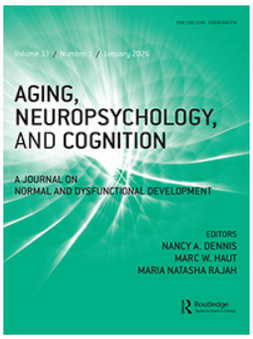

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Task-dependent cognitive effects of intermittent theta-burst stimulation across the adult lifespan

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ABSTRACT

Intermittent Theta-Burst Stimulation (iTBS) of the Dorsolateral Prefrontal Cortex (DLPFC) has the potential to enhance cognitive function by inducing long-term potentiation-like effects, modulating cortical excitability and network plasticity. However, the precise effects of iTBS across specific cognitive domains, age groups, and hemispheres remains unclear. Fifty-three adults aged 19–73 years, participated in a within-subject crossover designed study, receiving iTBS to the left and right DLPFC across two sessions, spaced one week apart. Cognitive tasks assessed four cognitive domains of attention, working memory, sequence learning, and inhibition. Processing speed and accuracy were assessed using time and hemisphere as fixed effects and age as a continuous variable in linear mixed effects and Bayesian models. There was an overall slowing of reaction time with age across all tasks. Brain stimulation reduced reaction times in attention and working memory tasks in all participants. Accuracy improved for working memory following iTBS, with a right hemisphere advantage. ITBS of the DLPFC influences cognition in a task-dependent manner. Improvements in attention were not influenced by hemisphere, suggesting a facilitation of top-up processing after DLPFC stimulation. Working memory enhancements were a dominant effect, especially following right hemisphere iTBS stimulation supporting lateralized optimization of visuospatial storage. These findings highlight iTBS as a potential noninvasive tool for cognitive enhancement. Future research should explore the longevity of these effects and their applicability in clinical populations.

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Aging; cognition; Dorsolateral Prefrontal Cortex (DLPFC); Transcranial Magnetic Stimulation (TMS); working memory

1. Introduction

Cognitive aging is associated with a decline in performance and slower processing speed on tasks involving perception, attention, inhibition, and working memory core components of executive functioning (Devitt & Schacter, 2016; Eckert et al., 2010; Salthouse & Ferrer-Caja, 2003). To compensate for neural challenges that affect cognition several theories have been presented that suggest hemispheric asymmetry reduction in older

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adults (HAROLD; Cabeza, 2002), alongside the Scaffolding Theory of Aging and Cognition (STAC) that posits older adults compensate for age-related neural decline by recruiting additional brain circuits, especially in the prefrontal cortex, to maintain cognitive performance through adaptive neuroplasticity (Reuter-Lorenz & Park, 2014). Increasing evidence shows that Transcranial Magnetic Stimulation (TMS) in the prefrontal cortex can improve cognitive function by inducing electromagnetic fields that modulate neural activity in targeted brain regions (Luber & Lisanby, 2014). Repetitive TMS (rTMS) applied at high frequencies (i.e., above 1 Hz) can induce cortical excitability and is a promising intervention to enhance neuroplasticity and cognition (Guse et al., 2010).

Specialized approaches to the delivery of rTMS, such as intermittent theta burst stimulation (iTBS), may have greater potential than traditional rTMS protocols. ITBS delivers bursts of high-frequency magnetic pulses, usually at 50 Hz, in a pattern of three pulses at 5 Hz, with an inter-burst interval of 200 ms, repeated every 10 seconds, for a total of 600 pulses per session to induce excitatory effects (Huang et al., 2005). ITBS generates greater and longer lasting effects on cortical excitability than traditional rTMS protocols (Huang et al., 2005) and mimics the brain's natural firing patterns. This may have greater effects on cognitive performance and induces a form of neuroplasticity akin to long term potentiation (LTP; Lee et al., 2021). ITBS is thought to enhance synaptic plasticity through mechanisms akin to long-term potentiation (LTP) by increasing the excitability of cortical circuits and facilitating functional connectivity within cognitive control networks (Huang et al., 2005; Suppa et al., 2016). Neuroimaging studies using fMRI have shown that iTBS can induce alterations in functional connectivity within the frontoparietal network (dorsal stream) and the default mode network, which are both implicated in cognitive aging and executive function (Abellaneda-Pérez et al., 2019; Esposito et al., 2022). Specifically, the rhythmic nature of iTBS mimics theta-gamma coupling which plays a critical role in working and long-term memory processes, attention, and concentration (Aftanas & Golocheikine, 2001; Klimesch, 1999; Pavlov & Kotchoubey, 2022).

ITBS shows promising effects on cognitive enhancement in healthy participants and patient populations. A recent systematic review and meta-analysis examining the efficacy of a single-session of iTBS in healthy subjects found a small positive effect on cognitive function across 30 included studies (Pabst et al., 2022). Systematic review evidence shows high-frequency rTMS interventions, including iTBS, can significantly improve global cognitive function in patients with mild cognitive impairment, Alzheimer's disease, and Parkinson's disease compared to sham stimulation (Chou et al., 2020; Jiang et al., 2020; Miller et al., 2023; Zhang et al., 2021). This effect is pronounced in studies stimulating the Dorsolateral Prefrontal Cortex (DLPFC) (Miller et al., 2023). The DLPFC is responsible for both complex cognitive functioning including working memory and sequence learning, and lower-level visual attention and inhibitory control. A few previous experimental studies have measured the cognitive effects of iTBS on the DLPFC in healthy subjects. The findings are mixed, with some studies demonstrating a significant improvement on working memory performance (Demeter et al., 2016; Hoy et al., 2016; Ngetich et al., 2022), others showing a clear neurophysiological effect with no enhancement of behavioral performance (Chung et al., 2018), or some showing predominantly practice effects (Feng et al., 2023; Ngetich et al., 2022). Additionally, the majority of these studies have focused on young adults, despite evidence that

cognitive function depends on the neural efficiency of the prefrontal cortex, which is vulnerable to the effects of aging (Gunning-Dixon & Raz, 2003; Raz et al., 1997). Given these age-related differences, it is essential to examine the effects of iTBS across different age groups, particularly in middle-aged and older adults, to determine whether the cognitive benefits extend beyond young populations.

Previous reviews have shown that many TMS studies stimulate either the left or right DLPFC, with insufficient justification for stimulating one hemisphere over another (Miller et al., 2023). The DLPFC is functionally lateralized, with the left hemisphere more strongly associated with verbal working memory and cognitive control, while the right hemisphere is implicated in visuospatial and attentional processing (Barbey, Colom, et al., 2013; Demakis, 2004; Mannarelli et al., 2015). Prior TMS research using high frequencies suggests that left DLPFC stimulation may enhance executive control and verbal processing, whereas right DLPFC stimulation is linked to improvements in attentional regulation (Hoy et al., 2016; Li et al., 2017; Vanderhasselt et al., 2007). However, few studies have directly compared the cognitive effects of stimulating both hemispheres within the same study design. In the current literature, there is a need to investigate the lateralized effects of stimulating the DLPFC. Furthermore, the majority of studies have assessed the impact of iTBS on tasks directly measuring or related to working memory, resulting in a sparsity of experimental evidence investigating the effects of iTBS on other cognitive functions. Attention and inhibition are core functions that rely on the integrity of the DLPFC and are critical for goal-directed behavior, cognitive flexibility, and impulse control. While enhancements in working memory and attentional control have been observed following iTBS (Hoy et al., 2016; Vanderhasselt et al., 2007), the effects on inhibitory processing remain unclear. However, one study did review effects in the Stroop task following left DLPFC iTBS stimulation and found improved inhibitory control (Viejo-Sobera et al., 2017) supporting lateralized inhibitory processing. Investigating these functions could provide insight into whether iTBS modulates broader cognitive control mechanisms beyond working memory. To our knowledge, no previous studies have investigated the effects of iTBS on inhibitory processing in healthy adults.

In this study, we applied iTBS to the left and right DLPFC in cognitively healthy subjects and measured the pre- and post-stimulation cognitive performance. We aimed to investigate the behavioral effects of iTBS on attention, working memory, sequence learning and inhibition, and compare the effects across the lifespan. We anticipated significant age-related differences in cognitive performance and hypothesized that older adults would perform slower and less accurately than younger and middle-aged adults. The focus of this study was to investigate the immediate cognitive effects of a single session of iTBS applied over each hemisphere, therefore we expected any iTBS-induced effects to be smaller than in multi-session studies (Huang et al., 2023; Pabst et al., 2022). However, some previous studies have shown significant cognitive enhancement following a single session of iTBS providing rationale for the current approach (Demeter et al., 2016; Hoy et al., 2016; Ngetich et al., 2022). Based on this literature, we hypothesized that iTBS applied over the DLPFC would result in enhanced cognitive performance in attention, working memory, inhibition and sequence learning, compared to sham stimulation.

2. Methods

2.1. Participants

Fifty-three cognitively healthy participants, aged 19 to 73 years (21 males, 24 females) took part in the study, including 23 young adults (19 to 30 years), 15 middle-aged adults (39 to 59 years) and 15 older adults (60+ years). Age group categories were identified following guidance from Goelz et al. (2023) that are shown to reflect neural and behavioral effects across age groups, but main analysis comprised age as a continuous variable. A sample size was based on a G*Power analysis for a mixed ANOVA design for within factors and between subject groups with a moderate effect size (f) = 0.25, alpha = 0.05, power (1-β) = 0.80 for 3 age groups, and a 2(time) ×2(hemisphere) ×4(cognitive task) design. This resulted in ~ 54 participant in total, i.e., 18 for each age group. Our recruitment did not quite reach this threshold in middle and older populations, but given the exploratory nature of the study 15 provides good representative sample in each age group for a pilot study. Participants were recruited via opportunity sampling including social media adverts, the School of Psychology's Participant Recruitment System or via the University of Leeds Older Adult Panel. All participants were right-handed and monolingual, with normal or corrected-to-normal vision. In line with the European Safety Guidelines for TMS (Rossi et al., 2021), participants were pre-screened for medical history and other contraindications for TMS application. Exclusion criteria included any history of psychiatric or neurological diseases, epilepsy, cardiovascular complications, regular-use medication, and other contraindications to TMS such as use of epileptogenic drugs, metal implants in the brain and pregnancy. Participants completed the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) and the Geriatric Depression Scale (GDS) Short Form (Yesavage & Sheikh, 1986). An information sheet was provided, and all participants gave written, informed consent. The study was fully compliant with the BPS ethics guidelines (Oates et al., 2021) in line with the Declaration of Helsinki (World Medical Association, 2013). The study was approved by the School of Psychology Research Ethics Committee at the University of Leeds (PSYC-347) on 29 October 2021. Participant demographic information is summarized in Table 1.

Table 1. Participant demographics. A reported as mean (standard deviation).

	Age		
Measure	Young	Middle	Older
N	15	15	15
Age (years)	20.93 (1.03)	54.27 (5.23)	66.33 (4.58)
Years of education	15.80 (2.1)	16.20 (1.9)	16.53 (2.4)
MoCA score (baseline)	27.93 (3.0)	28.13 (1.5)	27.87 (2.0)
GDS Session 1	0.93 (1.7)	1.40 (1.7)	0.67 (1.1)
GDS Session 2	0.73 (1.6)	1.13 (1.7)	0.73 (1.3)

N = sample size; GDS = Geriatric depression scale; MoCA = montreal cognitive assessment. MoCA scores ≤26 may indicate cognitive impairment in older adults. GDS score ≥5 indicates possible depression.

2.2. Experimental design

A single-blind, sham-controlled, crossover design was used, as shown in Figure 1. Participants completed two sessions, with each session lasting approximately 1 hour. To mitigate order effects, the order of receiving iTBS over the left or right DLPFC was randomized for each participant, and the order of cognitive tasks was randomized within and between participants using a random number generator. The sessions started with a brief explanation of the equipment and tasks, then written informed consent was obtained. In Session 1, participants completed the Medical History Questionnaire, the MoCA and GDS. Participants completed a baseline measure of performance on the cognitive tasks. Then participants received iTBS over the left or right DLPFC (F3 or F4) and completed the same four cognitive tasks again. In Session 2, participants received sham iTBS over the vertex and completed the cognitive tasks. Then in the same session, either left or right hemisphere iTBS was applied and participants again completed the four cognitive tasks.

In this experiment, the within-subjects factors included "time" (cognitive performance before and after iTBS) and "hemisphere" (left and right iTBS). "Age" served as a continuous variable. In the attention, inhibition and sequence learning tasks, the dependent variables were reaction time (RT, in milliseconds) and amplitude (in degrees or pixels) of saccadic eye movement from target location. In the working memory task, the dependent variables were response time (in milliseconds) and accuracy (% correct in the correct order) of mouse-clicks. The order of cognitive tasks and trials presented within tasks were randomized for each block and each participant, as illustrated in Figure 1.

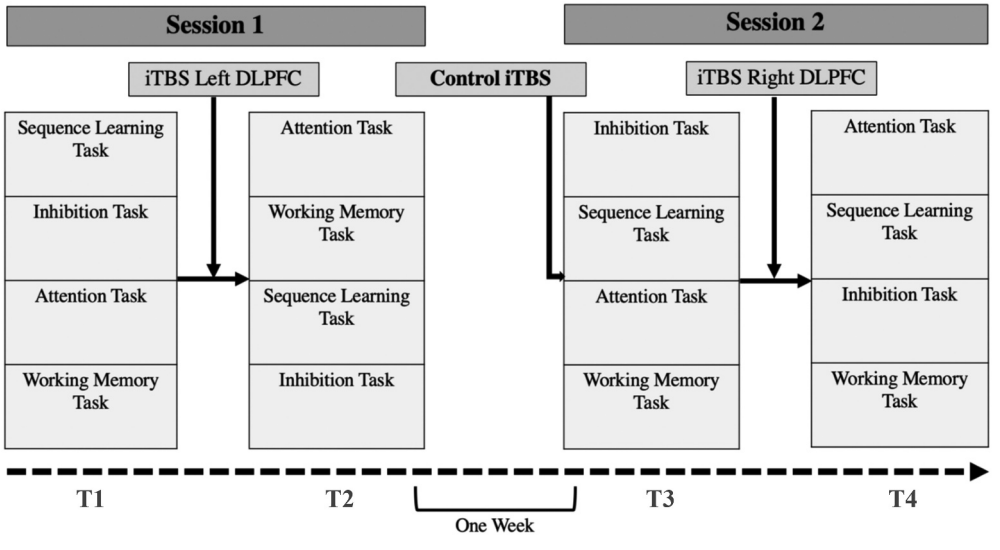

Figure 1. The experimental design with two sessions spaced 1 week apart. The time points of completing the cognitive tasks were as follows: T1 = baseline in session 1, T2 = after left or right iTBS in session 1, T3 = after sham iTBS in session 2, T4 = after left or right iTBS in session 2. The order of administering left and right iTBS was randomized for each participant.

2.3. Materials

2.3.1. Eye tracking

The cognitive tasks were designed on Experimental Builder software (SR Research Limited) and displayed on a CRT 19" Illyama computer with a 1024 × 768 display and 75 Hz refresh rate. Eye movements were recorded on an Eyelink II eye-tracking system (SR Research Ltd) with a sample frequency of 1000 Hz. Prior to the start of each task, a 9-point calibration and validation procedure was performed to ensure an accurate calibration between the screen and eye. The experimenter read the task instructions out loud before each task and verbally checked participants' understanding. The distance between the eye and the screen was 57 cm, with 1 cm on the screen equating to 1 degree of visual angle of the eye. The cognitive tasks were presented on a black background and performed in a dark room to minimize visual distractions, reduce reflective glare, and enhance pupil detection (due to pupil dilation in low light intensities). Overhead lights were turned on between tasks to control for visual adaptation and increase attentiveness.

2.3.2. Stimulation protocol

ITBS was administered using a Magstim-Rapid stimulator and a 70 mm figure-of-eight coil (2.6T). The coil was placed at a perpendicular angle to the skull and was held over the left DLPFC and right DLPFC, corresponding with positions F3 and F4 of the Standard International 10–20 EEG Positioning System (Jasper, 1958). This is a commonly used and well-established method for locating the DLPFC (Herwig et al., 2003). The positions were located by placing a functional Near Infrared Spectroscopy (fNIRS) cap on the head with the EEG positions printed on the top. The cap was aligned over position Cz on the scalp using the central point from naison to inion and ear to ear measurements (Herwig et al., 2003).

ITBS was delivered according to the protocol established by Huang et al. (2005); triplets of pulses delivered at a frequency of 50 Hz, repeated at 200 ms intervals (5 Hz), followed by an 800 ms rest period. This was administered for 190 s, resulting in a total of 600 pulses at a stimulator output of 40%. Previous research has shown that this output level produces effective cortical effects with this level of intensity (Suppa et al., 2016). The iTBS protocol was applied consistently across participants, rather than dosing stimulation according to individual motor threshold. This is due to evidence that motor threshold may not directly correlate with the excitability of the DLPFC (Tik et al., 2023). TMS is generally well-tolerated and painless (Najib & Horvath, 2014; Rossi et al., 2021; Taylor et al., 2018). This study adhered to established safety protocols for TMS, ensuring its safe application (Rossi et al., 2021).

In the control sham condition, stimulation was applied over the vertex (point Cz on the EEG 10–20 System) using the same iTBS parameters to mimic the psychosomatic sensations of the active stimulation. This is a well-established and appropriate control site for iTBS as vertex stimulation does not evoke increased BOLD activation at the stimulated site (Jung et al., 2016). In other words, sham stimulation of the vertex does not interfere with activity associated with cognitive processing and provides a good psychological control.

2.4. Stimuli

All trials and task orders were fully randomized. Each task was included in every session, and both the order of tasks and the trials within tasks were randomized across sessions and within individuals.

2.4.1. Attention

The attention task was a modified version of the cued-uncued attention task developed by Shimozaki (2010). The task measured RT (milliseconds) and amplitude (degrees) of saccades toward a visual target appearing horizontally to the left or right of a fixation cue, as seen in Figure 2. Prior to the target presentation, a cue appeared which either indicated the target location (cued) or did not (uncued). The cue was an arrow, 15 pixels in length, pointing left (<), or right (>) for cued trials, or was non-informative (< >) for uncued trials. Following this, a target appeared after a random interval (of 750, 1000, or 1250 ms), 5 or 10 degrees of visual angle (DVA) from the center of the screen and the trial ended after 1500 ms. The task consisted of 30 cued and 30 uncued trials, presented in two separate blocks (block order was randomized). These blocks were each followed by a 20 s rest period resulting in an overall task duration of 1 minute and 20 seconds.

2.4.2. Working memory

A modified version of the Corsi block tapping task (Corsi, 1972), known as the backward Corsi task was used to measure visuospatial working memory. As seen in Figure 3, during each trial 12 blue boxes appeared on a computer screen, with between 2 and 5 boxes flashing red in a sequence. Following a blank screen and a delay period of 0, 2, or 5 s, participants clicked the boxes in the reverse order of the sequence they viewed, before the next trial then appeared. Prior to the task, participants completed 2 practise trials containing sequences with 2 and 5 items which were not included in the analysis. The task

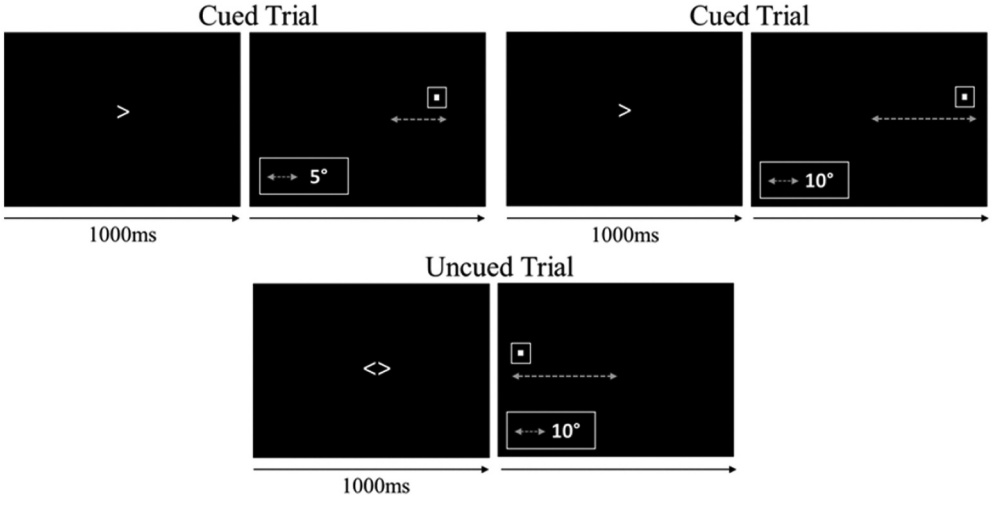

Figure 2. A diagram of the visual attention task. The top panel shows two examples of cued trials (5° and 10° DVA) and the lower panel the uncued trial (at 10° DVA).

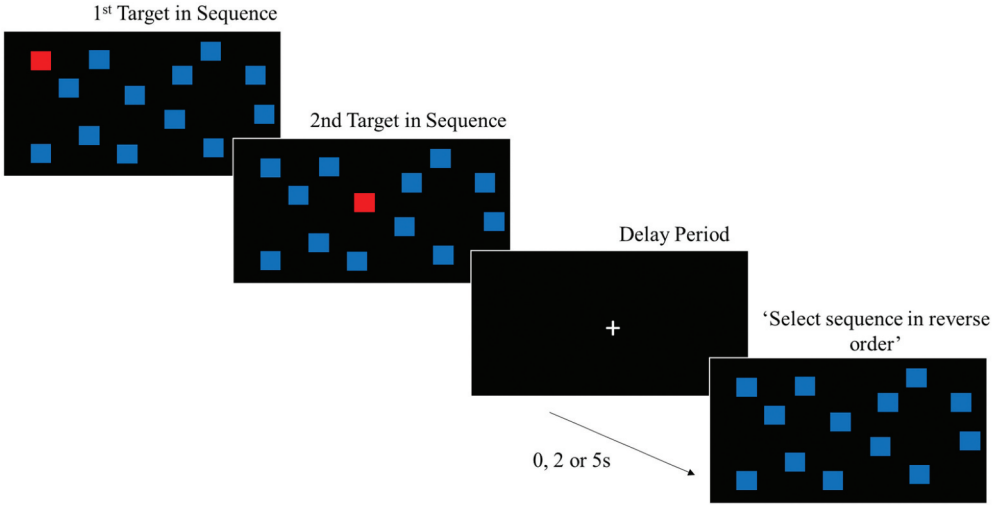

Figure 3. Representation of the backward Corsi block-tapping task. A blank screen with a fixation cross was shown during the delay period lasting 0, 2 or 5s.

contained 12 trial types (3 delays × 4 sequence lengths) with 3 blocks, resulting in a total of 36 trials per particicpant. A 30 s rest period was presented between blocks. The total task length was approximately 10 minutes. Measures included averaged response time (milliseconds) to each item in the sequence for all responses, and accuracy (%) of selecting the correct items in the correct order. Participants were given a maximum of 60 seconds to select the items in the sequence before the task automatically moved to the next trial.

2.4.3. Sequence learning

Sequence learning was measured using a saccade task (Burke et al., 2013), as seen in Figure 4. This measured visuospatial learning by assessing short latency predictive saccades. In this task, RT (milliseconds) and amplitude (degrees) for locating targets on predictive and non-predictive (random) sequences were measured. A central target (16-pixel diameter) was presented on the screen followed by three more target in a sequence. The visual targets sequentially jumped location

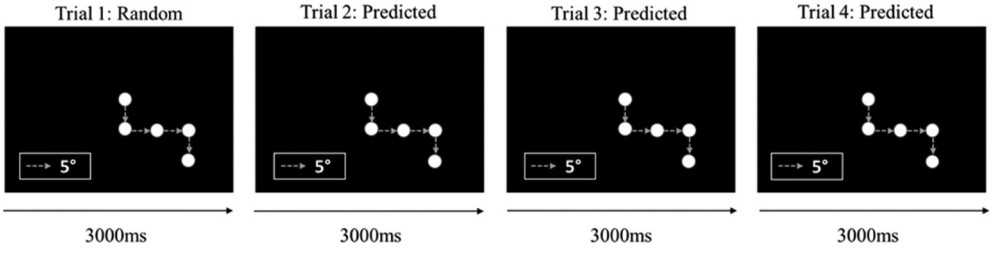

Figure 4. A diagram of the sequence learning task. Each target is presented sequentially with a 5° DVA step sequentially each for 750 ms resulting in a 3000 ms duration for each individual sequence. Sequences were presented 4 times before moving onto the next novel sequence presentation.

every 750 ms by 5 degrees of visual angle either up, down, left or right. The 4-target sequence was 3000 ms in duration and was repeated 4 times in a row (resulting in a 12s duration for each block), with a 10 second rest between each set of sequences. Participants performed 10 unique sets of sequences, resulting in a total of 40 trials and a task duration of 4 minutes.

2.4.4. Inhibition

An adapted version of the antisaccade task (Hallett) was used to measure inhibitory responses. This task measured RT (milliseconds) and amplitude (degrees) of saccades toward a target location. As shown in Figure 5, a central visual cue was presented for a randomized duration (either 750 ms or 1500 ms) and indicated whether or not participants should move their eyes toward the target. A green cue required participants to fixate upon a subsequently appearing boxed target to the left or right of this cue (15 pixels in length and width) (prosaccade). A red cue indicated that participants should move their eyes to the diametrically opposite position, not highlighted by a box (anti-saccade). The target was presented to the left or right of the cue at 5 or 10 DVA from the central circle, for 1500 ms to allow for accurate fixation. Both the target location and duration of the cue were randomized to avoid task prediction. Similarly to the attention task, 60 trials were presented in two blocks (30 prosaccade trials and 30 anti-saccade trials).

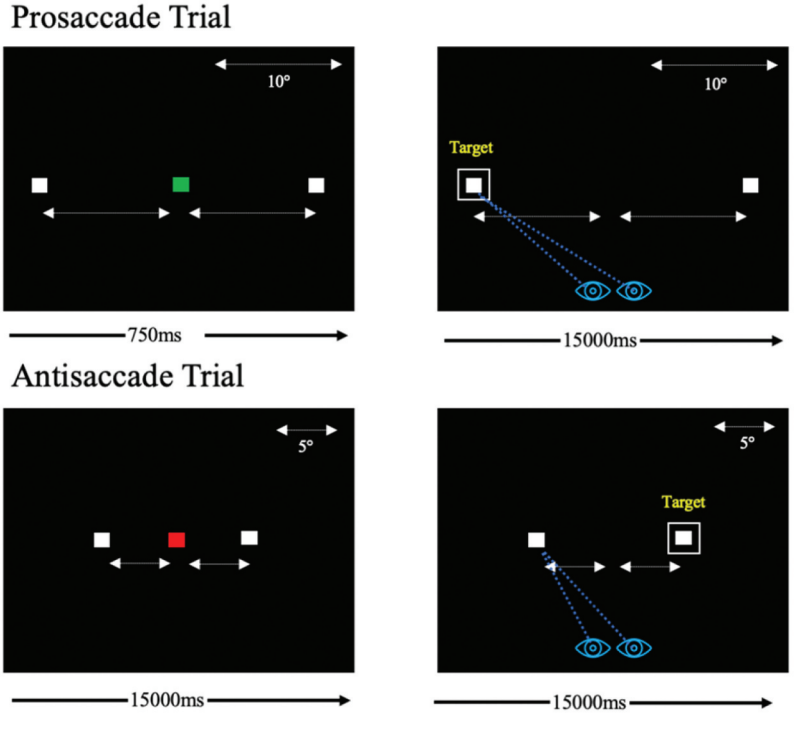

Figure 5. A diagram showing the inhibition task. The lower images show an example of the anti-saccade trial, and the upper images an example of a prosaccade trial.

2.5. Data analysis

2.5.1. Eye data processing

Continuous eye-tracking recordings were processed in EyeLink Data Viewer (version 4.2, SR Research Ltd) to convert measurements of saccadic eye movements into numeric data. For the attention and inhibition tasks, the target onset was identified for each trial to calculate the RT in milliseconds and amplitude in degrees of saccades identified using velocity profiles exceeding 30 deg/s toward (or away from) the target. The minimum amplitude of saccades was set to 2.0 degrees. For the sequence learning task, the RT (in milliseconds) and amplitude (in degrees or pixels) of saccades were identified for each target in the 4-target sequence, with a minimum amplitude of 2.0 degrees. For the working memory task, the onset of each mouse click event was extracted. Response time, in milliseconds, was calculated as the start of the trial onset to the last mouse click in the sequence. Accuracy was calculated as the percentage of correct blocks selected in the correct order. Following pre-processing, data was exported to MatLab 2022b (Mathworks Ltd) with files containing measures of saccade RTs, amplitudes and fixations for the attention, inhibition and sequence learning tasks, and response time and accuracy of mouse clicks for the working memory task.

2.5.2. Statistical analysis

Linear mixed-effects models (LMM), implemented in R Studio 2024.09.0, were fitted separately for each cognitive measure (reaction time, accuracy, and amplitude) using *Age* (continuous), *Time* (Before vs. After), and *Hemisphere* (Left vs. Right) as fixed factors, with random intercepts specified for participants to account for repeated measures. Interaction terms were included for all fixed effects. For reaction time data, a logarithmic transformation was applied to reduce skewness and approximate normality. Estimated marginal means (EMMs) were computed using the emmeans package to visualize predicted values across conditions, with 95% confidence intervals. Analyses were conducted in R (version 4.2.2) using the lme4 package for model fitting and emmeans for post hoc estimation. Model outputs including coefficients, bootstrapped confidence intervals, effect sizes, and approximate R^2 were also extracted.

To address potential violations of normality and improve robustness, parametric bootstrapping (1,000 iterations) was used to estimate confidence intervals for fixed effects. Partial eta-squared values and their confidence intervals were calculated to quantify effect sizes. Outliers, defined as observations ±3 z-scores from the mean within each age group and task, represented less than 1% of the data and were removed without replacement (see Supplementary Table S1 for details).

Complementary Bayesian hierarchical models were estimated using the brms package in R to examine the effects of intermittent theta-burst stimulation (iTBS) on behavioral and neurophysiological outcomes. Each model included fixed effects for Hemisphere, Time, and their interaction, with Age entered as a continuous covariate, and random intercepts for participants. For reaction time tasks, the dependent variable was log-transformed prior to modeling. Models assumed a Gaussian likelihood and were fit using weakly informative priors (Normal (0,1) for fixed effects; Cauchy (0,1) for random-effect standard deviations).

Posterior distributions were sampled using four chains of 4000 iterations each (1,000 warm-up), with adapt_delta = 0.95 to ensure convergence. For each parameter, we report posterior means and 95% credible intervals, along with two complementary indices of evidence: 1) Posterior Probability of Direction (PPD) that refers to the probability that the parameter's posterior lies on the same side of zero as its median, providing directional certainty of the effect, and 2) Region of Practical Equivalence (ROPE) that outlines the proportion of the posterior distribution within a predefined range around zero representing negligible effects. ROPE bounds were scaled to the outcome's variability ($\pm 0.10 \times SD$ of the response), following recommendations for domain-specific interpretation. Parameters were classified as meaningful if ≤5% of the posterior fell inside ROPE, as practically null if ≥95% fell inside ROPE, and undecided if outside these boundaries. Posterior distributions for key predictors were also plotted for each task using brms, bayestestR, and bayesplot.

3. Results

3.1. General age-related effects in cognitive tasks

As expected, age-related differences in reaction time were found across four cognitive tasks (see Figure 6). In all tasks, older adults exhibited longer reaction times compared to younger and middle-aged groups, with the largest differences observed in the Corsi task. Attention and Sequence Learning tasks showed moderate age-related increases, while Inhibition displayed a smaller effect. Subtask variations contributed additional variability but did not alter the overall age-related trend. These results highlight a consistent slowing of responses with age across diverse cognitive domains (see supplementary material Figures S1 and S2). Spline modeling revealed significant age effects mainly in the sequence learning task (Partial η^2 up to 0.064, see Figure 7), indicating that older participants exhibited disproportionately slower responses compared to younger adults, particularly beyond midlife.

Age-related differences in amplitude and accuracy across the four cognitive tasks is shown in Figures 8 and 9. Attention and Inhibition tasks showed relatively stable amplitude distance from the target across age groups of 0.5 degrees of visual angle, with minor variability. In contrast, Sequence Learning exhibited a pronounced increase in accuracy to the target for middle-aged and older adults compared to younger participants, indicating better accuracy onto the target in top-down processing that is internally generated with age. Accuracy in the Corsi task also declined with age, with older adults recalling the backward order of targets less accurately than younger adults. Subtask variations contributed additional variability, but did not alter the overall age-related trends. More specifically, spline modeling revealed significant age effects on accuracy in the Corsi task performance (Partial η^2 up to 0.23), indicating that accuracy varies markedly across the lifespan in a non-linear way with marked shift in middle-aged groups. Collectively, these findings underscore the importance of modeling age as a continuous, non-linear factor and highlight vulnerability or adaptability in visuospatial working memory across the adult lifespan.

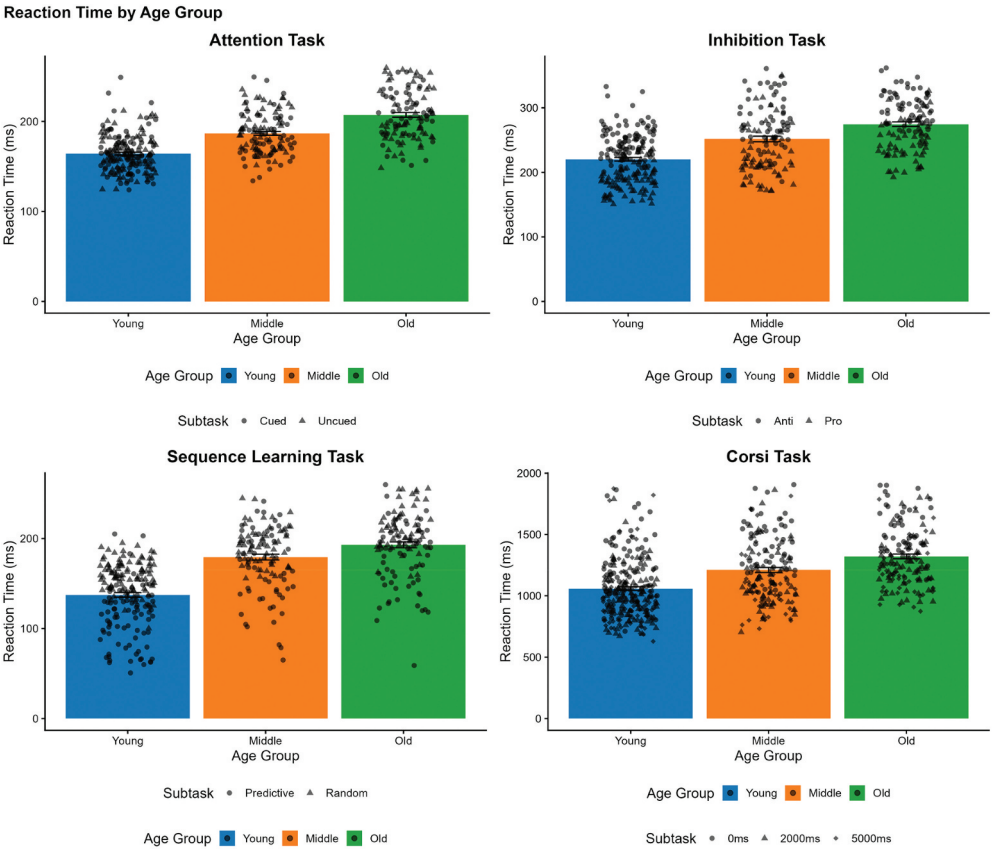

Figure 6. Bar plots show mean response in reaction time for each participant segregated by the three age groups (young-blue, middle-orange, old-green) across the four tasks represented in each of the four graphs. Error bars indicate ± standard error of the mean (SEM). Black and gray symbols represent individual participant data for the different sub-tasks within each age category. This visualization highlights age-related differences in reaction time while showing the variance in response across subtasks.

3.2. iTBS and hemisphere effects – linear mixed effects model (LMM)

3.2.1. Response time

A linear mixed-effects model examined reaction times (RT) during the attention task as a function of stimulation hemisphere (left vs. right) and time (before vs. after iTBS), with age as a continuous variable. There was a significant main effect of time, $F_{(1,154)} \approx 2.42$, $p = .02$, with faster RTs observed after stimulation (Estimate = −0.036, 95% CI [−0.064, −0.007], Partial Eta^2 = .43). The main effect of hemisphere was not significant ($p = .65$), nor was the hemisphere × time interaction ($p = .48$), indicating that improvements in RT were similar for left and right DLPFC stimulation. Age showed a robust effect ($p < .001$), with older participants exhibiting slower RTs overall (Estimate = 0.0047, 95% CI [0.0036, 0.0059]). These findings suggest that iTBS improved attentional processing speed regardless of stimulation hemisphere, while age remained a strong predictor of RT performance.

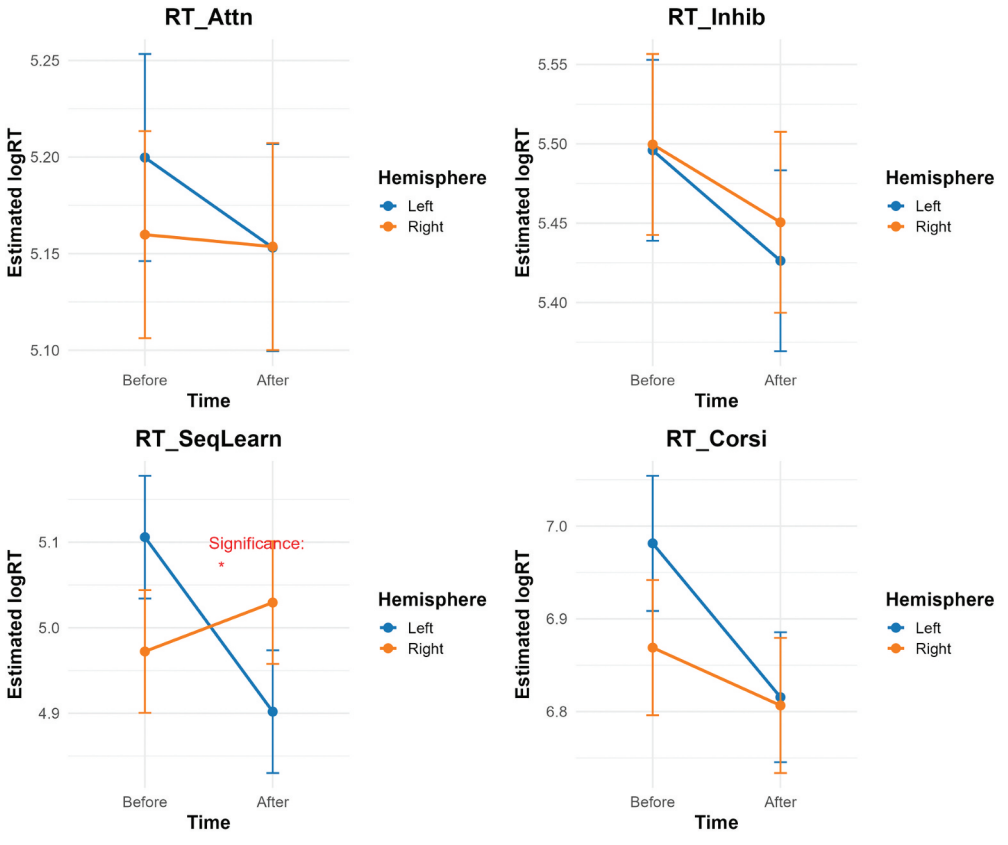

Figure 7. Estimated marginal means for log-transformed reaction time (RT) across time (before vs. After stimulation) and hemisphere (left vs. Right). Each panel represents a different cognitive task: (a) attention, (b) inhibition, (c) sequence learning, and (d) working memory (Corsi-back task). Lines indicate estimated means, and error bars represent ±1 standard error of the mean. Data were modelled using linear mixed-effects models with age as a covariate and participant as a random intercept. Please note a decrease reflects faster reaction times. * indicates a disproportionate significant decline from midlife with age.

For the inhibition task, a mixed-effects model revealed a significant main effect of hemisphere, ($F_{(1,154)} \approx -1.04$, $p = .02$), with faster RTs following stimulation of the right DLPFC compared to the left (Estimate = −0.012, 95% CI [−0.035, −0.011], Partial Eta^2 = .02). However, the main effect of time was not significant ($p = .45$), nor was the hemisphere × time interaction ($p = .33$), indicating that iTBS did not produce reliable pre-post changes in inhibition RT. Age was a strong predictor ($p < .001$), with older participants showing slower RTs (Estimate = 0.0045, 95% CI [0.0031, 0.0058]). These findings suggest that right DLPFC stimulation may confer a modest advantage for inhibitory control reaction time, while age-related slowing remains a dominant factor.

For the sequence learning task, mixed-effects modeling revealed no significant main effects of hemisphere ($p = .16$) or time ($p = .65$), and the hemisphere × time interaction was also non-significant ($p = .54$). This indicates that iTBS did not influence RT performance in sequence learning regardless of stimulation site. However, age was a strong predictor ($p < .001$), with older participants exhibiting slower RTs (Estimate = 0.0076, 95% CI [0.0061,

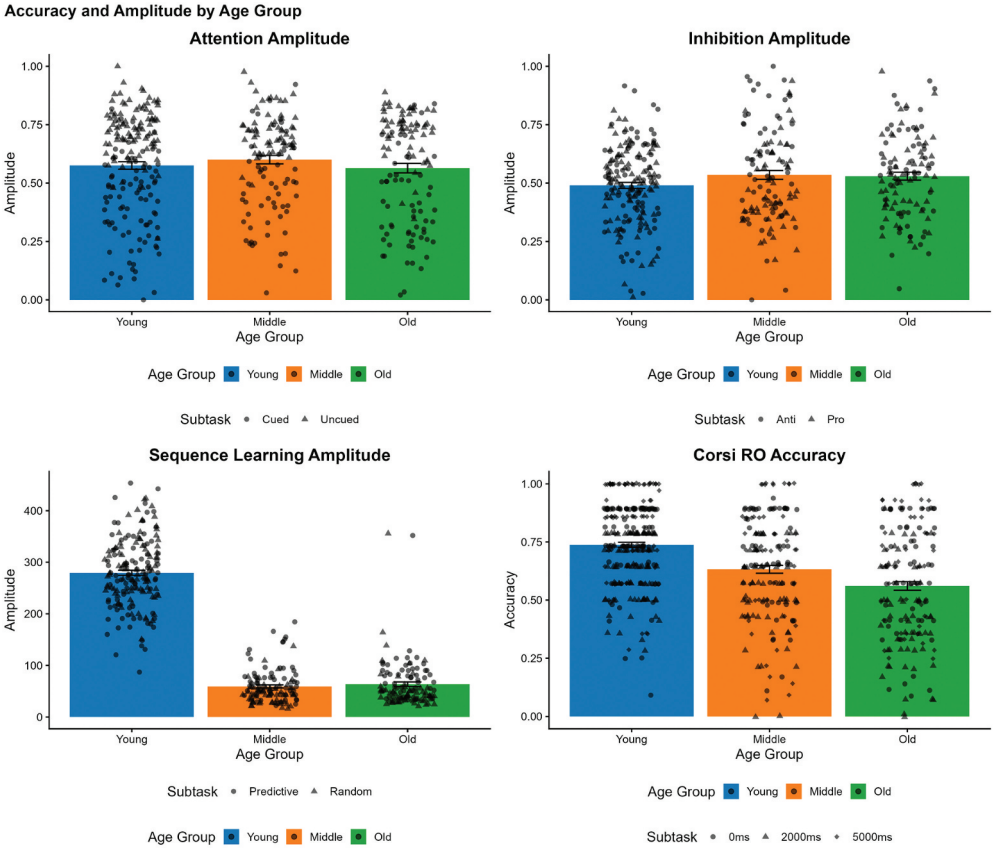

Figure 8. Bar plots show mean performance in amplitude and accuracy for three age groups (young-blue, middle-orange, old-green) across the four tasks as shown in each of the four graphs. Error bars indicate ± standard error of the mean (SEM). Black and gray symbols represent individual participant data for each sub-task showing distribution of performance within each age category.

0.0091]). These findings suggest that sequence learning RT is primarily driven by age-related factors rather than stimulation effects.

Finally, the Corsi task, mixed-effects modeling revealed a significant main effect of time, ($F_{(1,155)} \approx -4.07$, $p = .04$), with faster RTs observed after stimulation (Estimate = −0.077, 95% CI [−0.112, −0.037], Partial Eta^2 = .40). The main effect of hemisphere was not significant ($p = .17$), and the hemisphere × time interaction did not reach significance ($p = .07$) but revealed a trend, indicating that improvements in RT were trending toward greater improvements after right DLPFC stimulation. Age was a strong predictor ($p < .001$), with older participants exhibiting slower RTs (Estimate = 0.0051, 95% CI [0.0034, 0.0068]). These findings suggest that iTBS enhances visuospatial working memory speed regardless of stimulation hemisphere, while age remains a dominant factor

3.2.2. Amplitude and accuracy

For the attention task amplitudes, mixed-effects modeling revealed a small but statistically significant main effect of hemisphere, $p = .006$, with slightly higher accuracy following right

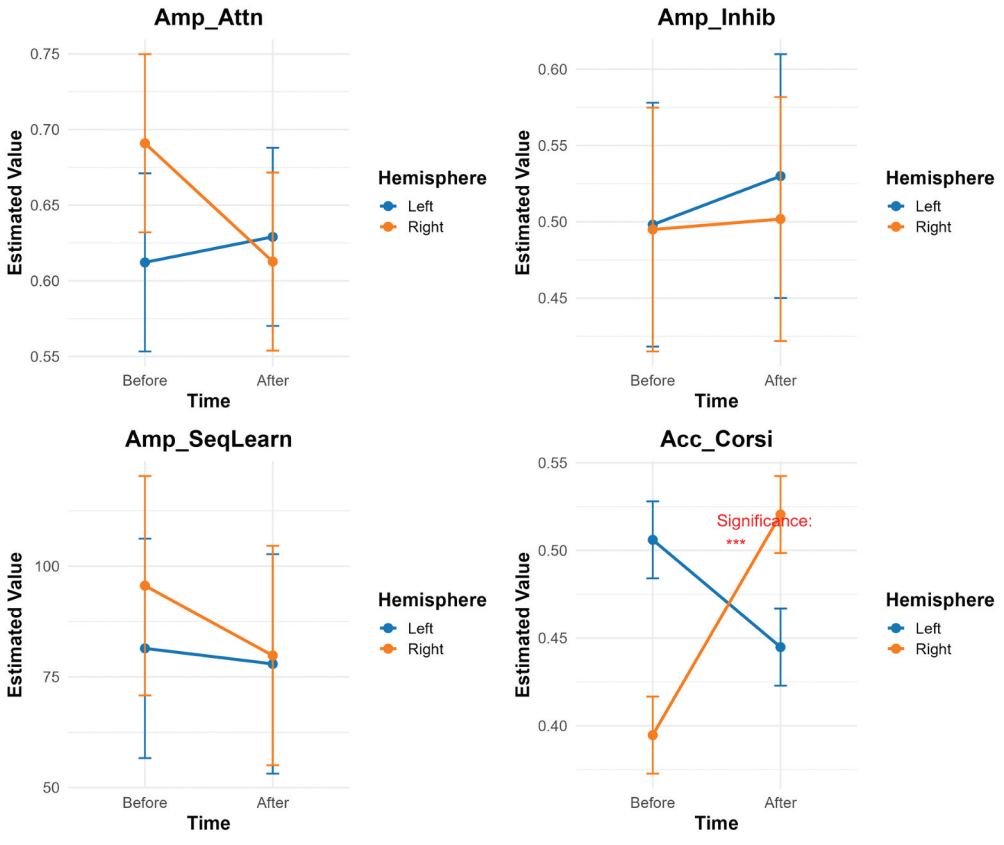

Figure 9. Estimated marginal means for amplitude and accuracy measures across time (before vs. After stimulation) and hemisphere (left vs. Right). Each panel represents a different cognitive measure: (a) attention, (b) inhibition, (c) sequence learning, and (d) working memory (Corsi-back task). Lines indicate estimated means, and error bars represent ±1 standard error of the mean. Data were modelled using linear mixed-effects models with age as a covariate and participant as a random intercept. Please note a decrease in amplitude reflects more accurate saccade to target, whereas an increase in accuracy reflects better performance (Corsi task). *** indicates plots where a significant ($p < 0.001$) age*hemisphere interaction occurred.

DLPFC stimulation compared to left (Estimate = 0.019, 95% CI [−0.017, 0.051], Partial Eta^2 = .006). The main effect of time was also significant ($p < .001$), indicating an increase in accuracy after stimulation (Estimate = −0.011, 95% CI [−0.045, 0.021]). Age was statistically significant ($p < .001$) but had no practical influence on accuracy (Estimate = −0.0001). The hemisphere × time interaction was not significant, suggesting that accuracy changes were not dependent on stimulation site.

For inhibition task amplitude, mixed-effects modeling revealed a statistically significant main effect of time, $p = .037$, with a slight increase in accuracy to the target after stimulation (Estimate = −0.032, 95% CI [−0.081, −0.013], Partial $Eta^2 \approx 0$). The main effect of hemisphere was also statistically significant ($p = .0097$), but the effect size was negligible (Estimate = −0.003, 95% CI [−0.048, 0.046]). Age was statistically significant ($p = .002$) but had no practical influence on accuracy (Estimate = 0.0011). The hemisphere × time interaction was not significant, indicating that accuracy changes were not dependent on stimulation site.

For sequence learning amplitude, mixed-effects modeling revealed no significant main effects of hemisphere ($p = .64$) or time ($p = .84$), and the hemisphere × time interaction was also non-significant. However, age was a strong predictor ($p < .001$), with older participants exhibiting markedly higher accuracy (Estimate = −4.98, 95% CI [−5.60, −4.35]). These findings suggest that sequence learning accuracy is primarily influenced by age-related factors rather than stimulation effects.

For visuospatial working memory accuracy, mixed-effects modeling revealed significant main effects of hemisphere ($p = .041$) and time ($p = .001$), with slightly higher accuracy following right hemisphere stimulation and an increase after stimulation overall (Hemisphere Estimate = −0.063, 95% CI [−0.083, −0.044]; Time Estimate = −0.036, 95% CI [−0.055, −0.018]). Age was not a significant predictor of this effect ($p = .24$). Importantly, the hemisphere × time interaction was substantial (Estimate = 0.114, 95% CI [0.085, 0.143]), indicating that the effect of iTBS stimulation from before and after was more dominant after right hemisphere stimulation, potentially reflecting differential neuroplastic responses in left versus right DLPFC in the backward Corsi task.

3.3. iTMS and hemisphere effects – Bayesian modelling

3.3.1. Reaction time

Posterior estimates converged well across all models as shown in Figure 10 ($\hat{R} \approx 1.000$; ESS > 1,300). For Time (After vs Before), only the Corsi task showed a credibly meaningful improvement [(logRT, β = −0.0767), 95% credible intervals (CrI, −0.1139, −0.0399), probability of direction (PPD = 0.9999 = very strong, and region of practical equivalence (ROPE = 0%)], corresponding to an estimated ~7.4% faster RT after iTBS. The Attention task also

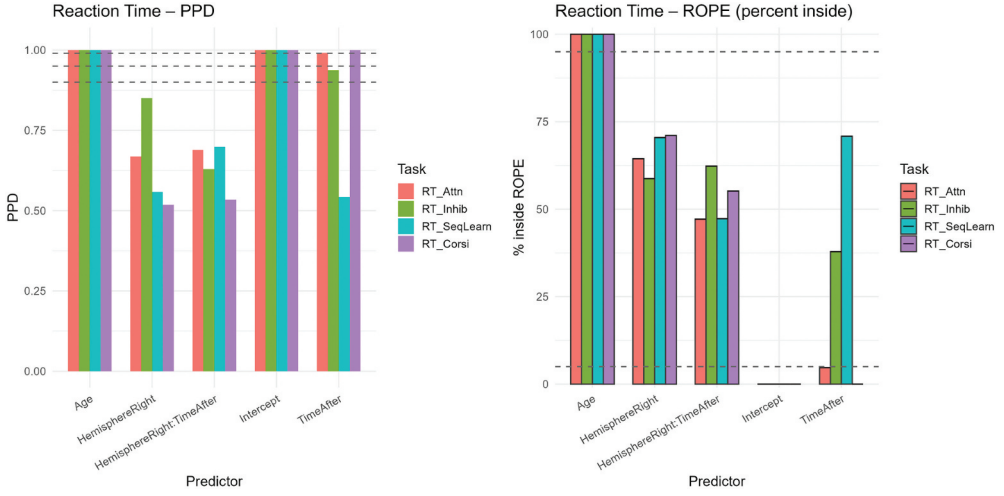

Figure 10. Posterior probability of direction (PPD) and percentage of posterior distribution inside the region of practical Equivalence (ROPE) for reaction time tasks. The left image shows PPD values for predictors across four tasks (attention – red, inhibition – green, sequence learning – blue, and Corsi-purple). Dashed lines indicate thresholds for moderate (0.90), strong (0.95), and very strong (0.99) evidence. The right graph shows the proportion of posterior samples within the ROPE (±0.1 SD), with dashed lines at 5% and 95% indicating meaningful and practically null effects respectively.

indicated faster responses after iTBS [β = −0.0364; CrI excludes 0; PPD = 0.991 = very strong, ROPE = 4.7%], suggesting a smaller yet practically meaningful effect of ~3.6% faster reaction times. For Inhibition, the time effect was modest and uncertain (β = −0.0180; CrI overlaps 0; PPD = 0.937 reflects moderate; ROPE = 37.9%, undecided; ~1.8% faster), and for Sequence Learning, the effect was negligible (β = 0.0026; CrI were wide; PPD = 0.542 reflecting a weak effect; ROPE = 70.8% with an undecided effect). Hemispheric main effects and Hemisphere × Time interactions were consistently weak (PPD ≤0.85) and largely inside ROPE (>45%), indicating no meaningful lateralization or interaction in these tasks. Age showed very strong directional certainty in all tasks (PPD = 1.0), but was 100% inside ROPE, confirming practically null age effects (~0.4–0.8% per unit).

In summary reaction time improvements After vs Before were robust and practically meaningful for Corsi, with a smaller but credible for Attention supporting LLM results. Bayesian modeling revealed negligible for Inhibition and Sequence Learning. The hemispheric and interaction effects were uniformly trivial, and age did not influence iTBS or hemisphere effects.

3.3.2. Amplitude and accuracy

Models converged well across all tasks ($\hat{R} \approx 1.000$; bulk ESS > 3,300). The amplitude in the attention task revealed that predictors had no meaningful effect shown in Figure 11. In addition, effect of time was a small and uncertain [β = −0.0115; 95% CrI (−0.0441, 0.0208); PPD = 0.752 ≈ weak effect; ROPE = 45.1% is undecided], and hemispheric and interaction effects were similarly negligible (PPD ≤0.87; ROPE > 30%). Age was also practically null (100% inside ROPE). The Inhibition amplitude change after iTBS, but this effect was

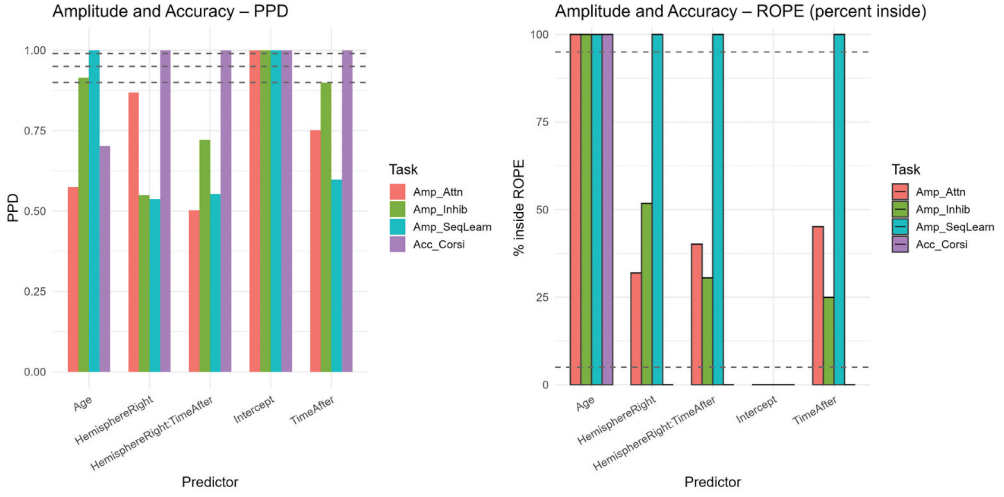

Figure 11. Posterior evidence for amplitude and accuracy predictors across tasks. The left graph shows posterior probability of direction (PPD) for each predictor, with dashed lines marking thresholds for moderate (0.90), strong (0.95), and very strong (0.99) evidence. The right graph shows the percentage of posterior samples inside the Region of Practical Equivalence (ROPE; dashed lines at 5% and 95%), indicating practical significance. Bars represent the four tasks: Attention (red), Inhibition (green), Sequence Learning (blue), and Corsi (purple).

modest and uncertain [β = −0.0315; CrI (−0.0790, 0.0174); PPD = 0.900 ≈ moderate effect; ROPE = 24.9% and is undecided], with hemispheric and interaction effects weak (PPD ≤0.72; ROPE > 30%). Age again showed a practically null effect for inhibition (100% inside ROPE). In the Sequence Learning task, all predictors for amplitude were fully inside ROPE (100%), indicating practically null effects despite some directional certainty for Age [β = −4.5376; CrI (−5.128, −3.898); PPD = 1.000]. Time and hemispheric effects were highly uncertain (PPD ≈0.54–0.60) and negligible. In contrast, the backward Corsi task revealed robust and practically meaningful effect. Participants revealed a clear improvement in accuracy after iTBS [β = −0.0363; CrI (−0.0563, −0.01660; PPD = 0.9998 was very strong; ROPE = 0%], regardless of hemisphere [β = −0.0633; CrI excludes 0; PPD = 1.000] and also the Hemisphere × Time interaction [β = 0.1146; CrI excludes 0; PPD = 1.000] were credibly non-null and outside the ROPE, indicating a stronger improvement post iTBS on the right hemisphere compared to the left. Age remained practically null indicating this was not driving this effect (100% inside ROPE).

4. Discussion

Age-related slowing in processing speed were dominant across all cognitive tasks in-line with previous literature (Verhaeghen, 2013). Our linear mixed-effects modeling highlighted this effect in age across all tasks in reaction time but isolated the attention and memory tasks particularly benefiting from increased reaction times post-iTBS, regardless of hemisphere. This positive effect in processing speed was also confirmed via Bayesian analysis which revealed a strong effect of iTBS in the Corsi, and weaker but meaningful effect in Attention across all participants. In terms of accuracy the attention task revealed more accurate saccades to the target post-iTBS, although the Bayesian results suggest that this effect was small and uncertain. Conversely, the Corsi task revealed consistent significant improvements in accuracy after iTBS stimulation that was particularly robust in the right hemisphere and that was strongly supported by our Bayesian analysis.

4.1. Effects of iTBS on processing speed and accuracy in cognitive tasks

This study found a reduction in RT and a smaller less convincing effect in saccade accuracy during the attention task following iTBS, which may reflect enhanced processing speed and neural efficiency of attentional processing following stimulation. There is limited research on the effects of iTBS/rTMS on attention in healthy subjects across the adult lifespan. However, consistent with the results of the current study, a meta-analysis has shown rTMS over the PFC resulted in a significant improvement in attention and processing speed in adults with attention deficit disorder (ADD) compared to control groups (Chen et al., 2023). The effects of iTBS on attentional processes could be explained by the increase in neural excitability induced by iTBS, heightening the neural response to stimuli, resulting in faster processing speed and improved attentional focus. Interestingly improvements were found regardless of hemisphere indicating both hemispheres contribute to orientating and executive control in this cued/uncued attention task. Typically, the right hemisphere is often associated with visuospatial attention and vigilance (Gitelman et al., 1999), and left with verbal working memory and goal maintenance (Arabacı

et al., 2024), although the cue-driven (top-down processing) used in this task is known to activate more bilateral dorsal frontoparietal circuitry (Corbetta & Shulman, 2002). Our findings are in-line with this top-down driven attention literature, whereby both hemispheres revealed positive effects to stimulation. This result may also reflect older adults tendency to additionally utilized bilateral activation in this task according to the classic theories of aging HAROLD – (Cabeza, 2002); STAC – (Reuter-Lorenz & Park, 2014) and neurophysiological evidence showing increased bilateral PFC activation with age (Ranchod et al., 2023).

Our finding that iTBS of the DLPFC improves response time and accuracy in working memory also is consistent with previous research, although most studies focus on older adult populations only. Systematic review evidence shows improvements on tasks which primarily measure working memory, following an intervention of high-frequency rTMS applied to the DLPFC over several days (Brunoni & Vanderhasselt, 2014; Chou et al., 2020; Jiang et al., 2020; Miller et al., 2023; Zhang et al., 2021). Such systematic reviews have shown that the majority of studies that have implemented high-frequency rTMS protocols stimulating the left hemisphere (Hoy et al., 2016; Ngetich et al., 2022). This is the first study to demonstrate improvements in response time on the Corsi working memory task across all adult age-ranges following a single session of iTBS. Furthermore, our results also provide new understanding that right hemisphere iTBS appears to be dominant for improving accuracy, while both contribute to faster response times. Evidence for right hemisphere dominance in visuospatial WM is consistent with a plethora of literature and models of RH dominance in visuospatial function (Corbetta & Shulman, 2002). A recent randomized crossover study reported that right DLPFC iTBS enhanced visuospatial WM performance in a 2-back task, improving both discriminability and reaction time, also supporting a causal role of rDLPFC in visuospatial WM (Ngetich et al., 2022). Aligned with this, lesion data and neuropsychological work also implicate right DLPFC in manipulating spatial information across broader memory contexts (Barbey, Koenigs, et al., 2013). Moreover, fMRI-guided iTBS to parietal cortex produces neural signatures of improved WM storage with hemisphere by stimulation interactions, strengthening the case that right lateralized frontoparietal circuits can be leveraged to boost visuospatial WM (Deng et al., 2022). Mechanistically, iTBS likely enhances WM via long term potentiation LTP like plasticity in frontoparietal control networks, entraining natural theta – gamma coupling that organizes item sequencing (theta) and maintenance (gamma) during the delay (Diao et al., 2022). Human neurophysiology shows iTBS elevates frontoparietal theta synchronization and parietal gamma power during WM, correlating with behavioral gains (Hoy et al., 2016). In visuospatial WM specifically, right DLPFC is tightly coupled with right parietal regions, and changes in activity correlate with behavioral improvements, suggesting that stimulation strengthens the storage buffer in posterior parietal cortex while prefrontal areas govern control and updating (Guevara et al., 2015).

It is notable that some younger participants were reaching ceiling levels in our 3–5 item delayed Corsi-back task prior to iTBS stimulation suggesting an already optimal performance. In younger participants, optimal performance can be achieved via unilateral brain activity possibly resulting in no significant benefit to our measures post iTBS (Cabeza, 2002). It is likely that older adult participants benefited most from iTBS via neural compensation mechanisms in this age group (Reuter-Lorenz & Park, 2014). According to the Hemispheric Asymmetry Reduction in Older adults (HAROLD - Cabeza, 2002), the brain

recruits additional cortical areas to compensate for age-related structural and functional decline, resulting in more bilateral activity in the PFC during complex tasks. The increase in activity induced in the right DLPFC following iTBS may provide the additional scaffolding needed for more optimal fronto-parietal coupling driving visuospatial working memory.

The results also revealed a single session of iTBS had no significant effects on performance on the sequence learning and inhibition tasks. This may be attributed to the wider neural networks associated with processing for sequence learning, such as the parietal and temporal lobes, rather than being limited to the DLPFC. Evidence shows that patients with parietal and temporal lesions exhibit deficits in spatial memory compared to healthy controls (Bohbot et al., 1998; Esfahani-Bayerl et al., 2016; Glikmann-Johnston et al., 2008; Shimozaki et al., 2003). Therefore, stimulating the DLPFC only, may not be sufficient for evoking a behavioral effect on a sequence learning task. In terms of inhibition, previous studies have found differences in processing between trials on the Go/NoGo task, a similar paradigm to the pro-antisaccade task in this study. Processing during the Go component is associated with theta-wave oscillations and activity in the parietal cortex, whereas the NoGo component is associated with beta-wave oscillations and activity in the lateral orbitofrontal cortex (Bokura et al., 2001; Karamacoska et al., 2018). Consequently, iTBS induced theta wave activity in the DLPFC may not be relevant for inducing performance improvements on the inhibition task.

4.2. Age-related differences in cognitive performance

In the present study, we found significant age-related differences in RT across all tasks, with consistently faster responses in young adults and slower responses in middle-age, with older-adults showing the slowest RT. This finding is consistent with two key theoretical models of cognitive aging. Firstly, the Speed-Accuracy Trade Off, proposes that the age-differences in cognitive performance can be accounted for by the tendency of younger adults to prioritize speed over accuracy, whereas older adults prioritize accuracy over speed (Salthouse, 1979). Secondly, the Processing-Speed Theory explains that there is a linear decline in cognitive performance due to reduced processing speed with increasing age (Salthouse, 1996). By using age as a continuous variable and including middle aged participants, our study demonstrates the gradual nature of this decline in most tasks, often missed in studies focusing solely on young and older adults. However, our mixed effects analysis using Age as a continuous variable revealed that in sequence learning tasks processing speed had a less linear trend, with a disproportionate slowing in RT beyond middle-age. This was also related to increased accuracy in older adults to the saccadic target in sequence learning supporting the focus of a accuracy over speed strategy.

Experimental research has shown older adults are slower than young adults on both simple visual tasks and more complex cognitive tasks (Ebaid & Crewther, 2019), which is consistent with our findings across various task types. Furthermore, age-related differences in processing speed are most pronounced in visuospatial tasks and in memory for locations, over verbal tasks and memory for letters (Jenkins et al., 2000).

Age-related decline in processing speed is a primary predictor of cognitive decline in older age (Eckert, 2011). Neural changes associated with aging, such as reductions in white matter integrity, synaptic density, and neurotransmitter availability, contribute to slower cognitive processing speeds in older adults (Murman, 2015). Therefore, our finding that iTBS can improve processing speed in working memory and attention is promising for the development of brain stimulation interventions to intercept age-related cognitive decline. It should be noted that there were 4 female participants aged 44, 45, 46 and 55 and within the peri and menopausal age bracket and one symptom of perimenopause is cognitive difficulty (Maki & Jaff, 2022). From these participants one reported being post- and the others pre-menopause. None of these participants reported any cognitive symptoms associated with this stage in life, and all scored > 26 in the MoCA indicating this was not a factor driving effects within the middle-aged group.

4.3. Strengths and limitations

The strengths of this study include the within-subject cross-over design approach where each individual acts as their own control, alongside within and between subject randomization thereby minimizing order effects and equalize potential psychological effects of receiving iTBS. Furthermore, all tasks were developed from well-established measures and were able to detect significant age-related differences in processing speed, demonstrating the validity of these tasks in measuring cognitive performance. An eye-tracking system recorded task-related eye movements and mouse-clicks providing highly precise measures of the RT/response time and amplitude/accuracy of responses. A further strength includes the use of a figure-of-eight coil to apply iTBS resulting in more targeted stimulation than other methods. Figure-of-eight TMS coils have been found to have a greater focality of 5 cm^2 tangential spread compared to 34 cm^2 for circular coils (Deng et al., 2013). Overall iTBS was well tolerated with minimal side effects reported by a few participants. Side effects were limited to facial twitching, a buzzing sensation at the site of stimulation and minimal headaches.

This study has several limitations which should be considered. Firstly, only a single session of iTBS was administered to each hemisphere, which may have constrained the potential behavioral effects. Repetitive TMS interventions typically administer at least 10 sessions of stimulation, as multiple sessions are required to induce LTP and establish clear sustained behavioral effects (Miller et al., 2023). Secondly, the use of sham stimulation in Session 2 May have resulted in psychological effects in the baseline measure of session 2. Alternatively, sham stimulation could be applied in a third session to clearly separate and assess any psychological (sham) effects. However, including a third session was not possible in this study due to limits on time and resources. Whilst sham stimulation is an effective mimic of actual TMS a dummy coil that mimics the sounds and sensations of stimulation while generating little to no magnetic field capable of inducing neural effects would also provide a more optimal solution of more formal blinding. Thirdly, this study did not use motor thresholding to dose the stimulation intensity for each participant. This may be considered a limitation as motor thresholding is common practise in TMS research (Rossi et al., 2021), although stimulating the DLPFC does

not induce a standard dose-response relationship. In addition, Tik et al. (2023) found significant individual variability in response to iTBS over the DLPFC, with some participants showing the strongest BOLD responses at below-threshold stimulation levels, while others showed the strongest responses at above-threshold levels, along with some atypical responders. This suggests that motor threshold may not directly correlate with the excitability of the DLPFC. Furthermore, determining the motor threshold involves identifying a minimum level at which to stimulate, whereas iTBS is applied at high frequencies ≥50 Hz which would be considered closer to a maximum level of stimulation intensity. A further limitation associated with the stimulation parameters was the fact that iTBS was applied over an fNIRS cap with an optode creating a 1 cm gap between the TMS coil and the scalp. This may have reduced the magnetic stimulation reaching the cortex as magnetic field strength decreases exponentially with distance (McConnell et al., 2001), and insufficient intensity will not cause neuronal depolarization. It may have been advisable to increase the stimulation intensity to account for this (Stokes et al., 2007). The study may also be limited by the use of the International EEG 10–20 System to locate the DLPFC rather than more accurate localization methods. Individual variation in brain shape and size (Reardon et al., 2018) mean it is more accurate to locate brain regions using neuronavigation techniques whereby individual MRI scans are co-registered to the participant's head to locate a region prior to stimulation. Nevertheless, the EEG 10–20 system has been found to be an appropriate system to use to locate the DLPFC in TMS studies at low cost (Herwig et al., 2003). Furthermore, the DLPFC is a large brain region located near the cortical surface, making it relatively easy to target with TMS using the EEG 10–20 system. It should also be noted that the accuracy measure in the Corsi – back task reached ceiling in some (mainly younger) participants (see Figure 8). This will have resulted in minimal improvement available to these participants post iTBS in this one measure. By using Age as a continuous variable and participants as random effects in our LMM and Bayesian model our findings we aimed to mitigate this, although the true strength of the intervention on accuracy measures in the Corsi task maybe weakened due to these ceiling effects. Finally, practice effects can be problematic in a repeated measure design, although the order of stimulation was counterbalanced, and a one-week washout period was implemented to minimize carryover effects. Eye movements tend to be less susceptible to practice effects due to their automaticity, minimal strategic learning, and stable baseline furthermore, reaction time improvements were observed only in attention and working memory tasks, rather than across all cognitive domains. This pattern suggests that generalized practice effects were unlikely to account for the observed changes, as improvements were domain-specific rather than global.

5. Conclusions

In conclusion, we have shown that a single session of iTBS on the DLPFC appears to have a positive effect on attention and working memory performance for younger and middle to older adults. These findings highlight the potential for using iTBS as a clinical intervention for age-related cognitive decline and potentially attention

deficit disorders. The observed improvements in cognitive performance suggest that the DLPFC plays an important role in attentional and working memory processing, therefore iTBS over this region may offer a promising avenue for therapeutic interventions aimed at mitigating cognitive decline. However, the cognitive improvements observed between sessions in the older adult group suggest that potential practice effects and psychological factors may have influenced the results. Further research is needed to explore between-session consolidatory effects specific to older adults. Further research is necessary to fully understand the underlying neuromodulatory processes supporting these effects and to ascertain the optimal stimulation parameters for clinical use.

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Author contributions

The author contributions to the manuscript using CRediT is as follows:.

AM (principal author) is responsible for data curation, formal analysis, investigation, methodology, project management, resources, software, visualization, writing – original draft.

RJA and RC are responsible for reviewing and editing the manuscript.

MB is responsible for conceptualization, formal analysis, programming, supervision, visualization and writing – review & editing.

Data availability statement

The data that support the findings of this study are openly available in the Open Science Framework reference DOI: https://doi.org/10.17605/OSF.IO/76FW5.

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