the undelayed tones ($t(24) = -2.332$, $p = .028$, $d = -.466$, corrected alpha = .025, two-tailed). See **Supplementary Fig. 2** for an illustration of the activation changes from early to late adaptation phases.



Supplementary Fig. 2. Results for the movement type x adaptation delay interaction plotted separately for early and late phases of adaptation. Exploratory comparisons of the adaptation phases revealed that the significant difference between adaptation delays in terms of reduced activation during exposure to delayed tones was mainly driven by early phases. The activation difference between the delays vanished during late phases of adaptation due to an activation increase for the delayed tones. Error bars indicate standard errors of the means. * $p < .05$, ** $p < .01$, *** $p < .001$.

5. fMRI results for the main effect of movement type

To assess whether movement-related processes were specific to active movement conditions in our study, we compared brain activations of active and passive conditions (Active > Passive) across adaptation and test phases. Since active conditions were associated with stronger activation in regions for motor processes, in left precentral gyrus and in the cerebellum (see **Supplementary Fig. 3** and **Table 3**), movement-related processes and thus sensorimotor predictions should be specific to the active conditions.



Supplementary Fig. 3. Group activations for the contrast Active > Passive. Across both adaptation and test phases active movements were associated with significantly stronger activations in left precentral gyrus and cerebellum.

Table 3

Group results for the main effect of movement type (Active > Passive) across adaptation and test phases.

Cluster peak	Cluster extent	Local peaks	Hem	Coordinates			T-val.	no. vox.	$p_{FWE\text{-}corr}$ (peak-level)	$p_{FWE\text{-}corr}$ (cluster-level)
				x	y	z				
PreCG			L	-36	-22	56	13.03	3277	< .001	< .001
(31.22%)	PostCG *(28.20%)*		L							
	SMA *(19.26%)*		L							
	SMA *(12.21%)*		R							
	PCL *(3.21%)*		L							
	SFG *(2.04%)*		L							
		PreCG	L	-34	-24	68	12.74		< .001	
		SMA	L	-4	-8	56	6.12		< .001	
Cereb			R	14	-50	-16	8.03	2179	< .001	< .001
IV/V	Vermis IV/V		.							
(21.80%)	*(20.01%)*		R							
	Cereb VI *(14.50%)*		.							
	Vermis VI *(11.79%)*		L							
	Cereb VI *(11.01%)*		R							
	LG *(10.37%)*									
		Vermis VI	.	2	-70	-10	7.61		< .001	
		Vermis IV/V	.	2	-48	0	6.70		< .001	
Caudate			L	-20	-18	20	5.48	1608	.001	< .001
(1mm; 5.97%)	Insula *(14.80%)*		L							
	Putamen *(14.05%)*		L							
	ROL *(6.41%)*		L							
	Pallidum *(4.91%)*		L							
	Thal VPL *(4.29%)*		L							
	Thal VL *(3.61%)*		L							
	TPOsup *(3.36%)*		L							
	IFGoperc *(3.23%)*		L							
		Insula	L	-46	6	0	5.40		.002	
		Putamen	L	-24	-10	12	5.11		.006	
Insula			R	44	8	2	5.20	737	.004	.001
(31.48%)	IFGoperc *(46.81%)*		R							
	ROL *(9.50%)*		R							
	TPOsup *(3.26%)*		R							
	PreCG *(2.31%)*		R							
		Insula	R	50	14	-4	5.13		.006	
		IFGoperc	R	60	12	16	4.49		.077	
Caudate			R	10	0	20	4.86	709	.018	.001
(2mm; 32.02%)	Pallidum *(13.96%)*		R							
	Putamen *(4.80%)*		R							
		Caudate	R	18	-4	22	4.73		.030	
		Caudate	R	18	-18	20	4.09		.287	
SPL			R	52	-40	58	4.71	95	.033	.469
(21.05%)	IPG *(74.74%)*		R							
	SMG *(3.16%)*		R							
		SMG	R	48	-38	44	3.31		.975	
Cereb VIII *(100%)*			R	22	-58	-52	3.85	112	.529	.386
		Cereb VIII	R	24	-50	-52	3.84		.541	
Thal PuM *[4.36mm]*			R	2	-20	16	3.67	102	.733	.433

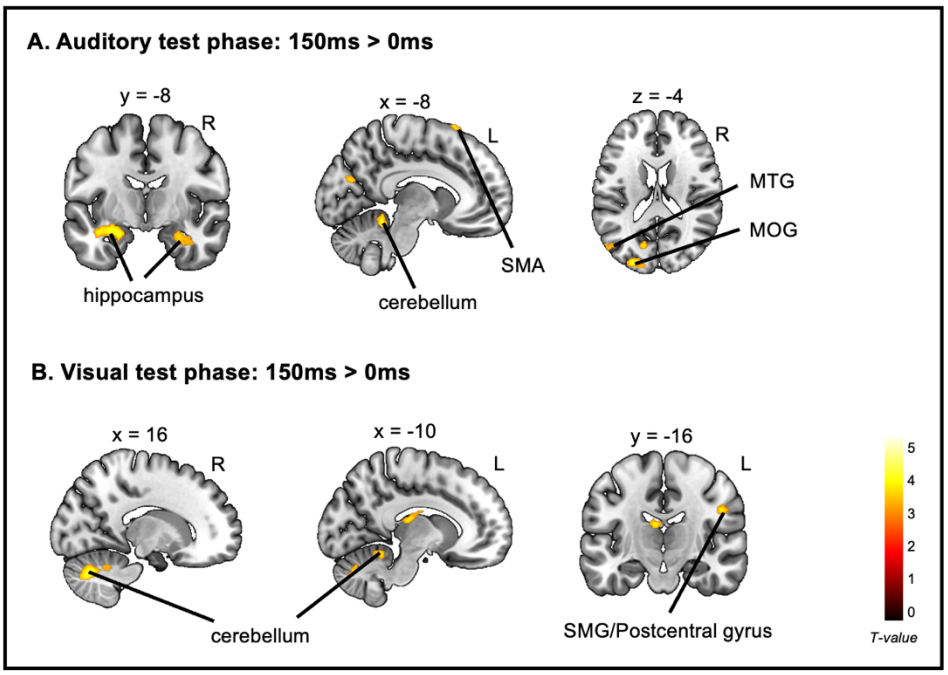
N = 25. Coordinates are listed in MNI space. Significance level: p < .001 uncorrected with a minimum cluster extent of 42 voxels (p < .05 Monte Carlo cluster level corrected). Additionally, FWE-corrected p-values at peak and cluster level are displayed. For peak voxels labeled as located outside gray matter the closest anatomical region is displayed with its distance to the peak in parentheses (in mm). The contribution of each anatomical region to the corresponding cluster is indicated in percent after the anatomical label. For better readability, only regions with a contribution > 2% are displayed. Cereb = cerebellum, FG = fusiform gyrus,

Hem. = hemisphere, IFGoperc = inferior frontal gyrus opercular part, IPG = inferior parietal gyrus, LG = lingual gyrus, PCL = paracentral lobule, PreCG = precentral gyrus, PostCG = postcentral gyrus, ROL = rolandic operculum, SFG = superior frontal gyrus, SMA = supplementary motor area, SMG = supramarginal gyrus, SPL = superior parietal lobe, Thal PuM = pulvinar medial thalamus, Thal VL = ventral lateral thalamus, Thal VPL = ventral posterolateral thalamus, TPOsup = temporal pole: superior temporal gyrus, R = right, L = left.

6. fMRI results for the main effect of adaptation delay (150ms > 0ms) separated by test modality

In our study, we did not find neural signatures for modality-transfer effects of temporal recalibration in terms of overlapping delay-dependent activations (conjunctions of the 150ms > 0ms contrasts for auditory and visual test modalities) or differences between the modalities (interactions of test modality and adaptation delay). Despite the non-significant interaction of adaptation delay and test modality, we explored the impact of the adaptation delay on activations during visual and auditory test phases separately. This exploration revealed that the delay-dependent activations in hippocampus (that appeared in the 150ms > 0ms contrast for test phases as reported in the main manuscript) were mainly driven by the auditory test modality (see **Supplementary Fig. 4A** and **Table 4**). This is also in line with the finding that the overlapping hippocampus activations during adaptation and test phases as reported in the conjunction analysis (Adaptation 150ms > 0ms ∩ Test 150ms > 0ms; Fig. 4) in the main manuscript, seemed to be mainly driven by the auditory test modality. Performing this conjunction analysis separately for both modalities revealed significant activations in left hippocampus for the auditory modality (x, y, z = -36, -10, -18, cluster size = 107 voxels, t = 4.00), but no significant activations occurred for the visual modality. The involvement of the hippocampus only for auditory stimuli may be attributed to the fact that the encoded novel temporal association between button presses and auditory stimuli, was not retrieved during the visual delay detection task. This could potentially indicate modality-specific processes in the hippocampus. However, since our data do not provide clear evidence for this due to the non-significant interaction, this explanation should be taken with caution. As opposed to that, cerebellar activations (which were also present in the 150ms > 0ms contrast for test phases as reported in the main manuscript) seemed to the mainly driven by the visual modality (including lobules VI, crus I, and crus II of the left cerebellar hemisphere, and lobules IV/V, VI, VIII, crus I, and crus II of the right cerebellar hemisphere; see **Supplementary Fig. 4B** and **Table 5**). This suggests that auditory temporal recalibration induced modulations of brain activation in this region also during delay detection in vision.

Finally, the fact that delay-dependent activations for auditory test phases also included visual processing regions, such as MOG, could speak for certain interactions between the two modalities in our task. Unimodal sensory processing regions have previously been found to play an important role not only in unimodal but also in multisensory processes (Ghazanfar & Schroeder, 2006) and neurons in visual cortex have been shown to also be responsive to auditory (Poremba et al., 2003) and audio-visual (Meijer et al., 2017) stimuli. While the delay-dependent visual activations in the auditory task may thus point to certain cross-modal interactions in the neural correlates of temporal recalibration, again it is important to note that differences or commonalities between the modalities were not strong enough in this study to lead to significant delay-dependent interaction or conjunction effects. Furthermore, recalibration-related activations for the visual modality during test did not lead to effects of temporal recalibration in behavior.



Supplementary Fig. 4. Group activations for the contrast 150ms > 0ms for auditory and visual modalities separately. The main effect of the adaptation delay (150ms > 0ms) across test modalities that is reported in the main manuscript mainly comprised activations in hippocampus and cerebellum. **A.** The hippocampal activations were mainly driven by the auditory test modality. **B.** The same contrast in the visual was mainly associated with activations in cerebellar regions.

Table 4

Group results for the main effect of adaptation delay (150ms > 0ms) during **auditory** test phases

Cluster peak	Cluster extent	Local peaks	Hem	Coordinates			T-val.	no. vox.	$p_{FWE\text{-}corr}$ (peak-level)	$p_{FWE\text{-}corr}$ (cluster-level)
				x	y	z				
Hipp *(65.22%)*	Parahipp *(10.43%)*		L	-28	-12	-18	4.57	345	.057	.029
	Amygdala *(3.19%)*		L							
		Parahipp	L	-26	-30	-20	3.28		.981	
Parahipp *(18.75%)*	Hipp *(52.21%)*		R	34	-20	-20	4.28	272	.161	.062
	FG *(5.15%)*		R							
	ITG *(4.41%)*		R							
		ITG *[2.00mm]*	R	46	-16	-20	4.07		.303	
		Hipp	R	36	-6	-24	3.55		.851	
MOG *(37.50%)*	SOG *(30.15%)*		L	-24	-88	18	3.95	272	.421	.062
	Cuneus *(20.96%)*		L							
	Calcarine *(8.82%)*		L							
		Cuneus	L	-14	-72	22	3.85		.533	
		MOG	L	-16	-92	16	3.67		.737	
MOG *(65.31%)*	IOG *(34.69%)*		L	-36	-88	-4	3.79	98	.598	.453
Cereb IV/V *(76.36%)*	Vermis III *(12.73%)*		L	-8	-44	-18	3.79	110	.603	.395
	Cereb III *(7.27%)*		L							
		Vermis III	.	6	-44	-14	3.23		.989	
SMA *(45.65%)*	SFG *(26.09%)*		L	-8	20	68	3.76	46	.631	.777
		SFG	L	-18	12	70	3.55		.848	
OFCpost *(84.44%)*	IFGorb *(11.11%)*		L	-34	30	-16	3.66	45	.739	.784
	OFClat *(2.22%)*		L							
	OFCant *(2.22%)*		L							
MTG *(64.84%)*	MOG *(24.18%)*		L	-52	-72	14	3.64	91	.759	.491
		MTG *[2.24mm]*	L	-50	-76	22	3.38		.952	
LG *(100%)*			R	16	-66	-8	3.48	51	.899	.743
MOG *(72.00%)*	SOG *(28.00%)*		R	34	-80	34	3.41	50	.937	.750
		SOG	R	24	-86	42	3.32		.973	

N = 25. Coordinates are listed in MNI space. Significance level: p < .001 uncorrected with a minimum cluster extent of 42 voxels (p < .05 Monte Carlo cluster level corrected). Additionally, FWE-corrected p-values at peak and cluster level are displayed. For peak voxels labeled as located outside gray matter the closest anatomical region is displayed with its distance to the peak in parentheses (in mm). The contribution of each anatomical region to the corresponding cluster is indicated in percent after the anatomical label. For better readability, only regions with a contribution > 2% are displayed. Hem = hemisphere, Cereb = cerebellum, FG = fusiform gyrus, Hipp = hippocampus, IFGorb = inferior orbitofrontal gyrus, IOG = inferior occipital gyrus, ITG = inferior temporal gyrus, LG = lingual gyrus, MOG = middle occipital gyrus, OFClat = lateral orbitofrontal cortex, OFCant = anterior orbitofrontal cortex, Parahipp = parahippocampal gyrus, SOG = superior occipital gyrus, R = right, L = left.

Table 5

Group results for the main effect of adaptation delay (150ms > 0ms) during **visual** test phases

Cluster peak	Cluster extent	Local peaks	Hem	Coordinates			T-val.	no. vox.	$p_{FWE\text{-}corr}$ (peak-level)	$p_{FWE\text{-}corr}$ (cluster-level)
				x	y	z				
Cereb VI			R	16	-68	-32	4.19	848	.214	<.001
(1.00mm, 28.18%)	Cereb VI *(10.97%)*		L							
	Cereb crus I *(9.67%)*		R							
	Cereb crus I *(7.55%)*		L							
	Cereb VIII *(7.19%)*		R							
	Vermis VII *(5.66%)*		.							
	Cereb crus II *(5.07%)*		R							
	Cereb crus II *(3.77%)*		L							
	Vermis VIII *(2.83%)*		.							
	Vermis VI *(2.71%)*		.							
	FG *(2.48%)*		R							
	Cereb IV/V *(2.36%)*		R							
		Cereb VI	L	-18	-66	-28	3.77		.621	
		Cereb VI	R	26	-58	-24	3.75		.640	
IFGorb *(83.05%)*	OFCpost *(16.95%)*		L	-34	30	-12	4.18	59	.221	.689
			L							
Thal PuM *(1.41mm, 8.48%)*	Thal LP *(8.48%)*		L	-8	-22	16	3.98	165	.388	.207
		Thal LP *[2.45mm]*	L	-6	-14	20	3.81		.580	
		Thal AV *[5.66mm]*	L	0	-8	18	3.50		.887	
SMG *(16.67%)*	PostCG *(55.56%)*		R	48	-16	30	3.81	54	.580	.723
			R							
Putamen *(1.00mm, 13.85%)*	Insula *(18.46%)*		R	32	16	-4	3.76	65	.630	.649
Cereb IV/V *(100%)*			L	-10	-48	-18	3.62	51	.788	.743
Cereb VI *(43.48%)*			L	-36	-68	-20	3.50	46	.888	.777
	FG *(54.35%)*		L							
	Cereb crus I *(2.17%)*		L							

N = 25. Coordinates are listed in MNI space. Significance level: $p < .001$ uncorrected with a minimum cluster extent of 42 voxels ($p < .05$ Monte Carlo cluster level corrected). Additionally, FWE-corrected p-values at peak and cluster level are displayed. For peak voxels labeled as located outside gray matter the closest anatomical region is displayed with its distance to the peak in parentheses (in mm). The contribution of each anatomical region to the corresponding cluster is indicated in percent after the anatomical label. For better readability, only regions with a contribution > 2% are displayed. Hem. = hemisphere, IFGorb = Inferior orbitofrontal gyrus, OFCpost = posterior orbital gyrus, PostCG = postcentral gyrus, SMG = supramarginal gyrus, Thal AV = thalamus, anteroventral nucleus, Thal LP = lateral posterior thalamus, Thal PuM = pulvinar medial thalamus, R = right, L = left.

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Study II: Publication Schmitter & Straube (2022)

Schmitter, C.V., & Straube, B. (2022). The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration. *Frontiers in Human Neuroscience, 16,* 998843, https://doi.org/10.3389/fnhum.2022.998843

frontiers | Frontiers in Human Neuroscience

TYPE Original Research
PUBLISHED 30 August 2022
DOI 10.3389/fnhum.2022.998843

OPEN ACCESS

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SPECIALTY SECTION
This article was submitted to Brain Imaging and Stimulation, a section of the journal Frontiers in Human Neuroscience

RECEIVED 20 July 2022
ACCEPTED 12 August 2022
PUBLISHED 30 August 2022

CITATION
Schmitter CV and Straube B (2022) The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration. *Front. Hum. Neurosci.* 16:998843. doi: 10.3389/fnhum.2022.998843

The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration

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The characteristic temporal relationship between actions and their sensory outcomes allows us to distinguish self- from externally generated sensory events. However, the complex sensory environment can cause transient delays between action and outcome calling for flexible recalibration of predicted sensorimotor timing. Since the neural underpinnings of this process are largely unknown this study investigated the involvement of the cerebellum by means of cerebellar transcranial direct current stimulation (ctDCS). While receiving anodal, cathodal, dual-hemisphere or sham ctDCS, in an adaptation phase, participants were exposed to constant delays of 150 ms between actively or passively generated button presses and visual sensory outcomes. Recalibration in the same (visual outcome) and in another sensory modality (auditory outcome) was assessed in a subsequent test phase during which variable delays between button press and visual or auditory outcome had to be detected. Results indicated that temporal recalibration occurred in audition after anodal ctDCS while it was absent in vision. As the adaptation modality was visual, effects in audition suggest that recalibration occurred on a supra-modal level. In active conditions, anodal ctDCS improved sensorimotor recalibration at the delay level closest to the adaptation delay, suggesting a precise cerebellar-dependent temporal recalibration mechanism. In passive conditions, the facilitation of inter-sensory recalibration by anodal ctDCS was overall stronger and tuned to larger delays. These findings point to a role of the cerebellum in supra-modal temporal recalibration across sensorimotor and perceptual domains, but the differential manifestation of the effect across delay levels in active and passive conditions points to differences in

the underlying mechanisms depending on the availability of action-based predictions. Furthermore, these results suggest that anodal ctDCS can be a promising tool for facilitating effects of temporal recalibration in sensorimotor and inter-sensory contexts.

KEYWORDS

sensorimotor temporal recalibration, sensorimotor adaptation, predictive processing, forward model, cerebellum, transcranial direct current stimulation, tDCS

Introduction

Despite the multitude of sensory signals that we are exposed to during daily interactions with the environment, we can effortlessly distinguish between those caused by our own actions and those with external origin. This ability relies heavily on the characteristic and highly predictable temporal relationship between actions and their sensory outcomes. For example, when clapping hands, the clap sound is strongly expected to be perceived near-instantaneously after the hands touch, by considering inherent delays in sound transmission and in sensory pathways. Such predictions about sensory action-outcomes are assumed to be generated by an internal forward model based on a copy of the motor commands (Blakemore et al., 1998; Wolpert et al., 1998; Elijah et al., 2016; Cao et al., 2017). Sensations that occur with the timing predicted for the action-outcome are likely to be attributed to the own action. A temporal mismatch, however, such as an unexpected long delay between action and outcome, elicits a prediction error and the attribution of sensations to an external event or agent (Haggard et al., 2002; Hughes et al., 2013; Imaizumi and Tanno, 2019; Zapparoli et al., 2020).

Notably, the complexity of the sensory environment can cause transient violations in the temporal relationship between action and outcome. For instance, additional delays can be imposed on the interval between an action and the perception of its outcome by changes in environmental conditions (e.g., dimmed light delaying signals from the retina; Matteson, 1971) or by changes in sensory processing (e.g., due to fatigue; Cai et al., 2018). Thus, it seems essential to dynamically recalibrate predictions about the timing of sensory action-outcomes to preserve accurate perception and attribution of agency even under frequently changing conditions (Stetson et al., 2006; Parsons et al., 2013; Cai et al., 2018). Such a recalibration of perception also has direct implications for motor functions, which have to be adapted to the changed temporal dynamics as well. An important everyday example is locomotion. Here, the adequate adaptation of temporal gait characteristics, e.g., step timing, to varying environmental conditions is an important indicator of the successful control of limb positions during locomotion (Hoogkamer and O'Brien, 2016; Gonzalez-Rubio et al., 2019).

Indeed, flexible recalibration of the perceived relative timing between actions and their sensory outcomes is an established phenomenon known as sensorimotor temporal recalibration. Evidence for this phenomenon can be derived from a range of studies that aimed at inducing a sensorimotor temporal recalibration effect (TRE) by repeatedly inserting a constant delay between a participant's action (like a button press) and its sensory outcome in form of a light flash or a brief tone (Stetson et al., 2006; Heron et al., 2009; Sugano et al., 2010, 2012, 2016, 2017; Stekelenburg et al., 2011; Tsujita and Ichikawa, 2012; Rohde and Ernst, 2013; Elijah et al., 2016; Cao et al., 2017; Cai et al., 2018; Arikan et al., 2021). After repeated exposure to such a manipulation, the delayed action-outcome was in fact perceived as occurring synchronously with the action (Sugano et al., 2010, Keetels and Vroomen, 2012; Sugano et al., 2012, 2016, 2017; Yamamoto and Kawabata, 2014) and shorter delays were less likely to be detected (Arikan et al., 2021). This indicates recalibration of the expected relative timing between action and outcome leading to a shift of synchrony perception toward the exposed delay. Moreover, undelayed outcomes were now frequently perceived as preceding the action (Stetson et al., 2006; Heron et al., 2009; Sugano et al., 2010; Stekelenburg et al., 2011; Tsujita and Ichikawa, 2012; Rohde and Ernst, 2013; Cai et al., 2018) suggesting that the constant delay was incorporated into the temporal prediction of the outcome.

Notably, while sensorimotor temporal recalibration finds support in a wide range of behavioral studies, evidence for the neural basis of this process remains sparse. The sensorimotor TRE could for instance be associated with in a shift of readiness potentials closer to movement onset indicating the involvement of action-based predictive mechanisms (Cai et al., 2018). Moreover, the illusory perception of an undelayed or very shortly delayed outcome as preceding the action after exposure to a constant delay was related to increased hemodynamic activation of brain areas involved in error-related processing such as anterior cingulate cortex and medial frontal cortex (Stetson et al., 2006). However, while these findings describe

correlates of the sensorimotor TRE in the brain, the neural mechanisms behind the process itself remain largely elusive.

The cerebellum has emerged as an important brain area regarding the generation of predictions about sensory action-outcomes. Since it receives and combines afferent inputs from sensory areas and efferent inputs from motor areas, its anatomy and location seem ideal for performing predictive forward model computations. It has consequently been proposed as critical brain structure for forward model related processes or even as the site of internal forward models itself (Miall et al., 1993; Wolpert et al., 1998; Imamizu et al., 2000; Blakemore et al., 2001; Ishikawa et al., 2016; Cao et al., 2017; Straube et al., 2017b; Arikan et al., 2019; van Kemenade et al., 2019; Tanaka et al., 2020; Welniarz et al., 2021). It is further well-known to be involved in potentially related processes such as motor control, adaptation and learning (Tseng et al., 2007; Synofzik et al., 2008; Shadmehr et al., 2010; Schlerf et al., 2012; Sokolov et al., 2017; Statton et al., 2018; Tanaka et al., 2020). This suggests that the cerebellum could also be a prime candidate area for the updating of action-outcome predictions and thus for the process of sensorimotor temporal recalibration.

It could be argued that the effects of sensorimotor temporal recalibration emerge simply due to recalibration of the perceived inter-sensory timing (e.g., between the tactile sensation at the end of the button press and the visual or auditory outcome) which is also known to be an important mechanism for dealing with differential and varying delays in the transmission and processing of sensations from different sensory modalities (Fujisaki et al., 2004; Vroomen et al., 2004; Hanson et al., 2008; van der Burg et al., 2013). Importantly however, the TRE appeared to be stronger when the action was self-initiated compared to conditions where the effector was passively touched (Stetson et al., 2006) or moved (Arikan et al., 2021). Since a TRE in such passive conditions can only be explained by inter-sensory temporal recalibration due to the absence of a motor command or the intention to act, the weaker effect in this condition points to a component in sensorimotor temporal recalibration that is specific to the processing of sensorimotor delays and can indeed be attributed to the adaptation of action-based predictions (Arikan et al., 2021).

These results also suggests that the involvement of regions known for action-outcome processing, such as the cerebellum, in temporal recalibration is specific to the sensorimotor context, but direct evidence for this claim is missing.

A recent MEG study reported first evidence for cerebellar contributions to temporal recalibration by investigating the M100 component known to reflect an early response to auditory stimuli. This component is typically attenuated for the processing of tones that occur in synchrony with a self-generated action compared to passive listening to externally presented tones. Here, after repeated exposure to a delayed tone, M100 attenuation also emerged for the delayed tones, but this effect was abolished after inhibition of the right cerebellum by TMS (Cao et al., 2017). While this points to a vital role of the cerebellum in temporal recalibration, it remains unclear whether this effect is indeed specific to sensorimotor as opposed to more general audio-tactile temporal recalibration and whether it can be linked to relevant changes in behavior.

Interestingly, the sensorimotor TRE could frequently be shown to transfer from one modality to another, such that the temporal perception of the action-outcome of one modality recalibrated to a delay previously inserted between the action and the outcome of another modality (Heron et al., 2009; Sugano et al., 2010, 2012; Arikan et al., 2021). This suggests that sensorimotor temporal recalibration does not occur in modality-specific circuits but rather on a supra-modal level, i.e., in the general predicted timing for sensory outcomes following an action. This assumption coincides with evidence that action-outcome predictions are simultaneously generated by the internal forward model for outcomes in multiple sensory modalities (van Kemenade et al., 2016, 2017; Straube et al., 2017b). Whether the neural correlates for the updating of action-outcome predictions, which might be assumed in the cerebellum, also perform this updating on a supra-modal level and are therefore responsible for the modality-transfer effects, remains to be determined.

In this study, we therefore used transcranial direct current stimulation (tDCS) on the cerebellum to address the question of whether it is related to temporal recalibration. We were specifically interested in the question of whether the relationship is unique to the sensorimotor context and whether the cerebellum contributes to the modality-transfer of recalibration effects. tDCS is a non-invasive brain stimulation technique that has already been used by a range of previous studies that investigated whether the stimulation of mainly frontal and parietal brain areas can influence the processing of sensory action outcomes. Frontal tDCS for instance facilitated the detection of delays between an action and its sensory outcome (Straube et al., 2017a, 2020) while stimulation of the pre-supplementary motor area (Cavazzana et al., 2015), angular gyrus (Khalighinejad and Haggard, 2015) or dorsolateral prefrontal cortex (Khalighinejad et al., 2016) modulated the intentional binding effect, i.e., an implicit measure for the perceived agency over a sensory event. Furthermore, visual cortex tDCS was able to influence the extent of the visuomotor TRE (Aytemür et al., 2017). The efficacy of cerebellar tDCS (ctDCS) has been shown for a variety of processes as well, e.g., for the modulation of motor learning (Shah et al., 2013; Celnik, 2015; Shimizu et al., 2017; Kumari et al., 2019) and adaptation (Jayaram et al., 2012; Doppelmayr et al., 2016; Yavari et al., 2016; Panico et al., 2018; Weightman et al., 2021), balance control (Ehsani et al., 2017) or procedural learning (Ferrucci et al., 2013; Gupta et al., 2018). Despite the presumable critical importance of the cerebellum for the predictive mechanisms underlying action-outcome processing, evidence for the impact of ctDCS in this context and especially when recalibration

of predictions is necessary due to repeated temporal action-outcome deviations is missing. Here, we tested if and to what extent ctDCS of different polarities can facilitate sensorimotor temporal recalibration.

Participants engaged in adaptation phases during which the temporal relationship between a button press and a visual sensory outcome was manipulated by introducing constant delays between button press and outcome. A subsequent delay detection task assessed if and to what extent these temporal incongruencies triggered temporal recalibration. Here, participants were asked to detect varying temporal delays between the button press and its sensory outcomes. The TRE was expected to manifest in decreased delay detection performance (especially for delays close to the adaptation delay) indicating a shift of predicted stimulus timing in the direction of the constant delay participants were previously exposed to. Importantly, button presses were either performed actively by the participants or passively by an electromagnetic passive button device. Since both passive and active movements were associated with similar tactile and proprioceptive sensations, this manipulation allowed us to disentangle effects of sensorimotor temporal recalibration due to adaptation of action-based predictions from effects due to inter-sensory temporal recalibration. Based on previous findings we expected a stronger TRE in active compared to passive movement conditions due to the additional involvement of predictive signals based on the motor commands (Stetson et al., 2006; Arikan et al., 2021). As actively compared to passively elicited sensory stimuli could previously be associated with generally enhanced delay detection performance (van Kemenade et al., 2016), an increased TRE due to the availability of action-based predictions could for example reflect an advantage in processing temporal prediction errors.

While the constant delay was always inserted between button presses and visual outcomes during adaptation (visuomotor or visuo-tactile temporal recalibration), the sensory modality in the delay detection task could be either visual or auditory. Based on the assumption that action-outcome predictions are generated for multiple sensory modalities (van Kemenade et al., 2016, 2017; Straube et al., 2017b) and based on previous observations (Heron et al., 2009; Sugano et al., 2010, 2012; Arikan et al., 2021) we expected the visuomotor or visuo-tactile temporal recalibration procedure to induce a TRE for both visual (visuomotor or visuo-tactile TRE) and auditory test modalities (audiomotor or audio-tactile TRE) and particularly so in active movement conditions due to recalibration of predictions on a supra-modal level.

This experimental paradigm was applied in four separate sessions for each participant during which they received 20 min of either anodal, cathodal, dual-hemisphere or sham ctDCS to investigate whether the TRE can be facilitated or impaired, respectively, depending on stimulation polarity, which might be attributed to changes in the sensitivity to temporal prediction errors or in the speed or precision of sensorimotor learning.

Anodal tDCS has frequently been shown to increase cortical excitability while it is decreased by cathodal tDCS (Nitsche and Paulus, 2000). Although such polarity-dependent effects seem to be more inconsistent for the cerebellum, similar directions of the effect have often been reported here as well (Grimaldi et al., 2016). Therefore, compared to sham stimulation, we expected temporal recalibration to be facilitated by anodal ctDCS on the bilateral cerebellum but to be impaired by cathodal ctDCS. Since dual-hemisphere tDCS could be demonstrated to increase stimulation effects (Vines et al., 2008; Kwon and Jang, 2012; Workman et al., 2020), presumably due to reduced inhibitory inter-hemispheric influences (Kwon and Jang, 2012), we furthermore explored whether stronger faciliatory effects on the TRE could be achieved by simultaneous anodal ctDCS of the right and cathodal ctDCS of the left cerebellar hemisphere compared to purely anodal ctDCS. Since we assumed ctDCS to influence action-based predictive mechanisms located in the cerebellum we expected greater polarity-dependent modulations of the TRE and its modality-transfer to occur in active movement conditions.

Materials and methods

Participants

Twenty-two right-handed healthy volunteers participated in the study (10 male; mean age: 25.18 years, *SD* = 4.59). All participants had normal or corrected-to-normal vision and normal hearing. They reported no history of psychiatric, neurological or movement disorders or of drug or alcohol abuse. Additionally, no one reported any contraindications for tDCS (e.g., electric, or metallic implants). According to a power analysis, this sample size should have been sufficient to reproduce effects of similar size as reported in previous studies with a similar experimental design (see section 1 in **Supplementary material** for further details). Participants provided written informed consent and received financial reimbursement for their participation. The study was conducted according to the Declaration of Helsinki and was approved by the local ethics commission of the medical faculty of University of Marburg, Germany.

Transcranial direct current stimulation

In each session, ctDCS was applied on the cerebellum with a DC stimulator (neuroConn GmbH, Ilmenau) and two rubber electrodes (5 × 7 cm) covered in saline-soaked sponges (0.9% NaCl).

For anodal and cathodal ctDCS, the center of the respective active electrode was placed on the midline 2 cm below the inion to target the bilateral cerebellum while the return electrode was attached to the right upper arm (onto the deltoid muscle). For dual-hemisphere ctDCS, electrodes were placed with their centers 2 cm below and 3 cm lateral to the inion targeting the right (anode) and the left cerebellar hemisphere (cathode), respectively. All electrodes were attached with rubber bands.

In each session, a current of 2 mA was applied for 20 min (+10 s fade in and fade out periods). For sham stimulation, sinus (HW) mode was used for a duration of 30 s. The stimulation parameters are in accordance with established tDCS safety guidelines (e.g., Bikson et al., 2017).

Equipment and stimuli

Participants were seated in a dimly lit room in front of a computer screen with a refresh rate of 60 Hz at a standardized distance of approximately 55 cm. During the experiment button presses were performed with the right index finger using a custom-made electromagnetic passive button. In active conditions, participants pressed the button actively themselves. In passive conditions, the button was pulled down automatically by an electromagnet with a maximum force of 4N. Participants' fingers were tied to the button with an elastic fabric band to ensure that it would smoothly follow the movement of the button in passive conditions.

When a button press was registered by the computer (i.e., the button reached the lowest position) the presentation of a visual or an auditory stimulus was triggered. The visual stimulus was composed of a Gabor patch (1° visual angle, spatial frequency: 2 cycles/degree) presented at the center of the screen. The auditory stimulus was a brief sine-wave tone (2000 Hz with 2 ms rise and fall) played through headphones. Both stimuli were presented for a duration of 33.4 ms each. Stimuli were created and presented using Octave and the Psychophysics Toolbox (Brainard, 1997).

To ensure that sensory outcome perception would not be influenced by direct visual or auditory feedback of the actual button press movements, the button was covered by a black box and pink noise was applied through the headphones at individually adjusted volume during the whole experiment.

Experimental design and task description

In each session, participants underwent multiple pairs of adaptation and test phases. Adaptation phases consisted of 18 consecutive button presses each followed by the presentation of the visual sensory outcome. Throughout an adaptation phase all button presses had to be performed either actively or were elicited passively (factor *movement type*). Importantly, the visual outcome occurred either directly after the button press was registered (0 ms delay) or after a constant delay of 150 ms (factor *adaptation delay*). While the 0 ms condition was assumed to match the natural expectation of temporal congruence between action and visual action-outcome (in active conditions) or between tactile or proprioceptive and visual sensory signals (in passive conditions), the constant delay was assumed to induce a prediction error and thus to trigger sensorimotor or inter-sensory temporal recalibration, respectively.

Each adaptation phase was followed by a test phase assessing the impact of the preceding adaptation phase on sensory perception. A test phase was composed of six individual test trials. In each trial the button was pressed once, either actively or passively (the movement type in each of the six test trials was identical to the one in the preceding adaptation phase). The button press triggered the presentation of either the visual or the auditory stimulus in each of the six test trials (factor *test modality*). In each trial one of six temporal delays (0, 83, 167, 250, 333, 417 ms; presented in frames: 0, 5, 10, 15, 20, 25) was inserted between button press and stimulus presentation. Thus, each delay appeared once in each test phase. Participants' task was to report whether they detected a delay between the button press and its sensory outcome by pressing one of two keys on the keyboard with their left hand. The order of delays was counterbalanced across test phases and the assignment of keys was counterbalanced across participants. The TRE was defined as the difference in the percentage of detected delays in this task following an adaptation phase with vs. without constant outcome delay. Worse delay detection performance after adaptation with the delay of 150 ms would reflect a shift of the expected timing of the sensory stimulus in the direction of the delay and thus temporal recalibration.

In summary, the factors *adaptation delay* (0 vs. 150 ms), *movement type* (active vs. passive) and *test modality* (visual vs. auditory) were combined to eight different experimental conditions. Together with the factor *stimulation* (anodal vs. cathodal vs. dual-hemisphere vs. sham ctDCS) this resulted in a $4 \times 2 \times 2 \times 2$ within-subjects design.

Procedure

Each participant went through all four stimulation conditions in four separate sessions. Intraindividual sessions were performed at least 24 h apart to prevent spill-over effects from the previous session. The order of stimulation conditions was counterbalanced across participants.

Each adaptation phase started with written instructions on the screen about the movement type of the upcoming button presses displayed for 1500 ms (see **Figure 1**). The instructions were displayed together with a fixation cross in the center of the screen which disappeared after another second

indicating that participants could start pressing the button or that the button started to move passively. During the adaptation phase, each button press triggered the presentation of the visual outcome that was either undelayed with respect to the button press or that was delayed by 150 ms. Actively generated button presses in the adaptation phases were trained to be performed in an interval of approximately 750 ms and with a duration of 500 ms. The button press duration in both adaptation and test phases was chosen to be larger than the maximum delay inserted between button press and outcome (i.e., 417 ms) to prevent delay detection from being disturbed by the upwards movement of the button for any of the tested delay levels. To assure comparable button press parameters between active and passive movement conditions, passive button press intervals as well as durations dynamically adapted to the mean of the respective preceding active conditions throughout the experiment. Adaptation phases always terminated automatically after 18 button presses.

Each test phase also started with the fixation cross and instructions about the movement type and outcome modality of the upcoming test trials (displayed for 1500 ms). The disappearance of the fixation cross initiated the first of six test trials. In active conditions, participants had 1500 ms to press the button once. Yet, they were instructed to press the button not immediately after the fixation cross had disappeared but to withhold their button press action for about 700 ms. This was to ensure that the button press was not triggered as a reflex upon a starting signal but as a self-initiated action (Rohde and Ernst, 2013; van Kemenade et al., 2016; Straube et al., 2020). The same button press latency was applied for passive test trials. Each button press was followed by the presentation of the visual or auditory outcome with one of the six levels of temporal delay. After an interval of 500 ms the question "Delay?" was presented on the screen for a maximum of 1500 ms during which participants had to indicate via keypress whether they detected a delay between the button press and the sensory outcome. Afterward the fixation cross appeared again for 500 ms and its disappearance cued the beginning of the next test trial. The last trial of each test phase was followed by a jittered inter-trial interval before the beginning of the next adaptation-test pair (500, 1000, and 1500 ms).

In one session, each of the eight experimental conditions was presented in eight pairs of adaptation and test phases. Since each of the six delay levels was presented once in a test phase, this procedure provided us with eight trials per delay and condition for the analyses. Four adaptation-test pairs of each condition occurred in sequence in a first task block during which tDCS stimulation was applied. After the first task block, tDCS electrodes were detached during a short break. The remaining four adaptation-test pairs of each condition were presented in a second task block after the break in the same order as in the first task block. The second task block was completed without tDCS stimulation. Within each task block conditions with 0 and 150ms adaptation delay were blocked to prevent potential spill-over effects due to rapid switching. Whether the block of 0 or 150 ms delay was presented first as well as the order of conditions within these blocks was counterbalanced across participants.

After each session potential side effects of the tDCS stimulation (e.g., itching sensations, headache, changes in visual perception, difficulties in concentration) were assessed with a custom-designed questionnaire of 28 items using ratings on a scale from one (no side effect) to five (strong side effect). During the first session, participants additionally went through a training procedure before the beginning of the stimulation in order to familiarize with the task. They were instructed to place their finger loosely on the button and not to apply any counter-pressure in passive movement conditions. For the adaptation phases, they were trained to perform the button presses in intervals of approximately 750 ms and for a duration of 500 ms while receiving feedback about their performance. For the test phases, participants were trained in each of the experimental conditions, once with the undelayed and once with the maximally delayed sensory outcome (417 ms) to familiarize with the stimuli and the delays. Here, they were provided with feedback about the actual presence of a delay in the respective trial. Participants were asked to answer as accurately, not as fast as possible. Finally, they went through a 10-min training of the experiment to further familiarize with the task and the alternation of adaptation and test phases.

Data analyses

Test trials for which no button press (0.8% of all trials) or response (1.4% of all trials) was registered were excluded from the analyses.

The proportion of detected test delays as a measure for delay detection performance was calculated separately for each participant and experimental condition. These data were then modeled by fitting psychometric functions in form of a cumulative Gaussian distribution function using the Psignifit toolbox version 4 (Schütt et al., 2016) for Python version 3.8.5 (Python Software Foundation[1]). Detection thresholds (i.e., the delay that was detected in 50% of all trials) and slopes (evaluated at the detection thresholds) were derived as summary measures from the psychometric functions. While the detection thresholds serve as a measure for the general delay detection performance (with lower values indicating better performance), the slopes represent the increment in detected delays when the amount of delay increases and thus indicate the discrimination ability between delay levels.

1 https://www.python.org/

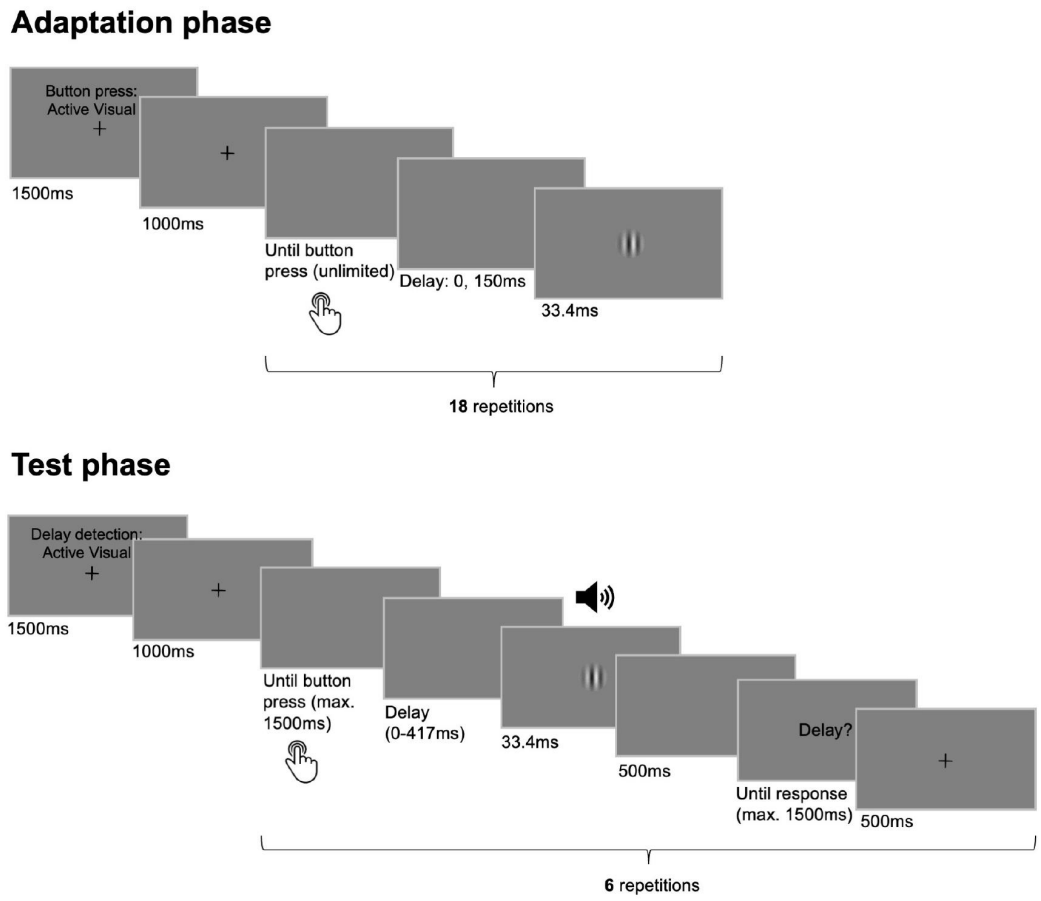

FIGURE 1
Trial sequence and timing of events. Participants went through multiple pairs of adaptation and test phases. During adaptation phases 18 button presses had to be performed either actively or they were elicited passively. Each button press was followed by the presentation of the visual outcome that appeared either undelayed with respect to the button press or that was delayed by 150 ms. In the following test phases composed of six test trials each, participants pressed the button once actively, or the button press was initiated passively. Here, the outcome followed the button press with one of six delay levels (0–417 ms) and participants' task was to judge the presence of a delay in each trial. While the sensory modality of the outcome was always visual during adaptation phases it could be visual or auditory during test phases.

In line with the pre-registered analysis plan[2], repeated-measures ANOVAs were performed to examine effects of temporal recalibration. But to get a more direct insight on the influence of the experimental manipulations on recalibration, the adaptation delay was not included as a factor in the analysis, but the TRE was used as a dependent variable. The TRE was quantified as the difference in detection thresholds in conditions with the adaptation delay of 150 ms vs. 0 ms. Positive values indicate a rightward shift of the psychometric function which corresponds to a decrease in delay detection performance after adaptation to the 150 ms delay as expected for temporal recalibration. Further, to better differentiate between the influence of ctDCS on the TRE in both test modalities, two repeated-measures ANOVAs were performed separately for the visual and auditory test modality, each including the factors *stimulation* and *movement type*. Similarly, repeated-measures ANOVAs were performed on the difference in slopes of conditions with 0 ms vs. 150 ms adaptation delay since temporal recalibration might also result in a lower ability to discriminate between delay levels represented in flatter slopes of the psychometric functions. *Post hoc* two-samples *t*-tests were used for significant main and interaction effects to inspect differences between movement types and stimulation conditions compared to the sham control condition. Additionally, in case of significant differences in the TRE between conditions, one-sample *t*-tests were further used to examine whether the respective TREs differed significantly from zero. As the TRE is defined as decreased delay detection performance after exposure to the adaptation delay of 150 ms, one-tailed *t*-tests were used.

2 https://osf.io/qhryx

For effects pointing in the negative direction, only descriptive results are reported. All ANOVAs and *t*-tests were conducted with JASP (Version 0.14.1; JASP Team, 2020).

Although the TRE has often been defined in terms of a shift in detection thresholds of psychometric functions fitted to the delay detection rates (Stetson et al., 2006; Stekelenburg et al., 2011; Tsujita and Ichikawa, 2012; Rohde and Ernst, 2013; Cai et al., 2018; Arikan et al., 2021), this analysis is limited to the fact that only the shift in the overall detection performance across all assessed delay levels is considered. However, it is also conceivable that shifts in detection performance after exposure to the constant adaptation delay are constrained to a specific delay range and might occur, e.g., only at the most uncertain delays or at delays which are close to the adaptation delay. After temporal recalibration these specific delays might be less likely to be detected even without a general shift in detection thresholds.

In that sense, we further explored the distribution of the TRE across the tested delay levels by generalized estimating equations (GEE) analyses using IBM SPSS Statistics (Version 25.0). Here, the difference in the percentage of detected delays between 150 vs. 0 ms adaptation delay conditions served as measure for the TRE which can be computed separately for each test delay level. For the regression coefficients an AR (1) working correlation structure and robust (sandwich) covariance estimators were used. The analysis was performed separately for visual and auditory test modalities and the respective models were composed of the factors *stimulation* (anodal, cathodal, dual-hemisphere, sham ctDCS), *movement type* (active, passive), and *test delay* (0, 83, 167, 250, 333, 417 ms). A full factorial model was used with all main and interaction effects of the included factors and the TRE was modeled with a linear link function. If indicated, post-hoc tests for differences in TRE between active and passive conditions as well as between stimulation conditions and the sham control condition were then calculated to further explore the direction of effects. Since this latter analysis was only done exploratory to investigate the potential influence of the test delay in the emergence of the TRE and *post hoc* tests were only calculated for significant main and interaction effects, the *p*-values reported here are not corrected for multiple comparisons.

Finally, differences in perceived side effects between the ctDCS stimulation conditions were assessed by paired-samples *t*-tests using the average score of all questionnaire items.

Results

Effects of temporal recalibration

Repeated-measures ANOVAs were performed on the TRE (difference in detection thresholds of 150 ms vs. 0 ms adaptation delay conditions) for each test modality (see section 2 in **Supplementary material** for a full overview of all effects of these analyses). For the visual modality, no main or interaction effects reached significance (all $p > 0.43$) suggesting that ctDCS did not influence the visuomotor or visuo-tactile TRE. Notably, according to one-sample *t*-tests, the TREs in the visual modality were also not significantly greater than zero in the sham control condition, neither the visuomotor TRE in active [$M = 11.518$, $SD = 41.310$, $t(21) = 1.308$, $p = 0.103$, $d = 0.279$, one-tailed], nor the visuo-tactile TRE in passive conditions [$M = -12.439$, $SD = 58.020$].

For the auditory test modality, the interaction of *stimulation* and *movement type* was significant [$F(3,63) = 2.810$, $p = 0.047$, $\eta_p^2 = 0.118$; see **Figure 2** for an overview of the psychometric functions fitted for these conditions]. According to post-hoc paired-samples *t*-tests, in passive conditions, anodal ctDCS increased the audio-tactile TRE compared to sham ctDCS [$t(21) = 3.090$, $p = 0.006$, $d = 0.659$, two-tailed; according to a Bonferroni corrected alpha of 0.05/3 (i.e., corrected for the three comparisons of ctDCS vs. sham) = 0.016; see **Figure 3A**]. More precisely, as further explored by one-sample t-tests, the audio-tactile TRE after anodal ctDCS was significantly greater than zero [$M = 14.174$, $SD = 36.473$, $t(21) = 1.823$, $p = 0.041$, $d = 0.389$, one-tailed], but was absent after sham ctDCS [$M = -22.293$, $SD = 46.460$].

No other stimulation condition elicited a TRE significantly different from the sham control condition for neither passive [cathodal vs. sham ctDCS: $t(21) = 1.522$, $p = 0.143$, $d = 0.324$; dual-hemisphere vs. sham ctDCS: $t(21) = 1.464$, $p = 0.158$, $d = 0.321$] nor active movement conditions [anodal vs. sham ctDCS: $t(21) = -0.232$, $p = 0.819$, $d = -0.049$; cathodal vs. sham ctDCS: $t(21) = -0.599$, $p = 0.556$, $d = -0.128$; dual-hemisphere vs. sham ctDCS: $t(21) = -0.390$, $p = 0.701$, $d = -0.083$].

Repeated-measures ANOVAs on the difference in slopes of the psychometric functions (between 0 ms vs. 150 ms adaptation delay conditions) did not reveal any significant main or interaction effects for either of the two test modalities (visual: all $p > 0.51$, auditory: all $p > 0.37$). Note that results derived from an alternative analysis approach with similar GEE analyses as described in section "Data analyses" including the factors *stimulation* and *movement type* led to comparable findings for all reported effects.

Distribution of temporal recalibration effects across test delays

We further explored stimulation-dependent modulations of the TRE across the delay levels used in the test phases by GEE analyses including the factors *test delay*, *stimulation,* and *movement type*. The TRE was here defined as difference in the percentage of detected delays between 150 and 0 ms adaptation delay conditions as this measure can be derived for each test delay level individually. Here, interaction effects including the

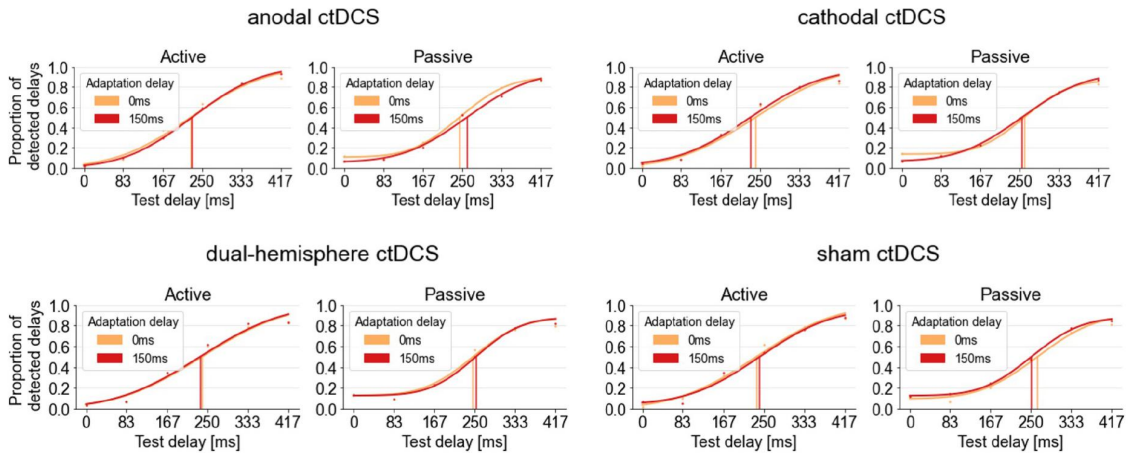

FIGURE 2
Psychometric functions fitted to the delay detection data for the auditory test modality. Group psychometric functions are displayed separately for each stimulation condition, movement type and adaptation delay. A TRE corresponds to a rightward shift of the psychometric functions for the 150 ms (red) compared to the 0 ms (orange) adaptation delay condition indicating decreased delay detection performance and thus temporal recalibration. Psychometric functions are displayed on group level only for illustration purposes. For the statistical analyses, the functions were fitted to and summary measures were derived from participants' individual detection rates.

factors *stimulation* and *test delay* were of interest (see section 3 in **Supplementary material** for a full overview of all effects of these analyses).

For the visual test modality, again, none of the interaction effects reached significance (all $p > 0.11$). The analyses for the auditory test modality revealed a significant interaction of *stimulation* and *test delay* [Wald Chi-Square (df = 15) = 82.104, $p < 0.001$] indicating that stimulation-dependent effects on the TRE differed here depending on the amount of temporal delay presented in the test phase. *Post hoc* tests specified that the facilitation of the TRE by anodal ctDCS compared to sham manifested for the test delay closest to the adaptation delay [167 ms, anodal vs. sham ctDCS: mean difference = 9.575, standard error = 3.527, df = 1, $p = 0.007$]. Again, the TRE was significantly greater than zero after anodal ctDCS for this delay level [$M = 5.855$, $SD = 12.403$, $t(21) = 2.214$, $p = 0.019$, $d = 0.472$, one-tailed] which was absent in the sham condition [$M = -3.720$, $SD = 12.981$]. Moreover, adaptation to the constant delay of 150 ms was associated with fewer false alarms (i.e., fewer delay responses for the undelayed condition) after anodal [0 ms, anodal vs. sham ctDCS: mean difference = 5.370, standard error = 2.497, df = 1, $p = 0.031$] and cathodal ctDCS [0 ms, cathodal vs. sham ctDCS: mean difference = 5.411, standard error = 2.752, df = 1, $p = 0.049$] compared to the sham control condition. TREs were significantly greater than zero after anodal as well as cathodal ctDCS at this delay level [anode: $M = 2.719$, $SD = 6.213$, $t(21) = 2.053$, $p = 0.026$, $d = 0.438$, one-tailed; cathode: $M = 2.760$, $SD = 7.094$, $t(21) = 1.825$, $p = 0.041$, $d = 0.389$, one-tailed], but not present after sham ctDCS [$M = -2.652$, $SD = 9.776$].

Finally, the interaction *stimulation* × *movement type* × *test delay* was significant [Wald Chi-Square (df = 15) = 37.183, $p = 0.001$]. Thus, we inspected the *post hoc* comparisons of anodal compared to sham ctDCS to investigate whether the faciliatory effects of anodal ctDCS differed across the range of test delays depending on the movement type. Accordingly, the facilitation of the effect for the 167 ms test delay by anodal ctDCS was specific to the audiomotor TRE in active movement conditions [active, 167 ms, anodal vs. sham ctDCS: mean difference = 10.498, standard error = 4.389, df = 1, $p = 0.017$; see **Figure 3B**]. According to a one-sample *t*-test, the audiomotor TRE after the anodal stimulation was significantly greater than zero [anode: $M = 6.953$, $SD = 17.556$, $t(21) = 1.858$, $p = 0.039$, $d = 0.396$, one-tailed; sham: $M = -3.544$, $SD = 20.423$], and did not differ significantly from the audio-tactile TRE induced for this delay level in passive conditions [anodal ctDCS, 167 ms, active vs. passive: mean difference = 2.197, standard error = 5.113, df = 1, $p = 0.667$].

In contrast, in passive movement conditions, the facilitation by anodal ctDCS occurred at a larger test delay level of 333 ms [passive, 333 ms, anodal vs. sham ctDCS: mean difference = 12.446, standard error = 5.081, df = 1, $p = 0.014$]. According to a one-sample *t*-test the audio-tactile TRE was significant here after anodal ctDCS [anode: $M = 8.144$,

$SD = 17.362$, $t(21) = 2.200$, $p = 0.020$, $d = 0.469$, one-tailed; sham: $M = -4.302$, $SD = 20.830$] and differed also weakly from the audiomotor TRE for this delay level in active conditions [anodal ctDCS, 333 ms, active vs. passive: mean difference = −9.280, standard error = 5.160, df = 1, $p = 0.072$].

Side effects of the stimulation

Overall, the magnitude of perceived side effects due to the tDCS stimulation was rated to be low [anodal ctDCS: mean = 1.429, $SD = 0.346$; cathodal ctDCS: mean = 1.326; $SD = 0.358$; dual-hemisphere ctDCS: mean = 1.209, $SD = 0.243$; sham ctDCS: mean = 1.253; $SD = 0.188$]. The comparison of perceived side effects between the ctDCS conditions compared to the sham control condition revealed a significant difference for anodal ctDCS [$t(21) = 3.106$, $p = 0.005$, $d = 0.662$, two-tailed; according to a Bonferroni corrected alpha of 0.05/6 (i.e., corrected for the pair-wise comparisons of all stimulation conditions) = 0.008]. There were no significant differences for the comparison of sham stimulation against cathodal [$t(21) = 1.089$, $p = 0.288$, $d = 0.232$, two-tailed] or dual-hemisphere ctDCS [$t(21) = -0.909$, $p = 0.373$, $d = -0.194$, two-tailed]. Furthermore, ratings for perceived side effects were significantly higher after anodal compared to dual-hemisphere ctDCS [$t(21) = 3.477$, $p = 0.002$, $d = 0.741$, two-tailed]. However, control analysis including side effects as covariate of no interest suggest that main results cannot be explained by side effects alone (see section 4 in **Supplementary material**).

Discussion

The complex and constantly changing sensory environment calls for flexible recalibration of the predicted timing between actions and their sensory outcomes. Since the neural underpinnings of sensorimotor temporal recalibration are largely unknown this study investigated the role of the cerebellum in this process by means of ctDCS. In an adaptation phase, participants were exposed to constant delays of 150 ms between actively or passively generated button presses and visual sensory outcomes while receiving either anodal, cathodal, dual-hemisphere or sham ctDCS. A delay detection task assessed if and to what extent the constant delays triggered a TRE in the visual and auditory modality. The results indicated that the exposure to constant delays did not result in a visuomotor or visuo-tactile TRE. However, a TRE occurred after anodal ctDCS in the auditory modality that was absent in the sham control condition. This effect was differentially distributed across the delay levels in the delay detection task depending on the movement type. In active conditions, anodal ctDCS facilitated the audiomotor TRE compared to sham stimulation at the delay level closest to the delay during the adaptation phase (167 ms), but at a larger delay level (333 ms) for the audio-tactile TRE in passive conditions.

These findings suggest a general role of the cerebellum in potentially supra-modal temporal recalibration across sensorimotor and perceptual domains, but the differential manifestation of the effect across tested delay levels in active and passive conditions point to differences in the underlying mechanisms depending on the availability of action-based predictions.

Effects of cerebellar transcranial direct current stimulation on temporal recalibration depending on the movement type (active versus passive)

We expected ctDCS to influence action-based prediction mechanisms in the cerebellum and therefore the TRE in both visual and auditory modalities specifically in active movement conditions. Indeed, in the auditory test modality anodal ctDCS facilitated the occurrence of the TRE compared to the sham control condition. Surprisingly however, this stimulation-dependent effect was not specific to active conditions, but an audio-tactile TRE appeared across the tested delay levels only in passive conditions. However, an inspection of the faciliatory effect of anodal ctDCS for the individual test delay levels revealed that in active conditions an audiomotor TRE could be elicited by anodal ctDCS specifically at the 167 ms delay which was the delay level closest to the constant delay of 150 ms used during the adaptation phases. In contrast, in passive conditions, a significant facilitatory effect of anodal ctDCS on the audio-tactile TRE occurred at the later 333 ms delay level, at which the influence of the same stimulation on the audiomotor TRE had already decreased.

This raises the question of why the effect of ctDCS generally extended to inter-sensory temporal recalibration and therefore also appeared in passive conditions, and what reason might underlie the different manifestation of the effects across the range of tested delays depending on the movement type.

Facilitation of temporal recalibration by anodal cerebellar transcranial direct current stimulation is not limited to the sensorimotor context

Since anodal tDCS is known to enhance cortical excitability (Nitsche and Paulus, 2000) the stronger recalibration effects observed in this stimulation condition are likely to be attributed to the facilitation of cerebellar-dependent mechanisms underlying temporal recalibration, e.g., by increasing the sensitivity to temporal prediction errors. Even though

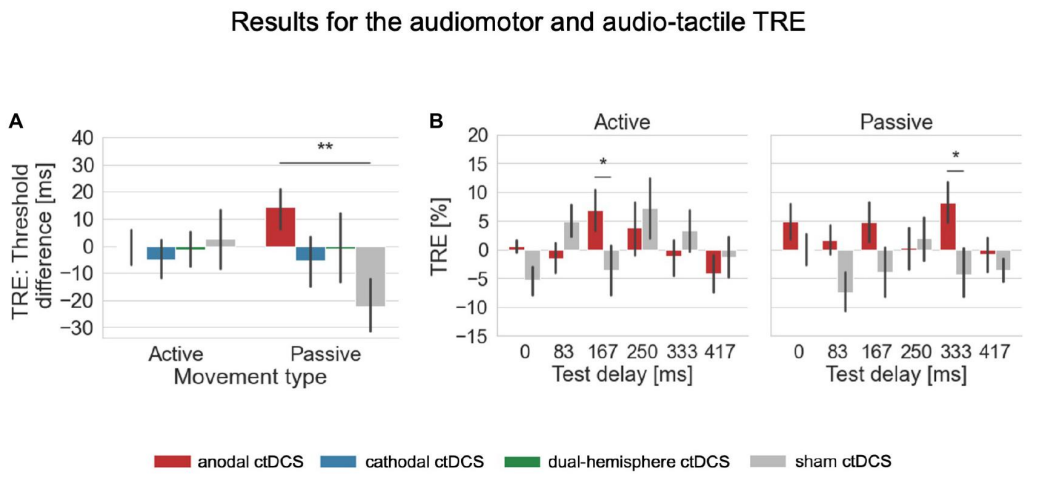

FIGURE 3
Results for the audiomotor and audio-tactile TRE. **(A)** For the overall shift in detection performance after temporal recalibration, the TRE was defined as the difference in detection thresholds derived from the fitted psychometric functions in conditions with the adaptation delay of 150 ms vs. 0 ms (where positive values indicate a rightward shift of the psychometric functions and thus worse performance after exposure to the 150ms delay indicating temporal recalibration into the expected direction). The audio-tactile TRE (in passive conditions) was here facilitated by anodal ctDCS compared to the sham control condition. **(B)** For a further exploration of the TRE across individual tested delay levels, the TRE was defined separately for each test delay as the difference in the percentage of detected delays between 0 and 150 ms adaptation delay conditions. For the audiomotor TRE (in active conditions), a facilitation by anodal ctDCS compared to sham occurred only for the test delay of 167 ms which was the one closest to the adaptation delay. For the audio-tactile TRE, the faciliatory effect was strongest at the larger test delay level of 333 ms. There were no significant main or interaction effects in both types of analyses on the TRE in the visual modality. Error bars indicate standard errors of the means. *$p < 0.05$, **$p < 0.01$.

this faciliatory effect was distributed differently across the tested delay levels in active and passive conditions, the fact that it was generally not limited to the active conditions, as we originally expected, but occurred even stronger in passive ones, suggests a role of the cerebellum not exclusively in sensorimotor but also in inter-sensory temporal recalibration.

Indeed, multiple studies support the involvement of the cerebellum in a variety of processes beyond sensorimotor functions ranging from perceptual processing (Baumann et al., 2015) and performance monitoring across domains of action, perception, and cognition (Peterburs and Desmond, 2016) to higher-level cognitive functions (Koziol et al., 2014). Traditionally, predictive processing in the cerebellum is often associated specifically with action-based predictions or with the detection of mismatches between expected and observed action-outcomes (Wolpert et al., 1998; Blakemore et al., 2001; Straube et al., 2017b; Arikan et al., 2019; van Kemenade et al., 2019). However, since cerebellar pathways do not only connect to motor areas, but also to a variety of other cortical areas including sensory regions (Strick et al., 2009; Sultan et al., 2012; Baumann et al., 2015), the cerebellum can be regarded as suitable for generating and updating predictive models in both motor and perceptual domains (Kotz et al., 2014). In this line it has been proposed that very similar mechanisms are at play for generating purely sensory predictions as for sensorimotor predictions (Schubotz, 2007) and that the posterior cerebellum completes similar tasks as the forward model in the action domain, but for perceptual processes with a timing aspect (O'Reilly et al., 2008). Indeed, the cerebellum has been shown to be relevant for temporal predictions also for action-independent sensory events and for the detection of mismatches between predicted and observed inter-sensory timing (Moberget et al., 2008; O'Reilly et al., 2008; Beudel et al., 2009; Coull et al., 2013; Kotz et al., 2014). In similar veins, although the cerebellum is commonly known for motor adaptation and thus for prediction adaptation in the action domain (Tseng et al., 2007; Synofzik et al., 2008; Izawa et al., 2012; Schlerf et al., 2012; Cao et al., 2017), recalibration of the expected timing of purely perceptual events could also be associated with the cerebellum, which suggests an important contribution to temporal recalibration of predictive models upon sensory prediction errors, but not exclusively for action-related processes (Roth et al., 2013).

Thus, in our study anodal ctDCS could have facilitated temporal recalibration particularly in an inter-sensory context by promoting the updating of the expected relative timing between tactile and auditory sensory signals. This adds evidence to the importance of the cerebellum for temporal recalibration of predictive mechanisms, however not exclusively within the motor domain as previously suggested (e.g., Cao et al., 2017), but also within the perceptual domain.

Anodal cerebellar transcranial direct current stimulation differentially impacts delay perception after temporal recalibration in the sensorimotor versus inter-sensory context

If anodal ctDCS facilitated the TRE identically in passive and active conditions, then this would suggest that the TRE in active conditions can be explained by the facilitation of inter-sensory recalibration mechanisms alone, since the additional availability of the motor commands would not provide any further explanatory contribution to the emergence of the effect in this condition. But notably, although anodal ctDCS facilitated the TRE in the auditory modality for both movement types, differences emerged in the manifestation of the effect when it is considered separately for the different delay levels used in the test phases. Thus, there may be differences in the exact underlying temporal recalibration mechanisms depending on the movement type.

For active conditions, the fact that the facilitation of the TRE by anodal ctDCS compared to sham occurred precisely at the delay level closest to the adaptation delay may point to a particularly accurate recalibration mechanism. This could be related to the fact that sensory action-outcomes are considered as particularly well predictable due to the availability of information on the motor commands (Blakemore et al., 1998; Wolpert et al., 1998; Elijah et al., 2016; Cao et al., 2017). It has been shown that this can result in sensory stimuli generated by self-induced actions being perceptually enhanced and leading to sharper neural representations compared to passively elicited sensory events (Yon et al., 2018). This is also reflected in our data in higher delay detection performance in active compared to passive conditions for auditory action-outcomes (see section 5 in **Supplementary material**). Such an enhanced perception of actively produced action-outcomes could also imply the generation of more precise error signals when a constant delay indicates a discrepancy between the temporal prediction and the actual occurrence of the outcome. Compared to passive conditions, the facilitation of cerebellar recalibration mechanisms could therefore also lead to a very precise shift in the prediction about the temporal occurrence of the action-outcome, affecting delay detection responses in the test phases only at the level close to the adapted delay. Thus, the facilitation of the audiomotor TRE by anodal ctDCS reaches significance only for the 167 ms delay while it decreases noticeably for larger delay levels.

Such a precise recalibration mechanism could be particularly important in a sensorimotor context, because in real-life situations, changes in the relative timing between actions and their outcomes have direct implications for motor behavior, as movements may need to be adjusted accordingly. Thus, precise sensorimotor temporal recalibration could be important to still enable accurate motor behavior under flexibly changing environmental conditions.

For passive conditions on the other hand, faciliatory effects of anodal ctDCS on the audio-tactile TRE appeared at larger delays (i.e., 333 ms). In part, this could be related to the fact that detection performance was generally worse in passive compared to active conditions. It might thus be that the perceptual performance at medium-size delay levels was generally too low for a strong recalibration effect to manifest here. Only at larger delay levels the recalibrated inter-sensory timing leads to significant decreases in delay detection performance. Nonetheless, the audio-tactile TRE induced by anodal ctDCS appears somewhat more distributed across the delay range, which becomes also apparent in the fact that the audio-tactile and audiomotor TRE do not differ significantly at the earlier 167 ms delay. But since the audiomotor TRE after anodal ctDCS decreases across delays after its early peak at the 167 ms delay, the relative impact of anodal ctDCS grows stronger for the audio-tactile TRE, resulting in significant differences between the audiomotor and audio-tactile TRE at the larger delay level of 333 ms. This somewhat broader distribution of the audio-tactile TRE after anodal ctDCS could also explain why it is overall, i.e., across all delay levels, stronger than the audiomotor TRE.

In conclusion, anodal ctDCS facilitated both the audio-tactile and the audiomotor TRE, but the differential manifestation of the effect across delay levels suggests the additional involvement of action-based predictive mechanisms for the emergence of the effect in active conditions potentially leading to a more precise audiomotor TRE. It should be noted though that these delay-dependent effects appeared to be rather weak and *post hoc* tests of this exploratory analysis are uncorrected for the multiple testing at each of the six delay levels and should therefore be interpreted with caution. Although the exact explanation for and interpretability of the differential manifestation of the sensorimotor and inter-sensory TRE as well as the overall rather weak recalibration effects in this study remains open, our findings nevertheless highlight the importance of not just focusing on the overall shift in perceptual thresholds (evaluated across all tested delay levels) during the investigation of temporal recalibration, but also at the exact manifestation of the effect at different delays.

Effects of cerebellar transcranial direct current stimulation on temporal recalibration depending on the sensory modality (visual versus auditory)

Since predictions about sensory action-outcomes are assumed to be generated on a supra-modal level, we expected that a TRE would manifest after the visual recalibration procedure in the visual, but also in the auditory test modality

in active movement conditions, and that anodal ctDCS would further boost these effects.

Surprisingly, however, without the influence of ctDCS, i.e., in the sham control condition, a TRE did not manifest for the visual modality in either active or passive conditions and did not transfer to the auditory modality either. Only after anodal ctDCS recalibration occurred in the auditory modality which was still absent in visual conditions. This raises the question of the reason for the resistance of the visual modality to behaviorally relevant recalibration in our study, as well as why the constantly delayed visual stimulus during adaptation phases nevertheless produced an auditory TRE after anodal ctDCS.

Resistance of the visual modality to temporal recalibration

Although recalibration of the perceived timing between actions and their visual sensory outcomes could be demonstrated in a range of previous studies (Cunningham et al., 2001; Heron et al., 2009; Keetels and Vroomen, 2012; Rohde and Ernst, 2013; Sugano et al., 2016; Aytemür et al., 2017; Arikan et al., 2021), a certain robustness of visual perception in the context of sensorimotor temporal recalibration has been reported earlier for instance by the absence of a behaviorally relevant visual sensorimotor TRE (Sugano et al., 2017). Additionally, an auditory sensorimotor TRE did often not transfer to the visual modality (Sugano et al., 2012; Arikan et al., 2021) while the opposite could frequently be demonstrated (Heron et al., 2009; Sugano et al., 2010, 2012; Arikan et al., 2021). Additionally, other phenomena based on similar sensorimotor prediction mechanisms like the intentional binding effect, i.e., an implicit measure for the experience of agency over action-outcomes, was found to be weaker for visual compared to auditory stimuli which might be related to the rather inaccurate time perception in the visual compared to the auditory modality (Ruess et al., 2018).

Similarly, in the context of inter-sensory timing, synchrony perception of visuo-tactile stimuli (as it is relevant for passive conditions in our study) has been shown to have rather low resolution as compared to, for example, audio-tactile stimuli (Fujisaki and Nishida, 2009). This implies that short temporal mismatches between visual and tactile sensory events might not be reliably detected and that the temporal relationship between both modalities could therefore be less prone to recalibration and its modulation by ctDCS (Hanson et al., 2008; but see: Harrar and Harris, 2008; Keetels and Vroomen, 2008).

Thus, in our study, the short temporal lag of 150 ms during the adaptation phase could have caused too noisy or unreliable prediction errors in the visual modality to induce recalibration of upcoming sensorimotor predictions or recalibration of inter-sensory timing and thus a behaviorally observable TRE in active or passive movement conditions. Nevertheless, we cannot rule out the possibility that the effects of temporal recalibration in general, as well as the effect of ctDCS on temporal recalibration, were so small for the visual modality that we are lacking sufficient statistical power in this study to detect these effects.

Facilitation of the temporal recalibration effect in auditory conditions suggests a supra-modal mechanism

The emergence of an audiomotor and audio-tactile TRE even though the sensory modality during the adaptation phase was visual would point to the recalibration of predictive or perceptual mechanisms that operate on a supra-modal level and not in modality-specific circuits. The fact that a TRE occurred indeed only in the auditory modality after anodal ctDCS in our study might be related to a generally more precise temporal perception and discrimination performance for auditory stimuli (Grondin, 2010; Grahn, 2012). This also implies a higher predictability of the temporal occurrence of auditory stimuli and predictability of sensory signals is known to be important for temporal recalibration to occur (Rohde et al., 2014).

Thus, our results suggest that the delayed visual stimulus in the adaptation phases still resulted in an updating of the perceived relative timing between the active or passive button movement and the feedback presentation, even though its effects were not measurable as TRE in the visual modality possibly because of the rather imprecise temporal perceptual acuity. However, with the faciliatory influence of anodal ctDCS, prediction error processing increased and resulted in a TRE now assessable in the auditory modality possibly due to the temporally more accurate perception.

Notably, we originally expected that anodal ctDCS would mainly promote the modality-transfer of the TRE in active conditions due to the facilitation of supra-modal sensorimotor recalibration mechanisms in the cerebellum, but the effect extended to passive conditions and thus to inter-sensory recalibration. Cross-modal transfer of the TRE in an inter-sensory context has also been shown in previous studies (di Luca et al., 2009; Arikan et al., 2021) and speaks here for general temporal recalibration mechanisms in the cerebellum that operate on a supra-modal level.

Nevertheless, it should be noted that due to the absence of effects in the visual modality conclusions about supra-modal recalibration mechanisms should be made with caution. Still, the fact that the visuomotor and visuo-tactile recalibration procedure could trigger an audiomotor or audio-tactile TRE, respectively, points to recalibration mechanisms in the cerebellum evoked by anodal ctDCS that are not modality specific.

Limitations and outlook

Some limitations of the study design and interpretability of the results should be considered. The potential of ctDCS in affecting performance in a variety of tasks has been demonstrated in an increasing number of studies (Grimaldi et al., 2016). Also in our study, anodal ctDCS appeared to facilitate recalibration effects in the auditory modality. It has to be noted though that the spatial resolution of this stimulation technique is known to be rather low. Therefore, we do not know exactly which parts of the cerebellum were targeted by the stimulation in our study, whether the effect was similar across subjects, or whether the stimulation effects have extended to nearby areas. At the same time, the anatomy and functionality of the cerebellum are very complex and different cerebellar areas are involved in different motor, perceptual or cognitive processes (Koziol et al., 2014; Baumann et al., 2015). This issue may explain why there were rather large individual differences in the obtained effects (as it becomes evident by the large standard errors) and may also provide an explanation for why we found effects of anodal ctDCS not only in active but also in passive conditions, since parts of the cerebellum, i.e., the posterior cerebellum, have been suggested as particularly important for recalibration in a purely sensory context (Roth et al., 2013). The use of high-definition tDCS may help to achieve more spatially defined effects in the future and thus to further disentangle contributions of the cerebellum to sensorimotor and inter-sensory temporal recalibration, respectively.

Furthermore, although anodal tDCS is generally thought to increase cortical excitability, the evidence for polarity-dependent effects of tDCS on the cerebellum is heterogeneous. While some studies find polarity-dependent effects in the expected direction (Galea et al., 2009; Jayaram et al., 2012), others failed to find a difference between anodal and cathodal ctDCS (Shah et al., 2013). This could be explained in part by the complex anatomy of the cerebellum, in which the orientation of neurons in different cerebellar areas may differ with respect to the induced electric fields (Grimaldi et al., 2016). Indeed, our findings don't show a clear pattern with respect to polarity-specific effects, as only anodal ctDCS had an impact on temporal recalibration. Although the reason for this remains open, it cannot be excluded that the perceived side effects of the tDCS stimulation which were particularly prominent after anodal ctDCS contributed to the emergence of behavioral effects specifically in this condition. Nonetheless, the specific and expected facilitation of recalibration effects by anodal ctDCS still argues for a polarity-dependent influence of the stimulation and therefore highlights anodal ctDCS as a potentially promising tool for modulating temporal recalibration in future research. However, the complex effects of this study also stress the importance of identifying additional brain areas next to the cerebellum which are involved in temporal recalibration mechanisms, e.g., by using fMRI, and that could constitute promising stimulation sites in future research on this topic.

It has to be noted that the recalibration effects in our study were overall rather small and not present without the facilitating influence of anodal ctDCS, i.e., in the sham control condition. The audio-tactile TRE in passive conditions seems to point even into the opposite direction than one would expect. Even though the reason for this remains unclear based on our data, considerably smaller shifts in temporal perception during recalibration compared to the magnitude of the actual adaptation delay has been reported previously (e.g., Stetson et al., 2006). The particularly weak effects in this study may indicate features in our experimental design that made pronounced temporal recalibration difficult to occur.

First, the size of the recalibration effect, or even the occurrence of the effect itself, could be related to the amount of attention deployed to the sensory stimuli during adaptation. For example, it has been reported that awareness of the constant delay between action and visual outcome is necessary to trigger the visual sensorimotor TRE (Tsujita and Ichikawa, 2016). Furthermore, the magnitude of recalibration to an asynchrony between visual and auditory sensory signals has been shown to increase particularly when attention is explicitly directed to the temporal relationship between the sensory stimuli as opposed to other stimulus features (Heron et al., 2010). In our study, we asked participants to pay close attention to the sensory stimuli also during the adaptation phases. However, we cannot directly infer how much attention the sensory stimuli actually received, as participants had no other task during adaptation than to press the button actively or let it be passively moved and to observe the visual stimuli. Thus, it is unclear whether too little attention to the stimuli during adaptation can contribute to an explanation of the small recalibration effects. In future studies, attention to the sensory stimuli could be more explicitly controlled by, for example, implementing an oddball task during the adaptation phase that requires close attention to the stimuli to complete the task.

Second, it could be argued that recalibration effects that have built up over the course of an adaptation phase decay relatively quickly over the course of a test phase, so that the last trials of the test phase are less affected by recalibration, resulting in lower overall recalibration effects. To counteract this, previous studies have used so-called top-up trials, in which subjects were quickly exposed to the adaptation delay again before each test trial (e.g., Rohde and Ernst, 2013). However, since our test phase consisted of only six test trials followed by another adaptation phase, we think it is unlikely that effects of recalibration wore off so quickly and a similar experimental procedure has also reliably led to recalibration effects before (Arikan et al., 2021).

Lastly, within our experimental procedure, conditions with the same adaptation delay (0 vs. 150 ms) were each presented in a block during and after stimulation, resulting in multiple changes of the adaptation delay within a session. While it was

intended to challenge the flexibility of recalibration mechanisms with this procedure, it is conceivable that the more frequent switching between adaptation delays in our experiment caused spill-over effects, thereby decreasing the overall size of the TRE or the time window available for the effect to build up before the adaptation delay changed again might have been too short. However, the rapid recalibration effects that could be observed even on a trial-by-trial basis at least in the inter-sensory domain (van der Burg et al., 2015; Lange et al., 2018) argue against that. Thus, the fact that anodal ctDCS was still able to elicit behaviorally relevant recalibration underlines the role of the cerebellum in flexibly adapting to just such rapid changes in the temporal relationship between an action and its sensory outcome or between the senses.

The prospect that anodal ctDCS may improve sensorimotor adaptation, has implications for neurological and psychiatric disorders known to have impairments in this process and potentially also in related processes like motor adaptation and learning. Patients with cerebellar ataxia for instance show impairments in the ability to adapt to visuomotor perturbations (Tseng et al., 2007) and exhibit problems in locomotor control, i.e., gait ataxia (Ilg and Timmann, 2013). Since the potential of anodal ctDCS for improving certain motor functions in such patient groups has already been demonstrated (Benussi et al., 2015, 2021; Wang et al., 2021), it may also be a promising tool to support rehabilitation of sensorimotor adaptation mechanisms, which are of great importance for motor performance in a variety of everyday tasks. One critical example is locomotion, whose successful functioning depends to a great extent on temporal perceptual recalibration mechanisms (Gonzalez-Rubio et al., 2019) as well as cerebellar processes (Morton and Bastian, 2006; Jayaram et al., 2012; Jossinger et al., 2020). Our results highlight the importance of the cerebellum in recalibration of sensorimotor and perceptual timing and therefore also stress its promising role as target for non-invasive brain stimulation in the context of rehabilitation of locomotor adaptation functions in these patients. First studies already demonstrated the efficacy of anodal ctDCS on posture and gait in this patient group (Benussi et al., 2015), providing a promising basis for future investigations of the specific conditions under which ctDCS may lead to improvements and long-lasting effects also in processes such as locomotor adaptation.

Beyond that, patients with schizophrenia spectrum disorder have been shown to have dysfunctions in forward model based predictive mechanisms (Ford et al., 2001; Bartolomeo et al., 2020; Uhlmann et al., 2020). Such a dysfunction, and especially the failure to adequately recalibrate internal model predictions to changes in the environment may underly symptoms of auditory hallucinations, i.e., when one's inner speech is misinterpreted as externally generated, or passivity phenomena, i.e., when outcomes of own actions are perceived as externally produced (Pynn and DeSouza, 2013). Therefore, based on the findings of this study, a promising avenue for future research is to investigate whether anodal ctDCS can improve recalibration mechanisms and thus symptomatology in patients with schizophrenia spectrum disorder.

Conclusion

The present study investigated the impact of ctDCS on visuomotor and visuo-tactile temporal recalibration and the manifestation of its effect on visual and auditory delay detection performance. We demonstrated that anodal ctDCS facilitated the TRE in the auditory modality in both active and passive conditions which points to a general role of the cerebellum in temporal recalibration across sensorimotor and perceptual domains. The fact that the effect occurred in the auditory modality even though the adaptation modality was visual further suggests that this temporal recalibration mechanism operates on a supra-modal level. The differential manifestation of the effect across tested delay levels in active and passive conditions, however, indicates a more precise cerebellar-dependent temporal recalibration mechanism in a sensorimotor context possibly due to the additional recalibration of action-based predictions.

Together these findings emphasize the role of the cerebellum in potentially supra-modal temporal recalibration mechanisms in both perceptual and sensorimotor domains, but there might be differences in the precision of recalibration depending on the availability of action-based predictions. Additionally, despite the complex pattern of observed effects, our findings suggest that anodal ctDCS can be a promising tool for facilitating effects of temporal recalibration in the sensorimotor, but explicitly also in the inter-sensory domain.

Data availability statement

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found below: doi: 10.5281/zenodo.6861087 (Zenodo), https://osf.io/qhryx (OSF preregistration).

Ethics statement

The studies involving human participants were reviewed and approved by Ethics Commission of the Medical Faculty of University of Marburg, Germany. The patients/participants provided their written informed consent to participate in this study.

Author contributions

BS and CS conceived and designed the study, and discussed and interpreted the data. CS was responsible for data acquisition and analysis, and wrote the manuscript. Both authors revised and approved the submitted version of the manuscript.

Funding

This research project was supported by the German Research Foundation (DFG project number: 286893149, *STR1146/9-2, STR1146/15-1, CRC/TRR135, A3* and the IRTG 1901) and by "The Adaptive Mind," funded by the Excellence Program of the Hessian Ministry of Higher Education, Science, Research and Art.

Acknowledgments

We thank Jens Sommer for technical support and Merle Gudjons, Amelie Heitzmann, and Muriel Reuter for assistance in data collection. Additionally, we thank Loes van Dam for helpful feedback on an earlier version of this manuscript.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnhum.2022.998843/full#supplementary-material

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Supplementary material for the research article: “The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration.”

1. Power analysis

The software MorePower 6.0.4 (Campbell & Thompson, 2012) was used to calculate the expected power for our main analysis, i.e., the 4 x 2 repeated-measures ANOVAs on the temporal recalibration effect (TRE) with the factors *stimulation* (anodal, cathodal, dual-hemisphere, sham ctDCS) and *movement type* (active, passive). We calculated the power for the 4 x 2 interaction effect which was of primary interest for our study. Previous studies on temporal recalibration (e.g., Arikan et al., 2021) or with a comparable task in a tDCS study design (Straube et al., 2017) reported large effects sizes with a comparable or even smaller sample size. Thus, considering our sample size of 22 participants and an expected effect size of $\eta_p^2 = 0.2$, this analysis results in an expected power of 91.2%. The effect size of $\eta_p^2 = 0.2$ corresponds to the average effect size of interaction effects found in a previous study of our lab with the same experimental design (Arikan et al., 2021). Using a more conservative effect size of $\eta_p^2 = 0.14$ which is by convention regarded as a large effect, still yields an expected power of 74.4%. Thus, based on effect sizes from previous studies, our sample size should provide us with sufficient power to find similar effects for the impact of cerebellar tDCS on our temporal recalibration experiment.

2. Supporting information for results on effects of temporal recalibration

For investigating the TRE induced by the recalibration procedure, repeated-measures ANOVAs were performed for each test modality with the factors *stimulation* and *movement type* (see section 3.1 in manuscript). **Table 1** and **Table 2** provide an overview of the main and interaction effects of these analyses. The TRE as dependent variable was quantified as the difference delay detection thresholds for conditions with the adaptation delay of 150 vs. 0ms (with positive values indicating a rightward shift of the psychometric functions and thus decreased detection performance after exposure to the 150ms adaptation delay indicating temporal recalibration).

Table 3 and **Table 4** summarize the results of the repeated-measures ANOVAs on the difference in slopes of the psychometric functions between 0ms vs. 150ms adaptation delay conditions.

Table 1. Results of the ANOVA on the TRE (threshold differences) for the visual test modality

Effect	df	F-value	p-value	η_p^2
stimulation	3	.565	.640	.026
movement type	1	.628	.437	.029
stimulation * movement type	3	.840	.477	.038

Table 2. Results of the ANOVA on the TRE (threshold differences) for the auditory test modality

Effect	df	F-value	p-value	η_p^2
stimulation	3	1.416	.246	.063
movement type	1	.074	.788	.004
stimulation * movement type	**3**	**2.810**	**.047**	**.118**

Table 3. Results of the ANOVA on slope differences for the visual test modality

Effect	df	F-value	p-value	η_p^2
stimulation	3	.399	.754	.019
movement type	1	.446	.511	.021
stimulation * movement type	3	.778	.511	.036

Table 4. Results of the ANOVA on slope differences for the auditory test modality

Effect	df	F-value	p-value	η_p^2
stimulation	3	1.064	.371	.048
movement type	1	.007	.933	< .001
stimulation * movement type	3	.798	.499	.037

3. Supporting information for results on the distribution of temporal recalibration effects across test delays

To explore the distribution of the TRE across the tested delay levels, GEE analyses were calculated for each test modality with the TRE as dependent variable including the factors *stimulation*, *movement type* and *test delay* (see section 3.2 in manuscript). **Table 5** and **Table 6** provide an overview of all effects of these analyses. Again, post-hoc tests were calculated for significant main and interaction effects of interest to quantify differences between active and passive conditions and between stimulation conditions and the sham control condition (see **Table 7**).

Table 5. Results of the GEE analysis on the TRE across test delays for the visual test modality

Effect	Wald-Chi-Square	df	p-value
stimulation	4.422	3	.219
movement type	.022	1	.881
test delay	**24.263**	**5**	**< .001**
stimulation * movement_type	4.638	3	.200
stimulation * test delay	21.595	15	.119
movement type * test delay	4.306	5	.506
stimulation * movement type * test delay	21.366	15	.125

Table 6. Results of the GEE analysis on the TRE across test delays for the auditory test modality

Effect	Wald-Chi-Square	df	p-value
stimulation	7.528	3	.057
movement type	.031	1	.860
test delay	6.133	5	.293
stimulation * movement_type	5.777	3	.123
stimulation * test delay	**82.104**	**15**	**< .001**
movement type * test delay	10.458	5	.063
stimulation * movement type * test delay	**37.183**	**15**	**.001**

Table 7. Post-hoc tests for significant interaction effects for the GEE analysis on the auditory test modality

	Mean diff.	Std. error	df	p-value	*95% Wald confidence interval for diff.* low	high
stimulation * test delay						
0ms: anodal vs. sham ctDCS	**5.371**	**2.497**	**1**	**.031**	**.477**	**10.265**
0ms: cathodal vs. sham ctDCS	**5.411**	**2.751**	**1**	**.049**	**.018**	**10.804**
0ms: dual-hem. vs. sham ctDCS	2.164	2.775	1	.435	-3.275	7.604
83ms: anodal vs. sham ctDCS	1.326	2.933	1	.651	-4.423	7.075
83ms: cathodal vs. sham ctDCS	1.542	2.962	1	.602	-4.263	7.347
83ms: dual-hem. vs. sham ctDCS	1.339	3.248	1	.680	-5.027	7.705
167ms: anodal vs. sham ctDCS	**9.575**	**3.527**	**1**	**.007**	**2.661**	**16.489**
167ms: cathodal vs. sham ctDCS	3.192	3.508	1	.363	-3.683	10.068
167ms: dual-hem. vs. sham ctDCS	3.068	4.535	1	.499	-5.821	11.957
250ms: anodal vs. sham ctDCS	-2.513	4.194	1	.549	-10.734	5.707
250ms: cathodal vs. sham ctDCS	-6.277	4.628	1	.175	-15.348	2.794
250ms: dual-hem. vs. sham ctDCS	-1.447	3.592	1	.687	-8.487	5.592
333ms: anodal vs. sham ctDCS	3.964	3.040	1	.192	-1.994	9.922
333ms: cathodal vs. sham ctDCS	-.582	4.598	1	.899	-9.595	8.431
333ms: dual-hem. vs. sham ctDCS	-2.408	3.257	1	.460	-8.791	3.976
417ms: anodal vs. sham ctDCS	-.081	2.561	1	.975	-5.100	4.938
417ms: cathodal vs. sham ctDCS	-.798	2.809	1	.776	-6.304	4.708
417ms: dual-hem. vs. sham ctDCS	2.083	3.522	1	.554	-4.820	8.987
stimulation * movement type * test delay						
0ms, active: anodal vs. sham ctDCS	5.763	3.093	1	.062	-.299	11.825
167ms, active: anodal vs. sham ctDCS	**10.498**	**4.389**	**1**	**.017**	**1.896**	**19.099**
83ms, passive: anodal vs. sham ctDCS	9.064	4.895	1	.064	-.530	18.657
167ms, passive: anodal vs. sham ctDCS	8.652	4.838	1	.074	-.829	18.134
333ms, passive: anodal vs. sham ctDCS	**12.446**	**5.081**	**1**	**.014**	**2.487**	**22.404**
83ms, passive: cathodal vs. sham ctDCS	**8.441**	**4.003**	**1**	**.035**	**.595**	**16.288**
0ms, active: dual-hem. vs. sham ctDCS	**5.357**	**2.499**	**1**	**.032**	**.459**	**10.255**
250ms, active: dual-hem. vs. sham ctDCS	-8.333	4.971	1	.094	-18.076	1.410

333ms, active: dual-hem. vs. sham ctDCS	**-6.602**	**2.377**	**1**	**.005**	**-11.260**	**-1.943**
0ms, sham ctDCS: active vs. passive	-5.086	3.051	1	.095	-11.067	.894
83ms, sham ctDCS: active vs. passive	**12.338**	**4.777**	**1**	**.010**	**2.975**	**21.701**
333ms, anodal ctDCS: active vs. passive	-9.280	5.160	1	.072	-19.394	.834
0ms, cathodal ctDCS: active vs. passive	**-11.364**	**4.706**	**1**	**.016**	**-20.587**	**2.140**

Note. For the three-way interaction, only tests at $p < .10$ are displayed for clarity.

4. Control analysis including stimulation side effects as covariate

Since significant differences in perceived side effects were found for anodal ctDCS compared to the sham control condition and compared to dual-hemisphere ctDCS (see section 3.3 in manuscript), we included stimulation side effects as covariate into the GEE analysis on the TRE for the auditory test modality with the factors *stimulation*, *movement type*, *test delay* (which is responsible for the main results of this study). Accordingly, the main results of this analysis cannot be attributed to side effects alone, as the interaction effects of interest (i.e., the two-way interaction of *stimulation* and *test delay* as well as the three-way interaction of *stimulation*, *movement type* and *test delay*) still reach significance (see **Table 8**).

Table 8. Results of the GEE analysis on the TRE across test delays for the auditory test modality including stimulation side effects as covariate

Effect	Wald-Chi-Square	df	p-value
stimulation	2.260	3	.520
movement type	.346	1	.556
test delay	3.522	5	.620
side effects	.316	1	.574
stimulation * movement_type	1.273	3	.736
stimulation * test delay	**33.829**	**15**	**.004**
stimulation * side effects	2.420	3	.490
movement type * test delay	7.532	5	.184
movement type * side effects	.342	1	.559
test delay * side effects	1.641	5	.896
stimulation * movement type * test delay	**45.065**	**15**	**< .001**
stimulation * movement type * side effects	.860	3	.835
stimulation * test delay * side effects	**62.307**	**15**	**< .001**

movement type * test delay * side effects	9.459	5	.092
stimulation * movement type * test delay * side effects	**54.293**	**15**	**< .001**

5. Differences in delay detection performance between active and passive movement types

To explore differences in delay detection performance between active and passive movement types, we compared the detection thresholds derived from the psychometric functions between active and passive conditions and separately for each test modality by means of paired-samples t-tests. Results for the auditory test modality revealed that smaller delays could be detected for active [*M* = 239.192, *SD* = 93.183] compared to passive conditions [*M* = 259.744, *SD* = 94.633; *t*(21) = -2.470, *p* = .022, *d* = -.527, two-sided;] indicating that self-generated action-outcomes were perceptually enhanced. For the visual test modality, there was no difference in delay detection thresholds between active [*M* = 243.810, *SD* = 89.473] and passive movement types [*M* = 243.765, *SD* = 94.444; *t*(21) = .005, *p* = .996, *d* = .001].

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Study III: Publication Schmitter & Straube (2024)

Schmitter, C. V., & Straube, B. (2024). Facilitation of sensorimotor temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals. *Scientific Reports*, *14*(1), 2627. https://doi.org/10.1038/s41598-024-53148-3

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Facilitation of sensorimotor temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals

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Core symptoms in patients with schizophrenia spectrum disorders (SSD), like hallucinations or ego-disturbances, have been associated with a failure of internal forward models to predict the sensory outcomes of self-generated actions. Importantly, forward model predictions must also be able to flexibly recalibrate to changing environmental conditions, for example to account for additional delays between action and outcome. We investigated whether transcranial direct current stimulation (tDCS) can be used to improve these sensorimotor temporal recalibration mechanisms in patients and healthy individuals. While receiving tDCS on the cerebellum, temporo-parietal junction, supplementary motor area, or sham stimulation, patients with SSD and healthy control participants were repeatedly exposed to delays between actively or passively elicited button presses and auditory outcomes. Effects of this procedure on temporal perception were assessed with a delay detection task. Similar recalibration outcomes and faciliatory effects of cerebellar tDCS on recalibration were observed in SSD and healthy individuals. Our findings indicate that sensorimotor recalibration mechanisms may be preserved in SSD and highlight the importance of the cerebellum in both patients and healthy individuals for this process. They further suggest that cerebellar tDCS could be a promising tool for addressing deficits in action-outcome monitoring and related adaptive sensorimotor processes in SSD.

Core symptoms in patients with schizophrenia and schizoaffective disorder (referred to as schizophrenia spectrum disorders, SSD) encompass hallucinations (e.g., perceiving the own inner speech as external voice) and ego-disturbances (e.g., perceiving own thoughts or actions as externally controlled). The emergence of these symptoms has been associated with a failure of adequately predicting the sensory outcomes of one´s own actions[1]. When performing an action, copies of the motor commands are thought to be used by an internal forward model to predict the action´s sensory outcomes. Re-afferent sensory input that is in line with the prediction is typically found to be associated with modulations in perceptual acuity and neural responses in multiple brain regions compared to input that deviates from the prediction, and is thus perceived as self-generated[2–4]. Dysfunctions in this predictive mechanism can result in the misattribution of self-generated sensory input as externally produced and lead to the symptoms in SSD described above[5–10].

Importantly though, forward model predictions are not rigid, but need to be able to flexibly recalibrate to preserve adequate distinction between self- and externally generated input even under dynamically changing environmental conditions. For instance, the outcome of an action can be transiently delayed under certain circumstances, e.g., a mouse click can lead to delayed responses from a computer[11]. Studies with healthy participants have frequently shown that after repeated exposure to a delayed action-outcome, the predicted sensory outcome timing shifted toward that delay. As consequence, the delayed outcome was perceived as occurring in synchrony with the action, a phenomenon known as the sensorimotor temporal recalibration effect (TRE)[12–16], and neural responses for the delayed outcome resembled the ones typically observed for undelayed outcomes[17]. To date, it remains unknown whether the dysfunctions in predictive mechanisms observed in SSD are due to a general

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failure of prediction generation or, more specifically, a failure of adequately recalibrating these predictions to the constantly changing requirements of the environment.

Neural correlates of the predictive processes based on the forward model have been identified in several brain regions. The cerebellum is most prominent in this regard since it has been suggested to play a vital role in the generation and updating of predictions about sensory action-outcomes[2,4,18–22]. Additionally, regions in parietal cortex, particularly the temporo-parietal junction (TPJ) or angular gyrus[9,23–26], and the supplementary motor area (SMA)[27,28] could be associated with the subjective feeling of control or agency over action-outcomes and the distinction between self- and externally generated stimuli. Interestingly, non-invasive brain stimulation techniques have demonstrated the potential to modulate these processes when applied to the respective brain regions. For instance, transcranial magnetic stimulation (TMS)[29] or transcranial direct current stimulation (tDCS)[30] of the cerebellum influenced the effect of sensorimotor temporal recalibration on perception in healthy individuals. Furthermore, tDCS on the angular gyrus[31], the pre-supplementary motor area[32,33], and frontal regions[34,35] modulated measures for agency and action-outcome-related processing, even in patients with SSD[36]. Thus, tDCS may also be a promising tool to enhance sensorimotor temporal recalibration mechanisms and thereby improve action-outcome processing and self-other distinction in patients with SSD.

Therefore, the present study investigated for the first time (1) whether sensorimotor temporal recalibration mechanisms are impaired in patients with SSD compared to healthy control (HC) participants, and (2) whether tDCS on the bilateral cerebellum, right SMA, or right TPJ can enhance recalibration and thus reduce potential deficits. Participants were exposed to delayed or undelayed tones following either actively performed or passively elicited button press movements, and the effects of this procedure on auditory and visual temporal perception were assessed with a delay detection task. The undelayed tone should align with the natural prediction of undelayed action-outcomes, while exposure to the delayed tones was expected to induce a TRE in terms of reduced delay detection performance. While active movements were expected to trigger sensorimotor temporal recalibration based in the forward model, passive movements were applied to control for recalibration effects due to changes in the expected inter-sensory timing between the tactile sensations during the button movement and the auditory or visual outcome[37–40]. We expected patients with SSD to exhibit reduced temporal recalibration compared to HC, specifically in active movement conditions, due to impaired recalibration of forward model predictions. We expected tDCS applied on the mentioned brain regions to enhance temporal recalibration in both groups, particularly in active conditions, due to the presumed importance of these regions in the generation and updating of forward model predictions.

Materials and methods

Participants

Twenty-four patients with SSD and 20 HC with no psychiatric diagnosis (10 female, mean age: 36.90, *SD* = 10.37) participated in the study. Two patients had to be excluded (see Supplementary Material S1), resulting in a final sample of 22 patients (11 female, mean age: 35.80, *SD* = 10.37). Fifteen patients were diagnosed with an ICD-10 diagnosis of schizophrenia, six patients with schizoaffective disorder, and one patient with an acute and transient psychotic disorder (for further details on sample characteristics see Supplementary Material S1). All participants had normal or corrected-to-normal visual acuity, normal hearing, and no history of neurological disorders. No contraindications for tDCS (e.g., electric, or metallic implants) were reported. Participants gave written informed consent and were financially reimbursed for their participation. The study was conducted according to the Declaration of Helsinki and was approved by the local ethics commission (Study 06/19) of the medical faculty of University of Marburg, Germany. The study was pre-registered in the German Clinical Trials Register (DRKS-ID: DRKS00025885; https://drks.de; date of registration: July 23, 2021).

Transcranial direct current stimulation

tDCS was applied using a DC stimulator (neuroConn GmbH, Ilmenau) and two rubber electrodes (5 × 7 cm) in saline-soaked sponges (0.9% NaCl). For all stimulation conditions, the anode was placed over the respective brain region since anodal tDCS has been shown to increase cortical excitability[41]. For stimulation of the bilateral cerebellum, the center of the anode was placed on the midline 2 cm below the inion. For tDCS on the right SMA and TPJ, electrodes were positioned according to the 10–20 EEG system. For stimulating the right SMA, the anode was placed on FC2 (10% of the distance between nasion and inion anteriorly to Cz; and 10% of the distance between the preauricular points to the right). tDCS on the right TPJ was applied by placing the anode between C4 and P4 (20% of the distance between nasion and inion posteriorly to Cz; and 20% of the distance between the preauricular points to the right). The right hemisphere was chosen based on previous findings indicating the involvement of right parietal and right supplementary motor regions in action-outcome processing in healthy individuals as well as in patients with SSD[9,36]. During the sham stimulation session, electrodes were attached similarly as for the cerebellar tDCS condition. In all conditions, the cathode was attached on the deltoid muscle of the right upper arm. A similar electrode montage with an extracephalic location for the return electrode has been successfully applied earlier in studies investigating effects of stimulating the cerebellum[42], SMA[32], and posterior parietal cortex[43] and was not accompanied with reduced stimulation outcomes compared to cephalic locations when a current of 2 mA was applied[44]. This montage also ensured that the obtained stimulation effects cannot be attributed to confounding influences of the cathode on neural excitability[44,45]. All electrodes were attached with rubber bands. The stimulation was applied with a current of 2 mA for 20 min (+ 10 s fade in and fade out periods). Next to these three active stimulation conditions, a sham stimulation condition was implemented by using sinus (half wave) mode for 30 s. Here, the current gradually increased during the first 15 s and then decreased again to generate the same subjective sensations (like tingling) due to changes in current intensity as in active stimulation conditions while no actual stimulation was applied. The stimulation parameters were chosen in accordance with

established tDCS safety guidelines[46]. Each participant experienced the four stimulation conditions (cerebellum, SMA, TPJ, sham) in four separate sessions. Sessions were performed at least 18 h apart to prevent residual effects from the previous stimulation. The stimulation conditions were applied in counterbalanced order, ensuring that in each group, across participants, each of the four stimulation conditions was applied approximately equally often during the first, second, third, or fourth session. Participants were sequentially assigned to one of the possible combinations of stimulation conditions and were unaware of the hypothesized effects of stimulating the respective brain region on task performance.

Equipment and stimuli

Participants performed the experiment in a dimly lit room in front of a computer screen. Button presses were executed with the right index finger using a custom-made electromagnetic passive button device. In active conditions, participants pressed the button actively by themselves. In passive conditions, the button was pulled down automatically by an electromagnet (max. force 4N). An elastic fabric band was used to attach the participants' fingers to the button to ensure that it smoothly followed its movement in passive conditions. When the button reached the lowest position, the presentation of an auditory or visual stimulus was triggered. The visual stimulus was a Gabor patch (1° visual angle, spatial frequency: 2 cycles/degree) which was presented at the center of the screen. The auditory stimulus was a brief sine-wave tone (2000 Hz with 2 ms rise and fall) presented through headphones. Both stimuli appeared for a duration of 33.4 ms. All stimuli were created and presented using Octave and the Psychophysics Toolbox[47]. To prevent any influence of the direct visual or auditory feedback from the actual button presses on sensory outcome perception, the button device was covered by a black box and pink noise was applied through headphones during the experiment. The intensity of the pink noise was adjusted individually for each participant until they indicated that they could no longer hear the inherent noise of the button device.

Experimental design and task description

The experiment consisted of an established temporal recalibration paradigm[22,30,48] in which participants were exposed to multiple pairs of adaptation and test phases. In adaptation phases, 18 consecutive button presses had to be executed each followed by the tone as auditory sensory outcome. The button presses were either performed actively or they were elicited passively (factor *movement type*). The tone occurred either immediately after the button press (undelayed, 0 ms delay) or was delayed by 200 ms (factor *adaptation delay*). Originally, we chose an adaptation delay of 150 ms as is had been used in previous studies with young healthy participants[30,48]. But given the lower delay detection performance observed among older participants, the adaptation delay was adjusted to 200 ms after collecting the data from the first four patients. Nonetheless, the data of all patients were included in the current analyses. Pairwise comparisons indicated that excluding the data of these four patients would not lead to differences in group-dependent effects on the overall effect of temporal recalibration (for details see Supplementary Material S3).

Each adaptation phase was followed by a test phase that assessed the impact of the adaptation delay on perception. A test phase consisted of six test trials for which the button had to be pressed once, either actively or passively. The movement type was the same as the one used in the previous adaptation phase. While the stimulus during adaptation phases was always auditory, in test phases, the button presses elicited either the auditory or the visual stimulus (factor *test modality*). This was done because the TRE has previously been shown to transfer between modalities, such that recalibration to a sensorimotor delay in one modality also affected temporal perception in another modality[13,48–50]. In a test phase, the sensory stimuli were either visual or auditory in all of the six test trials. In each test trial, the stimulus occurred with one of six test delay levels (0, 83, 167, 250, 333, 417 ms). Each of the test delays was used once in each test phase in counterbalanced order. Participants were instructed to report via keyboard presses after each trial whether they detected a delay between the button press and the stimulus. The TRE was defined as the difference in the proportion of detected delays after exposure to delayed vs. undelayed tones with worse performance for delayed tones reflecting a shift of the expected stimulus timing in the direction of the adapted delay, indicating temporal recalibration.

Procedure

An adaptation phase started with instructions displayed for 2000 ms indicating the movement type of the button presses (see Fig. 1). After the instructions disappeared, participants could start pressing the button or it started to move passively. Each button press was followed by the tone, either undelayed or delayed by 200 ms. After nine button presses, a fixation cross appeared on the screen for a jittered duration (1000, 1500, 2000, or 2500 ms) indicating a short break. After the fixation cross disappeared, the remaining nine button presses could be performed.

A test phase was initiated by instructions (2000 ms) about the movement type and stimulus modality of the following test trials. The cue "Ready" was presented for 1000 ms before each test trial. After the cue disappeared, participants had 2000 ms in active conditions to press the button. But they were instructed to wait for approx. another 700 ms to ensure that the movement was voluntary and not reflexive upon cue disappearance[36,51]. Passive movements were initiated after a jittered interval of 0, 500, 1000 ms. Each button press triggered the auditory or visual outcome with one of the six test delays. Afterwards, the question "Delay?" was presented and participants had 2000 ms to respond via keyboard press whether they detected a delay. After a pause of 500 ms the "Ready" cue initiated the next test trial. After the last trial of a test phase a jittered inter-trial interval (1000, 1500, 2000, 2500 ms) was inserted before the start of the next adaptation-test pair.

Each of the eight experimental conditions was presented with eight adaptation-test pairs per session. Within each session, conditions with the same adaptation delay were blocked to prevent spill-over effects due to rapid switching of delays. The first block of conditions with one of the adaptation delays took place while the

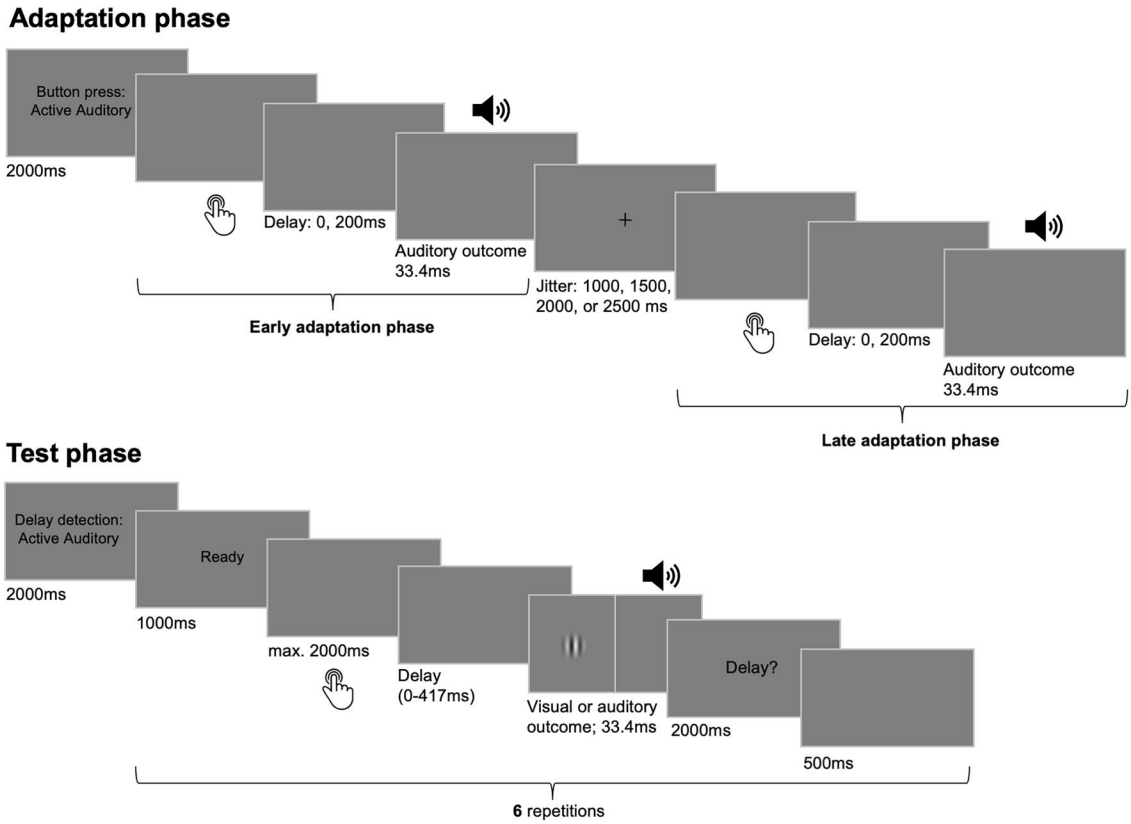

Figure 1. Trial sequence and timing of events. The experiment consisted of multiple pairs of adaptation and test phases. During adaptation phases, 18 button presses had to be performed either actively by participants or they were executed passively. A button press was followed by a delayed (200 ms) or undelayed tone. Adaptation phases were divided into two parts separated by a fixation cross presentation. In test phases, the button was pressed once in each test trial, either actively or passively. Here, the outcome occurred after one of six delays (0–417 ms) and participants had to report in each trial whether they detected a delay. The outcome modality was always auditory during adaptation, but it could be visual or auditory during test.

stimulation was applied. After this first task block, electrodes were detached. The conditions with the other adaptation delay were presented in a second task block without stimulation. Whether the undelayed or delayed tones were presented first as well as the order of conditions within blocks was counterbalanced across participants.

After each session, side effects due to the tDCS stimulation (e.g., itching sensations, headache, changes in visual perception, difficulties in concentration) had to be rated on a scale from one (no side effect) to five (strong side effect) using a custom-designed questionnaire of 28 items. During the first session, participants additionally went through a training procedure to familiarize with the task (see Supplementary Material S2).

Data analyses

Test trials for which no button press, or response were registered were excluded from the analyses. For SSD, 1.858% of all trials were excluded due to missing button presses, and 5.617% of trials due to missing responses. For HC, the button press was missing in 0.781% of all trials and the response in 3.503% of trials. The percentage of detected delays served as a measure for delay detection performances and was calculated for each participant and experimental condition. These data were forwarded into a mixed ANOVA with the between-participants factor *group* and the within-participants factors *stimulation*, *test modality*, *movement type*, and *adaptation delay*. We examined main and interaction effects including the factors *adaptation delay* and *group,* to test for the impact of the adaptation delay on temporal perception and the modulatory influence of the other experimental factors as well as group-dependent effects. For significant interaction effects with the *adaptation delay*, we calculated the TRE defined as the difference in the percentage of detected delays in conditions with the 200 ms compared to 0 ms adaptation delay. Positive values indicate worse detection performance after exposure to the 200 ms delay, reflecting a TRE into the expected direction. If indicated, post-hoc one-sided one-sample t-tests were used to assess whether the TRE was significantly greater than zero in the individual conditions of an interaction effect. Furthermore, two-samples t-tests were used to determine the difference in the TRE between the relevant conditions or groups. Since we had clear hypotheses regarding the direction of difference in TRE between conditions (i.e., a stronger TRE in HC vs. SSD, active vs. passive, auditory vs. visual conditions, and in active tDCS conditions vs. sham stimulation) one-sided t-tests were used. All post-hoc tests were Bonferroni-corrected if indicated. For significant interaction effects without the group factor, post-hoc tests were exploratorily performed

not only across but also individually for both groups to identify similarities in temporal recalibration effects for SSD and HC. Since the SSD group in our study was heterogeneous and comprised different diagnoses of the schizophrenia spectrum, the same analysis was also exploratorily performed for the subgroup of patients diagnosed with schizophrenia (F20; N = 15). Results of this exploratory analysis closely resembled the ones obtained with the entire SSD group and are reported in Supplementary Material S7. Finally, we tested for differences in perceived stimulation side effects between the groups and stimulation conditions by a mixed ANOVA with the factors *group* and *stimulation* (results are reported the Supplementary Material S4). All analyses were performed in JASP (Version 0.14.1)[52].

Results

A mixed ANOVA with the between-participants factor *group* (SSD, HC) and the within-participants factors *stimulation* (cerebellum, SMA, TPJ, sham), *test modality* (auditory, visual), *movement type* (active, passive), and *adaptation delay* (0 ms, 200 ms) was conducted on the percentage of detected delays. Results revealed no significant main effect of *group* [$F(1, 40) = 0.239$, $p = 0.628$, $\eta_p^2 = 0.006$], indicating that patients did not differ from HC in general delay detection abilities [HC: *Mean* = 37.138, *SD* = 8.845; SSD: *Mean* = 41.758, *SD* = 17.393]. Furthermore, none of the interaction effects including the factors *group* and *adaptation delay* were significant (all $p > 0.139$), thus providing no evidence for impairments in temporal recalibration and differences in the effectiveness of tDCS in patients with SSD (see Supplementary Material S3 for a summary of all effects).

However, across groups and conditions, there was a significant main effect of the *adaptation delay* [$F(1, 40) = 14.033$, $p < 0.001$, $\eta_p^2 = 0.260$]. Thus, participants' perception recalibrated to the 200 ms delay between button press and auditory outcome, leading to a significant TRE in terms of reduced delay detection performance [*Mean TRE* = 3.197, *SD* = 5.439; see Table 1 for an overview of effects computed individually for both groups and Fig. 2 for an illustration of effects]. Additionally, the interaction of *movement type* and *adaptation delay* was significant [$F(1, 40) = 8.762$, $p = 0.005$, $\eta_p^2 = 0.180$].

Post-hoc tests revealed that the TRE was significantly greater than zero in both active [*Mean TRE* = 4.103, *SD* = 4.586, $t(41) = 5.799$, $p < 0.001$, $d = 0.895$, $\alpha_{corr} = 0.025$] and passive conditions [*Mean TRE* = 2.291, *SD* = 6.830, $t(41) = 2.174$, $p = 0.018$, $d = 0.335$, $\alpha_{corr} = 0.025$], but was significantly stronger in active ones [*Mean difference* = 1.812, *SD* = 4.124, $t(41) = 2.848$, $p = 0.003$, $d = 0.439$]. Furthermore, there was a significant *test modality* and *adaptation delay* interaction [$F(1, 40) = 9.229$, $p = 0.004$, $\eta_p^2 = 0.187$]. While the TRE was significantly greater than zero for both, audition [*Mean TRE* = 4.279, *SD* = 5.939, $t(41) = 4.669$, $p < 0.001$, $d = 0.720$, $\alpha_{corr} = 0.025$] and vision [*Mean TRE* = 2.115, *SD* = 5.871, $t(41) = 2.335$, $p = 0.012$, $d = 0.360$, $\alpha_{corr} = 0.025$], indicating a modality transfer of the TRE, it remained significantly larger in auditory (unimodal) than in visual (cross-modal) conditions [*Mean difference* = 2.164, *SD* = 4.599, $t(41) = 3.050$, $p = 0.002$, $d = 0.471$]. The interaction of the three factors *movement type*, *test modality*, and *adaptation delay* [$F(1, 40) = 7.781$, $p = 0.008$, $\eta_p^2 = 0.163$] further indicated that the active–passive difference in the TRE was specific to auditory outcomes [*Mean difference* = 4.187, *SD* = 5.872, $t(41) = 4.622$, $p < 0.001$, $d = 0.713$, $\alpha_{corr} = 0.025$; Active: *Mean TRE* = 6.373, *SD* = 6.255, $t(41) = 6.603$, $p < 0.001$, $d = 1.019$, $\alpha_{corr} = 0.025$; Passive: *Mean TRE* = 2.185, *SD* = 6.976, $t(41) = 2.030$, $p = 0.024$, $d = 0.313$, $\alpha_{corr} = 0.025$] but did not transfer to the visual modality [*Mean difference* = − 0.563, *SD* = 7.625, $t(41) = -0.478$, $p = 0.682$, $d = -0.074$, $\alpha_{corr} = 0.025$; Active: *Mean TRE* = 1.834, *SD* = 4.662, $t(41) = 2.549$, $p = 0.007$, $d = 0.393$, $\alpha_{corr} = 0.025$; Passive: *Mean TRE* = 2.396, *SD* = 8.733, $t(41) = 1.778$, $p = 0.041$, $d = 0.274$, $\alpha_{corr} = 0.025$].

Regarding the influence of tDCS on temporal recalibration, according to the interaction of *stimulation* and *adaptation delay* [$F(3, 120) = 2.800$, $p = 0.043$, $\eta_p^2 = 0.065$] and subsequent post-hoc tests, across groups, the TRE was significantly stronger after cerebellar tDCS compared to sham stimulation [*Mean difference* = 3.071, *SD* = 8.050, $t(41) = 2.472$, $p = 0.009$, $d = 0.381$, $\alpha_{corr} = 0.016$; Sham: *Mean TRE* = 2.028, *SD* = 6.250, $t(41) = 2.103$, $p = 0.021$, $d = 0.324$, $\alpha_{corr} = 0.025$; Cerebellum: *Mean TRE* = 5.099, *SD* = 8.183, $t(41) = 4.038$, $p < 0.001$, $d = 0.623$, $\alpha_{corr} = 0.025$], but not after tDCS on the right SMA [*Mean difference* = 0.640, *SD* = 7.643, $t(41) = 0.542$, $p = 0.295$, $d = 0.084$, $\alpha_{corr} = 0.016$] or the right TPJ [*Mean difference* = 0.967, *SD* = 6.257, $t(41) = 1.001$, $p = 0.161$, $d = 0.155$, $\alpha_{corr} = 0.016$]. Finally, the significant four-way interaction of *stimulation*, *movement type*, *test modality*, and *adaptation delay* [$F(3, 120) = 3.343$, $p = 0.022$, $\eta_p^2 = 0.077$] further revealed that, across groups, the faciliatory influence of cerebellar tDCS on the TRE occurred specifically for active and auditory conditions [*Mean difference* = 5.188, *SD* = 14.052, $t(41) = 2.393$, $p = 0.011$, $d = 0.369$, $\alpha_{corr} = 0.0125$; Sham: *Mean TRE* = 4.518, *SD* = 9.580, $t(41) = 3.057$, $p = 0.002$, $d = 0.472$, $\alpha_{corr} = 0.025$; Cerebellum: *Mean TRE* = 9.707, *SD* = 12.633, $t(41) = 4.979$, $p < 0.001$, $d = 0.768$, $\alpha_{corr} = 0.025$], but was absent in passive/auditory [*Mean difference* = 3.109, *SD* = 16.246, $t(41) = 1.240$, $p = 0.111$, $d = 0.191$, $\alpha_{corr} = 0.0125$], active/visual [*Mean difference* = 1.405, *SD* = 9.725, $t(41) = 0.937$, $p = 0.177$, $d = 0.145$, $\alpha_{corr} = 0.0125$], and in passive/visual conditions [*Mean difference* = 2.581, *SD* = 10.710, $t(41) = 1.562$, $p = 0.063$, $d = 0.241$, $\alpha_{corr} = 0.0125$].

Discussion

In this study, we investigated for the first time the commonalities and differences in sensorimotor temporal recalibration mechanisms between HC and SSD and whether tDCS on relevant regions could facilitate recalibration effects. We found similar effects of sensorimotor temporal recalibration in both groups indicating that recalibration mechanisms may be preserved in SSD. Furthermore, the faciliatory impact of cerebellar tDCS on these effects in both groups highlights the importance of the cerebellum for recalibrating forward model predictions in response to environmental changes.

Regardless of the tDCS stimulation, both HC and SSD showed a significant TRE across conditions, and specifically so for active movements. Furthermore, no group differences in the TRE were observed depending on the movement type, test modality, or stimulation condition. Thus, our study does not provide evidence for a fundamental impairment in sensorimotor temporal recalibration in SSD, but rather suggests commonalities in

TRE	Group	Mean ± SD	t-value	p-value	α_{corr}	Cohen's d
Across conditions	**HC**	**2.218 ± 4.033**	**2.459**	**.011***	**.05**	**.532**
	SSD	**4.087 ± 7.684**	**2.495**	**.012***	**.05**	**.550**
Active	**HC**	**3.584 ± 3.233**	**4.959**	**< .001*****	**.025**	**1.109**
	SSD	**4.575 ± 7.826**	**2.742**	**.006*****	**.025**	**.585**
Passive	HC	.852 ± 5.802	.656	.260	.025	.147
	SSD	3.599 ± 8.733	1.933	.033	.025	.412
Active > Passive	**HC**	**2.733 ± 4.813**	**2.539**	**.010***	**.05**	**.568**
	SSD	.976 ± 6.231	.735	.235	.05	.157
Auditory	**HC**	**3.883 ± 4.283**	**4.055**	**< .001*****	**.025**	**.907**
	SSD	**4.639 ± 8.528**	**2.551**	**.009****	**.025**	**.544**
Visual	HC	.553 ± 4.878	.507	.309	.025	.113
	SSD	3.535 ± 8.196	2.023	.028	.025	.431
Auditory > Visual	**HC**	**3.331 ± 4.382**	**3.399**	**.003****	**.05**	**.760**
	SSD	1.103 ± 6.605	.784	.442	.05	.167
Auditory: Active	**HC**	**5.816 ± 3.905**	**6.661**	**< .001*****	**.025**	**1.490**
	SSD	**6.879 ± 10.410**	**3.099**	**.003****	**.025**	**.661**
Auditory: Passive	HC	1.950 ± 6.342	1.375	.092	.025	.308
	SSD	2.399 ± 9.244	1.217	.119	.025	.259
Visual: Active	HC	1.353 ± 4.391	1.278	.092	.025	.308
	SSD	2.271 ± 7.292	1.461	.079	.025	.311
Visual: Passive	HC	− .247 ± 7.377	− .150	.559	.025	− .033
	SSD	4.799 ± 10.894	2.066	.026	.025	.441
Auditory: Active > Passive	**HC**	**3.866 ± 6.128**	**2.821**	**.005****	**.025**	**.631**
	SSD	**4.480 ± 9.834**	**2.137**	**.022***	**.025**	**.456**
Visual: Active > Passive	HC	1.600 ± 7.226	.990	.167	.025	.221
	SSD	− 2.528 ± 8.659	− 1.370	.907	.025	− .292
Sham	HC	1.160 ± 5.923	.876	.196	.025	.196
	SSD	2.817 ± 7.883	1.676	.054	.025	.357
Cerebellum	**HC**	**3.145 ± 6.441**	**2.184**	**.021***	**.025**	**.488**
	SSD	**6.875 ± 12.585**	**2.562**	**.009****	**.025**	**.546**
Cerebellum > Sham	HC	1.985 ± 7.617	1.165	.129	.05	.261
	SSD	4.058 ± 11.499	1.655	.056	.05	.353
Active/Auditory: Sham	**HC**	**3.699 ± 7.323**	**2.259**	**.018***	**.025**	**.505**
	SSD	5.263 ± 14.656	1.684	.053	.025	.359
Active/Auditory: Cerebellum	**HC**	**9.181 ± 7.356**	**5.581**	**< .001*****	**.025**	**1.248**
	SSD	**10.184 ± 18.052**	**2.646**	**.008****	**.025**	**.564**
Active/Auditory: Cerebellum > Sham	**HC**	**8.328 ± 12.974**	**2.313**	**.016***	**.05**	**.517**
	SSD	4.921 ± 20.334	1.135	.135	.05	.242

Table 1. TREs for individual conditions and comparisons of conditions, evaluated individually for both groups. The TRE is defined as the difference in the percentage of detected delays between conditions with the 200 ms vs. 0 ms delay during preceding adaptation phases. For individual conditions, one-sample t-tests were used to assess whether the TRE was significantly greater than zero. Difference in TRE between conditions were assessed with two-samples t-tests. All t-tests were Bonferroni corrected. The corrected alpha level used for each test is displayed in the column α_{corr}. Significant tests are presented with bold values. *$p < .05$, **$p < .01$, ***$p < .001$.

recalibration mechanisms between SSD and HC. Predictable action-outcomes, i.e., outcomes in active conditions in our study, are typically associated with perceptual differences compared to externally generated sensory input[2–4]. However, this difference is often found to be reduced in SSD which is usually considered as an indicator of impairments of the forward model in predicting the sensory outcomes of self-generated actions[5,7–9]. In our study, overall group differences in delay detection performances between actively and passively generated stimuli appeared to have been too small or associated with too much variance to manifest in a significant interaction effect (see also Supplementary Material S8 for study limitations). Nevertheless, according to supplementary analyses (see Supplementary Material S5), patients with SSD exhibited a reduced difference between active and passive delay detection rates for a specific test delay level, indicating that the previously reported deficit[5,7–9,36] also weakly manifested in our data. Importantly, due to the absence of differences in temporal recalibration between the groups, our findings suggest that the aberrant processing associated with self-generated action-outcomes

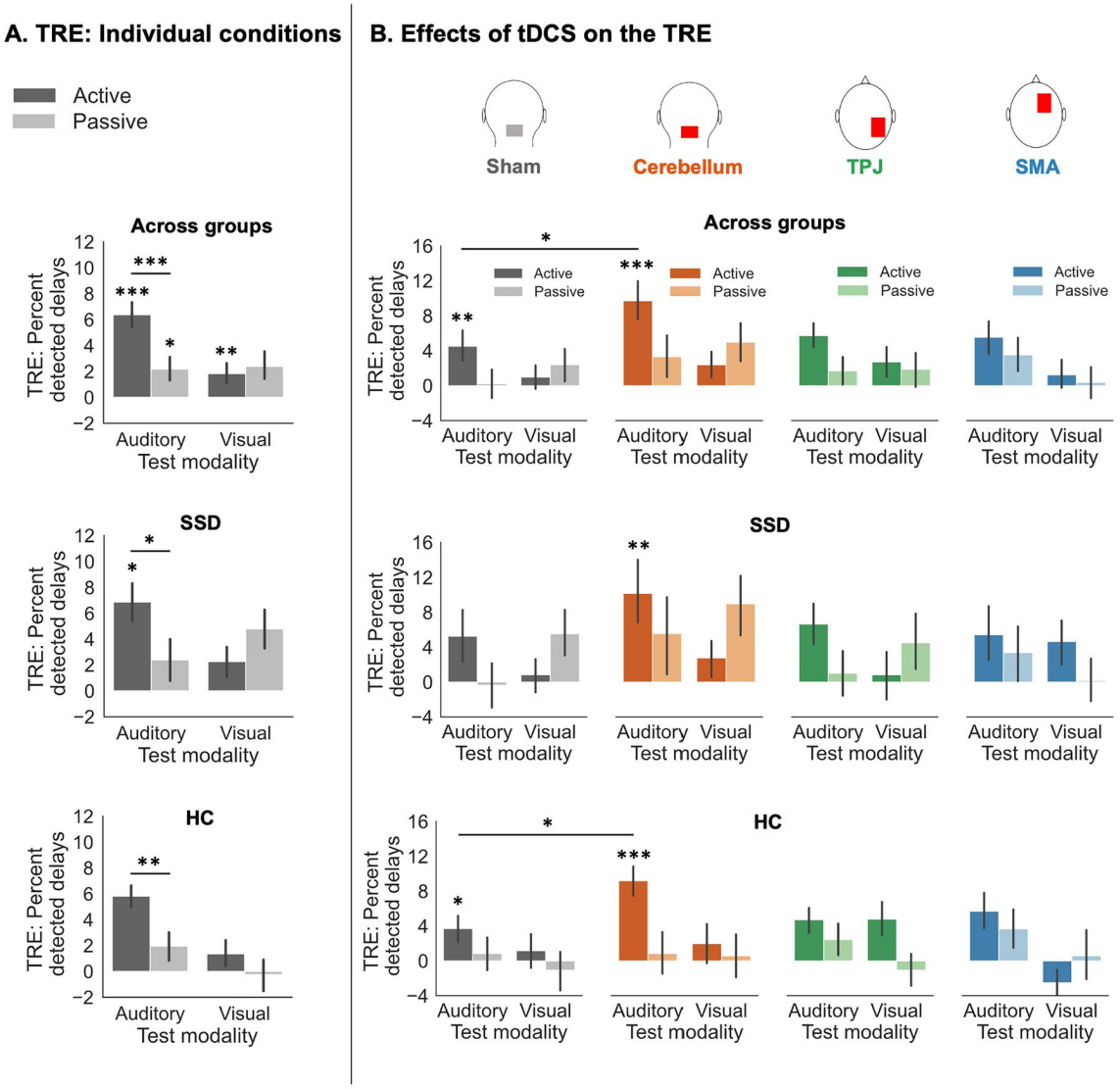

Figure 2. Temporal recalibration effects. (**A**) The TRE, defined as the difference in the percentage of detected delays between conditions with the 200 ms vs. 0 ms delay during preceding adaptation phases, is displayed for each experimental condition (i.e., for both test modalities and movement types), across groups, as well as separately for both groups. In both groups, for auditory (unimodal) conditions, the TRE was significantly larger in active compared to passive movement conditions. (**B**) The TRE is displayed for each of the four stimulation conditions, again across groups and separately for both groups. Across groups and for HC alone, cerebellar tDCS significantly facilitated the TRE compared to sham stimulation. For SSD, cerebellar tDCS induced a significant TRE which was absent during sham stimulation. Error bars indicate standard errors of the mean. $^{*}p > .05$, $^{**}p < .01$, $^{***}p < .001$.

in SSD cannot be attributed to dysfunctions in flexibly recalibrating forward model predictions in response to changes in environmental conditions, such as varying action-outcome delays. Instead, they point to a more general failure in the prediction generation process in SSD.

Importantly, cerebellar tDCS facilitated the TRE in both groups. In HC, the TRE increased significantly with cerebellar tDCS compared to sham stimulation. In SSD, cerebellar tDCS was able to induce a significant TRE which was absent with sham stimulation. The cerebellum has frequently been suggested as the site of internal forward models[2,4,18–21]. The adaptation of these predictions when required due to changing environmental conditions could also be associated with processes in the cerebellum[19,22,29,30,53,54]. Thus, the facilitatory impact of cerebellar tDCS on the TRE suggests that the recalibration of these predictive processes in the cerebellum was amplified by the stimulation, which is in line with previous studies demonstrating a facilitatory influence of cerebellar stimulation on sensorimotor temporal recalibration mechanisms in healthy participants[29,30]. This is further supported by the fact that the TRE was generally larger in active than in passive conditions for both groups in our study. In both active and passive conditions, the TRE can be associated with the recalibration of the expected inter-sensory timing between the tactile sensation of the button movement and the visual or auditory outcome. A stronger TRE for active movements thus suggests that, next to inter-sensory recalibration mechanisms, the

recalibration of forward model predictions additionally contributed to the TRE in this condition[48,55]. Moreover, the fact that the faciliatory impact of cerebellar tDCS was specific to active conditions further indicates that it specifically amplified the recalibration of forward model predictions in this region.

Furthermore, according to supplementary analyses, across groups, the TRE in active and auditory conditions appeared to be larger after cerebellar tDCS compared to tDCS applied to the TPJ or SMA (see Supplementary Material S6). Although both TPJ and SMA have often been associated with processes closely related to forward model-based predictive mechanisms, such as the sense of agency[9,23–28], they do not to appear as strongly linked to the recalibration of action-outcome predictions as the cerebellum. This suggests that these regions are more likely to play a role at a different processing stage, such as in the generation of efference copy signals[56] or the comparison of predictions and outcomes[25,26]. This emphasizes once again the central role of the cerebellum in generating forward model predictions and in adapting them to additional action-outcome delays[19,22,29,30], and that this adaptability can consequently be most effectively amplified by means of cerebellar tDCS in patients and healthy individuals.

Beyond that, the faciliatory impact of cerebellar tDCS on the TRE appeared to be specific to auditory conditions for both groups. Since the adaptation delay was always inserted between the button press and the auditory outcome, a transfer of the TRE to vision, especially for active conditions, would suggest that forward model predictions are generated and recalibrated simultaneously for sensory outcomes of different modalities. This would indicate that recalibration results in changes in the general predicted timing for sensory action-outcomes rather than in modality-specific changes[13,48–50]. Although the adaptation procedure had an impact on temporal perception in the visual domain in our study, leading to a visual TRE across the groups, cerebellar tDCS did not affect the size of this modality-transfer effect. Furthermore, the transfer of the TRE to vision was not stronger in active than in passive conditions. Thus, these findings do not speak for the presence of supra-modal predictive mechanisms in the cerebellum. Instead, the modality-transfer can rather be explained by the supra-modal recalibration of inter-sensory matching mechanisms, assumed to be involved in both active and passive conditions, leading to changes in the expected timing between tactile, auditory, and visual outcomes[57]. Importantly though, the TRE across active and passive conditions was larger for auditory than for visual stimuli. Thus, there was only a partial transfer of the effect to vision. For sensorimotor, i.e., active conditions, a general superiority of the TRE due to recalibration to auditory compared to visual action-outcome delays has also been reported previously[15]. And while a transfer of the TRE from audition to vision has been found in a few studies[49,50], others failed to replicate this finding[13,22,48]. This may be related to the fact that temporal perception is less precise for vision than for audition and the temporal predictability of visual signals is therefore thought to be worse compared to auditory ones[58,59]. Hence, it may be assumed that due to the lower temporal predictability or higher levels of noise associated with visual sensory stimuli, visual perception is generally less prone to small changes in inter-sensory or in action-outcome delays.

Overall, the fact that cerebellar tDCS had a similar impact on the TRE for both groups highlights the importance of cerebellum-based predictive processes, which play a vital role in the adaptation to action-outcome delays in both healthy individuals and patients with SSD. This could also imply the potential of cerebellar tDCS to facilitate related adaptive processes in SSD, which are tightly connected to the cerebellum as well and have frequently been reported to be impaired in these patients. Among them is the process of sensorimotor adaptation, i.e., the adaptation of movements in response to a discrepancy between predicted and observed sensory outcomes of these movements[60–62]. For instance, compared to healthy individuals, patients exhibited impaired sensorimotor adaptation abilities in tasks where movements had to adapt to shifted or rotated visual feedback[63–65], and reduced saccade adaptation[66,67]. These adaptation deficits in SSD may also be explained by dysfunctions in accurately building and updating internal forward models in the cerebellum to minimize the error between predicted and perceived sensory action-outcomes[65,67]. In healthy individuals, tDCS on the cerebellum already showed the potential to improve sensorimotor adaptation performances in similar tasks[68–70]. Initial evidence in non-clinical psychosis further demonstrated the effectiveness of cerebellar tDCS in ameliorating sensorimotor learning deficits[71]. Since cerebellar tDCS had a faciliatory impact on sensorimotor temporal recalibration in both groups in our study, these findings emphasize the potential of this technique to also improve these related adaptive processes in SSD. Furthermore, intact sensorimotor recalibration mechanisms which can be further amplified by cerebellar tDCS could also represent a valuable resource of patients with SSD. For instance, it might be conceivable to train sensorimotor adaptation abilities or the general ability of the forward model to generate appropriate action-outcome predictions and thereby to improve self-other distinction, action-outcome monitoring, and ultimately related clinical symptoms in SSD. Concurrent stimulation of the cerebellum via tDCS may be able to enhance respective training outcomes. However, it is important to note that while our study suggests similar behavioral temporal recalibration effects between patients and healthy individuals, as well as similar effects of cerebellar tDCS on recalibration, further neural correlates of sensorimotor temporal recalibration mechanisms have not yet been investigated in SSD. Future fMRI or EEG studies (for example see[22,72,73]) could prove useful in this regard to determine whether the similar behavioral recalibration effects observed between the groups are also accompanied by similar neural processing during recalibration, or whether differences emerge at the neural level, indicating dysfunctional recalibration-related neural processes.

In conclusion, our study points to similar sensorimotor temporal recalibration mechanisms in HC and SSD and highlights the importance of the cerebellum in both groups for this process. Our results suggest that cerebellar tDCS may constitute a promising tool for addressing deficits in related predictive or adaptive processes based on the forward model in the cerebellum, and potentially linked symptomatology in SSD.

Data availability

The data that support the findings of this study are openly available in Zenodo at: https://doi.org/10.5281/zenodo.10047376.

Received: 30 October 2023; Accepted: 29 January 2024
Published online: 01 February 2024

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Acknowledgements

We thank Jens Sommer for technical support and Michelle Achenbach, Trâm Đỗ, Luca Grolms, Lisa Herberstein, and Sabrina Nasri-Roudsari for assistance in data collection and patient recruitment.

Author contributions

BS and CS conceived and designed the study, and discussed and interpreted the data. CS was responsible for data acquisition and analysis and wrote the manuscript. Both authors revised and approved the submitted version of the manuscript.

Funding

Open Access funding enabled and organized by Projekt DEAL. This research project was supported by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation): STR1146/15-1 (Project Number: 429442932), STR1146/9-2 (Project Number: 286893149) and by "The Adaptive Mind," funded by the Excellence Program of the Hessian Ministry of Higher Education, Science, Research and Art.

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-024-53148-3.

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Supplementary material for the research article: "Facilitation of temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals"

S1. Sample characteristics

Initially, 24 patients with SSD were included in the study, but two of them dropped out before finishing all sessions due to a loss of interest in participating. The final samples of HC and SSD were matched in terms of sex and the level of education (see **Supplementary Table 1**). There were no significant age difference between the groups [independent-samples t-test: $t(40) = .435$, $p = .666$, $d = .134$].

Before the first tDCS session, patients were invited to an additional session during which their diagnosis was verified with the Structured Clinical Interview for DSM-IV (SCID).[1] Furthermore, additional clinical scales and neuropsychological tests were applied during this session (results are summarized in **Supplementary Table 1**). For HC, the same neuropsychological tests were applied during the tDCS sessions.

Supplementary Table 1. Demographics and clinical characteristics.

	SSD (N = 22)	**HC** (N = 20)
Demographics		
Male/Female	11/11	10/10
Age	35.636 +/- 10.363	37.050 +/- 10.699
Higher Education	13	14
Antipsychotic medication		
None	4	20
FGA	2[a]	-
SGA	18	-
Neuropsychological tests		
Attention		
d2 score	163.23 +/- 39.43	175.47 +/- 44.24[b]
Executive functions		
TMT-A (sec.)	26.76 +/- 7.90	23.94 +/- 9.80
TMT-B (sec.)	**72.32 +/- 22.56**	**54.52 +/- 22.90**
Short term memory		
WAIS: FS score	7.50 +/- 1.44	7.65 +/- 1.75
WAIS: BS score	6.14 +/- 1.21	6.60 +/- 1.43
Clinical scales		
SAPS score	18.04 +/- 13.27	
SANS score	13.64 +/- 11.17	
BDI score	0.62 +/- 0.53	
GAF score	60.50 +/- 15.91	
SOFAS score	78.0 +/- 14.01	

Note. FGA = First generation antipsychotics, SGA = Second generation antipsychotics, d2: d2 test of attention,[2] TMT: Trial Making Test,[3] WAIS: Wechsler Adult Intelligence Scale,[4] FS: Forward span, BS:

Backward span, SAPS: Scale for the Assessment of Positive Symptoms,[5] SANS: Scale for the Assessment of Negative Symptoms,[6] BDI: Beck Depression Inventory,[7] GAF: Global Assessment of Functioning,[8] SOFAS: Social and Occupational Functioning Assessment Scale.[9] For continuous variables the mean +/- standard deviation is displayed. Significant differences between HC and SSD are presented with bold values [TMT-B: $t(40) = -2.536$, $p = .015$, $d = -.784$; there were no group differences for any other comparisons: all $p > .260$]. [a]Two patients were medicated with both FGA and SGA. [b]N = 19.

S2. Training Procedure

To ensure that button presses were correctly performed and that participants were familiar with the task, all participants went through a training procedure during the first tDCS session prior to the stimulation. They were trained to let their finger be moved by the button device in passive condition without applying any counter-pressure. They were also trained to perform the button presses with the correct timing, i.e., in intervals of approx. 800ms in adaptation phases and for a duration of approx. 500ms (in both adaptation and test phases). The button presses were chosen to last for 500ms to ensure that stimuli were presented before the upward movement of the button for all test delay levels (the max. delay was 417ms), since it may interfere with delay detection. Even though participants were trained to perform the active button presses with the parameters described above, further measures were taken during the experiment to assure comparable button press parameters for active and passive movement conditions: Passive button press intervals and durations adapted to the mean of the respective preceding active conditions. Adaptation phases always terminated automatically after nine button presses in each of the two parts. If participants completed the button presses too fast in active conditions during a part of the adaptation phase (i.e., faster than 8000ms), the jitter between the adaptation phases (when moving too fast in the first part) or the instruction text for the following test phase (when moving too fast in the second part) were extended by the remaining time. Additionally, participants trained the test phases for each experimental condition, once with no delay and once with the maximum delay between button movement and outcome (417ms) to familiarize with the stimuli and the delays. During the training of test trials, they received feedback about the actual presence of a delay. Responses about the presence of a delay were instructed to be given as accurately, but not as fast as possible. Lastly, they went through in a 10-minute training of the experiment to further familiarize with the task.

S3. Overview of all main and interaction effects for the main analysis

A mixed ANOVA with the between-participants factor *group* and the within-participants factors *stimulation*, *test modality*, *movement type*, and *adaptation delay* was used to assess the impact of these variables on the percentage of detected delays during the

test phases. Of main importance were main and interaction effects including the factor *adaptation delay* since modulations of delay detection performances were expected to occur after exposure to the delayed (200ms) vs. undelayed tone during adaptation phases. **Supplementary Table 2** provides an overview of all effects of this analysis. Please refer to the main manuscript for an interpretation and discussion of the relevant effects. Furthermore, note that excluding the first four patients for which the adaptation delay had been set to 150ms instead of 200ms, did not yield group differences in the overall TRE [$t(36) = 1.508$, $p = .140$, $d = .490$, two-sided], indicating that these patients did not fundamentally affect the reported temporal recalibration results.

Supplementary Table 2. Results of the ANOVA testing for differences in delay detection performances between the experimental conditions

Effect	Sum of Squares	df	Mean Square	F-val.	p-val.	η_p^2
Group	1042.879	1	1042.879	0.239	0.628	0.006
Residuals	174743,407	40	4368.585			
Stimulation	1889.121	3	629.707	3.228	0.025	0.075
Stimulation * Group	579.187	3	193.062	0.990	0.400	0.024
Residuals	23411.494	120	195.096			
Test modality	276.511	1	276.511	1.072	0.307	0.026
Test modality * Group	300.903	1	300.903	1.167	0.286	0.028
Residuals	10313.270	40	257.832			
Movement type	8490.601	1	8490.601	23.817	< .001	0.373
Movement type * Group	15.472	1	15.472	0.043	0.836	0.001
Residuals	14259.492	40	356.487			
Adaptation delay	3381.799	1	3381.799	14.033	< .001	0.260
Adaptation delay * Group	64.406	1	64.406	0.267	0.608	0.007
Residuals	9639.504	40	240.988			
Stimulation * Test modality	41.766	3	13.922	0.487	0.692	0.012
Stimulation * Test modality * Group	20.466	3	6.822	0.239	0.869	0.006
Residuals	3429.039	120	28.575			
Stimulation * Movement type	498.654	3	166.218	2.905	0.038	0.068
Stimulation * Movement type * Group	1.018	3	0.339	0.006	0.999	1.483e -4
Residuals	6865.225	120	57.210			
Test modality * Movement type	3085.947	1	3085.947	57.555	< .001	0.590
Test modality * Movement type * Group	4.002	1	4.002	0.075	0.786	0.002
Residuals	2144.706	40	53.618			
Stimulation * Adaptation delay	442.776	3	147.592	2.800	0.043	0.065
Stimulation * Adaptation delay * Group	28.934	3	9.645	0.183	0.908	0.005
Residuals	6324.609	120	52.705			
Test modality * Adaptation delay	398.065	1	398.065	9.229	0.004	0.187
Test modality * Adaptation delay * Group	8.787	1	8.787	0.204	0.654	0.005
Residuals	1725.286	40	43.132			
Movement type * Adaptation delay	289.127	1	289.127	8.762	0.005	0.180
Movement type * Adaptation delay * Group	74.661	1	74.661	2.263	0.140	0.054
Residuals	1319.897	40	32.997			
Stimulation * Test modality * Movement type	81.283	3	27.094	1.558	0.203	0.037

Stimulation * Test modality * Movement type * Group	17.785	3	5.928	0.341	0.796	0.008
Residuals	2086.397	120	17.387			
Stimulation * Test modality * Adaptation delay	117.841	3	39.280	1.425	0.239	0.034
Stimulation * Test modality * Adaptation delay * Group	18.754	3	6.251	0.227	0.878	0.006
Residuals	3307.155	120	27.560			
Stimulation * Movement type * Adaptation delay	15.263	3	5.088	0.131	0.941	0.003
Stimulation * Movement type * Adaptation delay * Group	19.708	3	6.569	0.169	0.917	0.004
Residuals	4656.530	120	38.804			
Test modality * Movement type * Adaptation delay	460.901	1	460.901	7.781	0.008	0.163
Test modality * Movement type * Adaptation delay * Group	33.242	1	33.242	0.561	0.458	0.014
Residuals	2369.495	40	59.237			
Stimulation * Test modality * Movement type * Adaptation delay	179.676	3	59.892	3.343	0.022	0.077
Stimulation * Test modality * Movement type * Adaptation delay * Group	5.751	3	1.917	0.107	0.956	0.003
Residuals	2149.907	120	17.916			

Note. N_{HC} = 20, N_{SSD} = 22

S4. Stimulation side effects

After each session, participants reported on a custom-designed questionnaire whether they perceived any side effects due to the tDCS stimulation [on a scale from one (no side effect) to five (strong side effect) for 28 items]. To test for potential differences in perceived stimulation side effects between groups and stimulation conditions, we conducted a mixed ANOVA with the between-participants factor *group* and the within-participants factor *stimulation*. A full overview of the results is displayed in **Supplementary Table 3**. There was a significant main effect of *group* indicating that patients with SSD (*Mean* = 1.608, *SD* = .441) reported stronger perceived side effects than HC (*Mean* = 1.229, *SD* = .281). Importantly, since there were no group differences in the TRE or in the impact of tDCS on the TRE in our study, this difference in perceived stimulation side effects should not have influenced our reported main results. There was no significant main effect of *stimulation* and no interaction of the factors *group* and *stimulation*, indicating that the amount of perceived side effects did not differ between the different stimulation conditions.

Supplementary Table 3. Results of the ANOVA testing for differences in perceived stimulation side effects.

Effect	Sum of Squares	df	Mean Square	F-val.	p-val.	η_p^2
Group	6.030	1	6.030	18.459	< .001	.316
Residuals	13.067	40	.327			
Stimulation	.357	3	.119	1.535	.209	.037
Stimulation * Group	.421	3	.140	1.810	.149	.043
Residuals	9.307	120	.078			

Note. N_{HC} = 20, N_{SSD} = 22

S5. Group-dependent differences in delay detection performance between active and passive conditions

The rationale of the present study was based on the established finding that patients with SSD show impairments in predicting the sensory outcomes of self-generated actions which manifests in reduced perceptual differences between actively vs. passively elicited stimuli in SSD compared to HC.[10-13] Here, we investigated whether this impairment may partly be attributed to dysfunctional sensorimotor temporal recalibration mechanisms. Thus, firstly, the question arises as to whether there was such a general impairment in predicting sensory action-outcomes in patients, meaning whether they showed a reduced difference in the processing of actively vs. passively generated stimuli in our study.

Both groups detected more delays in active compared to passive conditions. According to paired-samples t-tests, this difference was significant in HC [*Mean difference* = 6.591, *SD* = 6.561, $t(19) = 4.493$, $p < .001$, $d = 1.005$, two-sided], but failed to reach significance for SSD [*Mean difference* = 3.635, *SD* = 9.135, $t(21) = 1.866$, $p = .076$, $d = .398$, two-sided]. Nonetheless, this group difference appeared to be not strong enough or the variance within the groups might have been too large to lead to a significant *group* x *movement type* interaction in the ANOVA reported in the main manuscript.

However, since it may be reasonable to assume that the active-passive difference in delay detection occurs for certain delay levels only, we also conducted a generalized estimating equations (GEE) analysis using IBM SPSS Statistics (Version 27.0) with the active-passive difference in the percentage of detected delays as dependent variable, which was computed separately for each of the six delay levels used during the test phases. An AR (1) working correlation structure and robust (sandwich) covariance estimators were used for the regression coefficients. The factors, *stimulation* (cerebellum, TPJ, SMA, sham), *test modality* (auditory, visual), *test delay* (0, 83, 167,

250, 333, 417ms), and *group* (HC, SSD) were included in a full factorial model testing for all main and interaction effects. The active-passive difference was modeled with a linear link function. Importantly, this analysis revealed a significant interaction of *group* and *test delay* [Wald Chi-Square (df = 5) = 13.332, p = .020]. According to post-hoc tests, the active-passive difference was significantly stronger in HC than in SSD for test stimuli delayed by 250ms [mean difference = 11.512, standard error = 3.928, df = 1, p = .003].

Hence, for an individual medium-sized delay level, patients showed reduced differences in the perception of actively vs. passively elicited stimuli. Importantly, the medium-sized delay levels are the ones for which most prominent active-passive differences can be assumed due to floor or ceiling effects at very small or large delays, respectively. Thus, to a given extent, there are indications for the aberrant processing of actively generated action-outcomes in SSD in in our study, but we cannot provide evidence for the attribution of this impairment to dysfunctional temporal recalibration mechanisms.

S6. Exploratory comparisons between effects of the three active stimulation conditions on the TRE

We also explored whether the TRE with cerebellar tDCS, particularly in active and auditory conditions, was not only significantly larger compared to sham stimulation (as reported in the main manuscript), but whether it was also significantly larger compared to tDCS of the TPJ or SMA. To this end, by means of one-sided two-samples t-tests, we compared the TRE in these conditions between cerebellar tDCS and the other two active tDCS conditions.

Across groups, the TRE was significantly larger with cerebellar tDCS compared to tDCS of the TPJ [Across groups: Mean difference = 3.983, SD = 13.713, t(41) = 1.960, p = .028, d = .302; SSD: Mean difference = 3.538, SD = 18.248, t(21) = .909, p = .187, d = .194; HC: Mean difference = 4.473, SD = 9.928, t(19) = 2.015, p = .029, d = .451]. Similarly, across patients and HC, the TRE was significantly larger with cerebellar tDCS compared to tDCS of the SMA [Across groups: Mean difference = 4.164, SD = 15.541, t(41) = 1.736, p = .045, d = .268; SSD: Mean difference = 4.764, SD = 19.575, t(21) = 1.141, p = .133, d = .243; HC: Mean difference = 3.503, SD = 12.095, t(19) = 1.295, p = .105, d = .290]. Furthermore, according to a two-sided, two-samples t-test, the TRE did not differ significantly between TPJ and SMA stimulation [Across groups: Mean difference = .180, SD = 11.268, t(41) = .104, p = .918, d = .016; SSD: Mean difference = 1.226, SD = 14.588, t(21) = .394, p = .698, d = .084; HC: Mean difference = -.970, SD = 9.769, t(19) = -.444, p = .662, d = -.099].

Thus, the effects across both groups indicate the superiority of cerebellar tDCS in facilitating the TRE not only in comparison to sham stimulation but also in comparison to tDCS of the TPJ and SMA. It must be noted though that the tests for each individual group seemed to have lacked sufficient statistical power to consistently reveal significant differences between stimulation conditions. Nonetheless, these results provide further evidence for the importance specifically of the cerebellum in the recalibration of forward model predictions, as compared to the TPJ and SMA which were also frequently associated with processes related to the forward model, such as action-outcome processing and the sense of agency. Furthermore, they emphasize that the cerebellum may be the most promising stimulation site for enhancing the adaptability of forward model predictions.

S7. Exploratory analysis of patient subgroups

The SSD group in our study did not only consist of patients with a F20 diagnosis of schizophrenia (SZ) but also included a small group of patients diagnosed with a schizoaffective disorder (SZA). To test whether the results reported in the main manuscript are driven by the SZA group and do not reflect the pattern in the SZ group, the main analyses were exploratorily performed for the subgroup of patients with SZ (N = 15). Since our sample only comprised 6 patients with SZA, the data pattern for this group was inspected descriptively only.

Results of all main and interaction effects of the mixed ANOVA with the factors *group* (SZ, HC), *movement type* (active, passive), *test modality* (visual, auditory), and *adaptation delay* (0ms, 200ms) are depicted in **Supplementary Table 4** and in **Supplementary Fig. 1**. An overview of effects computed individually for the SZ group are additionally provided in **Supplementary Table 5**. As in the analysis with the entire SSD sample reported in the main manuscript, there was no significant main effect of *group* [$F(1, 33) = .010$, $p = .922$, $\eta_p^2 < .001$] and no interaction effects including the factors *group* and *adaptation delay* (all $p > .068$). Across groups and conditions, there was a significant main effect of the *adaptation delay* [$F(1, 33) = 13.934$, $p < .001$, $\eta_p^2 = .297$], indicating significant temporal recalibration [*Mean TRE* = 3.334, *SD* = 5.319]. The significant interaction of *movement type* and *adaptation delay* [$F(1, 33) = 14.242$, $p = < .001$, $\eta_p^2 = 0.301$] revealed that the TRE was significantly greater than zero in both active [*Mean TRE* = 4.647, *SD* = 4.390, $t(34) = 6.263$, $p < .001$, $d = 1.059$, $\alpha_{corr} = .025$] and passive conditions [*Mean TRE* = 2.020, *SD* = 6.715, $t(34) = 1.780$, $p = .042$, $d = .301$, $\alpha_{corr} = .025$], but was significantly stronger in active ones [*Mean difference* = 2.627, *SD* = 3.944, $t(34) = 3.940$, $p < .001$, $d = .666$]. According to the

significant *test modality* and *adaptation delay* interaction [$F(1, 33) = 7.293$, $p = .011$, $\eta_p^2 = .181$], the TRE was significantly greater than zero for both, audition [*Mean TRE* = 4.366, *SD* = 5.730, $t(34) = 4.508$, $p < .001$, $d = .762$, $\alpha_{corr} = .025$] and vision [*Mean TRE* = 2.301, *SD* = 5.734, $t(34) = 2.374$, $p = .012$, $d = .401$, $\alpha_{corr} = .025$], but remained significantly larger in auditory (unimodal) than in visual (cross-modal) conditions [*Mean difference* = 2.065, *SD* = 4.273, $t(34) = 2.859$, $p = .004$, $d = .483$]. The significant interaction of the three factors *movement type*, *test modality*, and *adaptation delay* [$F(1, 33) = 5.265$, $p = .028$, $\eta_p^2 = .138$] further indicated that the active-passive difference in the TRE was specific to auditory outcomes [*Mean difference* = 4.662, *SD* = 6.442, $t(34) = 4.281$, $p < .001$, $d = .724$, $\alpha_{corr} = .025$; Active: *Mean TRE* = 6.698, *SD* = 6.120, $t(34) = 6.474$, $p < .001$, $d = 1.094$, $\alpha_{corr} = .025$; Passive: *Mean TRE* = 2.035, *SD* = 6.997, $t(34) = 1.721$, $p = .047$, $d = .291$, $\alpha_{corr} = .025$] but did not transfer to the visual modality [*Mean difference* = .592, *SD* = 6.641, $t(34) = .527$, $p = .301$, $d = .089$, $\alpha_{corr} = .025$; Active: *Mean TRE* = 2.597, *SD* = 4.495, $t(34) = 3.418$, $p = < .001$, $d = .578$, $\alpha_{corr} = .025$; Passive: *Mean TRE* = 2.005, *SD* = 8.223, $t(34) = 1.443$, $p = .079$, $d = .244$, $\alpha_{corr} = .025$].

Regarding stimulation dependent effects, the significant interaction of *stimulation* and *adaptation delay* [$F(3, 99) = 3.333$, $p = .023$, $\eta_p^2 = .092$] revealed that the TRE was significantly stronger after cerebellar tDCS compared to sham stimulation [*Mean difference* = 3.772, *SD* = 7.892, $t(34) = 2.827$, $p = .004$, $d = .478$, $\alpha_{corr} = .016$; Sham: *Mean TRE* = 1.692, *SD* = 6.476, $t(34) = 1.545$, $p = .066$, $d = .401$, $\alpha_{corr} = .025$; Cerebellum: *Mean TRE* = 5.463, *SD* = 7.750, $t(34) = 4.171$, $p < .001$, $d = .705$, $\alpha_{corr} = .025$], but not after tDCS on the right SMA [*Mean difference* = 1.012, *SD* = 8.645, $t(34) = .693$, $p = .247$, $d = .117$, $\alpha_{corr} = .016$] or the right TPJ [*Mean difference* = 1.784, *SD* = 6.244, $t(34) = 1.691$, $p = .050$, $d = .286$, $\alpha_{corr} = .016$]. Contrary to the analysis reported in the main manuscript, the four-way interaction of *stimulation*, *movement type*, *test modality*, and *adaptation delay* did not reach significance [$F(3, 99) = .232$, $p = .874$, $\eta_p^2 = .007$].

Overall, the results of this analysis limited to the subgroup of patients with SZ show strong similarities to the results reported with the entire SSD sample in the main manuscript, with comparable TREs for patients and HC, and a faciliatory impact of cerebellar tDCS on the TRE. Minor differences between the analyses, such as the non-significant four-way interaction when only including SZ patients, may be attributed to the smaller sample size and thus reduced statistical power in the SZ subgroup. Furthermore, although the number of SZA patients in our sample was very small, the pattern of results in this subgroup also aligns with that of the SZ subgroup and the combined SSD group (see **Supplementary Fig. 2**). These results could suggest that the underlying temporal

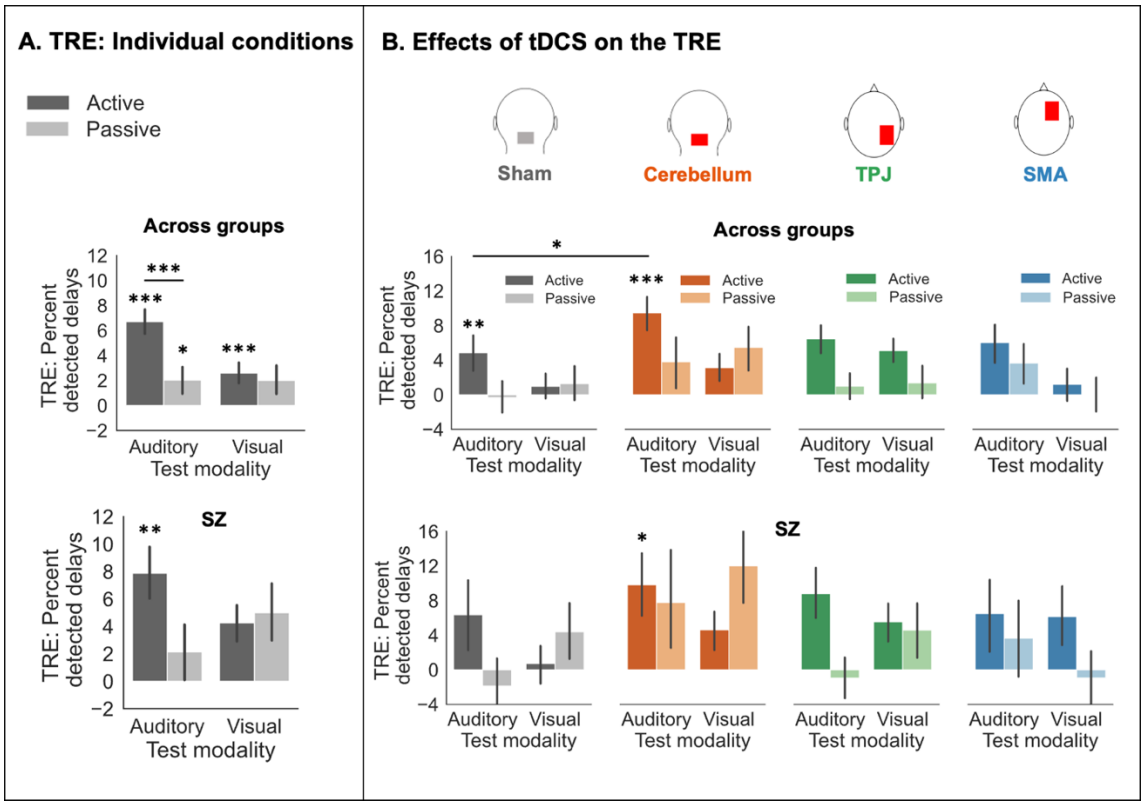
recalibration mechanisms and cerebellar processes are comparable for different diagnoses of the schizophrenia spectrum. This is in line with previous findings demonstrating that similar deficits in processing self-generated action-outcomes are associated with SZ and SZA,[14] indicating commonalities in sensorimotor functions and their impairments in psychosis with and without affective symptomatology. However, it is important to emphasize that due to the small sample sizes in the patient subgroups in the present study, conclusions about the subgroup results should be taken with caution.

Supplementary Table 4. Results of the ANOVA testing for differences in delay detection performances between the experimental conditions only including the subgroup of patients diagnosed with a F20 diagnosis of schizophrenia.

Effect	Sum of Squares	df	Mean Square	F-val.	p-val.	η_p^2
Group	36.626	1	36.626	0.010	0.922	2.970 e -4
Residuals	123266.193	33	3735.339			
Stimulation	2345.506	3	781.835	4.064	0.009	0.110
Stimulation * Group	716.295	3	238.765	1.241	0.299	0.036
Residuals	19045.700	99	192.381			
Test modality	665.489	1	665.489	3.133	0.086	0.087
Test modality * Group	117.060	1	117.060	0.551	0.463	0.016
Residuals	7009.874	33	212.420			
Movement type	8353.120	1	8353.120	37.985	< .001	0.535
Movement type * Group	106.324	1	106.324	0.483	0.492	0.014
Residuals	7256.944	33	219.907			
Adaptation delay	3207.381	1	3207.381	13.934	< .001	0.297
Adaptation delay * Group	98.913	1	98.913	0.430	0.517	0.013
Residuals	7596.323	33	230.192			
Stimulation * Test modality	112.140	3	37.380	1.259	0.293	0.037
Stimulation * Test modality * Group	21.372	3	7.124	0.240	0.868	0.007
Residuals	2939.090	99	29.688			
Stimulation * Movement type	231.092	3	77.031	1.363	0.259	0.040
Stimulation * Movement type * Group	39.864	3	13.288	0.235	0.872	0.007
Residuals	5595.882	99	56.524			
Test modality * Movement type	2520.472	1	2520.472	62.251	< .001	0.654
Test modality * Movement type * Group	11.838	1	11.838	0.292	0.592	0.009
Residuals	1336.136	33	40.489			
Stimulation * Adaptation delay	551.740	3	183.913	3.333	0.023	0.092
Stimulation * Adaptation delay * Group	134.200	3	44.733	0.811	0.491	0.024
Residuals	5462.450	99	55.176			
Test modality * Adaptation delay	269.260	1	269.260	7.293	0.011	0.181
Test modality * Adaptation delay * Group	23.427	1	23.427	0.635	0.431	0.019
Residuals	1218.355	33	36.920			
Movement type * Adaptation delay	412.343	1	412.343	14.242	< .001	0.301
Movement type * Adaptation delay * Group	102.564	1	102.564	3.543	0.069	0.097
Residuals	955.419	33	28.952			
Stimulation * Test modality * Movement type	37.519	3	12.506	0.637	0.593	0.019

Stimulation * Test modality * Movement type * Group	28.846	3	9.615	0.490	0.690	0.015
Residuals	1944.185	99	19.638			
Stimulation * Test modality * Adaptation delay	138.749	3	46.250	1.814	0.149	0.052
Stimulation * Test modality * Adaptation delay * Group	8.956	3	2.985	0.117	0.950	0.004
Residuals	2523.582	99	25.491			
Stimulation * Movement type * Adaptation delay	101.036	3	33.679	0.951	0.419	0.028
Stimulation * Movement type * Adaptation delay * Group	3.637	3	1.212	0.034	0.991	0.001
Residuals	3504.506	99	35.399			
Test modality * Movement type * Adaptation delay	294.782		294.782	5.265	0.028	0.138
Test modality * Movement type * Adaptation delay * Group	4.851	1	4.851	0.087	0.770	0.003
Residuals	1847.790	33	55.994			
Stimulation * Test modality * Movement type * Adaptation delay	138.584	3	46.195	2.176	0.096	0.062
Stimulation * Test modality * Movement type * Adaptation delay * Group	14.775	3	4.925	0.232	0.874	0.007
Residuals	2101.705	99	21.229			

Note. N_{HC} = 20, N_{SZ} = 15



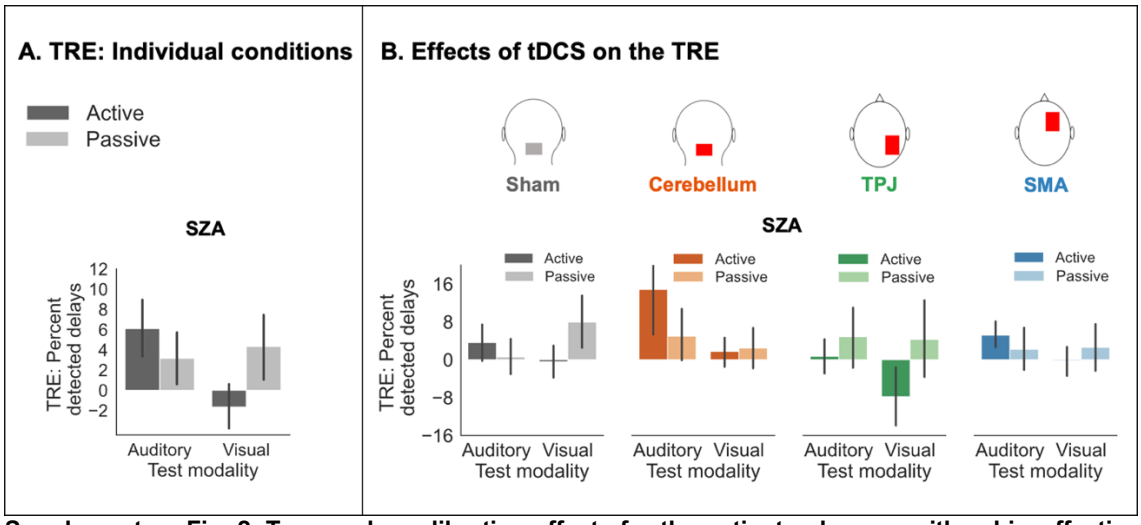
Supplementary Fig. 1. Temporal recalibration effects for the patient subgroup with schizophrenia. **A:** The TRE, defined as the difference in the percentage of detected delays between conditions with the 200ms vs. 0ms delay during preceding adaptation phases, is displayed for each experimental condition (i.e., for both test modalities and movement types), across HC and patients diagnosed with a F20 diagnosis of schizophrenia (SZ; N = 15), as well as separately for SZ patients. **B:** The TRE is displayed for each of the

four stimulation conditions, again across HC and SZ patients and separately for SZ patients. Error bars indicate standard errors of the mean. *p > .05, **p < .01, ***p < .001.

Supplementary Table 5. TREs for individual conditions and comparisons of conditions, evaluated for the subgroup of patients diagnosed with a F20 diagnosis of schizophrenia.

TRE	Mean+/-SD	t-value	p-value	α_{corr}	Cohen´s d
Across conditions	**4.821 +/- 8.199**	**2.278**	**.019***	**.05**	**.588**
Active	**6.064 +/ 8.207**	**2.862**	**.006*****	**.025**	**.739**
Passive	3.578 +/- 9.160	1.513	.076	.025	.391
Active > Passive	2.486 +/- 5.802	1.659	.060	.05	.428
Auditory	5.010 +/- 9.122	2.127	.026	.025	.549
Visual	4.632 +/- 8.439	2.126	.026	.025	.549
Auditory > Visual	.378 +/- 6.323	.231	.410	.05	.060
Auditory: Active	**7.872 +/- 11.416**	**2.671**	**.009****	**.025**	**.690**
Auditory: Passive	2.148 +/- 9.598	.867	.200	.025	.224
Visual: Active	**4.256 +/- 7.284**	**2.263**	**.020***	**.025**	**.584**
Visual: Passive	5.009 +/- 10.618	1.827	.045	.025	.472
Auditory: Active > Passive	**5.724 +/- 10.586**	**2.094**	**.027**	**.025**	**.541**
Visual: Active > Passive	-.752 +/- 6.836	-.426	.662	.025	-.110
Sham	2.401 +/- 8.866	1.049	.156	.025	.271
Cerebellum	**8.554 +/- 12.707**	**2.607**	**.010****	**.025**	**.673**
Cerebellum > Sham		**2.116**	**.026***	**.05**	**.546**
Active/Auditory: Sham	6.372 +/- 16.801	1.469	.082	.025	.379
Active/Auditory: Cerebellum	**9.832 +/- 15.441**	**2.466**	**.014***	**.025**	**.637**
Active/Auditory: Cerebellum > Sham	3.461 +/- 18.389	.729	.239	.05	.188

Note. The TRE is defined as the difference in the percentage of detected delays between conditions with the 200ms vs. 0ms delay during preceding adaptation phases. For individual conditions, one-sample t-tests were used to assess whether the TRE was significantly greater than zero. Difference in TRE between conditions were assessed with two-samples t-tests. All t-tests were Bonferroni corrected. The corrected alpha level used for each test is displayed in the column α_{corr}. Significant tests are presented with bold values. N_{SZ} = 15. *p < .05, **p < .01, ***p < .001.



Supplementary Fig. 2. Temporal recalibration effects for the patient subgroup with schizoaffective disorder. A: The TRE, defined as the difference in the percentage of detected delays between conditions with the 200ms vs. 0ms delay during preceding adaptation phases, is displayed for each experimental condition (i.e., for both test modalities and movement types) for the subgroup of patients diagnosed with schizoaffective disorder (SZA; N = 6). **B:** The TRE is displayed for each of the four stimulation conditions. Error bars indicate standard errors of the mean.

S8. Limitations

The results of our study do not provide evidence for impaired sensorimotor temporal recalibration mechanisms in patients with SSD, as there were no significant differences compared to the HC group. This could indicate that sensorimotor recalibration abilities may be a useful resource of patients with SSD that could be exploited to train predictive mechanisms based on the forward model and to thereby improve self-other differentiation and action-outcome monitoring. Importantly, however, the absence of group differences in recalibration does not necessarily speak against the existence of an impairment in patients; it is also conceivable that certain characteristics of our study have masked differences between the groups.

Firstly, previous studies on potentially related adaptive processes, namely on sensorimotor adaptation, could show that patients were able to adapt their movements to the introduced action feedback perturbations, but they adapted slower[15] and the adaptation process was associated with more errors[16] compared to HC. Our study design did not allow for the investigation of the time course of temporal recalibration effects. Adaptation and test phases were blocked, which only allowed us to assess the impact of the adaptation delay on perception once at the end of an adaptation phase. Thus, future study designs should consider that the time course of adaptation could provide important information regarding potential impairments in patients.

Secondly, the majority of patients in our sample were under antipsychotic medication at the time of the study. This could have compensated for potentially existing deficits, since antipsychotics are known to particularly target positive symptoms, such as hallucinations and delusions, which are believed to be associated with the dysfunctions in predictive mechanisms of the forward model investigated here.[10-13,17,18] Additionally, the patients exhibited on average a relatively high level of functioning and displayed only moderate levels of symptoms at the time of testing, as indicated by the SANS and SAPS scores (see **Supplementary Table 1**). Therefore, it should be noted that it remains open whether group differences in sensorimotor temporal recalibration might have emerged in a sample characterized by higher average symptom scores and a larger number of patients. Although our data indicate that recalibration processes are comparable between patients and healthy individuals, cerebellar tDCS may also have the potential to normalize patients' recalibration performance if they exhibit impairments in this process.

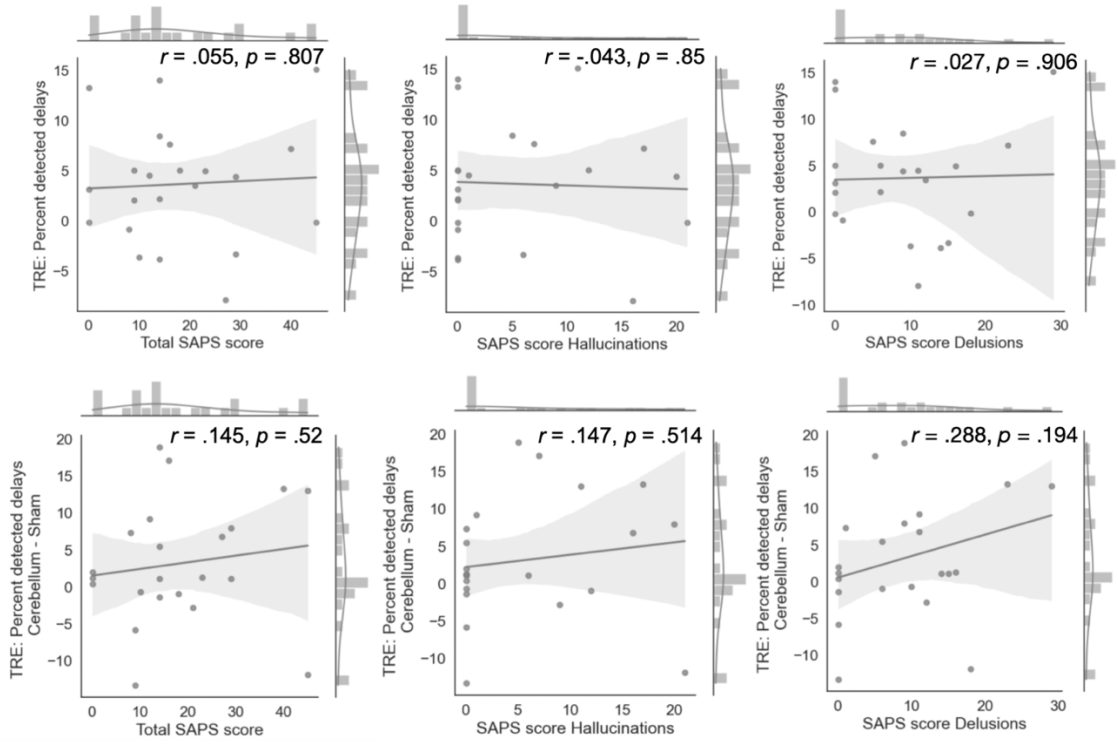
Thirdly, the variance in temporal recalibration and stimulation effects appeared to be high in our study, particularly in the patient group. While this may partly be explained by the relatively low sample sizes, it could also suggest that there are individual differences in whether patients exhibit dysfunctions in sensorimotor temporal recalibration mechanisms. Likewise, there could be individual differences in the effectiveness of tDCS on enhancing recalibration effects. Hence, it would be useful to determine under which conditions patients may exhibit dysfunctions in temporal recalibration or profit from tDCS. A relevant factor could, for instance, be the presence the above-mentioned symptoms related to the presumed deficits in predictive mechanisms. In our study, exploratory correlation analyses did not reveal a relationship between temporal recalibration and these symptoms (see supplementary material S9), but future studies with larger sample sizes could specifically investigate the determining factors for the occurrence of a potential deficit in this process and the effectiveness of tDCS on facilitating the underlying predictive mechanisms. Furthermore, variability in stimulation-dependent effects may also arise due to individual differences in participants' cerebellar anatomy and connectivity pattern with other brain regions.[19] Thus, future studies could apply individually adjusted stimulation protocols according to the participants' individual anatomy.

Finally, it should be acknowledged that the actual mechanism underlying sensorimotor temporal recalibration are not yet fully understood. A recent and ongoing debate has cast doubt on the suitability of the forward model framework for explaining the processing of all types of action-outcomes. It has been suggested that external outcomes of an action

which are not body-related, such as the abstract visual and auditory stimuli employed in the present study, may be subject to more general predictive mechanisms that operate across perceptual and motor domains, as opposed to forward model predictions based on efference copy signals.[20-22] Importantly though, the difference in the TRE between active and passive movement conditions observed here as well as in previous studies[23-26] indicates that there are unique characteristics in predictive mechanisms depending on whether an active action is involved, as proposed by the forward model framework. Nonetheless, the exact neural mechanisms by which action-outcome predictions are generated and recalibrated in regions like the cerebellum remain to be more closely examined.

S9. Exploratory correlation analyses of the TRE and SAPS score

Dysfunctions in predictive mechanisms of the forward model, i.e., in adequately predicting the sensory outcomes of self-generated actions, are assumed to partly underly symptoms in SSD, such as hallucinations (e.g., perceiving the own inner speech as external voice) and ego-disturbances or delusions of control (e.g., perceiving own thoughts or actions as externally controlled).[27] Thus, it is conceivable that the severity of these symptoms correlates with the ability to recalibrate forward model predictions in response to changes in environmental conditions. To test this, we performed exploratory correlation analyses between the TRE and the total SAPS score as well as the SAPS subscales for hallucinations and delusions obtained from the patients. Furthermore, we tested whether the amount of facilitation of the TRE by cerebellar tDCS correlated with the same clinical measures. All correlations were performed with the SciPy package (version 1.11.1) for Python (version 3.11; https://www.python.org/). However, none of these correlations reached significance (see **Supplementary Fig. 3**). This could either indicate that the emergence of the TRE did not depend on the severity of the respective symptoms in our study but may also be explained by the relatively small sample of 22 patients, which might have resulted in insufficient statistical power for such effects to emerge (see also supplementary material S8).



Supplementary Fig. 3. Upper row: Correlations between the TRE and the SAPS score (total score and for the subscales on hallucinations and delusions) of the SSD group are displayed. **Lower row:** Correlations are displayed between the same SAPS scores and the amount of facilitation of the TRE by cerebellar tDCS compared to sham stimulation.

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II. Manuscript Contributions

Study I:

Schmitter, C.V., Kufer, K., Steinsträter, O., Sommer, J., Kircher, T., & Straube, B. (2023). Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements. *Human Brain Mapping*, hbm.26508. https://doi.org/10.1002/hbm.26508

Contribution: 75%

Conceptualization	BS, **CS**, TK
Methodology	BS, **CS**, JS, KK, TK
Software	OS
Investigation and Recruitment	**CS**, KK
Formal analysis	**CS**
Interpretation	BS, **CS**, KK
Writing – Original Draft	**CS**
Writing – Review & Editing	BS, **CS**, KK, TK
Visualization	**CS**
Supervision	BS, TK
Funding acquisition	BS, TK

Study II:

Schmitter, C.V., & Straube, B. (2022). The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration. *Frontiers in Human Neuroscience*, *16*, 998843. https://doi.org/10.3389/fnhum.2022.998843

Contribution: 90%

Conceptualization	BS, **CS**
Methodology	BS, **CS**
Software	**CS**
Investigation and Recruitment	**CS**
Formal analysis	**CS**
Interpretation	BS, **CS**
Writing – Original Draft	**CS**

Writing – Review & Editing	BS, **CS**
Visualization	**CS**
Supervision	BS
Funding acquisition	BS

Study III:

Schmitter, C.V., & Straube, B. (2024). Facilitation of sensorimotor temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals. *Scientific Reports*, *14*(1), 2627. https://doi.org/10.1038/s41598-024-53148-3

Contribution: 90%

Conceptualization	BS, **CS**
Methodology	BS, **CS**
Software	**CS**
Investigation and Recruitment	**CS**
Formal analysis	**CS**
Interpretation	BS, **CS**
Writing – Original Draft	**CS**
Writing – Review & Editing	BS, **CS**
Visualization	**CS**
Supervision	BS
Funding acquisition	BS

III. List of Publications

Kufer, K., **Schmitter, C.V.**, Kircher, T., & Straube, B. (2024). Temporal recalibration in response to delayed visual feedback of active versus passive actions: An fMRI study. *Scientific Reports, 14*(1), 4632. https://doi.org/10.1038/s41598-024-54660-2

Schmitter, C.V., Kufer, K., Steinsträter, O., Sommer, J., Kircher, T., & Straube, B. (2023). Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements. *Human Brain Mapping*, hbm.26508. https://doi.org/10.1002/hbm.26508

Schmitter, C.V., Steinsträter, O., Kircher, T., van Kemenade, B.M., & Straube, B. (2021). Commonalities and differences in predictive neural processing of discrete vs. continuous action feedback. *NeuroImage*, *229*, 117745. https://doi.org/10.1016/j.neuroimage.2021.117745

Schmitter, C.V., & Straube, B. (2024). Facilitation of sensorimotor temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals. *Scientific Reports*, *14*(1), 2627. https://doi.org/10.1038/s41598-024-53148-3

Schmitter, C.V., & Straube, B. (2022). The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration. *Frontiers in Human Neuroscience*, *16*, 998843. https://doi.org/10.3389/fnhum.2022.998843

Schülke, R., **Schmitter, C.V.**, & Straube, B. (2023). Improving causality perception judgements in schizophrenia spectrum disorder via transcranial direct current stimulation. *Journal of Psychiatry and Neuroscience*, *48*(4), E245–E254. https://doi.org/10.1503/jpn.220184

IV. Curriculum Vitae

Die folgenden Seiten 141 – 142 (Curriculum Vitae) enthalten persönliche Daten und sind deshalb nicht Bestandteil dieser Veröffentlichung.

V. Verzeichnis der akademischen Lehrenden

Meine akademischen Lehrenden waren:

In Marburg:

Dr. Beatriz Arias Martin
Dr. Antonia Barke
Prof. Dr. Annette Borchers
Prof. Dr. Eva-Lotta Brakemeier
Prof. Dr. Frank Bremmer
Prof. Dr. Moritz Bünemann
Prof. Dr. Hanna Christiansen
Prof. Dr. Carsten Culmsee
Prof. Dr. Niels Decher
Prof. Dr. Dominik Endres
Dr. Karin Funsch
Dr. Jose C. García Alanis
Dr. Patricia Garrido-Vasquez
Prof. Dr. Julia A. Glombiewski
Prof. Dr. Mario Gollwitzer
Dipl.-Psych. Marianne Hannuschke
Dr. Anna Heuer
Prof. Dr. Uwe Homberg
Prof. Dr. Andreas Jansen
Dr. Franziska Jeromin
Prof. Dr. Tilo Kircher
Prof. Dr. Florian Klapproth
Dr. Kristina Klaus-Schiffer
Dr. Ina Kluge
Dr. Stefan König
Prof. Dr. Harald Lachnit
Dr. Gunnar Lemmer
Prof. Dr. Stephanie Mehl
Prof. Dr. Urs Nater
Prof. Dr. Igor Nenadić
Prof. Dr. Katja Nieweg
Prof. Dr. Johannes Oberwinkler
Prof. Dr. Dominik Oliver
Prof. Dr. Kathleen Otto
Prof. Dr. Martin Peper
Prof. Dr. Martin Pinquart
Prof. Dr. Timothy David Plant
Prof. Dr. Winfried Rief
Prof. Dr. Lothar Schmidt-Atzert
Prof. Dr. Anna Schubö
Prof. Dr. Alexander Schütz
Prof. Dr. Rainer Schwarting
Prof. Dr. Malte Schwinger
Prof. Dr. Gerhard Stemmler
Dr. Hannah Margraf
Dr. Jutta Margraf-Stiksrud
Dr. Hans Onno Röttgers
Prof. Dr. Marco Rust
Prof. Dr. Joachim Schachtner
Dr. Christian Schales
Dr. Ulrich Schu
Dr. Jana Strahler
Prof. Dr. Benjamin Straube
Prof. Dr. Kati Thieme
Dr. Anna Thorwart
Prof. Dr. Lars Timmermann
Dr. Jan Tünnermann
Dr. Metin Üngör
Prof. Dr. Bianca van Kemenade
Prof. Dr. Ulrich Wagner
Prof. Dr. Eberhard Weihe
Dr. Cornelia Weise
Prof. Dr. Richard Wiese
Dr. Markus Wöhr

In Stockholm:

Prof. Dr. Johan Lundström
Prof. Dr. Mats Olsson

VI. Danksagung

An erster Stelle möchte ich mich herzlich bei meinem Betreuer Benjamin Straube für die umfassende Unterstützung dieser Arbeit bedanken. Die vielen anregenden und motivierenden Diskussionen in stets angenehmer Atmosphäre sowie die Unterstützung bei sämtlichen Herausforderungen haben stark dazu beigetragen, dass die letzten vier Jahre eine sehr positive und lehrreiche Erfahrung für mich waren.

Mein besonderer Dank gilt auch allen Koautoren der Studien in dieser Dissertation für die hervorragende Zusammenarbeit. Ein besonderer Dank geht an Jens Sommer und Olaf Steinsträter, die maßgeblich zur Umsetzung des technischen Setups der Studien beigetragen haben und immer sofort zur Stelle waren, wenn Fragen oder Probleme aufgetreten sind. Außerdem möchte ich mich bei allen Hiwis bedanken, die sehr viel Arbeit investiert haben, um die umfangreichen Daten für die Studien dieser Dissertation zu sammeln. Ein besonderer Dank geht auch an das MRT-Team, Mecky Wallnig und Rita Werner, die die MRT-Messungen dieser Arbeit maßgeblich unterstützt haben.

Ein großes Dankeschön geht ebenso an das TNM-Lab dafür, dass immer eine angenehme Arbeitsatmosphäre geherrscht hat und gegenseitige Unterstützung selbstverständlich war. Weiterhin möchte ich mich bei den Mitgliedern des IRTG 1901 „The Brain in Action“ und des TAM („The Adaptive Mind“) Projektes bedanken. Ein Teil dieser Gruppen gewesen sein zu dürfen, hat wertvolle Möglichkeiten zum Austausch und zur fachlichen Weiterentwicklung geboten.

Schließlich gilt mein aufrichtiger Dank meiner Familie und meinen Freunden für die vielseitige moralische Unterstützung während der letzten Jahre und insbesondere während der Zeit der Promotion.

VII. Ehrenwörtliche Erklärung

Ich erkläre ehrenwörtlich, dass ich die dem Fachbereich Medizin Marburg zur Promotionsprüfung eingereichte Arbeit mit dem Titel „Neural correlates and neural stimulation of temporal recalibration mechanisms in sensorimotor and inter-sensory contexts“ in der Klinik für Psychiatrie und Psychotherapie unter der Leitung von Prof. Dr. Tilo Kircher mit Unterstützung durch Prof. Dr. Benjamin Straube ohne sonstige Hilfe selbst durchgeführt und bei der Abfassung der Arbeit keine anderen als die in der Dissertation aufgeführten Hilfsmittel benutzt habe. Ich habe bisher an keinem in- oder ausländischen Medizinischen Fachbereich ein Gesuch um Zulassung zur Promotion eingereicht, noch die vorliegende oder eine andere Arbeit als Dissertation vorgelegt.

Ich versichere, dass ich sämtliche wörtlichen oder sinngemäßen Übernahmen und Zitate kenntlich gemacht habe.

Mit dem Einsatz von Software zur Erkennung von Plagiaten bin ich einverstanden.

Die vorliegende Arbeit wurde (oder wird) in folgenden Publikationsorganen veröffentlicht:

Schmitter, C.V., Kufer, K., Steinsträter, O., Sommer, J., Kircher, T., & Straube, B. (2023). Neural correlates of temporal recalibration to delayed auditory feedback of active and passive movements. *Human Brain Mapping*, hbm.26508. https://doi.org/10.1002/hbm.26508

Schmitter, C.V., & Straube, B. (2024). Facilitation of sensorimotor temporal recalibration mechanisms by cerebellar tDCS in patients with schizophrenia spectrum disorders and healthy individuals. Scientific Reports, 14(1), 2627. https://doi.org/10.1038/s41598-024-53148-3

Schmitter, C.V., & Straube, B. (2022). The impact of cerebellar transcranial direct current stimulation (tDCS) on sensorimotor and inter-sensory temporal recalibration. *Frontiers in Human Neuroscience*, *16*, 998843. https://doi.org/10.3389/fnhum.2022.998843

Schmitter, C.V., Steinsträter, O., & Straube, B. (2023). *Neural correlates of sensorimotor temporal recalibration in schizophrenia spectrum disorder (SSD): Pliot results from fMRI and tDCS.* Posterbeitrag zum Gießen International Schizophrenia Symposium (GISS) in Gießen.

Ort, Datum, Unterschrift Doktorandin

Die Hinweise zur Erkennung von Plagiaten habe ich zur Kenntnis genommen.

Ort, Datum, Unterschrift Referent