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# Unwanted memory intrusions recruit broad motor suppression

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## Abstract

Quickly preventing the retrieval of (inappropriate) long term memories might recruit a similar control mechanism as rapid action-stopping. A very specific characteristic of rapid action-stopping is ‘global motor suppression:’ when a single response is rapidly stopped there is a broad skeletomotor suppression. This is shown by the technique of Transcranial Magnetic Stimulation (TMS) placed over a task-irrelevant part of primary motor cortex (M1) to measure motor evoked potentials (MEPs). Here we used this same TMS method to test if rapidly preventing long-term memory retrieval also shows this broad skeletomotor suppression effect. Twenty human participants underwent a Think/No-Think task. In a first phase, they learned word pairs. In a second phase, they received the left-hand word as a cue and had to either retrieve the associated right-hand word (“Think”) or to stop retrieval (“No-Think”). At the end of each trial, they reported whether they had experienced an intrusion of the associated memory. Behaviorally, on No-Think trials, they reported fewer intrusions than Think trials, and the reporting of intrusions decreased with practice. Physiologically, we observed that the MEP, measured from the hand (which was irrelevant to the task), was reduced on No-Think trials in the time frame 300 to 500ms, especially on trials where they did report an intrusion. This unexpected result contradicted our pre-registered prediction that we would find such a decrease on No-Think trials, where the intrusion was not reported. These data suggest that one form of executive control over (inappropriate) long term memory retrieval is a rapid and broad stop, akin to action-stopping, that is triggered by the intrusion itself.

## INTRODUCTION

The ability to control our actions and thoughts is essential to many daily life endeavors such as stopping one’s step into the street if a car approaches or pushing disruptive intrusive thoughts out of mind when we are trying to focus on work. It has been suggested that there may be a functional and perhaps anatomical similarity between rapid action-stopping and preventing memory intrusions (Anderson & Green, 2001; Castiglione, Wagner, Anderson, & Aron, 2019; Depue, Orr, Smolker, Naaz, & Banich, 2016; Guo, Schmitz, Mur, Ferreira, & Anderson, 2018; Anderson & Hulbert, 2021). Such research has compared tests of rapid action-stopping such as the stop signal paradigm with a test of rapid intrusion prevention known as the Think/No-Think paradigm. In the Stop Signal Task subjects are presented with, for example, a white letter (e.g. ‘T’ or ‘K’) and instructed to respond as fast as they

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can by saying the letter out loud. On a minority of trials, before they speak, the letter subsequently turns red (at varying delay intervals), signaling the subjects to stop the initiated speech response (Logan & Cowan, 1984). In the Think/No-Think paradigm (Anderson & Green, 2001) participants are first asked to learn word pairs (cue word + target word). Then, for each pair, they are given a cue word alone and asked to either recall the matching target word if the cue is green (Think trials) or to try to 'suppress' the memory of the matching target word if the cue is red (No-Think trials). It is possible to track the intrusion of the target word into consciousness by presenting a rating scale after each trial, asking the subject to rate the extent to which the target word came to mind (Benoit, Hulbert, Huddleston, & Anderson, 2015; Castiglione et al., 2019; Hellerstedt, Johansson, & Anderson, 2016; Levy & Anderson, 2012). Behavioral results show a steady decrease in reported intrusions with practice on No-Think trials (Castiglione et al., 2019; Hu, Bergstrom, Gagnepain, & Anderson, 2017; Levy & Anderson, 2012).

One basis for a common mechanism between rapid action-stopping and preventing intrusions is that meta-analysis of fMRI results from Think/No-Think and Stop Signal Task response inhibition shows that No-Think trials and Stop trials elicit overlapping activations in right lateral prefrontal cortex (Guo et al., 2018). Another basis for a common mechanism is that scalp Electrocephalography (EEG) showed that both No-Think and Stop trials elicit increased power of oscillations in the beta band range within about 300ms over right lateral frontal electrodes (Castiglione et al., 2019). Here we tested the idea of a common mechanism using a different approach, that of single-pulse Transcranial Magnetic Stimulation (TMS) induced motor evoked potential (MEP) – a measure of motor excitability.

In TMS studies of the stop signal paradigm, a single pulse of TMS is delivered over the primary motor cortex (M1) on trials with a stop signal, at timepoints meant to overlap with the putative stopping process in the brain. Importantly, in such studies, TMS is done over a muscle representation that is not related to the task. It has been shown that stopping the hand leads to a MEP reduction in the leg (Badry et al., 2009; Majid, Cai, George, Verbruggen, & Aron, 2012), stopping the eyes leads to a MEP reduction of the hand (Wessel, Reynoso, & Aron, 2013) and stopping speech leads to reduced MEPs of the hand (Cai, Oldenkamp, & Aron, 2012; Wessel & Aron, 2017; Wessel et al., 2016). This broad stopping-induced reduction of MEPs for task-irrelevant muscle representation is thought to be an effect of a fast cortico-subthalamic 'hyperdirect' pathway globally shutting off the skeletomotor system via the basal ganglia (Wessel et al., 2016). Here we tested whether this global MEP reduction also occurs when people try to stop retrieval of a long-term memory. Our reasoning was that even though it is possible to stop a particular response selectively (Majid et al., 2012), it appears that global suppression is a fast default and therefore might also operate in the case of preventing inappropriate memory retrieval. If present on No-Think trials (Intrusion or No-Intrusion), this global effect may play a functional role, such as shutting down all responses, regardless of their modality (whether cognitive or motoric); this might be faster and more efficient than selectively stopping specific responses. Or it might simply mean that global motor suppression is a byproduct of this stopping system, which occurs even when a different modality is stopped (e.g. thoughts).

In each participant we ran the Think/No-Think task and then the vocal Stop Signal Task. TMS was delivered over left M1 and MEPs were recorded from the right hand via electromyography. TMS was delivered to generate a motor evoked potential (MEP) at specific points in time, designed to overlap with putative stopping of retrieval and stopping of action. There are two theories about when thought stopping occurs during a No-Think trial. One theory (supported by Castiglione et al., 2019) is that stopping occurs early in the trial, at around 300ms, preventing intrusions from coming to mind; if this were the case, we would expect to find decreased MEPs for NT No-Intrusion compared to NT Intrusion. A second theory is that stopping may instead be triggered following the intrusion, in order to "shut the intrusion out of awareness" (Guo et al., 2019); in this case we would expect decreased MEPs for NT Intrusion compared to NT No-Intrusion trials (i.e. global stopping only occurred following intrusions). While both these alternatives are possible, guided by our previous results (Castiglione et al., 2019) we thought the first case was more likely. Specifically, given the finding from scalp EEG, that No-Think No-Intrusion elicited increased beta band power around 300ms after the No-Think cue compared to No-Think Intrusion (Castiglione et al., 2019), we predicted that MEPs would be reduced on No-Think No-Intrusion compared to No-Think Intrusion, Think and baseline trials, in the time frame of 300, 400 or 500ms (possibly at different times for different subjects).

## METHODS

Link to pre-registration document: https://osf.io/qhgpt/?view_only=c2118b1b35ef40659e12f62c7fc5e6f5

### Recruitment, sample size justification, exclusion and replacement criteria:

**Recruitment.—**Subjects within the 18-26 age range were recruited through flyers posted on the UCSD campus and paid $20 per hour. Inclusion criteria were: normal/corrected to normal vision, no previous history of neurological illness or learning disabilities, no current use of psychoactive medications and English as a primary language since early childhood (0-3 years).

**Sample size.—**We collected data from 24 subjects, to achieve a fully analyzable sample size of n=20 subjects (4 subjects were excluded due to noncompliance with one or more of our exclusion criteria). We could not run a power analysis because no prior study had examined motor excitability during the Think/No-Think task. However, previous studies measuring MEPs of a task-unrelated muscle using TMS have used sample sizes n<20 (Cai et al., 2012; Greenhouse, Sias, Labruna, & Ivry, 2015; Wessel et al., 2016).

**Data Exclusion.—**Exclusion criteria were: a) inability to reach training threshold on word pairs in the requisite time (at least 50% word pairs) b) use of intentional strategies to think about the target word during No-Think trials (assessed by a post-experimental questionnaire), c) technical failures in EMG recording, d) the failure to reach a balanced number of No-Think trials with and without intrusions (at least a 70%-30% ratio), where each TMS pulse time (300ms, 400ms and 500ms from the No-Think cue) includes at least 20 trials, e) outlier behavior on the Stop Signal Task, i.e. p(stopping)<30% or p(stopping)>70%, Go RT excessively slow (i.e. over 800ms), or Go omissions > 15%.

### Think/No-Think task:

**Training phase:** During this phase, subjects learned a total of 60 word pairs of which 24 were later presented to them as “Think stimuli,” 24 as “No-Think” stimuli and 12 as filler pairs for practicing the task. These were the same word pairs used in Castiglione et al. (2019). The assignment of “Think” or “No-Think” to each word pair was counterbalanced across subjects through 3 assignment lists (list A, list B and list C). The training was divided into 2 parts (30 learned words per part). During Part 1, subjects observed 30 word pairs appearing in random order on a black background for 2 seconds (Fig.1A). A testing phase followed, where subjects were presented, in random order, with the left-hand word from each word pair and were instructed to say the right-hand word out loud. They were given visual feedback of the correct response either right after their response or after 4 seconds if no response was given. Part 2 was identical to Part 1, but the remaining 30 word pairs were used instead. After Parts 1 and 2, subjects were tested on recall of the overall 60 word pairs. No feedback was given for this testing phase. Responses were recorded (both manually by the experimenter and through a microphone) in order to assess whether the subject reached 50% of correct answers; subjects who did not were excluded from the study. Manual records were compared to microphone recordings afterwards by an experimenter blind to the word pair conditions.

**Think/No-Think phase:** Subjects performed this phase of the task on all 24 Think (T) and 24 NT (NT) pairs, which were each presented 9 times, for a total of 468 trials. The 468 trials were divided into 9 blocks of 52 trials each. Each block randomly presented 1 repetition of every T and NT word pair (for a total of 48 experimental trials) plus 4 additional trials - for which the word pairs were randomly picked from the T and NT pairs - that were used as baseline MEP measurements. Each word pair was consistently presented either as a T pair or as a NT pair. First, the subjects did two practice cycles of the task which used filler word pairs for both T and NT trials. Between the two practice cycles, they completed a diagnostic questionnaire to verify that the instructions were understood and applied correctly (if not, feedback was given on how to correct behavior for the next practice cycle). Then the actual task started: a fixation cross first appeared, jittered around 500ms. Then, for each trial, the left-hand word from a word pair was presented on the screen either in red, cueing the subject to prevent/stop the memory of the matching word (NT trial), or in green, cueing the subject to silently remember the matching word (T trial) (Fig. 1A). For NT trials, subjects were instructed to use a *direct suppression* strategy, i.e. they were asked to simply block the target word from awareness instead of substituting it with any other thought, word or idea. On each experimental trial (excluding baseline trials), a single pulse of TMS was delivered over the right first dorsal interosseus (FDI) area of the motor cortex at either 300ms, 400ms or 500ms after the cue (whether on a T or NT trials) (Fig. 1B). These times were selected based on our hypothesis that global stopping occurs as a preventive mechanism during NT No-Intrusion trials, and specifically based on the following observations: a) in Castiglione (2019) the average beta increase (marking thought stopping) was around 300ms, b) our existing work (Jana et al., 2020) showed that right frontal beta in stopping preceded global motor suppression by around 20 to 50ms roughly, ergo the global MEP decrease should be expected at 20 to 50ms after 300ms, c) our work on global motor suppression for the stop signal task (Jana et al., 2020) showed that MEPs are suppressed for about 100ms or more (leading to our choice of 500ms as maximum time). For each condition (T and NT), there were 72 trials where TMS was delivered at each of 300ms, 400ms and 500ms. On the 36 baseline trials (4 trials per block), the TMS pulse occurred 250ms before the cue. The word stayed on the screen for 3 seconds. After each trial (T and NT), a rating scale was presented on the screen, asking the subject to rate from 1 to 3 (1=never, 2=early, 3=late) by pressing the corresponding number key, if and when the matching word had come to mind during the trial. After the third block, the same diagnostic questionnaire from the training phase was administered to ensure subjects were still following the instructions. Word-pair display order was counterbalanced across participants.

### Stop Signal Task:

In the last part of the experiment, subjects performed 4 blocks of a vocal Stop Signal Task, mainly as a validating tool for our MEP methods. There were 4 blocks of 100 trials each. At the beginning of each block, a fixation cross was displayed. After approximately 500ms, either a letter ‘T’ or a letter ‘B’ was displayed in white in the center of the screen and the subject was instructed to answer quickly by pronouncing the letter in a microphone. On approximately 25% of the trials, after the letter appeared, it turned red (a stop signal). For these Stop trials, the stop signal was presented with a dynamically adjusted delay starting at 200ms after the letter appeared; after failed stops the delay was shortened (by 50ms increments), whereas after successful stops it was prolonged (by 50ms increments). Subjects had 1 second to respond. On each trial, a single pulse of TMS was delivered over the FDI area of the left motor cortex. On Stop trials, this pulse was delivered 170ms after the stop signal; this timing was calculated based on evidence suggesting that implementation of action stopping can be measured from EMG around this time (Hannah, Muralidharan, Sundby, & Aron, 2019; Nord et al., 2019; Raud & Huster, 2017). On Go trials the TMS pulse time was yoked to that of stop trials. In each block ~10 trials were randomly selected to be baseline trials, where TMS was delivered 250ms before the go cue, for a total of ~40 baseline trials. The inter-trial interval varied depending on the response time to create a standardized trial duration of 3000ms.

### EMG and TMS:

Electromyography (EMG) was recorded using a belly-tendon montage with 10-mm-diameter Ag-AgCl hydrogel electrodes, from the FDI muscle of the right hand (using the metacarpophalangeal joint of the index finger as reference electrode location). The EMG signal was amplified using a Grass QP511 Quad AC amplifier (Grass Technologies, West Warwick, RI), with a bandpass filter between 30 Hz and 1kHz. Data was sampled at 2 kHz with a CED Micro 1401-2 and was recorded using CED Signal version 4 (Cambridge Electronic Design, Cambridge, UK) (Fig. 1B). Single pulses of transcranial magnetic stimulation (TMS) were delivered with a 7 cm figure-of-eight coil, using a TMS device (PowerMag Lab 100, MAG&More GMBH, Munich, Germany). The pulse shape generated had a biphasic waveform, with the initial phase of induced current in the brain being oriented from posterior-to-anterior across the anterior bank of the central sulcus.

During hot-spotting, the area that elicits the best motor response in the right FDI muscle was established over left M1 with the coil held about 45 degrees to the mid-sagittal line. The optimal position was marked on the scalp to ensure the coil was held in the same location throughout the experiment. A supra-threshold pulse (minimum stimulus intensity that produced > 1mV motor-evoked potentials (MEPs) in 5/10 trials) was first found. TMS was applied at 110% of this supra-threshold pulse (Mean intensity=54.64% of maximum output; min=36%, max=70%).

## ANALYSIS AND PREDICTIONS

Behaviorally, for the Think/No-Think task we expected that intrusions would decrease for NT trials across time (Castiglione et al., 2019; Hu et al., 2017; Levy & Anderson, 2012). While another behavioral measure of Think/No-Think is subsequent forgetting (i.e. phase 3 of the task), we did not run the typical final recall test for the Think No-Think task. This was because we were particularly interested in the punctate and “online” aspect of preventing/stopping intrusions after a No-Think cue is given, regardless of its long-term effects (the purpose of the final recall test is instead to verify the long-term effects of multiple intrusion suppressions, at the end of the Think/No-Think task). For MEPs we predicted beneath-baseline reductions in the time frame of 300, 400 and 500ms (possibly at different times for different subjects) on NT trials, more for trials without an intrusion. For the Stop Signal Task, we expected that behavioral performance would be typical and that MEPs would be reduced after the stop signal and before SSRT (Badry et al., 2009; Cai et al., 2012; Logan & Cowan, 1984; Majid et al., 2012; Wessel et al., 2013).

### Behavioral analysis:

**Think/No-Think task:** We calculated the intrusion proportion over time (over the 9 blocks). To do so, we collapsed early and late intrusions and considered only two conditions: Intrusion and No-Intrusion trials. This was done due to the lack of MEP measurements in each intrusion condition (early and late) once the data were divided into the three TMS pulse times (leading to fewer than 10 trials per condition/TMS pulse time). For each participant there was 1 repetition for each NT word pair per block, and 9 blocks in total, i.e. 9 repetitions for each word pair. For each participant, the dependent measure was the proportion of intrusions at each repetition, separately for T trials and NT trials (where a max of 1.0 means every NT or T trial in that block was coded as intrusion and 0 means no NT or T trial was coded as intrusion). We ran a 2-way repeated measures ANOVA with the factors Repetition (0–9 repetitions) and Condition (T versus NT). Based on previous observations (Benoit et al., 2015; Castiglione et al., 2019; Hellerstedt et al., 2016; Levy & Anderson, 2012) we predicted a main effect, such that intrusions would decrease across time.

**Stop Signal Task:** Mean RTs were calculated for both Go and Stop trials, as well as mean Stop Signal delay. Specifically, the RTs for Go trials were calculated by taking the mean of all trials where subjects responded correctly to a Go signal (they made the correct cued response). The SSRTs were computed (according to a recent consensus document by Verbruggen et. al 2019) by using the integration method with replacement of Go omissions.

We verified that RTs of Failed Stop trials were faster than Go RTs (as required by the race model, (Logan & Cowan, 1984).

## TMS and EMG:

### EMG data analysis was performed in MATLAB2015b (The MathWorks).

**MEP:** MEP amplitude was extracted from the EMG signal recorded from the right FDI. The root mean square (RMS) of a baseline period of 100ms prior to the TMS pulse was calculated and trials were excluded if the RMS crossed 0.05mV. MEP amplitude for each trial was calculated by taking the peak-to-peak difference between the maximum and minimum amplitude of the EMG signal, for a period of 10ms to 50ms after the TMS pulse. The mean MEP amplitude was calculated for each condition (T, NT Intrusion, NT No-Intrusion) at each TMS pulse time (200ms, 300ms, 400ms after the stimulus), and normalized by dividing by the amplitude of the mean baseline MEP (from the inter-trial interval TMS pulses).

**Think/No-Think task:** Our goal was to establish whether stopping retrieval (NT trials, and in particular those without any intrusion), would lead to decreased MEPs compared to baseline but also compared to trials where retrieval was *not* stopped (T trials); this was to make sure that MEP suppression was specific to stopping retrieval. As in our pre-registered document, we had planned to use a linear mixed effect model to do this comparison, using TMS pulse time (300ms, 400ms, 500ms) as a random factor to track the potential variability across-subjects in the time of MEP decrease. However, we later realized that it would not be possible to compare NT trials to both baseline and T at the same time using a linear mixed effect model. We therefore decided to run three one-sample t-tests to test the difference of NT MEP simultaneously from Baseline MEP and T MEP. To do so we dropped the factor “TMS pulse time” by choosing, for each subject and for each condition, the smallest mean(MEP) among the 300ms, 400ms and 500ms TMS pulse times. We were then left with one MEP score per subject per condition. For the T condition, we only kept trials where the subject did think about the target.

In **t-test 1**, we computed **A**. the difference [BaselineMEP – No-Think No-IntrusionMEP], **B**. the difference [BaselineMEP – ThinkMEP], and ran a one-sample t-test of **A–B**. We expected A to be significantly greater than B.

In **t-test 2**, we repeated t-test 1 but for NT Intrusion by computing **A**. the difference [BaselineMEP – No-Think IntrusionMEP], **B**: the difference [BaselineMEP – ThinkMEP], and ran a one-sample t-test of **A–B**. We expected A and B to not be different.

In **t-test 3**, we compared NT No-Intrusion to NT Intrusion by computing **A**. the difference [BaselineMEP – No-Think No-IntrusionMEP], **B**. the difference [BaselineMEP – No-Think IntrusionMEP], and ran a one-sample t-test of **A-B**. We expected to find a significant difference where A>B (NT No-Intrusion is more suppressed than NT Intrusion).

Multiple comparisons were corrected using the Holm-Bonferroni method.

We had to drop an additional comparison we had planned in our preregistered document: that between first and second halves, as we did not have enough MEP measurements per condition and per TMS pulse time once dividing the data in halves.

To evaluate if the muscle was equally at rest between conditions before the TMS pulse occurred, we conducted a repeated measures ANOVA analyzing the mean EMG in the 100ms before the pulse (for T, NT No-Intrusion, NT Intrusion).

**Stop Signal Task:** In order to validate our methods, we aimed to replicate previous results showing reduced MEP for Successful Stop trials compared to Go and baseline trials. In order to do so, we ran one-sample t-tests of the difference in MEP amplitude for Successful Stop vs. Go, Successful Stop vs. Failed Stop and Successful Stop vs. baseline. Multiple comparisons were corrected using the Holm-Bonferroni method.

To evaluate if the muscle was equally at rest across conditions before the TMS pulse occurred, we conducted a repeated measures ANOVA on the mean EMG in the 100ms before the pulse (for Go, Successful Stop, Failed Stop and baseline).

## RESULTS:

### Behavioral analysis:

**Think/No-Think task:** For the intrusion analysis we ran a 2-way repeated measures ANOVA with the factors Repetition (0–9 repetitions) and Condition (No-Think vs. Think). There was a main effect of Condition, $F(1,342) = 663.199$, $P < 0.001$, partial eta sq. = 0.659, and a significant interaction between Repetition and Task $F(8,342) = 5.160$, $P < 0.001$ (Fig. 1C), indicating that intrusions significantly decreased across the repetitions for NT trials, while they remained at a constant and high level across the repetitions for T trials. This shows that participants were performing the task as in previous studies (Castiglione et al., 2019; Hu et al., 2017; Levy & Anderson, 2012).

**Stop Signal task:** Behavioral Stop Signal Task results were typical. Go RT was slower than Failed Stop RT in all participants, in line with the race model (mean Go RT = 507ms, mean Failed Stop RT = 485ms). The percentage of successful stop trials was 48% on average with very few errors on go trials (~4%). The Stop Signal delay yielding 48% correct stops was 281ms and SSRT was 214ms.

### TMS and EMG:

**MEP:** MEPs from the task-unrelated right FDI were measured to test the globality of a putative stopping process on NT trials. MEP was normalized for each subject by dividing the mean MEP amplitude in each condition (T, NT Intrusion and NT No-Intrusion) and each TMS pulse time (300ms, 400ms, 500ms) by the mean baseline MEP amplitude for that subject.

**Think No-Think task:** We examined MEPs for our three main conditions: T trials, where participants thought about the target word, NT No-Intrusion trials, where participants successfully prevented retrieval of the target word, and NT Intrusion trials, where even though prompted not to think about the target word, participants experienced an intrusion (Fig. 2A). As explained in the Methods above, for each subject, and each condition, we selected the minimum MEP score among the 300ms, 400ms and 500ms conditions (Fig. 2B – see supplementary Fig.1 for all-subjects MEP graphs). We then conducted three tests (Fig. 2C).

**T-test 1:** The first test examined our main pre-registered prediction that MEPs for NT No-Intrusion would be reduced compared to baseline, and more so compared to T. Contrary to our prediction, this test [(Baseline MEP – No-Think No-IntrusionMEP) – (Baseline MEP – ThinkMEP)], showed a non-significant effect (m=0.02, t(19)=1.162, p=0.259, d=0.260, 95% CI[−0.09 0.06]).

**T-test 2**: We now tested whether MEPs for NT Intrusion would be reduced relative to baseline, and more so compared to Think. Surprisingly, this one sample t-test of the difference [(Baseline MEP – No-Think IntrusionMEP) – (Baseline MEP – ThinkMEP)], did show a significant effect (m=0.07, t(19)=3.340, p=0.003, d=0.747, 95% CI[0.03 0.11]), and this held after Bonferroni correction (for 3 tests, the significance threshold is 0.05/3 = 0.017).

**T-test 3**: We now tested if the reduction for NT Intrusion vs. baseline was greater than the reduction of NT No-Intrusion vs. baseline. This one-sample t-test of the difference [(Baseline MEP – No-Think IntrusionMEP) – (Baseline MEP – No-Think No-IntrusionMEP)], was not significant (m=0.04, t(19)= 1.920, p=0.07, d=0.429, 95% CI[−0.02 0.06]).

For the EMG activity in the 100ms before the TMS pulse, a repeated measures ANOVA showed no significant difference across conditions (T, NT No-Intrusion, NT Intrusion), confirming the muscle was equally at rest.

**Stop Signal Task:** Because of technical issues we were only able to use Stop Signal Task data for 10 of our participants. The main analysis, Successful Stop MEP < Go MEP, showed the anticipated reduction in MEP of a large effect size (n=3) (m=0.13, t(9)=2.732, p=0.069 after Bonferroni correction, d=0.864, 95% CI[0.02 0.24]), confirming previous results (Cai et al., 2012; Wessel et al., 2016). This non-significant result must be taken in context of the large effect size, replication, and the fact that at n=10 we were underpowered, and this result is also Bonferroni corrected.

The comparison between Successful Stop MEP and Baseline also showed the anticipated result, albeit of moderate effect size (m=0.09, t(9)= 1.929, p=0.257 after Bonferroni correction, d=0.61, 95% CI[−0.01 0.20]). The difference between Successful Stop and Failed Stop was not significant.

For the EMG activity in the 100ms before the TMS pulse, a repeated measures ANOVA showed no significant difference for mean EMG across conditions (Go, Successful Stop, Failed Stop) confirming that the muscle was equally at rest.

## DISCUSSION:

We wanted to know whether stopping retrieval of an unwanted word would induce a global MEP suppression, a well-known effect of action-stopping in the Stop Signal Task (Badry et al., 2009; Cai et al., 2012; Majid et al., 2012; Wessel et al., 2013). We predicted that MEP amplitude would be reduced on those trials where participants successfully stop retrieval (NT No-Intrusion trials). However, the results only showed a weak and non-significant reduction of NT No-Intrusion from Think. Instead, and unexpectedly, we found a result for NT Intrusion trials, i.e. the MEPs for these trials were more decreased from baseline, than Think trials were. Additionally, we validated our ‘global suppression’ methods by showing that MEPs in the Stop Signal Task were reduced for Stop Success < Go trials with large effect size (d=0.864), even though only in 10 subjects.

Thus, on trials with self-reported intrusions in a verbal Think/No-Think task there was a reduction of MEPs from the task-irrelevant hand within 500ms. This striking result could be taken to imply that the detection of an intrusion triggers a control process that, akin to action-stopping (and leading to similar global effects), must quickly shut-down an unwanted thought that intruded into awareness (Guo et al., 2018; Levy & Anderson, 2012). We suppose the following occurs on such trials. First, an intrusion occurs within ~500ms. Second, the intrusion is detected, and a stop-like process is quickly triggered, with global effects – something we imagine functions as a clearing/gating process (below we will discuss the adaptive value of this mechanism). Third, when probed on whether they experienced an intrusion, participants have enough residual memory of it (from before it was cleared out) that they report experiencing one.

This observation of a control process that is related specifically to intrusions fits other observations in the literature. First, comparing the Go/No-Go task, the Stop Signal Task and the Think/No-Think task, Guo et al. (2018) found greater cortical overlap for the comparison of the Think/No-Think and Stop Signal Task (than for the comparison of the Think/No-Think and Go/No-Go task), suggesting that *cancelling ongoing retrieval* might be more pertinent during NT, compared to *preventing* retrieval. Second, cancelling an intrusion induces different hippocampal fMRI activation than preventing an intrusion (Levy & Anderson, 2012) – something that has been interpreted as more hippocampal downregulation. Third, cancelling intrusions triggers greater inhibitory modulation of the hippocampus by the dorsolateral prefrontal cortex (Benoit et al., 2015; Guo et al., 2018; Levy & Anderson, 2012). In actuality, it is likely that both mechanisms (cancelling and preventing) play a role on NT trials. Notably, in an earlier study we showed that right frontal beta (an EEG signature of action-stopping) was recruited more on NT No-Intrusion trials than NT Intrusion trials, within a mere 300ms (Castiglione et al., 2019). This is compatible with the NT cue (red color) quickly triggering a process to prevent retrieval, resulting in a NT No-Intrusion trial.

Thus, we suggest that NT trials may recruit two types of stopping. As soon as a red cue is presented, a No-Go-like preventive stop is triggered to “shut the gate” and *prevent* the intrusion of the target word (similarly to the way action must be prevented in a No-Go trial). When this preventive stopping is not implemented strongly/early enough or fails to be triggered, an intrusion will make its way into awareness. This early preventive stop, successfully triggered in NT No-Intrusion trials, and possibly absent in NT Intrusion trials, may explain the early difference in EEG recording (right frontal beta) between these two trial types observed by Castiglione et al. (2019). Specifically, there was a greater early increase in right frontal beta in NT No-Intrusion indicating that a preventive stop was successfully triggered in these trials compared to NT Intrusion trials. On the other hand, on NT trials where prevention failed and an intrusion occurred, a Stop-like process may be recruited to *cancel* retrieval (similarly to the way an ongoing action must be stopped in a Stop trial). We attribute the global effects of the MEP reduction on NT Intrusion trials to this fast Stop-like process.

While we theorize that the right frontal beta increase may represent a marker of preventing intrusion, and global MEP reduction a marker of cancelling ongoing intrusions, these markers may not be exclusive to the respective processes. For example, right frontal beta increase may occur during intrusion cancellation as well (in fact, in the action domain this marker has been linked primarily to cancellation). However, we suggest that, because intrusions happen at unpredictable (and untraceable) times during a trial, increased beta would occur at different times and so be washed out in averaging that is locked to the NT cue. Similarly, while we did not find a significant MEP reduction for NT No-Intrusion trials, it is possible that a rapid process that *prevents* retrieval would produce a global MEP reduction. If so, we would expect this to occur at an early timepoint; here we measured the MEP at 300, 400 and 500ms, which might have been too late (or these punctate measurements may have missed the specific time). Future studies could further probe these two putative control processes by 1) recording EEG and MEP simultaneously to compare the time of right frontal beta power increase to that of MEP suppression, and 2) placing the MEP recordings across a wider time window.

Questions remain about the lack of differences in MEPS between some of our conditions. We conjecture that the lack of a significant reduction for NT No-Intrusion versus Think in our 300-500ms time window may have been due to the NT No-Intrusion MEP decreasing earlier than 300ms (i.e. an early global MEP suppression occurs to preventively stop retrieval, a NoGo-like event). Accordingly, the lack of a significant difference between NT No-Intrusion and NT Intrusion MEP may be due to NT No-Intrusion MEPs decreasing earlier than 300ms, and this effect “smearing” into the 300ms-500ms time window. It should also be noted that NT Intrusion trials are a mix of successful and failed intrusion stopping trials. Yet we were not able to assess whether intrusions were successfully stopped after they occurred (even though we instructed participants to stop intrusions whenever they arose, we have no measurement of their success at doing so). Indeed, even if stopping intervenes after an intrusion (via a MEP decrease), we can’t know whether this MEP decrease occurs quickly enough or strongly enough to successfully cancel the ongoing intrusion. If a large MEP suppression is what is needed to yield a successful cancelation of an intrusion, once averaging across both successful and failed NT Intrusion trials, the overall MEP reduction for NT Intrusion trials will be partly “washed out.” Accordingly, while this averaged NT Intrusion MEP may still be reduced compared to Think, it will not be significantly smaller than No-Think No Intrusion. Future studies could work on developing tools to measure the success of intrusion-cancelation, for example by revealing the time of reconstructions of memory representations through EEG.

An alternative interpretation of our main result that MEPs were reduced for NT Intrusion vs. baseline (and also compared to the difference of T vs. baseline) is that this reflects an arousal/difficulty/error-detection process. For example, MEPs reflect multiple influences on the motor system at many levels, including catecholaminergic enervation of primary motor cortex (Gorelova, Seamans, & Yang, 2002). However, we think this is unlikely because the MEP reduction was quite quick (somewhere in the range of 300, 400, or 500ms across subjects), possibly too soon for subjects to register an error, when pattern completion via hippocampus probably takes at least several hundred ms (Staresina & Wimber, 2019).

It could be argued that the MEP suppression observed during NT Intrusion trials actually relates to stopping vocal responses, rather than stopping memory retrieval. Note, however, that in the Think/No-Think task, subjects had to withhold a vocal response (motoric withholding). This is known to produce a broad suppression of the motor system, impacting MEP amplitudes in finger muscles (Wessel et al., 2016). However, in our study speech responses are withheld both during Think trials (where subjects think about the matching word without saying it out loud) and No-Think trials (where subjects both don’t say or think about the matching word). Therefore, if the MEP suppression we observed during No Think Intrusion trials was a result of withholding a speech response (rather than stopping retrieval), we would observe no difference between No-Think Intrusion and Think trials. Or, alternatively, one might even expect to see a greater MEP suppression during Think trials, since in these trials subjects are allowed to think about the matching word which might trigger an even greater impulse to say it out loud. But what we actually observed was that No-Think Intrusion trials had reduced MEPs compared to Think trials. We argue this cannot be explained on the simple withholding-of-a-motoric-response account.

Several events other than action stopping also give rise to MEP suppression in a task irrelevant muscle (action selection, action initiation, action with-holding). Such events arguably involve a form of inhibitory control, be it choice selection (suppress all alternatives), action initiation (withhold until the time is right), action with-holding (see Duque et al., 2017 for a review). In the case of stopping (action or retrieval), it is unclear whether this global MEP suppression has a specific functional role (globally shutting down all modalities to promptly interrupt any ongoing processes, among which is the “unwanted process”), or whether it is a byproduct of inhibition as implemented by the stop-system (regardless of the modality inhibited). We now show something similar for attempting to prevent an intrusion on No-Think trials; it is plausible that all of these events require varying degrees of gating of basal ganglia output, manifested as global motor system suppression.

In conclusion we show that when participants are instructed to prevent the retrieval of a long-term memory in response to a cue, and they experience an intrusion of the unwanted memory, then the motor excitability of a task-unrelated muscle is decreased. Because this “global” MEP reduction is similar to the one observed during action-stopping, we suggest a cancelling mechanism might intervene to cancel the intrusion when subjects experience unwanted retrieval. This raises the question of why in there a broad reduction of motor excitability while we are trying to suppress ongoing unwanted retrieval. We suppose that urgency recruits a non-selective stopping process that, regardless of the modality it needs to stop, shuts down all responses (across cognitive and motor domains) (Wessel & Aron, 2017) – this might have the adaptive function of gating a particular interrupter to preserve focus on a vital task. An alternative explanation of the broad reduction of motor excitability relates to the structure of the current Think/No-Think task, which required linguistic operations that might be motoric. In this way, stopping an unwanted word from coming to mind is like stopping a motor program. This, in turn, raises the question of whether the effect we see here of global MEP reduction would be evident in a non-linguistic version of the Think/No-Think task. In any event, the current results show that a broad motor suppression appears to be recruited by the detection of an unwanted memory intrusion. We tentatively suggest that this is because the requirement to control an intrusion needs to be very quick, and so the brain calls upon the fastest stopping process it has, one that comes along with a broad effect. This theory has interesting implications, for example that differences in the triggering of this mechanism could explain individual differences in mental distractibility.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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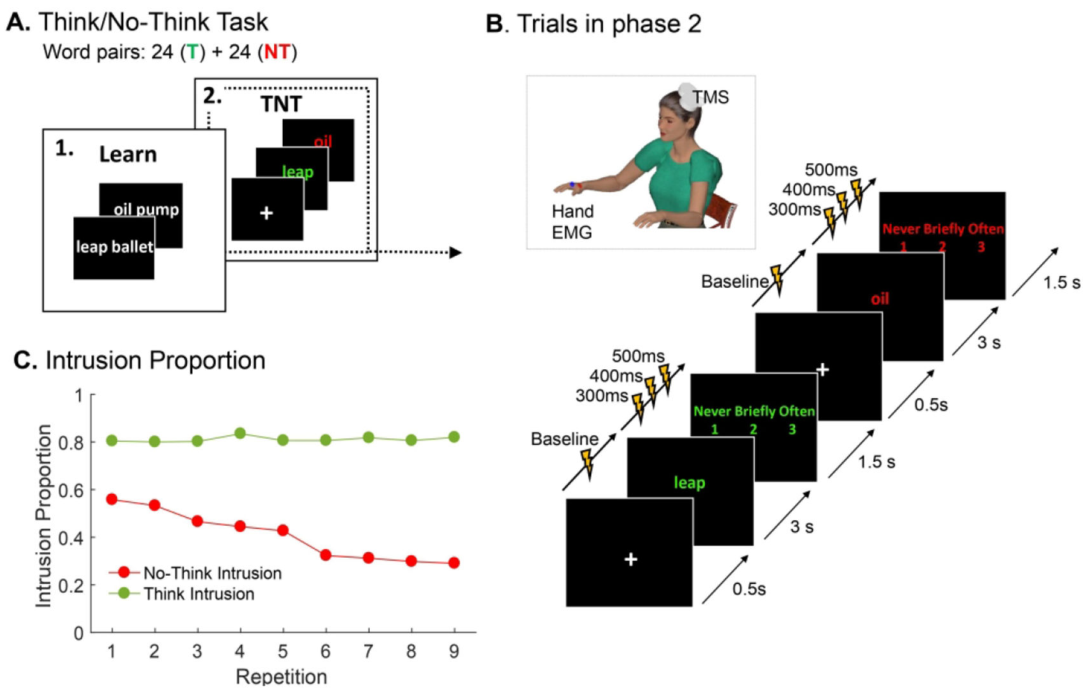


**Fig. 1.**

The Think/No-Think task. A. The two phases of the task. Phase 1: learning of word pairs. Phase 2: Think/No-Think. On each trial, the left-hand word from a pair is shown either in green, cuing the subject to think about the target word, or in red, cuing the subjects to prevent the retrieval of the target word. B. Example trials where a Think and then a No-Think cue are shown for 3s, each followed by an intrusion rating asking whether/when the subject had an intrusion of the target word. On each trial, a single pulse of TMS is delivered at either 300ms, 400ms or 500ms after the cue (experimental trials) or at 250ms before the cue (baseline trials). C. Intrusion proportion for Think (green) and NT (red) trials across the 9 blocks. Early and late intrusions were collapsed leading to only two conditions: Intrusion and No-Intrusion. Intrusion proportion was calculated from 0 to 1 for each block (where a max of 1.0 means every NT or T trial in that block was coded as intrusion and 0 means no NT or T trial was coded as intrusion).

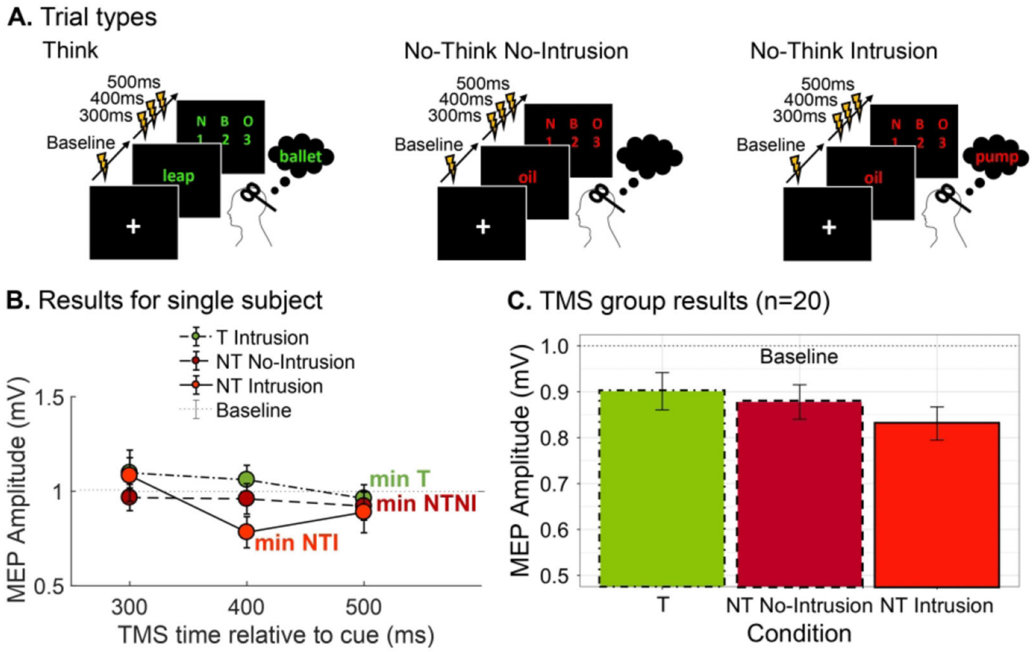


**Fig. 2.**

Results for the motor-evoked potential. A. Trial types: Think (T), where participants thought about the target word, NT No-Intrusion (NTNI), where participants successfully prevented retrieval of the target word, and NT Intrusion (NTI), where even though prompted not to think about the target word, participants experienced an intrusion. B. Selection in a single subject of the minimum MEP score per condition (T, NTNI, NTI) across the 3 TMS times (300ms ,400ms ,500ms). In this case, the NTI score selected is at 400ms, the NTNI score at 500ms and the T score at 500ms. C. Overall results of the average MEP per conditions across 20 subjects.