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Research Report

Enhanced mind-matter interactions following rTMS induced frontal lobe inhibition

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ABSTRACT

A major barrier to acceptance of psi is that effects are small and hard to replicate. To address this issue, we developed a novel neurobiological model to study this controversial phenomenon based upon the concept that the brain may act as a psi-inhibitory filter. Our previous research in individuals with frontal lobe damage suggests that this filter includes the left medial middle frontal region. We report our findings in healthy participants with rTMS induced reversible brain lesions. In support of our *a priori* hypothesis, we found a significant psi effect following rTMS inhibition of the left medial middle frontal lobe. This significant effect was found using a *post hoc* weighting procedure aligned with our overarching hypothesis. This suggests that the brain may inhibit psi and that individuals with neurological or reversible rTMS induced frontal lesions may comprise an enriched sample for detection and replication of this controversial phenomenon. Our findings are potentially transformative for the way we view interactions between the brain and seemingly random events.

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1. Introduction

Psi is a controversial phenomenon that includes telepathy (mind-mind connections), clairvoyance (perceiving distant objects or events), precognition (perceiving future events), and mind-matter interactions (psychokinesis) (Radin, 2006). Although there is a well-established literature discussing the empirical evidence for psi, including psychokinesis (Acunzo, Evrard, & Rabeyron, 2013; Cardeña, 2018; Nelson, 2015; Radin, 2006; Varvoglis & Bancel, 2015; Vernon, 2021; Walach, Horan, Hinterberger, & von Lucadou, 2020) arguments against the existence of psi include that the effects are small (Bosch, Steinkamp, & Boller, 2006) and hard to replicate under controlled experimental conditions (Jahn et al., 2000; Moulton & Kosslyn, 2008; Walach & Jonas, 2007). Moreover, although theories to explain psi have been proposed (Radin, 2006), none are considered adequate. Nevertheless, psi would be of great fundamental importance if genuine (Bosch et al., 2006). Thus, further well-designed and adequately powered studies of psi are warranted, especially those that may provide insights into underlying mechanisms. Moreover, since putative psi effects must involve the brain, neurobiological models to study these phenomena are essential to advance the field.

As we previously noted (Freedman et al., 2018), one would expect that if psi abilities are real, they should have developed as prominent human traits due to their potentially great significance. However, this has clearly not been the case. Thus, there may have been a strong evolutionary advantage for the emergence of neurobiological mechanisms to inhibit these phenomena. The benefits of inhibiting psi might include preventing exposure to constant bombardment with irrelevant stimuli from telepathy, precognition, and clairvoyance that might divert attention away from environmental events threatening survival. The same notion might also apply to inhibiting mind-matter interactions that could cause chaos in the environment. This concept is in keeping with the "attention to life" theory proposed by Henri Bergson in the early 1900s in which he postulated that the nervous system may have evolved to inhibit psi as a protective mechanism to screen individuals from stimuli that are of no interest or benefit to them (Bergson, 1914; Ehrenwald, 1975, 1978). These stimuli could create a significant distraction that could have a negative effect on survival. Thus, neural mechanisms that filter these stimuli, as well as filtering neural output resulting in mind-matter interactions, may help explain why psi effects are so small and difficult to detect. Based on this concept, we developed a novel neurobiological model to study these effects (Freedman et al., 2018; Freedman, Jeffers, Saeger, Binns, & Black, 2003). This model suggests that the frontal lobes of the brain act as a filter to inhibit psi and implies that humans may have innate psi abilities that are suppressed by this frontal lobe filter.

In support of our neurobiological model of psi inhibition by the frontal lobes, we reported significant mind-matter interactions in two individuals with frontal brain lesions (Freedman et al., 2003, 2018). One had a tension pneumocephalus and the other had behavioral variant frontotemporal dementia associated with a mutation in the C9ORF72 gene. The primary area of lesion overlap in the two participants was in the left medial middle frontal region involving Brodmann areas 9, 10, and 32. The experimental task was to influence output of a Random Event Generator translated into movement of an arrow on a computer screen to the right or left. Compared to a well-designed control condition, both individuals demonstrated a significant effect in moving the arrow on the screen contralateral to the side of their primary lesion overlap, i.e., to the right.

Based on our findings in the two individuals with damage to their frontal lobes, we adopted a new approach to help determine whether the left medial middle frontal region of brain acts a filter to inhibit psi. This was the use of repetitive transcranial magnetic stimulation (rTMS) to induce reversible brain lesions in the left medial middle frontal region in healthy participants. This approach made it feasible to test a relatively large number of individuals, whereas it is difficult to find many research participants with neurological disorders affecting their medial frontal brain region.

As in our previous studies, the experimental measure of psi involved the type of mind-matter interactions known as micro-psychokinesis, or micro-PK (Williams, 2021). Micro-PK involves an effect on small events such as the output of a random number generator that would produce random outputs in the absence of a micro-PK effect (Cardeña, 2018) and that are only detectable through statistical means (Varvoglis & Bancel, 2015). The specific task in our study was to influence the output of a Random Event Generator (REG) translated into movement of an arrow on a computer screen to the right or left. Our *a priori* hypothesis, as pre-specified in our BIAL Foundation grant that funded this research, was that healthy participants with reversible rTMS induced lesions affecting the left medial middle frontal brain region will show larger right intention effects on this mind-matter interaction task compared to healthy participants without rTMS induced lesions. In addition to our *a priori* hypothesis, we explored the effects of rTMS induced lesions affecting the right medial middle frontal region. We report our findings using rTMS in a well-powered study involving healthy participants (n = 108).

2. Materials and methods

2.1. Ethical considerations

The study received ethics approval by Clinical Trials Ontario (application #1511). The lead REB site is Baycrest Health Sciences in Toronto (application #12–51). Written informed consent was obtained prior to enrolling participants in the study.

2.2. Participants

One hundred and eight healthy participants were recruited from the Rotman Participant Database. Table 1 shows demographic information, as well as performance scores on the Montreal Cognitive Assessment (MoCA), a screening test of cognitive function (Nasreddine et al., 2005). Exclusion criteria were history of neurological disorders affecting the brain, major depressive disorder within 90 days of study entry,

Table 1 – Demographic and clinical characteristics of participants.

	Intention on first 500 trials:	Left rTMS		Right rTMS		Sham rTMS		Effect Size[a]
		Left	Right	Left	Right	Left	Right	
Count		18	18	18	18	18	18	
Sex	female:male	11: 7	8: 10	9: 9	12: 6	12: 6	11: 7	c = .17
	Prop (female)	.61	.44	.50	.67	.67	.61	
Age (years)	mean	36.3	39.9	40.2	31.9	39.6	39.7	.03
	sd	18.1	19.5	21.3	16.5	20.4	17.9	
	min, max	20, 72	21, 73	20, 73	20, 73	21,78	22, 70	
Education (years)	mean	16.9	15.9	17.0	15.8	16.7	16.6	.05
	sd	2.0	2.2	2.1	1.9	1.5	3.0	
	min, max	13, 20	12, 22	13, 21	11, 20	15, 20	13, 25	
MoCA scores	mean	27.3	27.6	26.3	27.2	28.1	26.6	.08
	sd	1.9	2.3	2.3	1.5	1.9	2.2	
	min, max	23, 30	22, 30	22, 30	25, 30	23, 30	21, 30	

[a] Eta-squared for continuous data; Pearson's contingency coefficient for binary data.

active psychiatric disorder, and past history of psychosis or other significant psychiatric disorders such as obsessive compulsive disorder, generalized anxiety disorder, and bipolar disorder (DSM-5, 2013). Sample size of 36 participants per stimulation arm with 500 intention and 500 control trials for each direction was determined based on 95 % power to detect a small interaction (f = .001) with analysis of variance between the virtual left lesion contrast (Left rTMS v. Sham rTMS) and right intention effect (intention v. control) assuming small correlation between repeated measures (r = .10) and specifying an alpha level of 5 %.

Participants were screened using a standard questionnaire for rTMS candidates (Rossi, Hallett, Rossini, Pascual-Leone, & The Safety of TMS Consensus Group, 2009). Individuals who received TMS in the past were excluded to avoid recognition of the difference between actual and sham stimulation. Participants were randomly assigned to one of three groups according to stimulation: rTMS induced left medial middle frontal lesion (n = 36), rTMS induced right medial middle frontal lesion (n = 36), and sham rTMS (n = 36). Participants were also evenly allocated to start with either left intention trials or right intention trials. Participants were allocated to six possible arms, i.e., Stimulation (3) × Order (2), by random permutation in blocks of six.

2.3. *Procedures*

2.3.1. *Transcranial magnetic stimulation*

TMS was administered using a Magstim Super Rapid 2 Plus machine equipped with a Magstim D70 Air Film figure-8 shaped coil (70 mm outer coil diameter) and was delivered with the handle of the coil pointing backward at 45° from the midsagittal line. The optimal position for activating the first dorsal interosseus (FDI) muscle of the right hand, i.e, the hotspot, was identified and marked with a skin marker. This position was close to C3. For determination of the active motor threshold (AMT), maximum FDI muscle contraction was first measured with the integrated electromyography (EMG) level visualized on an oscilloscope (Tektronix TBS1052B). The amplified EMG signal was fed through an analog integrator (Digitimer NL703) with a time constant of 200 msec. AMT was defined as the lowest intensity eliciting Motor Evoked Potentials (MEPs) of at least 200 μV peak-to-peak amplitude in 5 of 10 trials during slight isometric contraction of the FDI muscle (20 % of maximum voluntary contraction). The stimulus intensity was expressed as a percentage of the maximum stimulator output.

A protocol of rTMS, known as theta burst stimulation (TBS), has been developed as a rapid way of changing cortical excitability. Continuous TBS (cTBS) reduces cortical excitability with an effect lasting about 20–30 min (Huang, Edwards, Rounis, Bhatia, & Rothwell, 2005). Previous studies showed that cTBS produces a virtual lesion effect. For example, cTBS of the left superior temporal cortex induced temporary impairment in semantic processing (Bruckner, Kiefer, & Kammer, 2013) and cTBS of the right posterior parietal cortex caused visual extinction in the left visual field (Vesia, Niemeier, Black, & Staines, 2015).

cTBS was delivered to the medial middle frontal region, targeting Brodmann areas 9, 10, and 32. cTBS consisted of three pulse bursts at 50 Hz delivered every 200 ms (5 Hz) for 40 s (600 pulses total) at 90 % AMT. This was adjusted to 95.4 % to equalize the applied energy when switching from the Magstim D70 Air Film figure-8 shaped coil, used to determine AMT, to the air cooled Magstim 3910-00 coil used for rTMS (Magstim Inc., personal communication). Sham stimulation was administered using a Magstim 3950-00 D70 Air Film coil. This coil effectively eliminates stimulation immediately under its center, producing instead a diffuse oval of magnetic field energy 3–7 cm from the center, peaking at 25.3 % of the energy produced by the active coil (Smith & Peterchev, 2018). The sham intensity was set at 150 % AMT with a maximum set at 50 % of stimulator output. Table 2 shows the intensities for the AMT, active rTMS, and sham rTMS.

The rTMS coil was oriented vertically against the forehead with the handle pointing superiorly. A target site corresponding to 1 cm superior and approximately 3 cm to the right or left of the nasion was selected, depending on whether the participant was randomized to the right or left stimulation condition. The rTMS target sites were Fp1 or Fp2 depending on the side of stimulation. Sham stimulation was used to control for the effects of sensation to ensure that our findings with active rTMS could be attributable to actual medial middle

Table 2 – Summary Statistics for Active Motor Thresholds, as well as rTMS and Sham Intensities.

		Left rTMS		Right rTMS		Sham rTMS	
	Intention on first 500 trials:	Left	Right	Left	Right	Left	Right
AMT (% of stimulator output)	mean	39.9	38.4	39.1	40.6	41.3	43.8
	sd	5.6	5.5	5.2	6.3	7.8	8.0
	missing[a]	0	2	1	2	1	0
	min, max	29, 50	30, 48	32, 50	33, 59	25, 60	30, 55
Stimulation Intensity[b]	mean	38.0	36.6	37.2	38.6	49.2	49.7
(% Stimulator Output)	sd	5.4	5.3	5.1	6.1	2.8	1.2
	missing	0	2	1	2	0	0
	min, max	28, 48	29, 46	31, 48	31, 56	38,50	45,50

AMT = Active Motor Threshold, sd = standard deviation.
[a] Missing values due to omission in saving data.
[b] Stimulation intensities for left and right rTMS were 90 % AMT; Stimulus intensities for sham rTMS were 150 % AMT with maximum set at 50 %.

frontal region stimulation. Participants randomized to the sham condition group received sham stimulation in the same location as the left rTMS group. The timing and sound from the sham coil mimicked the stimulation from the active treatment coil. However, no significant stimulation was delivered to the target site in the brain.

2.4. *Mind - matter interactions*

As previously described (Freedman et al., 2003, 2018), the experimental task was to influence the numerical output of a portable Random Event Generator (REG) that produced 0s and 1s with equal probability at a rate of 200 bits per second (Jahn et al., 2000). Each sample of 200 bits comprised a trial. The numerical output of the REG was translated into movement of an arrow on a computer screen to the right (Intention Right) or left (Intention Left). Outcome per trial was the sum of 200 consecutive bits with expected sum per trial equal to 100. The REG was obtained from Psyleron, Inc.

The arrow moved in steps whose size and direction represented the accumulating deviations of trials from the expected value of 100. The midline of the screen was set at 100. The formula for location of the arrow relative to the midline is as follows: $D_k = (n_1 - 100) + (n_2 - 100) + (n_3 - 100) + \ldots..+ (n_k - 100)$ where D_k = deviation from expected value of 100 after trial k and n_j = random number generated by the REG over 1 s (sum of 200 consecutive 0s and 1s) on the *j*th trial where $j = 1$ to k. If $n_k - 100$ is negative, the arrow moves toward the left. If $n_k - 100$ is positive, the arrow moves toward the right.

The time between rTMS administration and the first experimental session was about 2–3 min. Participants were tested in a soundproof booth. They sat in front of a computer monitor showing the arrow pointing to the right or left (Fig. 1). They were asked to concentrate on moving the arrow in the direction that it was pointing. The arrow tip started at the midline for each block of trials and moved to the right or left on the screen in small steps according to the cumulative deviation from 100. If the arrow tip was to the right of midline, this represented a cumulative deviation greater than 100. If the tip was to the left of midline, the deviation was less than 100. The order of direction was counterbalanced across

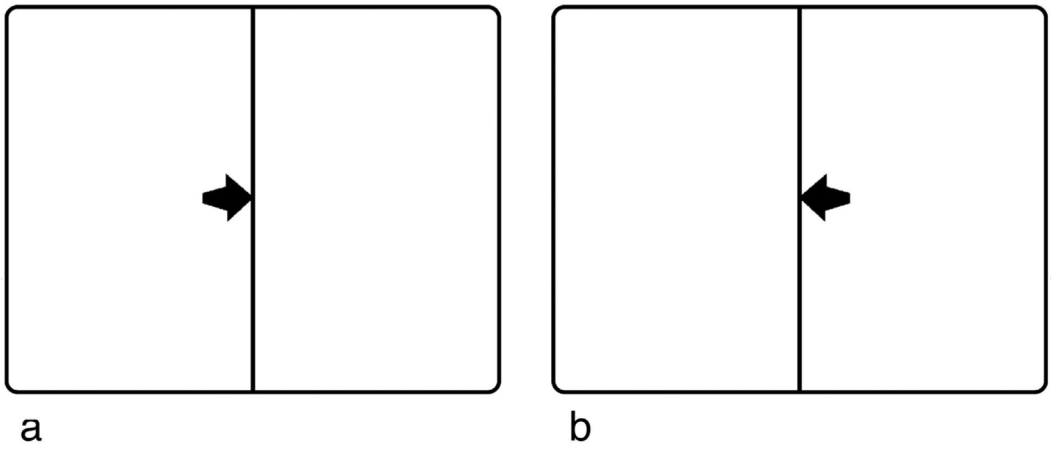

Fig. 1 – Computer screen showing initial position of arrow for each intention. a) Intention Right; b) Intention Left
This figure was adapted from a similar figure that first appeared in the Journal of Scientific Exploration. vol. 17, no. 4, pp. 651–668, 2003, under the title "Effects of frontal lobe lesions on intentionality and random physical phenomena" (Freedman et al., 2003) and has been adapted with permission.

participants, i.e., four sets of trials in the order Left Intention, Right Intention, Left Control, Right Control or Right Intention, Left Intention, Right Control, Left Control. Prior to administration of the intention trials, participants were administered rTMS under one of three stimulation types: right rTMS, left rTMS, or sham rTMS.

As previously described (Freedman et al., 2018), participants were given instructions that included the following: "There are some people who believe that if we concentrate on something hard enough, we can affect how things happen. We would like to see if there is a possibility that people can influence something just by concentrating on it." Participants were instructed to face the computer screen displaying an arrow pointing in the right or in the left direction with the tip at the midline. The experimenter continued with the instructions: "Now on this screen there is an arrow. When we are ready to start, I would like you to concentrate on making the arrow move in the direction that it is pointing. Here it is pointing to the (left/right). The arrow may sometimes be on the right and sometimes on the left side of the screen, but I want you to try to keep the arrow on the (left/right) side as much as possible. The line down the middle divides the screen into the left and right sides. There will be 5 sessions of about 2 min, lasting 10 min in total during which the arrow will be moving. Then we will move on to the next session. Remember, I would like you to try to keep the arrow on the (left/right) side as much as possible. Do you have any questions?" The experimenter says "left" when the arrow is pointing to the left and "right" when the arrow is pointing to the right.

Each intention, i.e., Right or Left, consisted of 500 trials presented in 5 blocks of 100 trials and lasted approximately 10 min. At the end of each 100-trial block, the experimenter confirmed that the participant understood the task, answered any questions, and initiated the next block. This took about 15–20 s. The position of the arrow tip was reset to the midline after each block. After the third block, the participant was asked to indicate the direction they were intending to move the arrow. After the first 500 trials, the experimenter set up the second session and read a short version of the instructions again, indicating that this time the participant was to move the arrow in the opposite direction. There was a delay of approximately 1 min between the end of the first session and the start of the second session. The two sessions took about 20 min to complete.

Immediately after the 500 Right and 500 Left Intention trials were completed, the participant left the room and a control run of 1,000 trials was run without the participant in the room. The control trials were run in two blocks of 500 trials and followed the same order of intentions that the participant completed. After the first block of 500 control trials, i.e., 8 min and 20 s after the control program was initiated, the experimenter entered the room to perform a key press that initiated the second block of 500 control trials and then left the room. This took about 15–30 s.

Thus, participants were each administered 2,000 trials. The first half were intention trials in which they were asked to move an arrow on a computer screen to the right or left. The movement of the arrow reflected the output of the REG. The second half were control trials which were administered after the participant exited the room. Within each of these two sessions, sets of 500 trials were either Right or Left.

2.5. Data analysis methods

The analysis plan to test the single *a priori* hypothesis with a single cross-product term in a linear model was pre-specified in the BIAL Foundation grant that funded this research. However, it was not pre-registered. To isolate the *a priori* hypothesis that healthy participants with reversible rTMS induced lesions affecting the left medial middle frontal brain region will show larger right intention effects on a mind-matter interaction task compared to healthy participants without rTMS induced lesions, we coded the three factors in the following way: a Direction contrast set to 0 for right trials and 1 for left trials, an Intention contrast set to +1 for intention trials and −1 for control trials, and two contrasts for rTMS group with left frontal stimulation as the reference category, *i.e.* StimSham set to +1 for participants with sham stimulation and zero otherwise and StimRight set to +1 for participants with right frontal stimulation and zero otherwise. Since right trials are coded as zero, the hypothesis is tested directly by the two-way cross-product of StimSham by Intention.

We ran a linear mixed effects model for trial-level REG output with random Intercept and random Intention effect for participants. The following variables were entered into the model: Intention (intention v. control trials), Direction (left v. right trials), StimSham (sham v. left stimulation) and StimRight (right v. left stimulation). We also included all appropriate two-way and three-way interaction terms. Since the *a priori* hypothesis was that the experimental effect (Intention v. Control) for Right Intention trials would be greater after Left rTMS than after Sham stimulation, the *a priori* focus was on the Intention x Sham Stimulation cross-product term. We report in the text, for each relevant variable, the model parameter estimate in the original scale ($\widehat{\beta}$), 95 % confidence interval, test t-statistic, p-value, and measure of the size of effect calculated as $d = \mathrm{sqrt}(4t^2/df)$.

Since the duration of transient rTMS-induced suppression of neural function required to reduce putative psi inhibition on the experimental task is unknown, we applied a scientifically valid weighting procedure to give more weight to observations from intention trials which were closer in time to the stimulation and less weight to later intention trials. A sigmoidal weight function was specified taking on values between one and zero with mid-taper around the break between the first 500 trials and second 500 trials and slope that reduced weighting from .73 to .27 over 120 trials, i.e., 60 trials before and after the break. Since prior to collecting their control trials, the participant was escorted out of the room where the intention trials were administered and the REG was located, weighting for these control trials was increased rapidly back towards one with an arctan function that reached a weight of .90 around the 79th control trial. The linear mixed effects model was run with and without this weighting.

Regarding further justification for the weighting, cTBS was initially shown to reduce the amplitude of motor-evoked potentials for 20–60 min (Huang et al., 2005), although the exact mean duration and variability are unknown. A subsequent

meta-analysis found that the effects of cTBS progressively decreased over 60 min (Chung, Hill, Rogasch, Hoy, & Fitzgerald, 2016). However, these estimates are derived solely from studies of motor cortex excitability. Whether a similar time course of modulation of higher cognitive processes can be expected from stimulation of other cortical regions is currently unknown. Therefore, implementing a weighting procedure accounts for the effectiveness of cTBS wearing off over the course of the experiment (Chung et al., 2016), while comparing the results from different breakpoints corresponding to different durations.

Although the weighting procedure was added *post hoc*, this does not alter the conclusion that our *a priori* hypothesis was confirmed. The reason is that our *a priori* hypothesis is about the existence of an effect rather than its duration. Moreover, the study was not designed to identify how long the effect of rTMS induced lesions would last. Without direct data pointing to duration of rTMS effects on left medial middle frontal region function, it was assumed that effects would last about 20–30 min. Given that assumption, collection of 1,000 intention trials over approximately 20 min was considered feasible and sufficient. While weighting of trials was not pre-specified in the analysis plan, it is a standard method to reduce the influence of observations that might not reflect exposure.

Hypothesis tests were performed at an α-level of 5 %. Model parameters and statistics were calculated using the lme4 and lmerTest packages in R (version 4.2.2). Nelder-Mead optimization was implemented to obtain Maximum Likelihood estimates.

2.6. *Calibration of REG*

To look for non-random patterns in the bits being generated by the REG, we harvested a sequence of bits six times on five different days before data collection, on six different days around mid-point of data collection, and on three different days at the end of data collection. On each day, the bits were collected for about 2 h and 15 min, resulting in harvested sequences of 1.7 million bits. The sequences of bits were submitted individually to the National Institute of Standards and Technology (NIST) suite of fifteen randomness tests (Rukhin et al., 2014), some with subtests resulting in 188 tests on each sequence. The cost of a false negative was considered substantively higher than the cost of a false positive for these screening tests because we did not want to falsely conclude that the REG output was random. Each was performed at an alpha level of 1 % even with the expectation that one to three positive tests might arise even if the sequence were random. This process was completed before beginning the data collection phase of the study, at the mid-point of the study, and at the end to ensure that the device continued to perform without bias.

Over the 15 sequences harvested from the REG, each of two returned no positive tests, each of five returned one positive test, each of six returned two positive tests, and each of two returned three positive tests. Twenty-three of the positive tests were from the 148-subtest Nonperiodic Templates test, eight of which indicated an unexpected count of four to six consecutive numbers in 9-bit strings. Three of the remaining positive tests were from the Random Excursions test with unexpected number of visits to −2, −3, or +8 during random walks defined by the sequence. The only other positive test was a single instance of the Runs test which indicated slower oscillation between consecutive numbers than expected. Twenty-three positive tests was not considered abnormal from 15 applications of the suite of up to 188 hypothesis tests. Additionally, no consistent deviation from randomness was noted from these 18 positive tests.

3. Results

Six randomized participants, two from each of the three rTMS interventions, did not complete the study. Three participants withdrew prior to, or during, rTMS administration. The other three participants did not understand the REG instructions. These six participants were replaced at the end of the planned allocation schedule with an additional six participants who were deterministically allocated to the intervention and order previously assigned to the original withdrawn participants.

Demographic and clinical characteristics of the 108 participants included in the data analyses are summarized in Table 1. Since participants were allocated randomly to each of the six study arms, it is not surprising that only small effects were observed between the arms on sex, age, and years of education. A medium difference was noted on the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) with scores on average slightly higher for the Sham rTMS participants whose first experimental trials were to move the arrow to the left.

Active Motor Threshold (AMT) levels used to determine rTMS intensity are summarized in Table 2. Fig. 2 displays the cumulative REG output for each of the 500 trial blocks averaged across participants within Left, Right, or Sham rTMS interventions and by order of intention for each intervention. Blue lines represent Left trials and red lines represent Right trials. The grey dashed line represents the weighting function (not on the same scale as the cumulative average) used to focus on the initial intention trials when the effect is expected to be stronger. This representation shows a sinusoidal function through the intention trials with weights starting close to 1, tapering through .5 around the 500th trial, continuing through the second 500 trials close to zero, and followed by an arc-tangent function rising rapidly toward 1 for the control trials.

We initially assumed sufficient rTMS efficacy over the entire duration of the observation window. Based on that assumption, an unweighted random effects model did not show a significant interaction ($\widehat{\beta} = -.06$, LCL = −.16, UCL = .05, t = −1.02, $p = .31$, $d = .11$) between the Sham Stimulation contrast (Left rTMS v. Sham rTMS) and the Experimental contrast (Intention v. Control) among the Right trials. We also note that while this model did not converge, the estimates for this focal interaction are not substantively different from those reported below for the weighted analysis.

In order to focus analysis on the earlier trials when the rTMS effect might be expected to be stronger, we applied weighting with a logistic function tapering over the Intention trials and then increasing rapidly to an asymptote of 1 during the control trials with an arctan function (Table 3).

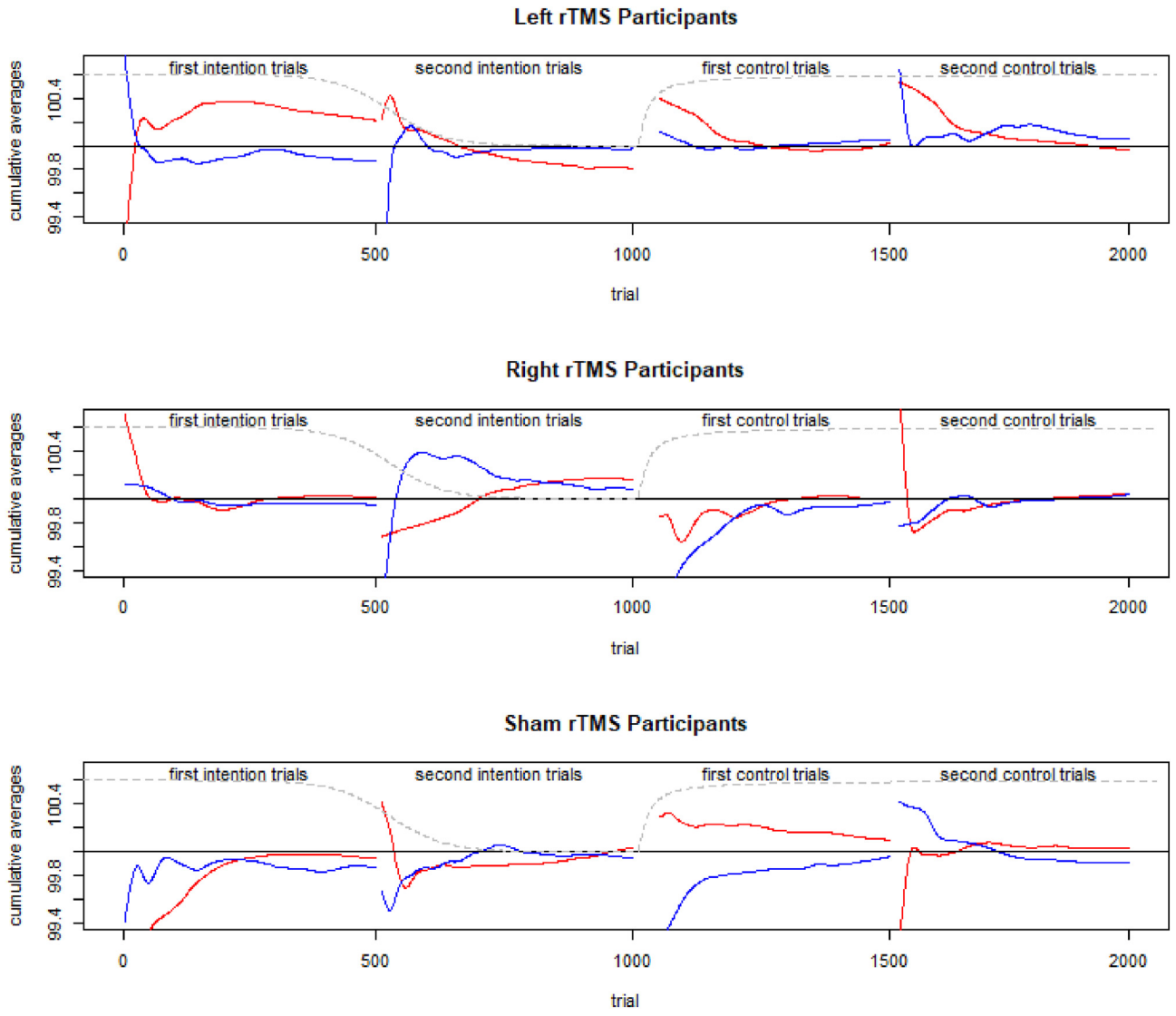

Fig. 2 – Cumulative average REG output across first and second 500 Intention and Control trials for each of the three rTMS conditions (Right, Left, Sham). Cumulative Average REG output greater than 100 corresponds to the arrow tip being on the right. Red = Intention Right; Blue = Intention Left. Grey dashed line represents the weighting function (not on the same scale as the cumulative average).

With the midpoint of the weighting taper located around the 500th intention trial, REG output for Right trials was not found to be statistically different between Left rTMS and Sham rTMS participants (t = −1.89, $p = .060$). For the Left rTMS groups, REG output was significantly higher for Right Intention than Right Control trials ($\widehat{\beta} = .11$, LCL = .03, UCL = .20, t = 2.59, $p = .010$, $d = .35$). Specifically targeting the *a priori* hypothesis, a significant interaction was detected between the Intention contrast (i.e., Intention v. Control trials) and the Sham stimulation contrast (i.e., Left rTMS v. Sham rTMS) for Right trials ($\widehat{\beta} = -.17$, LCL = −.29, UCL = −.05, t = −2.80, $p = .006$, $d = .38$). Fig. 2 shows the cumulative average REG output accumulated across each of four sets of 500 trials for participants in the Left (top), Right (middle), and Sham (bottom) rTMS groups. Cumulative average REG output greater than 100 indicates a position of the arrow tip on the right side of the screen. The model also shows that the differential Intention effect for Right trials between Left Stimulation and Sham Stimulation participants is significantly greater than for Left trials ($\widehat{\beta} = .24$, LCL = .08, UCL = .40, t = 2.95, $p = .003$, $d = .27$).

Fig. 3 shows boxplots for the average REG output for (a) the first 500 intention and first 500 control trials and (b) for the second 500 intention and second 500 control trials. In Fig. 3a, it is worth noting that average REG output for the first 500 Right Intention trials administered to the Left rTMS participants shows a relatively symmetrical distribution, no outlying observations, and about three-quarters of the values greater than 100. Average REG output greater than 100 indicates a position of the arrow tip on the right side of the screen.

As can be seen in the bottom panel of Fig. 2, the Right Control trials ("first control trials" and to a lesser degree the

Table 3 – Estimates for the weighted linear mixed effects model with random intercept and intention effects.

	Weighted (mid-taper around 300th trial)					Weighted (mid-taper around 500th trial)					Weighted (mid-taper around 700th trial)				
	Estimate	Std. Error	df	t value	Pr(>|t|)	Estimate	Std. Error	df	t value	Pr(>|t|)	Estimate	Std. Error	df	t value	Pr(>|t|)
(Intercept)	.15206	.05002	148	3.04	.0028**	.11053	.04174	225	2.648	.00867**	.0638	.03850	368	1.657	.09832
StimSham	−.14514	.07074	148	−2.052	.04194*	−.11157	.05903	225	−1.890	.06006	−.07477	.05445	368	−1.373	.17048
StimRight	−.13093	.07074	148	−1.851	.06616	−.09863	.05903	225	−1.671	.09615	−.04423	.05445	368	−.812	.41716
Intention	.15387	.05230	155	2.942	.00376**	.11239	.04333	222	2.594	.01012*	.06583	.04068	316	1.618	.10659
Direction	−.16245	.07043	170	−2.307	.02228*	−.13485	.05809	480	−2.321	.02069*	−.08066	.05386	12060	−1.498	.13424
StmS×I	**−.20509**	**.07396**	**155**	**−2.773**	**.00624****	**−.17154**	**.06128**	**222**	**−2.799**	**.00557****	**−.1349**	**.05752**	**316**	**−2.344**	**.01968***
StmR × I	−.16483	.07396	155	−2.228	.02729*	−.13253	.06128	222	−2.163	.03162*	−.07822	.05752	316	−1.360	.17487
StmS × D	.05947	.09960	170	.597	.55123	.05004	.08216	480	.609	.54276	.02494	.07617	12060	.327	.74337
StmR × D	.12716	.09960	170	1.277	.20344	.11574	.08216	480	1.409	.15956	.07715	.07617	12060	1.013	.31112
I × D	−.22548	.07033	169	−3.206	.00161**	−.19798	.05803	476	−3.412	.00070***	−.1441	.05381	11650	−2.678	.00741**
StmS × I × D	.25181	.09946	169	2.532	.01226*	.24243	.08206	476	2.954	.00329**	.2175	.07610	11650	2.859	.00426**
StmR × I × D	.21139	.09946	169	2.125	.03499*	.19998	.08206	476	2.437	.01518*	.1616	.07610	11650	2.123	.03375*

Fixed effect estimates and test statistics for the linear mixed effects model with weighting function tapering at three occasions during the intention trials. The primary analysis with the taper placed around the 500th trial weights the first 500 trials close to 1, the second 500 intention trials close to zero and the 1,000 control trials close to 1. StimRight = Right rTMS (+1) v. Left rTMS (0); StimSham = Sham rTMS (+1) v. Left rTMS (0); Intention = Intention Contrast (Intention (+1) v. Control (−1)); Direction = Direction Contrast (Left (+1) v. Right (0)); Since Right direction trials are coded as zero, the hypothesis is directly tested by the two-way StimS × I interaction term crossing the Intention contrast (Intention v. Control trials) with the Stimulation contrast (Sham v. Left stimulation participants). Regardless of whether we taper the weighting around the midpoint of the intention trials, i.e., between the first 500 and the second 500 intention trials or earlier (e.g., around the 300th trial) or later (e.g., around the 700th trial), the StimSham × Intention was found to be significant, i.e., detection of a significant effect was not sensitive to the selection of a specific mid-point of taper.
*p < .05, **p < .01, ***p < .001.

"second control trials") returned higher REG output after the Sham participants were administered their Intention trials. Since this contrast of Right Intention trials versus Right Control trials among the Sham rTMS participants served as a control for the Right Intention versus Right Control contrast in the Left rTMS participants, we wanted to confirm that an effect was observed in the Left rTMS participants rather than the effect being due to an inverted effect observed in the Sham rTMS participants. Since the Left Stimulation participants were coded as the reference category by the pair of Stimulation contrasts, this was confirmed by the Intention effect – reported above – which was significant (t = 2.59, $p = .010$).

4. Discussion

As predicted by our *a priori* hypothesis, we demonstrated that healthy participants with reversible rTMS induced lesions targeting the left medial middle frontal brain region showed larger right intention effects on a mind-matter interaction task compared to healthy participants without rTMS induced lesions. This significant effect was found only after we applied a *post hoc* weighting procedure aligned with our overarching hypothesis. We applied the weighting procedure in the statistical analysis because neural inhibition due to rTMS was expected to decline over time. Although rTMS effects can last for 20–30 min, the exact duration in our study was not fully known, especially since the intensity required for putative psi effects may vary with demands of the experimental task. To account for the expected decline in rTMS induced neural suppression, we applied greater weighting to the intention trials that were closer in time to the stimulation than to trials that occurred later. Regardless of whether we set the midpoint of the taper around the transition between the first and second set of 500 intention trials, around the 300th trial or around the 700th trial, the mind-matter interaction effect following the induced left medial middle frontal lesion was significant. Thus, our findings appear robust regardless of how the weighting is applied.

Thus, we replicated the previous findings which we reported in two participants with brain lesions, i.e., twice in an individual with a brain lesion due to a tension pneumocephalus (Freedman et al., 2003) and once in a case with behavioral variant frontotemporal dementia due to a mutation in the C9ORF72 gene (Freedman et al., 2018). These robust findings across different brain pathologies in neurological patients, as well in healthy participants with reversible rTMS induced brain lesions, support the concept that the brain acts as a filter to inhibit psi and that the left medial middle frontal region, involving one or more of Brodmann areas 9, 10, and 32, is a key anatomical component of this filter.

Although our findings suggest that the left medial middle frontal region inhibits psi, the mechanisms by which this might occur are unknown. In this regard, we previously noted mental states that have been associated with psi (Freedman et al., 2018). These include mental immersion leading to a loss of awareness of oneself and immediate surroundings (Jahn & Dunne, 1987) and altered states such as meditation (Honorton, 1977) and hypnosis (Honorton, 1977; Stanford & Stein, 1994), in which there may be a reduction in self-

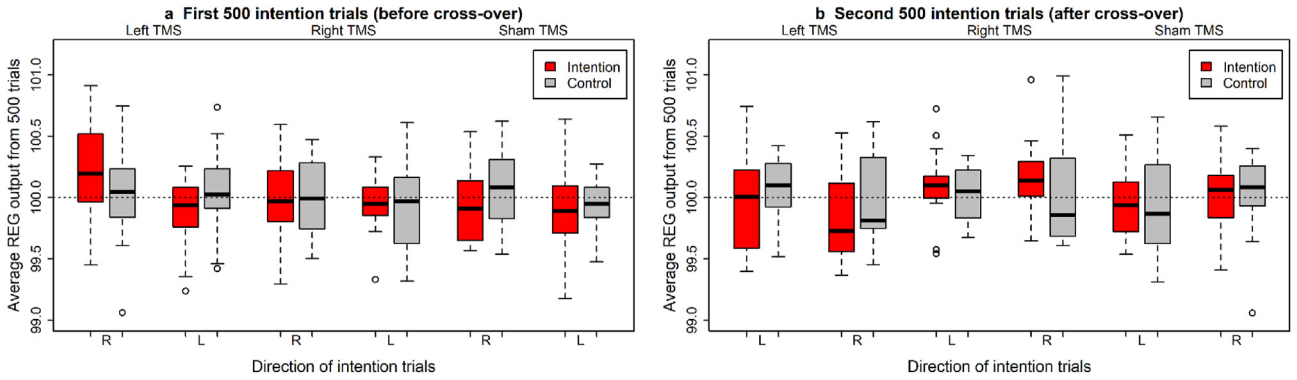

Fig. 3 – Boxplots for the average REG output in the Left, Right, and Sham rTMS groups. (3a) First 500 intention and first 500 control trials. (3b) Second 500 intention and second 500 control trials. Average REG output greater than 100 corresponds to the arrow tip being on the right. R=Right Intention; L = Left Intention; Heavy Line = median; Boxes in graph before and after crossover represent the participant groups in the same order. Thus, those who started with right intention trials before crossover continued with left intention trials after crossover; Boxes represent 25th to 75th percentile. Open circles = outlying the bulk of observations.

awareness (Vaitl et al., 2005). Thus, since the medial middle frontal region is involved in mediating self-awareness (Amodio & Frith, 2006; Morin, 2007, 2011), and since reduced self-awareness may facilitate psi (Honorton, 1977; Jahn & Dunne, 1987; Stanford & Stein, 1994; Vaitl et al., 2005), we previously postulated that damage to this area may enhance psi through a reduction in self-awareness (Freedman et al., 2018). We also suggested that in addition to reduced self-awareness, relatively good attention was required for psi effects to occur (Freedman et al., 2003, 2018).

The requirement for reduced self-awareness combined with good attention to facilitate psi may help explain why inhibition of the left medial middle frontal region was associated with a significant mind-matter interaction effect in moving an arrow on a computer screen to the right, i.e., contralateral to the side of the induced rTMS lesion. In addition to our pre-planned hypothesis related to the left medial middle frontal region, we explored the effects of rTMS induced lesions affecting the right medial middle frontal region. When there was an induced rTMS lesion in the right medial middle frontal region, the difference between left intention and right intention effects, each versus control, was significantly attenuated compared to left rTMS. In fact, based on Fig. 3a, any effect due to the right sided rTMS inhibition appears to be negligible. Although the right hemisphere has a prominent role in mediating self-awareness (Keenan, Rubio, Racioppi, Johnson, & Barnacz, 2005), it also has a major role in mediating attention (Mesulam, 1981). Since ability to focus attention may be necessary for psi effects to occur, reduced attention due to rTMS inhibition following right-sided stimulation may have interfered with the emergence of psi effects. In contrast, rTMS induced lesions in the left medial middle frontal region may have resulted in a combination of reduced self-awareness with preserved attention, i.e., the cognitive profile that may be necessary to facilitate psi effects. Further research is needed to test this hypothesis.

A comment is warranted about the noise reduction model of parapsychology (Cardeña, 2018; Honorton, 1974, 1977; Storm & Rock, 2009), self-awareness, and the concept of the brain as a psi-inhibitory filter (Bergson, 1914; Ehrenwald, 1975, 1978). The noise reduction model conceptualizes psi as a weak cognitive signal that is usually masked by internal cognitive and external noise (Storm & Rock, 2009). According to this model, reducing the noise should enhance detection of psi. Since self-awareness may represent a form of internal noise, reduction in self-awareness as a psychological mechanism that may facilitate psi is in keeping with the noise reduction model as related to internal noise. However, the relation between the noise reduction model and the brain filter hypothesis, which forms the basis of our work, is unclear with respect to external noise. The reason is that psi phenomena are part of the external noise based on the brain filter hypothesis (Bergson, 1914; Ehrenwald, 1975, 1978). Thus, according to the brain filter hypothesis, reducing external noise as a whole would also reduce psi.

An observation that requires discussion relates to the right intention control data in the Sham stimulation group. These control data showed higher REG output, which corresponds to movement of the arrow to the right, as compared to the Right Intention trials. This inverted effect in the Sham group could have artifactually contributed to significant statistical interaction showing a larger Right Intention effect following left sided rTMS compared to Sham stimulation since in both cases the comparison is to control data. To address this issue, we examined the Right Intention versus Right Control data within the Left Stimulation group alone and found a significant Right Intention effect. This suggests that the significant mind-matter interaction effect was not an artifact of an inverted effect among Sham control participants.

Finally, the current study, together with our previous research (Freedman et al., 2003, 2018), suggests that individuals with frontal brain lesions may comprise an enriched sample for detection of psi effects. Thus, studying participants with neurological or reversible rTMS induced frontal lesions may facilitate detection and replication of psi effects in well-controlled studies. Our work also provides a rationale to further replicate our findings using transcranial direct current

stimulation (tDCS), a procedure which can produce reversible deactivation of neuronal populations. In addition, our findings suggest a possible neuroanatomical mechanism for putative emergence of psi in other circumstances, such as with use of psychedelics. For psychedelics, this is based on reduction of cerebral blood flow in medial prefrontal cortex after infusion of psilocybin (Carhart-Harris et al., 2012; Luke, 2022).

There are limitations to our study. First, although we targeted rTMS to inhibit function in Brodmann areas 9, 10, and 32, it is difficult to be certain that the stimulation was actually delivered to these areas. However, the stimulation should have at least been close to these regions. Second, although control data were collected in close temporal proximity to the data generated when the participant was trying to influence the movement of the arrow, the control data were not collected at exactly the same time and thus are not a perfect match for the intention data. Despite this, it is unlikely that this led to an artifactually significant result because we submitted output from the REG to the National Institute of Standards and Technology (NIST) suite of fifteen randomness tests (Rukhin et al., 2014) and did not find any consistent deviation from randomness. Thirdly, sham does not produce the identical sensation and muscle twitching as with real rTMS. This is not likely to have caused false positive results since we did not include participants who were familiar with rTMS. Thus, participants in the Sham Group would not likely have detected that they received Sham stimulation. Finally, although our *a priori* hypothesis was pre-specified in the BIAL Foundation grant that funded this research, the study was not pre-registered. Future replication studies are encouraged and should utilize a pre-registered framework.

5. Conclusions

Our findings in healthy participants with rTMS induced reversible brain lesions are potentially transformative for the way we view interactions between the brain and seemingly random events. They replicate our previously published findings in individuals with damage to their frontal lobes and support the concept that the brain serves as a filter to block psi effects. This may help explain why these effects are so small and hard to replicate in healthy participants.

Our findings also suggest that individuals with neurological or reversible rTMS induced frontal lesions in the left medial middle frontal region may comprise an enriched sample for more reliable detection and replication of psi effects. Thus, studies with a focus on this group may significantly advance research in the area of psi and help bring this controversial phenomenon into the realm of mainstream science.

Data availability

All data used in the manuscript will be made publicly available on Open Science Framework at osf.io/6rzy8 (Freedman, Binns, Meltzer, Hashimi, & Chen, 2024) except data that are personally identifying or sensitive. Our Research Ethics Board has determined that the latter data fields are comprised of age in years, years of education, and the MoCA score. However, the omitted fields will be made available to researchers on request.

Transparency and open promotion (TOP) guidelines

No part of the study procedures was pre-registered prior to the research being conducted. In addition, no part of the study analyses was pre-registered prior to the research being conducted. However, the analysis plan to test the single *a priori* hypothesis with a single cross-product term in a linear model was pre-specified in the BIAL Foundation grant that funded this research. The overall methodology was also pre-specified in the BIAL grant application.

We report how we determined our sample size, all data exclusions, all inclusion/exclusion criteria, whether inclusion/exclusion were established prior to data analysis, all manipulations, and all measures in the study. We confirm that inclusion/exclusion criteria were established prior to data analysis. Anonymised data, digital study materials, data dictionary, and analysis script are publicly available on Open Science Framework at osf.io/6rzy8 (Freedman et al., 2024).

Author contributions

Morris Freedman: Conceptualization; Funding Acquisition; Investigation; Methodology; Project Administration; Resources; Supervision; Writing – Original Draft Preparation; Writing – Review and Editing. **Malcolm Binns**: Conceptualization; Formal Analysis; Funding Acquisition; Investigation; Methodology; Supervision; Visualization; Writing – Original Draft Preparation; Writing – Review and Editing. **Jed Meltzer**: Formal Analysis; Investigation; Methodology; Resources; Supervision; Writing – Review and Editing. **Rohila Hashimi**: Investigation; Methodology; Project Administration; Writing – Original Draft Preparation; Writing – Review and Editing. **Robert Chen**: Conceptualization; Funding Acquisition; Investigation; Methodology; Supervision; Writing – Review and Editing.

Declaration of competing interest

None.

Open practices

The study in this article earned Open Data and Open Material badges for transparent practices. The data and materials used in this study are available at: https://osf.io/6rzy8

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