Anterior Cingulate Cortex Signals the Need to Control Intrusive Thoughts During Motivated Forgetting

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ow do people limit awareness of unwanted 35 memories? Evidence suggests that when 36 unwelcome memories intrude, a retrieval 37 stopping process engages the right dorsolateral pre- 38 frontal cortex (rDLPFC; Anderson et al., 2004) to 39 inhibit hippocampal activity (Benoit and Anderson, 40 2012; Benoit et al., 2015; Gagnepain et al., 2017) 41 and disrupt retrieval. It remains unknown how and 42 when the need to engage prefrontal control is de- 43 tected, and whether control operates proactively to 44 prevent an unwelcome memory from being retrieved, 45 or must respond reactively, to counteract its intru- 46 sion. We hypothesized that dorsal anterior cingu-13 late cortex (dACC) achieves this function by detect-14 ing signals indicating that an unwanted trace is 47 15 emerging in awareness, and transmitting the need 16 for inhibitory control to right DLPFC (Alexander and 17 Brown, 2011; Botvinick et al., 2001). During a memory suppression task, we measured trial-by-trial vari-19 ations in dACC's theta power and N2 amplitude, two 20 electroencephalographic (EEG) markers of the need for enhanced control (Cavanagh and Frank, 2014). With simultaneous EEG-fMRI recordings, we tracked 23 dynamic interactions between the dACC, rDLPFC 24 and hippocampus during suppression. EEG analyses revealed a clear role of dACC in detecting 26 the need for memory control, and in upregulating prefrontal inhibition. Importantly, we identified 28 dACC contributions before episodic retrieval could 29 have occurred (500 ms) and afterwards, indicating 30 distinct proactive and reactive control signalling. 31 Stronger proactive control by the dACC led to re-63 32 duced hippocampal activity and diminished over-33 all blood-oxygen-level-dependent (BOLD) signal in

dACC and rDLPFC, suggesting that pre-empting retrieval early reduced overall control demands. However, when dACC activity followed the likely onset of recollection, retrieval was cancelled reactively: effective connectivity analyses revealed robust communication from dACC to rDLPFC and from rDLPFC to hippocampus, tied to successful forgetting. Together, our findings support a model in which dACC detects the emergence of unwanted content, triggering top-down inhibitory control, and in which rDLPFC countermands intruding thoughts that penetrate awareness.

Introduction

When people suppress unwanted memories, the dACC is among the regions more active, but its contribution to inhibitory control over memory remains undefined. In non-memory contexts, major theoretical accounts agree that dACC monitors ongoing processing and detects information indicating a need to intensify cognitive control, and that dACC communicates this demand to prefrontal regions that implement control (Alexander and Brown, 2011, 2015; Botvinick, 2007; Botvinick et al., 2001; Cavanagh and Frank, 2014; Vassena et al., 2020). The conflict monitoring theory (Botvinick et al., 2001) proposes that dACC is sensitive to cognitive conflict, and that processed conflict signals initiate strategic adjustments in cognitive control to prevent future conflict. Accounts derived from the predicted response outcome model (PRO, Alexander and Brown, 2011) point out that surprising events typically increase the activation of this region, so they maintain that dACC plays a specific role in calculating surprise (Vassena et al., 2020). Following these

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ideas, we hypothesized that, during motivated forget- 57 1 ting, dACC dynamically regulates mnemonic inhibition 58 by computing signals that indicate a need to control un- 59 welcome content. On one hand, these warning signals 60 may originate from reminders that foreshadow an un- 61 wanted memory's intrusion, triggering proactive control 62 to prevent retrieval; on the other hand, they may derive 63 directly from an unwanted memory's reactivation, which 64 may elicit cognitive conflict and a need to purge the in- 65 9 truding memory from mind (Levy and Anderson, 2012). 66 10 Specifically, when proactive control fails to prevent re- 67 trieval, intrusion-related activity would drive stronger sig- 68 nals in dACC as the demands for cognitive control in- 69 13 crease, and this would initiate a reactive mechanism en-70 14 gaging rDLPFC and downregulating the hippocampus 71 15 (Benoit et al., 2015; Gagnepain et al., 2017; Levy and 72 16 Anderson, 2012). We hypothesized that dACC would 73 17 transmit these signals to prefrontal regions to amplify 74 18 top-down inhibition over regions driving retrieval of the 75 19 offending memory. 20

To test these hypotheses, we acquired simultaneous 77 21 EEG-fMRI recordings as participants performed a mem-78 ory suppression task. This multimodal approach allowed 23 us to relate temporally precise signatures of the need 24 for enhanced cognitive control to BOLD signals to track 25 dynamic interactions between the dACC, rDLPFC and 26 hippocampus during suppression (Figure 1). Following 27 an EEG-informed fMRI approach, we first tested, on a 28 trial-by-trial basis, the coupling between BOLD signals 29 in the foregoing regions and proactive control. We in-30 dexed proactive control via measures of frontal midline 31 theta power and N2 amplitude arising prior to the likely 32 recollection of the intruding memory. We hypothesized 33 that, whereas proactive control prepares the system to 34 inhibit hippocampal retrieval, those trials with poorer 35 proactive control would lead to increased demands for 36 intrusion-control later in the trial, reactively triggering el-37 evated activity in both dACC and rDLPFC. To tie these 38 prefrontal interactions to mnemonic control, we exam-39 ined how engaging dACC/rDLPFC related the suppres-40 sion of hippocampal retrieval processes by testing the 41 coupling of prefrontal activity with theta oscillatory ac-42 tivity from hippocampal EEG sources. We included 43 temporally resolved EEG source analyses to investigate 44 whether regional modulations occurred before or after 45 likely recollection onset. Finally, we captured the dy- $_{\scriptscriptstyle 101}$ 46 namics of information flow during reactive control of un-47 wanted memories by calculating Granger causality be-48 tween EEG sources. These analyses allowed us to mea-49 sure whether dACC transmits control signals to rDLPFC, and whether rDLPFC, in turn, intensifies top-down inhibition of the hippocampus, facilitating motivated forgetting. 52

Results

⁵⁴ The memory suppression task was a version of the 111

55 Think/No-Think (TNT) paradigm (Anderson and Green, 112

⁵⁶ 2001) as shown in **Figure S1**. First, participants (n=24)

encoded unrelated cue-associate word pairs and were trained to recall the associate given the cue. Then, participants entered the TNT phase, wherein they were presented with cues from studied items as reminders and directed to control the retrieval process, while we acquired simultaneous EEG-fMRI recordings. On each trial of the Think condition, participants received the cue word within a green frame and were asked to recall and think about its associate; on No-Think trials, by contrast, participants received the cue within a red frame and were asked to prevent the associate from entering consciousness. In a final phase, we performed two memory tests. On the same-probe (SP) test, participants received each cue word again and tried to recall its associate. On the independent-probe (IP) test, participants instead received a novel category name and were asked to recall a word that belonged to that category from among the studied associates. We also tested memory for items that participants learned during the training phase, but that had not appeared during the TNT phase, providing a baseline estimate of retention for items that had neither been retrieved nor suppressed.

Behaviour and confirmatory fMRI data analyses

We replicated key findings from previous studies (Anderson and Green, 2001; Anderson and Hulbert, 2021). As expected, participants recalled fewer associate words in the No-Think than in the Baseline condition (SP test: t(23)=4.65; p<0.001; IP test: t(23)=4.74; p<0.001 and overall memory test: t(23)=6.16; p<0.001; Figure S2). The below-baseline recall performance for No-Think items reflects suppression-induced forgetting (SIF) and confirms that participants successfully engaged inhibitory control mechanisms during retrieval suppression, which impaired memory. Although memory performance was lower on the IP test than on the SP test (Test type effect: F(1,23)=94.52; p<0.001), SIF generalized across both tests (Condition main effect: F(1.23)=24.00; p<0.001; Condition*Group interaction: F<1)(Anderson and Green, 2001; Anderson et al., 2004). In contrast, voluntary retrieval did not affect recall of Think items compared to baseline (overall memory test: p=0.30; SP test: p=0.15) (cf. Anderson and Green, 2001). Nevertheless, using different cues at recall than those studied and practiced was detrimental for retrieval (IP test: t(23)=-2.55; p<0.05), as has been previously reported, which is consistent with the encoding specificity principle (for a detailed discussion, see Paz-Alonso et al., 2009).

To confirm that suppressing associate words engaged dACC and rDLPFC, we analysed fMRI data comparing the activation between NT and T trials from the TNT phase. Using a priori dACC and rDLPFC ROIs taken from a meta-analysis of 16 retrieval suppression studies (Apšvalka et al., 2020), we observed greater activity during retrieval suppression than voluntary retrieval (dACC: +6, +23, +41; p(FWE)<0.05, small volume corrected [SVC]; rDLPFC: +36, +38, +32; p(FWE)<0.01,



Figure 1. Summary of expected relationships between EEG measures and BOLD signals associated with proactive and reactive control. The upper panel represents a hypothetical timeline of brain processes after encountering a reminder (dog's bone toy) associated with an unwanted memory (the death of a beloved dog). Proactive control (blue dot) is triggered before episodic retrieval of associated memories starts in the hippocampus, whereas reactive control (green dot) is triggered after, because of conflict generated by intrusions. The lower panels summarize the expected effects of enhanced proactive (blue boxes) and reactive (green boxes) control, according to the model. These effects imply specific relationships between EEG measures and BOLD signals, which were tested using the methods listed (brown text). Please, refer to the main text for more details.

SVC). With the opposite contrast (NT<T), we also confirmed decreased activity during retrieval suppression relative to voluntary retrieval in the hippocampus (left hip-10 pocampus: -33, -34, -10; p(FWE)<0.001, SVC; right hip- 11 pocampus: +24, -25, -13; p(FWE)<0.05, SVC). Impor- 12 tantly, these deactivations were below the level observed 13 Gagnepain et al., 2017). In addition, an exploratory analin a perceptual baseline condition in which participants 14 ysis using the overall contrast between No-Think and

viewed unpaired single words presented within a grey frame (left hippocampus: -33, -31, -10; p(FWE)<0.005, SVC; right hippocampus: +30, -25, -19; p(FWE)<0.05, SVC), consistent with the view that retrieval suppression downregulates hippocampal activity (Depue et al., 2007;

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Think trials revealed BOLD activation patterns consistent with previous observations (for reviews, see Anderson et al., 2016; Anderson and Hanslmayr, 2014). Additional activations arose in mostly right-lateralized regions, including supplementary motor area, premotor cortex, inferior frontal gyrus, and parietal lobe, whereas additional deactivations occurred in brain areas that support the representation of visual memories, among other regions (**Table S1**; **Figure S3**).

Early engagement of dACC's theta control mechanism predicts reduced demands on dACC and rDLPFC for intrusion control

People who see a reminder to an unwanted thought and 13 engage inhibitory control early enough may prevent the 14 unwelcome memory from intruding. Achieving this form 15 of proactive control requires a mechanism that detects 16 the need for increased control upon seeing a reminder. In natural settings, people may learn to identify warning 18 features of stimuli that foreshadow unpleasant thoughts 19 and use these features to initiate proactive suppression. 20 We hypothesized that one of the key roles of dACC dur-21 ing motivated forgetting is to trigger this proactive mechanism to entirely prevent awareness of unwelcome con-23 tent. This proactive mechanism may be initiated in the 24 TNT task when participants process the red No-Think 25 cues as task signals to stop retrieval. Related to this 26 possibility, a previous EEG study gave participants advanced warning about whether each upcoming trial re-28 quired suppression or retrieval; they found that anticipat-29 ing the need for retrieval suppression increased theta 30 power in dACC and left DLPFC sources in No-Think rel-31 ative to Think trials within 500 ms after the suppression 32 task warning (Waldhauser et al., 2015). Indeed, in non-33 memory tasks, increased midline and prefrontal theta ac-34 tivity typically reflects enhanced cognitive control, and is 35 a common mechanism by which anterior cingulate and 36 medial prefrontal cortices detect the need for control and communicate it to lateral prefrontal cortex (Cavanagh 38 and Frank, 2014). 39

Guided by these findings, we used theta power local-40 ized to dACC sources as an index of dACC engagement 41 in upregulating inhibitory control during memory sup-42 pression and sought to relate this effect to BOLD signal 100 43 in the dACC and rDLPFC. To focus on proactive control, 101 44 we measured dACC-theta within an early time window 102 45 after cue onset and before the likely retrieval of the as-103 46 sociates (~500 ms, Staresina and Wimber, 2019). Our 104 47 hypothesis implies two main predictions about how early 105 48 dACC-theta power should relate to BOLD signals. First, 10 if dACC is engaged in proactive control, we should ex-107 50 pect elevated theta power during the early time window.¹⁰⁸ However, provided that proactive control prepares the 109 52 brain for mnemonic inhibition, facilitating retrieval stop-110 ping, successful engagement of this mechanism should 111 54 prevent intrusions, reducing aggregate demands on in-112 55 hibitory control over the full 3-second duration of the trial ¹¹³ 56

(think of the adage: *"a stitch in time, saves nine"*). Therefore, although theta activity is generated by the dACC, a robust early theta response should, paradoxically, predict less aggregate dACC BOLD signal during the trial, reflecting the diminished need for intrusion control. Similarly, a robust early dACC-theta response should lead to less rDLPFC BOLD signal over the duration of the trial.

To test whether these salutary effects of proactive control emerge, we measured trial-by-trial variations of EEG theta power in dACC sources within an early time window (300-450 ms; 4-8 Hz) where frontal midline theta power started to increase in No-Think relative to Think (Figure 2A). We then used this measure as a parametric modulator for an EEG-informed fMRI analysis. Consistent with our first prediction, trials with enhanced early dACC-theta power were associated with reduced BOLD signal in the dACC ROI, an effect specific to memory suppression (No Think: p=0.03; No Think<Think: p<0.05; Figure 2D; see also Table S2). To test the second prediction, we used the same parametric modulator but restricted the contrasts to the rDLPFC ROI. BOLD signal in the rDLPFC ROI was also reduced in trials with enhanced early dACC theta power, and this effect was also specific to suppression (No Think: p<0.01; No Think<Think: p<0.05; Figure 2D; see also Table S2).

We sought converging evidence for the role of proactive control in reducing demands on dACC and rDLPFC by focusing on a well-established ERP component related to memory suppression. Previous studies have demonstrated the suppression N2 effect (more negativegoing wave in No-Think than in Think), which appears to index the engagement of early inhibitory control during suppression; it correlates with the N2 effect of motor-stopping (Mecklinger et al., 2009), with SIF, and with the consequent reduction in distressing intrusions of lab-analogue traumatic memories (Streb et al., 2016). Taking into account its early latency and medial frontal topography, we hypothesized that this suppression N2 may be partly generated in dACC and reflect an aspect of the same frontal midline theta mechanism that processes the need for control (Cavanagh and Frank, 2014) after seeing the No-Think cues. Replicating prior studies (Bergström et al., 2009; Chen et al., 2012; Mecklinger et al., 2009; Streb et al., 2016; Waldhauser et al., 2012), mean ERP amplitudes during No-Think trials were significantly more negative than they were during Think trials between 300-450 ms (300-400 ms: t-mean(23)=-2.20, t-cluster=-15.5, pcluster=0.04; 350-450 ms: t-mean(23)=-2.70, t-cluster=-27.0, p-cluster=0.004) at frontocentral, right frontal and right temporal electrodes; Figure 2B). The N2 effect was localized at the right supplementary motor area (SMA, BA6: 10, 0, 60, p<0.001; Figure 2C), and supporting our hypothesis, at other frontal midline regions including the dACC (peak voxel: 10, 20, 40, p<0.001). To be consistent with how N2 is measured in other studies, we created a pooled frontocentral channel (Fz, FC1 and FC



37 Figure 2. Early frontal midline theta signals in dACC during retrieval suppression reflect proactive control. (A) Time-frequency 38 and scalp topographic maps showing increases in frontal midline theta 39 power during No-Think relative to Think. There was a cluster of frontocentral channels showing significant effects between 4-6 Hz and 250-800 ms (p<0.05). We extracted theta power from dACC sources within $\,^{\scriptscriptstyle 41}$ 300-450 ms, as a measure of proactive control. (B) Decreased am- 42 plitude of ERP waveform in No-Think (red) relative to Think (green; 43 p-cluster<0.05). Gray shadow indicates the time window 300-450 ms considered for N2 wave analyses. (C) Increased power in dACC sources during the suppression-N2 (300-450 ms; p<0.01, corrected 45 with permutations and maximal statistic). (D) BOLD signals in dACC and rDLPFC were reduced in trials with increased dACC-theta power during retrieval suppression but not during retrieval. Similarly, BOLD signals in dACC and rDLPFC were reduced in trials with larger N2 signals during retrieval suppression. *p<0.05; **p<0.005; ~p=0.052. Error bars represent standard error of the mean. T=Think; NT=No- 50 Think. (E) Individuals with larger the N2 showed more suppressioninduced forgetting. Scatter plot shows a correlation between the N2 effect (ERP amplitude in Think minus No Think) and forgetting scores 52 (z-SIF). Each participant's forgetting z-SIF was obtained by z-scoring 53 its suppression-induced forgetting (SIF) index relative to the SIF of all $_{\rm 54}$ participants receiving the same items in the same conditions (counterbalancing group). This transformation isolates suppression effects, by correcting for irrelevant variability in forgetting due to differences in memorability of items across counterbalancing groups. (F) Scalp topo- 57 graphic and source maps showing increases in alpha power over left occipito-temporal regions (left fusiform gyrus) between 250-500 ms in 50 trials with large N2 signals (p-cluster<0.05).

2) and compared again the amplitudes of No-Think and ⁶¹
Think trials within the 300-450 ms window. This fronto-⁶²
central channel showed peak differences between 332-⁶³
348 ms (all t(23)<-2.70, p-corrected<0.05), confirming ⁶⁴

that the N2 effect likely was generated before participants recollected the associate and agreeing with a proactive control role. Importantly, participants with a larger N2 effect (more negative going N2 in No-Think relative to Think trials) showed higher SIF scores (r=0.42; p<0.05; 1 outlier; **Figure 2E**); indeed, only high forgetters showed differences in amplitude during this time window (332-348 ms, all t(11)<-2.88, p-corrected<0.05; **Figure S4**) but not low forgetters (all t(11)>-1.66, pcorrected>0.24). Our results confirm previous findings and suggest that the N2 effect reflects early control processes in dACC that facilitate memory inhibition (Bergström et al., 2009; Mecklinger et al., 2009).

If the N2 reflects early inhibitory control, increases in this component, just as with dACC-theta power, should be negatively related to BOLD signal in both the dACC and rDLPFC. To test this, we extracted trial-by-trial variations of the N2 amplitude at the frontocentral channel. Then, we used this measure to build a parametric modulator for an EEG-informed fMRI analysis. Consistent with our hypothesis, trials with larger (more negative) frontocentral N2 amplitudes were accompanied by reduced BOLD signal in the dACC ROI (p<0.05) specifically in No-Think trials (p<0.05; Figure 2D; see also Table S3). Similarly, trials with larger (more negative) frontocentral N2 amplitudes during memory suppression were associated with reduced BOLD signal in the rDLPFC ROI (p<0.05), although the differences relative to voluntary retrieval did not achieve significance (p=0.052). Taken together, the timing of the N2 component and the negative relationship to overall BOLD signal across the full duration of the trial suggest that the N2 effect, like dACCtheta, indexes proactive inhibitory control over memory. This proactive mechanism contributes to stopping retrieval processes, reducing the occurrence of intrusions, and pre-empting any need for further engagement of dACC and rDLPFC during the suppression trial.

To further scrutinise this hypothesis, we tested whether the N2 was associated with EEG oscillatory markers of elevated cognitive control. Firstly, we expected to link the N2 with early increases in frontal midline theta activity; and secondly, we expected to find enhanced alpha/beta band activity in regions involved or under top-down inhibitory control (Castiglione et al., 2019; Fellner et al., 2020; Waldhauser et al., 2015). To test this, we split sensors' TFRs on No-Think trials based on the amplitude of the frontocentral N2 as an index of proactive control. Trials with larger (more negative) N2 amplitudes showed, in addition to frontocentral theta power increases, increased alpha power relative to trials with smaller N2 amplitudes. Effects were maximal at frontal (4-8 Hz: 200-500 ms; 9-12 Hz, 350-450 ms; all t>2.46, t-cluster=226.9; p-cluster=0.01) and occipitoparietal sensors (9-12 Hz: 250-500 ms; all t>2.55, t-cluster=132.8; p-cluster=0.057; Figure 2F). Alpha power differences were maximal in two clusters of brain sources, one including left temporal and occipital areas (peak voxel: -50, -50, 0, BA37; t=4.54, pcluster=0.038) and another one maximal in right me-57
dial superior frontal gyrus (peak voxel: 10, 70, 10, 58
BA10; t=4.07, p-cluster=0.019). These findings suggest 59
a possible mechanistic link between frontal midline theta 60
and posterior alpha power increases (Waldhauser et 61
al., 2015). This suggests that successfully pre-empting 62
intrusion-related conflict via early proactive control might 63
be partly achieved by increasing local inhibition in visual
cortical areas and suppressing cortical memory repre sentations (Gagnepain et al., 2014).

Delayed evoked responses in dACC during suppression may reflect the detection of control demands caused by intrusions

When early control fails to suppress cue-driven retrieval, 14 unwanted memories may intrude into awareness, cre-15 ating cognitive conflict, driving higher demands on in-16 hibitory control over memory (Levy and Anderson, 2012). 17 We hypothesized that, in addition to its role in signalling 18 early control demands in response to the task cues, 19 dACC detects intrusions as 'alarm' signals that indicate 20 the need to further increase inhibitory control (Alexander 21 and Brown, 2011). If intruding recollections trigger such a delayed control response, modulations in the evoked 23 activity of dACC should arise after the latency where rec-24 ollection could start (~500 ms, Staresina and Wimber, 25 2019). To test this prediction, we extracted source time 26 courses (0.5-30 Hz) from all voxels within our dACC ROI and compared the mean amplitudes observed during 28 No-Think and Think trials across all time points after cue 29 onset (0-1 s). Accordingly, dACC amplitude was more 30 negative during No-Think trials than during Think tri-31 als between 548-708 ms (t-mean(23)=-2.51, t-cluster=-32 793.6, p-cluster=0.0064; Figure 3A). Amplitude differ- 65 33 ences were only significant in dACC sources oriented ra-34 dially to the top of the head, consistent with the topogra-35 phy of ERPs related to novelty, conflict, or error process-36 ing (Cavanagh et al., 2012). These ERPs are thought to be part of the same frontal midline theta mechanism 38 for realizing the need for cognitive control (Cavanagh 39 and Frank, 2014); therefore, we expected that these 40 delayed control signals in dACC particularly would in-41 volve theta band activity. Indeed, amplitude differences 42 were explained by delta/theta band evoked activity (0.5-43 8 Hz: 428-728 ms, t-mean(23)=-2.51, t-cluster=-1511, 44 p-cluster=0.0046) and were not significant for alpha/beta 45 evoked activity (8-30Hz: all p-clusters>0.33). 46 If intruding recollections drive these delayed dACC 47 evoked responses, these signals should be more evident 48 for individuals likely to experience intrusions. Agreeing 49 with this, only low forgetters, who should have experi- 80 50

enced more overall conflict due to intrusions (Gagnepain ⁸¹
et al., 2017), showed more negative amplitudes in the ⁸²
No-Think than the Think condition between 552-704 ms ⁸³
(t-mean(11)=-2.68, t-cluster=-769.8, p-cluster=0.0044).
In contrast, high forgetters, who were more efficient at ⁸⁵
implementing inhibitory control and forgetting the asso-⁸⁶

ciates, showed no amplitude differences in this later window. These findings are in line with our hypothesis that dACC is also involved in the late adjustment of inhibitory control when unwanted memories emerge. Moreover, they suggest that late evoked theta responses in dACC reflect cognitive conflict and control demand signals driven by intrusions.



Figure 3. Time courses and Granger Causality analysis of delayed dACC and rDLPFC effects. (A and B) Mean evoked activity (0.5-30 Hz) in dACC (A) and rDLPFC (B) showing significant differences between each condition in a delayed time window (548-708 ms and 504-640 ms, respectively). Horizontal grey bars indicate the significant time windows (p-cluster<0.05). EEG source time courses were reconstructed from the ROIs showed in the brain representations. (C) Granger causality spectra of information flow between dACC and rDLPFC sources (450-1450 ms) in trials associated with high and low conflict (large or small dACC activity in the 428-728 ms window, 0.5-8 Hz). In trials with more conflict-related activity, the information flow goes primarily from dACC to DLPFC between 2-12.5 Hz. Horizontal grey bar indicates the significant frequency window (p-cluster<0.05). Light shadowed areas represent standard error of the mean.

Intrusions trigger dACC to communicate the need to increase inhibitory control to rDLPFC through a theta mechanism

Once an intrusion is detected, the need for increased control should be transmitted to prefrontal areas that implement mnemonic inhibition. We hypothesized that dACC communicates an intrusion-control signal to rDLPFC through a mechanism of interareal neural coupling mediated by theta band activity (Cavanagh and Frank, 2014; Smith et al., 2019). To test this idea, we first investigated whether rDLPFC evoked activity showed modulations reflecting the reception of dACC signals. We reconstructed source time courses (0.5-30 Hz) from all voxels within the rDLPFC ROI and compared their mean amplitudes across No-Think and Think trials for all time points after cue onset (0-1 s). rDLPFC amplitude was more negative in No-Think than in Think trials at latencies overlapping the dACC effect associated with putative intrusion control (sources with left-right orientation: 408-588 ms, t-mean(23)=-2.56, t-cluster=1.374, p-cluster=0.008; sources with inferior-superior orientation: 504-640 ms, t-mean(23)=-2.53, t-cluster=-1.425, p-

cluster=0.016; Figure 3B). Then, we performed a whole- 57 1 brain source analysis within dACC's delayed control win- 58 dow (0.5-8 Hz; 428-728 ms) to verify that these modula- 59 tions were regionally specific and not caused by stronger 60 nearby sources. We expected that, if dACC and rDLPFC 61 5 were particularly engaged in control processes triggered 62 6 by intrusions, these regions should show activity differ- 63 ences significantly larger than those shown prior to cue 64 8 onset. Agreeing with this, two frontal clusters exhib- 65 9 ited above-baseline effects: one in the right hemisphere 10 comprising superior frontal gyrus, middle frontal gyrus 67 11 and anterior cingulate cortex (peak voxel: 30, 30, 40, 68 BA8; t=3.75, p-cluster=0.0086; Figure S5) and another 13 in the left hemisphere comprising inferior frontal gyrus 14 and insula (peak voxel: -50, 20, 0, BA47; t=3.84, p-15 cluster=0.037). We confirmed that dACC and rDLPFC 16 ROIs showed significant effects (p<0.05, corrected with 17 permutations and maximal statistics). 18

Finally, we looked for functional coupling between 19 dACC and rDLPFC, indicating the transmission of the 20 control demands. We investigated the directionality of 21 the interaction between dACC and rDLPFC by applying nonparametric Granger causality analyses to a 1-s win-23 dow after the N2 (450-1450 ms). In trials with larger 24 intrusion-control signals (more negative evoked activity 25 in dACC), the information flow in the direction of dACC to 26 rDLPFC was higher than that from rDLPFC to dACC for 27 theta and alpha frequency bands (2-12.5 Hz, p=0.0064, 28 corrected with cluster-based permutation test). In trials 29 with smaller dACC signals, there was no preferred direc-30 tion in the information flow (p-cluster>0.44; interaction 31 effect: p-cluster=0.09; Figure 3C). Our results support ... 32 our hypothesis, showing that dACC and rDLPFC were 33 maximally engaged around the time that unwanted mem-34 ories may have been retrieved. Strikingly, stronger re-35 sponses in dACC generated Granger causal influences 36 on rDLPFC activity within the theta and alpha frequency 37 bands, consistent with a process communicating the 38 need to intensify memory control. 39

Early control processes involving dACC contribute to later hippocampal downregulation

An intruding memory may not endure very long in aware-42 ness if inhibitory mechanisms already have been pre-43 pared at the time the intrusions occur. We hypothe-44 sized that proactive control early in the trial would fa-45 cilitate the later down-regulation of memory-related net-46 works, and that decreased theta oscillatory activity as-71 47 sociated with retrieval (Waldhauser et al., 2015) should 72 48 reflect the impact of this suppression. We tested this 49 hypothesis by median-splitting No-Think trials accord-74 50 ing by their N2 amplitude (proactive control) and then 75 looking for reflections of suppressed activity in sen-76 sor TFRs by applying the contrast larger<smaller N2 amplitude. Indeed, trials with larger N2 amplitudes 54 79 showed reduced theta oscillatory power between 650-55 1850 ms after cue onset in left frontal, central and pari- 80 56

etal sensors, relative to those with smaller N2 amplitudes (**Figure 4A**; 4-9 Hz; all t<-2.42, t-cluster=-493.9; p-cluster<0.001). In trials with smaller N2 amplitudes (where proactive control was reduced) theta oscillatory activity persisted above baseline levels for the whole epoch. Consistent with our hypothesis, the greatest reduction in theta was localized in the left hippocampus (peak voxel: -30, -30, -10; t=-4.56, p-cluster=0.0038; **Figure 4B**), but both hippocampi showed theta power decreases in ROI TFR analyses (left hippocampus: all t<-1.97; p-cluster<0.005; right hippocampus: all t<-1.84, p-cluster=0.014; **Figure 4C**).



Figure 4. Effect of proactive control on theta power activity and BOLD signals in the hippocampus. (A) TFRs from all sensors showing decreased theta power in trials associated with strong proactive control (large N2 signal) relative to trials with weak proactive control (small N2 signal; p-cluster<0.05). Right panel shows the scalp topography of the effects in the framed time window (4-6 Hz, 650-1850 ms). (B) Sources of the peak theta power decreases were localized in left hippocampus (p-cluster<0.05). (C) ROI average of hippocampus zscored power time courses for trials associated with strong and weak proactive control. Horizontal grey bars indicate the time window of significant differences between conditions in the ROI time-frequency analysis (p-cluster<0.05). (D) BOLD signals in the hippocampus were reduced in trials with increased dACC theta power (300-450 ms) during retrieval suppression but not during retrieval. Similarly, BOLD signals in the hippocampus were reduced in trials with larger (more negative) dACC N2 amplitudes during retrieval suppression but not during retrieval. *p<0.05; **p<0.005; ***p<0.0005. Light shadowed areas (C) and error bars (D) represent standard error of the mean.

These findings suggest that early proactive control processes contributed to the later stopping of hippocampal retrieval. To verify the localization of these effects to the hippocampus, we performed several additional analyses. First, we related EEG theta activity reconstructed from hippocampal sources to hippocampal BOLD signal. EEG-informed fMRI analysis using mean hippocampal theta power (4-6 Hz, 650-1850 ms) as a parametric modulator revealed a positive correlation between theta power and hippocampal ROIs BOLD signals (right: p < 0.005, uncorrected; SVC, p[FWE]=0.067;

left: p<0.05, uncorrected; Figure 5A) across all tri- 57 1 als, consistent with the hypothesis that our hippocampal 58 theta sources reflected hippocampal processing. Next, 59 we sought converging evidence of proactive mnemonic 500 control by relating trial-by-trial variations in early dACC- 61 5 theta power to hippocampal BOLD signals during re- 62 6 trieval suppression. We found that trials with increased 63 dACC-theta power showed stronger hippocampal deacti- 64 vations, specifically during memory suppression (Figure 65 9 **4D**). We confirmed with an alternative EEG-informed 66 10 fMRI analysis that more negative N2 amplitudes, ex- 67 11 tracted trial-by-trial from the dACC ROI, also correlated 68 with reduced hippocampal BOLD signals, again specifi- 69 13 cally during memory suppression (SVC, p[FEW]<0.05; 14 Figure 4D). Together, these parallel findings strongly 15 support our hypothesis that dACC triggers proactive in-16 hibitory control to stop retrieval of unwanted memories 17 by the hippocampus. 18

The delayed latency (650-1850ms) of the theta sup-19 pression effect suggests that although proactive con-20 trol processes may help to prevent intrusions, they also 21 enhance readiness to purge intruding thoughts from awareness when they do occur, overlapping with and 23 likely facilitating hippocampal downregulation by reac-24 tive control processes. To examine whether a reac-25 tive hippocampal downregulation arose, we analyzed 26 the time course of hippocampal theta activity as an in-27 dex of hippocampal retrieval. Specifically, we exam-28 ined those trials associated with higher putative intru-29 sion control, to determine the presence of (a) an early 30 increase in hippocampal retrieval activity followed by 31 (b) hippocampal activity suppression. To test this, we 32 divided No-Think trials according to the power of the 33 intrusion-control signals they exhibited in dACC (2-8 Hz; 34 428-728 ms). In trials with larger intrusion control sig-35 nals, hippocampal theta power (2-8 Hz) was increased 36 only during the first half of the epoch (left: 300-1600 ms, 37 t-mean=3.16, t cluster=p-cluster<0.001; right: 0-1700 38 ms, t-mean=2.81, t cluster=p-cluster<0.01), relative to 39 trials showing smaller intrusion-control signals. The fact 40 that no significant differences emerged in hippocampal 41 theta power during the second half of the epoch is con-42 sistent with reactive suppression of hippocampal theta 43 in response to an intrusive recollection. 44

RDLPFC down-regulates the hippocampus in 45 response to dACC intrusion-related control signals 46

The foregoing findings suggest that early and delayed 47 control mechanisms during memory suppression con-48 tribute to hippocampal down-regulation, which is ex-49 pressed as theta power decreases. Particularly, when 50 early control fails to prevent unwanted memories from intruding, dACC generates signals indicating the need for intrusion-control. These signals may dynamically adjust inhibitory control mechanisms in the rDLPFC to 54 downregulate hippocampal activity (Benoit et al., 2015) 55 to purge the intruding memories. Consistent with 56

this intrusion-purging hypothesis (Levy and Anderson, 2012), during suppression, increased BOLD signals in rDLPFC and dACC were coupled to decreased theta power in bilateral hippocampal sources after the onset of recollection (650-1850ms) (DLPFC and right hippocampus: SVC, p[FWE]=0.02; and left hippocampus: p<0.005, uncorrected; dACC and right hippocampus: SVC, p FEW=0.01), and the latter theta suppression effect was itself associated with hippocampal downregulation (Figure 5A). These findings suggest that hippocampal theta power decreases (observed after retrieval onset) may arise from increased prefrontal inhibitory control.



Figure 5. Downregulation of hippocampus by reactive control. (A) EEG-informed fMRI parametric analyses using hippocampal theta power as regressor. Voxels in dACC (orange) and rDLPFC (burgundy) showing significant (p<0.005) negative correlation with theta power reconstructed from sources of right hippocampus ROI (cyan). Bar plots show that theta power in the right hippocampus was (i) positively coupled to BOLD signal in this region and (ii) reduced in trials with increased dACC and rDLPFC BOLD signals during retrieval suppression. (B and C) Granger causality spectra of information flow between rDLPFC and right hippocampus sources in No-Think and Think (B) and trials associated with high and low conflict (large or small dACC activity in the 548-708 ms time window; C). In No-Think and in trials with more conflict-related activity, the information flow goes primarily from rDLPFC to right hippocampus in low beta band. Horizontal grey bars indicate the significant frequency windows (p-cluster<0.05). Error bars (A) and light shadowed areas (B,C) represent standard error of the mean. GC=granger causality values.

To examine whether rDLPFC and dACC activity during intrusion-control may be causally related to hippocampal theta decreases, we used nonparametric Granger causality focusing on a 1-s window after the N2 (450-1450 ms). First, we investigated the direction of information flow between rDLPFC and hippocampus. This analysis revealed a higher top-down than bottom-up information flow during retrieval suppression in the theta band (DLPFC to left hippocampus, 2.0-6.5 Hz, p=0.021, corrected with cluster-based permutations; interaction effect: 2-5.6 Hz, p-cluster<0.05) and in the low beta band (DLPFC to right hippocampus, 12.6-17.8 Hz, p=0.023, corrected with cluster-based permutations; Figure 5B). Importantly, the increased top-down information flow in the beta range specifically arose during trials with

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larger intrusion-control signals in dACC (12.2-17.4 Hz, 57 p-cluster=0.023; interaction effect: 12.3-15.4 Hz, p- 58 cluster=0.023; Figure 5C), consistent with the possibility 59 that dACC triggered the rDLPFC top-down mechanism 60 that caused hippocampal down-regulation. To test this 61 idea, we identified trials in which the suppressive impact 62 6 of the hippocampus was clear and examined the influ- 63 ence of dACC on rDLPFC; we split No-Think trials ac- 64 cording to the mean theta power in hippocampal sources 65 9 (4-6Hz, 650-1850 ms) and computed Granger causality 66 analyses within that window. We found that trials with re- 67 duced hippocampal theta showed a higher information 68 flow in the theta band (4-9.73 Hz, p-cluster<0.05) from 69 13 dACC to rDLPFC than in the opposite direction, consis- 70 14 tent with a role of dACC in triggering elevated control. 71 15 Together, these findings point to a late influence of the 72 16 rDLPFC on the hippocampus and suggest that beta os-73 17 cillations mediate a reactive top-down inhibitory control 74 18 mechanism triggered in response to intrusions detected 75 19 by the dACC. 20

Top-down inhibitory control from the rDLPFC to the 77 21 hippocampus may facilitate forgetting of the suppressed 78 memories (Anderson and Hulbert, 2021; Apšvalka et al., 79 23 2020; Benoit et al., 2015; Gagnepain et al., 2014). We 💀 24 tested this possibility by dividing participants into those 81 25 who showed higher or lower SIF scores. High forgetters 82 26 showed a greater top-down than bottom-up information 83 flow from rDLPFC to right hippocampus for suppression ⁸⁴ 28 items that they successfully forgot, relative to those that 85 29 they remembered (19.8-23.0 Hz, p-cluster=0.031). In 86 30 contrast, less successful forgetters showed the opposite 87 31 pattern, with a higher top-down than bottom-up informa-32 tion flow for suppression items that they later remem- 89 33 bered (11.6-17.6 Hz, p-cluster=0.006). These findings 90 34 suggest that in low forgetters, the reactive engagement 91 35 of top-down inhibitory control in response to intrusions 92 36 is related to persisting memory for intruding thoughts. 93 37

Discussion

Our findings reveal a central role of dACC in triggering 97 inhibitory control that causes motivated forgetting. The 98 40 data suggest that dACC can signal the need for inhi-99 41 bition proactively, in response to environmental cues,100 42 or reactively, to counter intrusive thoughts themselves.¹⁰¹ 43 Two key findings support dACC's proactive role in pre-102 44 venting retrieval. First, frontal-midline theta mechanisms 103 45 partly originated in dACC and emerged in an early win-104 46 dow (300-450 ms after No-Think task cue) prior to the 105 47 likely onset of episodic recollection; and second, later 106 in the trial, these early effects were associated with re-107 49 duced BOLD signals and theta power in the hippocam-108 50 pus, consistent with reduced retrieval activity. These 109 51 findings suggest that rapidly detecting the need for sup-110 52 pression from an environmental signal (in this case, the III task cue) engages proactive control by dACC to pre-112 54 vent intrusions. Consistent with this interpretation, trials 113 55 with increased early theta signals from dACC were ac-114 56

companied by lower overall BOLD activations of dACC and rDLPFC, reflecting reduced conflict processing and lower demands on prefrontal control when recollection was quickly mitigated. Thus, rapid early control was beneficial; as they old adage says, "a stitch in time, saves nine." These effects echo those of a prior fMRI study investigating the benefits of forgetting on neural processing during a retrieval-induced forgetting task (Kuhl et al., 2007). That study showed that, as competing memories were suppressed across retrieval practice trials, the demands to detect and overcome conflict were reduced. and so activations in ACC and lateral prefrontal cortex declined. Similar conflict reduction benefits (associations between successful memory control and reduced conflict processing) have been shown in a range of studies (see Anderson and Hulbert, 2021 for a review).

Importantly, our results suggest that proactive control did not simply prevent retrieval but also facilitated forgetting. Several observations support this conclusion. Firstly, individuals with stronger signatures of proactive control showed superior suppression-induced forgetting, complementing earlier findings linking the suppression N2 (i.e., more negative-going frontocentral ERPs around 300-450 ms Mecklinger et al., 2009) to better SIF (Bergström et al., 2009), and to fewer distressing intrusions after analogue trauma (Streb et al., 2016). Second, proactive control engages processes that could plausibly contribute to forgetting. For example, the N2 was partly generated in dACC and associated with early (<500 ms) frontal midline theta power increases, an activity pattern likely reflecting the detection and communication of the need for control to prefrontal cortex (Cavanagh and Frank, 2014). These mechanisms could trigger early inhibitory control targeting regions supporting memory. Indeed, early N2-associated increases in alpha oscillatory power (a typical correlate of cortical inhibition Klimesch, 2012) in left fusiform gyrus may be an example: given that down-regulation of this fusiform region by DLPFC during suppression is known to disrupt visual memory traces of the associates (Gagnepain et al., 2014), elevated alpha power in visual cortex may both limit the reinstatement of associated words and suppress their memory traces, resembling the downregulation of item-specific memories (Fellner et al., 2020). We also linked early proactive control signals to decreased hippocampal theta oscillatory power during a later time window (650-1850 ms), an effect previously linked to successful suppression-induced forgetting [19]. The current hippocampal modulations started during earlier time windows (~300 ms), suggesting that early control reduced hippocampal theta oscillations, affecting later hippocampal-cortical theta networks. Given that hippocampal pattern completion appears to begin around 500 ms after cue onset (Staresina and Wimber, 2019), the 650-1850 ms window offers an opportunity for rDLPFC action over the hippocampus (Apšvalka et al., 2020; Benoit and Anderson, 2012; Benoit et al., 2015; Depue et al., 2007; Gagnepain et al., 2017) to

inhibit memory traces, stopping intrusions. Indeed, we 59 1 found significant causal influence of rDLPFC on both hip- 60 pocampi within 450-1450 ms only during suppression. 61 Together, these findings suggest that proactive control 62 facilitates forgetting by increasing inhibition in regions 63 where memories would be reactivated, and, by magni- 64 fying the impact of intrusion-control mechanisms (see 65 also Hanslmayr et al., 2009; Waldhauser et al., 2015). Critically, however, the dACC also triggered inhibitory 67 9 control reactively in a time window during which un-10 wanted memories could have been involuntarily re- 69 11 trieved. Our findings suggest that dACC detects conflict 70 caused by intruding memories and communicates the 71 13 need for control to rDLPFC, which in turn increases top- 72 14 down inhibition over the hippocampus. Supporting this 73 15 conclusion, we found, during retrieval suppression, peak 74 16 dACC and rDLPFC source activities in a delayed time 75 17 window, coinciding with the likely onset of conscious 76 18 retrieval. dACC activity in this window (552-704 ms) 77 19 was particularly large for low forgetters, suggesting that 78 20 these signals reflected intrusion-related conflict. More- 79 21 over, dACC amplitude increases were due to delta/theta 80 activity, which is a preferred rhythm for the coherent fir- 81 23 ing of dACC and DLPFC's neurons during conflict pro- 82 24 cessing, and for cross-areal coordination to implement 83 25 control (Smith et al., 2019). Precisely, using dACC 84 26 amplitude in this window (0.5-8 Hz; 428-728 ms) as a so 27 proxy for conflict, we found that high conflict was asso- 86 28 ciated with high information flow from dACC to rDLPFC 87 29 in delta/theta band and from rDLPFC to right hippocam- *** 30 pus in beta band. The greater the activation in dACC ⁸⁹ 31 and rDLPFC, and the stronger their theta-mediated com- 90 32 munication, the stronger was the implementation of con- 91 33 trol over hippocampal activity (reflected by decreases in 92 34 retrieval-related theta). 35

Prefrontal control over hippocampal activity, once 94 36 triggered by dACC, appears to be achieved via beta 95 37 phase synchronization. During retrieval suppression, 96 38 the rDLPFC increased its communication with the right 97 39 hippocampus in the low beta band, an effect not found 98 40 during retrieval trials. This higher information flow, more- 99 41 over, arose specifically on high conflict trials, consistent 100 42 with the need to intensify top-down control to purge in-101 43 trusions from awareness. Elevated communication with 102 44 the hippocampus in the beta band during intrusions inte-103 45 grates prior evidence that had separately illustrated the 104 46 importance of intrusions and beta activity in inhibitory 105 47 control over memory. On the one hand, fMRI studies 106 48 have found that intrusions elicit greater rDLPFC acti-49 vation (Benoit et al., 2015), stronger hippocampal sup-50 pression (Benoit et al., 2015; Gagnepain et al., 2017; 51 Levy and Anderson, 2012), and more robust fronto-52 hippocampal interactions to suppress retrieval (Benoit 109 et al., 2015; Gagnepain et al., 2017), although the os-110 54 cillatory mechanisms of this intrusion effects were not 111 55 established. On the other hand, the importance of beta $^{112}_{113}$ 56 oscillations to memory inhibition has grown increasingly $\frac{1}{114}$ clear but has not linked this activity to reactive control 115

over intrusions. For example, it has previously been shown that (a) at the scalp level, retrieval suppression increases long-range synchronization in low beta frequency band (15-19 Hz) (Waldhauser et al., 2015), suggesting that this rhythm (together with alpha) might mediate top-down control; (b) at the intracranial level, directed forgetting instructions elicit DLPFC-hippocampal interactions in the low beta range (15-18 Hz) (Oehrn et al., 2018), with greater information flow from DLPFC to hippocampus when people were instructed to forget an item, but not when instructed to remember it; and (c) stopping actions and stopping retrieval elicit a common right frontal low beta component (Castiglione et al., 2019). Taken together with the current results, these findings point to a key role of beta oscillations in the top-down control over hippocampal processing by the rDLPFC, a demand that is especially acute during the reactive control of intrusions.

Overall, the validity of our model should be further investigated with high-density EEG, magnetoencephalography, and direct electrophysiological recordings in the involved regions. EEG and fMRI recordings might display spurious correlations introduced by head movements (Fellner et al., 2016), although control analyses indicate that our effects are not due to movement (see Supplemental Information). EEG motion artifacts were spatially filtered out with beamforming when using source activities as parametric modulators or removed by discarding outliers. On the other hand, source reconstruction accuracy is known to be affected by low signal-to-noise ratio (especially for deep sources in the hippocampus), among other factors. We minimized this problem by following methodological recommendations (Ruzich et al., 2019).

In summary, this study provides evidence that theta mechanisms in dACC are key to triggering inhibitory control by rDLPFC during motivated forgetting. These mechanisms can be proactively engaged by external warning stimuli, helping to rapidly pre-empt unwanted thoughts. Additionally, they are strongly activated during a later time window after hippocampal retrieval likely has occurred, consistent with a reactive control response to intrusions that enhances hippocampal downregulation by the rDLPFC. This impact of prefrontal cortex on hippocampal activity is achieved by rDLPFC-hippocampal beta interactions critical to clearing the mind from unwanted thoughts and to hastening the demise of memories we would prefer not to have.

Materials and Methods

Participants

A total of 24 participants (12 females, mean \pm SD age, 21.4 \pm 2.0 years) were recruited through the Southwest University undergraduate participant pool. All had normal or corrected-to-normal vision and had no history of psychiatric or neurological illness. To check whether the participants had adequate sleep prior to the experiment, they answered questions about their sleep state upon arrival at the laboratory; all of them were in line with our requirements. None of the participants

had experienced the experimental task before. The Ethics Commit tee of Southwest University approved the study. Written informed con sents were obtained from all participants according to the declaration
of Helsinki after detailed explanation of the experiment protocol. All the

participants received monetary compensation after their participation. 70

Stimuli

Stimuli
128 neutral words were selected from the Thesaurus of Modern Chi-

⁸ nese to form 68 pairs of weakly related words. Within each pair, a

word was used as cue and the other word as associate. Each asso ciate word was a member of a unique semantic category, so it could be

later recalled using that extra-list category name as cue. 48 word pairs

were divided into three sets of 16 word pairs, which rotated across par-

ticipants through the conditions (Think, No-Think, and Baseline). The

remaining 16 pairs were used as fillers for practice. 8 additional single words were included during the TNT task in a Perceptual baseline 7

¹⁶ condition.

Experimental paradigm

The experiment consisted of three phases: study, TNT, and final memory test.

20 Study phase

First, participants studied all the 64 cue-associate word pairs. On each 21 trial, both words were displayed visually, side by side, on a black background for 5 s. Each trial was separated by an inter-stimulus interval 23 (ISI) with a fixation cross for 600 ms. Then, participants were trained 24 to recall the associate words given the cues. On each trial, a cue 25 appeared at the center of the screen for 5 s, and participants were 26 27 asked to recall and say out loud the corresponding associate word. Participants' responses were recorded. After every trial, the associate 28 word was displayed as feedback for 2 s. All word pairs were repeat-95 29 edly trained until participants correctly provided at least 50% of all the 96 30 associate words. Finally, participants were tested again by displaying 97 31 each cue, but the associate feedback was omitted. This test was used 33 to identify the word pairs that participants successfully learned before qq entering the TNT phase and restrict (conditionalize) the analyses to 100 34 those trials corresponding to learned associations. 35 101

36 TNT phase

Participants performed this part of the experiment inside the fMRI scan-104 37 ner and stimuli were displayed on a back-projection screen mounted 38 above participants' heads. At the beginning of this phase, participants 106 39 practiced the task on 16 fillers. Afterwards, short diagnostic question-107 40 naires were administered to assess whether participants understood 108 41 the instructions, and questions were clarified. The proper task was di- $^{\rm 109}$ 42 vided into 6 blocks separated by 1-min breaks. Each block consisted $^{\scriptscriptstyle \rm 110}$ 43 of 80 trials, where all cues from the Think (16) and No-Think (16) con-111 44 ditions, together with Perceptual baseline words (8), were presented 45 twice. In sum, each cue word was presented 12 times during this 112 46 phase. Each trial started with a fixation cross (variable ISI between 113 47 500 ms and 1200 ms). Then, a cue word appeared within a coloured 114 48 frame for 3 s. The trial ended with a blank screen (ISI=1.5 s). For cues $\frac{1}{115}$ 49 within green frames (Think), participants were asked to think of the as-50 sociate word and keep it in mind while the cue was on the screen. For cues within red frames (No-Think), participants were asked to pay full 52 attention to the cue and prevent the associate word from coming into 119 mind during the whole trial. Instructions encouraged that participants 120 54 followed a direct suppression strategy (Benoit and Anderson, 2012; 55 Bergström et al., 2009), by emphasizing that they should suppress 122 56 retrieval and avoid replacing the associate with alternative words or 123 57 thoughts. For words within a grey frame, participants were just asked 124 58 to pay attention to them. 59

60 Final memory test

Memory for all studied word pairs was evaluated, including Baseline items that were excluded from the TNT phase. Until this phase, participants were unaware of a final memory assessment to prevent the influence of anticipatory mechanisms on forgetting scores and were initially told that the experiment was about attention and their ability ¹³⁰ to ignore distraction. Participants performed two types of final tests: same probe (SP) and independent probe (IP), with the order of these tests counterbalanced across participants. On the SP test, each cue was presented again, and participants were asked to recall and say out loud the associate word, as they did during the training phase. On the IP test, each unique category name was given as cue and participants were asked to recall and say out loud a member of this category, from those associate words they initially studied. At the end of the experiment, participants completed a questionnaire to determine whether they followed the instructions to suppress retrieval during No-Think trials.

Equipment

EEG

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EEG data were recorded by 32 Ag/CI electrodes that were placed on the scalp according to the international 10/20 system. The data were digitized at 5 kHz, referenced online to FCz using a non-magnetic MRIcompatible EEG system (BrainAmp MR plus, Brain products, Munich, Germany). Impedances were kept below 10 k before recording. Electrocardiogram (ECG) was simultaneously acquired from each participant. The EEG amplifier used a rechargeable power pack that was placed outside the scanner bore. To ensure the temporal stability of the EEG acquisition in relation to the switching of the gradients during the MR acquisition, a SyncBox (SyncBox MainUnit, Brain Products GmbH, Gilching, Germany) was used to synchronize the amplifier system with the MRI scanner's system. Fiber optic cables transmitted the amplified and digitized EEG signal to the recording computer, which was outside the scanner room. An Adapter (BrainAmp USB-Adapter, Brain products, Gilching, Germany) was used to convert optical into electrical signal.

fMRI

All images were acquired using a 3T Siemens Trio scanner. Α T2-weighted gradient echo planar imaging (EPI) sequence (TR/TE=1500/29 ms, FOV=192 × 192 mm2, flip angle=90 deg, acquisition matrix=64 × 64, thickness/gap=5/0.5 mm, in-plane resolution=3.0 × 3.0 mm2, axial slices=25) was used for functional image acquisition. The first three volumes of each sequence were discarded to account for magnetization saturation effects. All subjects were scanned in six blocks, where each block lasted 435 s and contained 290 volumes. After the first three blocks, a T1 was acquired for 5 min, where participants were told to relax and hold still. The 3D spoiled gradient recalled (SPGR) sequence used the following parameters: TR/TE=8.5/3.4 ms, FOV=240 × 240 mm2, flip angle=12 deg, acquisition matrix=512 × 512, thickness=1 mm with no gap. The high-resolution T1-weighted structural volume provided an anatomical reference for the functional scan. We minimized head movements by using a cushioned head fixation device.

Behavioural Data Analysis

Recall accuracies at the final memory test were estimated for Think, No-Think and Baseline conditions, and for each test type (SP and IP) separately. The analyses were conditionalized: only word pairs learned in the study phase (determined by the memory test prior the TNT phase) were considered. Recall accuracies were computed as a ratio between the number of word pairs correctly recalled at the final test and the total number of word pairs that were learned at study. These measures were compared using a two-way analysis of variance (ANOVA) with the memory condition (No-Think and Baseline) and test type (SP and IP) as factors, to determine whether there was belowbaseline forgetting. Paired-samples T-tests were applied to assess the effect of memory suppression and memory retrieval on final recall performance within each test type. We conducted all behavioural statistical analyses in SPSS Statistics 19.0.

EEG data preprocessing

Main fMRI gradient and ballistocardiogram (BCG) artifacts were first removed from the EEG data acquired during the TNT phase, following standard template subtraction procedures. Subsequently, data were

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down-sampled to 250 Hz and digitally filtered within 0.1-45 Hz using 70 1 a Chebyshev II-type filter. Temporal independent component analysis (ICA; Bell and Sejnowski, 1995) was subsequently applied to attenuate ocular artifacts (e.g., blinks, saccades), fronto-temporal muscular activity of small intensity and residual BCG and imaging artifacts. Ar-74 tifactual components were visually selected on the base of their characteristic time courses, topographic amplitude distributions, signal features (i.e., kurtosis, energy) and spectral characteristics (Mayeli et al., 77 2016). Continuous EEG data was divided into 5000-ms segments rel-9 ative to the onset of all words presented during the TNT phase (Think, 79 10 No-Think and Perceptual Baseline). Each segment included 500 ms of pre-stimulus baseline and 4500 ms of post-stimulus period. Segments that were contaminated by jumps, movement or strong muscular ac-13 tivity were removed. Finally, EEG signals were re-referenced to the 33 14 average for further analyses. All following analyses were conditionalized as the behavioural measures by including only trials belonging to 16 85 word pairs that were learned at study. 17

18 ERP analyses

ERPs were computed within the 1250-ms epoch comprising 250 ms 19 of pre-stimulus baseline and 1000 ms of post-stimulus period. The 20 suppression-N2 component was identified by visual inspection of the 21 grand-mean ERPs of frontocentral sensors, around the latencies reported in previous studies (Mecklinger et al., 2009). Statistical com-23 parisons between No-Think and Think N2 waveforms were limited to 24 the 300-450 ms time window. A first analysis contrasted the mean 25 amplitudes of all sensors in two overlapping 100-ms windows using 26 non-parametric paired T-tests. Cluster-based permutation tests with 27 5000 Monte Carlo randomizations were applied to correct for multi-28 ple comparisons across time and sensors. Each iteration assigned 29 random conditions labels to each trial and extracted the cluster of sen-30 sors (p<0.05, one-tailed) with maximal (negative) summed statistic. 31 To determine the precise time window of the N2 effect, a second anal-32 ysis contrasted amplitudes from all time points of a pooled frontocen-33 tral channel (Fz, FC1 and FC2). To correct for multiple comparisons 34 across time points, another permutation test with 5000 Monte Carlo 35 randomizations was applied, based on the maximal (negative) statis-36 tic. To investigate the relationship between the N2 effect and forgetting, 37 robust Pearson correlations were computed between the differential 38 waveform of the pooled channel (mean Think minus No-Think ampli-39 tude within the significant window) and the mean SIF in both memory $^{110}_{111}$ 40 41 tests.

Time-frequency analyses

Time-frequency representations (TFRs) were computed on data-115 43 padded wider epochs (-3000-5500 ms) to prevent edge filter ef-116 44 fects. Epochs were convolved with 6-cycles and 3-cycles wavelets 117 45 and then cropped to obtain 2-30 Hz spectral power between -500 $^{\rm 118}$ 46 ms pre-stimulus to 3000 ms post-stimulus, in 50 ms by 1 Hz time-119 47 frequency bins. To further reduce the contribution of noise, participants ¹²⁰ 48 TFRs were normalized using a single-trial baseline correction method 121 49 (Grandchamp and Delorme, 2011). First, power values of each time-122 50 frequency bin and channel were z-transformed using the mean power 123 51 and standard deviation across all trials. After trial average, TFRs were 124 converted into z-power change relative to baseline (-500 ms to 0 ms 125 53 pre-cue window) by subtracting the mean baseline z-power value from 126 54 all time points of each frequency bin and channel. Within-condition 127 55 relative power increases or decreases were determined by contrasting 128 56 each time point against the mean baseline value at each frequency bin 129 57 using non-parametric paired T-tests. P-values were computed through 130 58 5000 Monte Carlo randomizations. Then, false discovery rate (FDR) 131 59 procedure (Benjamini and Hochberg, 1995) was applied (p<0.05) to 132 60 correct for multiple comparisons across time-frequency bins and scalp 133 61 locations. TFRs were contrasted between Think and No-Think condi-134 62 tions using cluster-based permutation tests with 5000 Monte Carlo ran-135 domizations to correct for multiple comparisons across time-frequency 136 64 bins and scalp locations. Each iteration assigned random conditions ¹³⁷ 65 labels to each trial and extracted the cluster of sensors and time-138 66 frequency bins (p<0.05) with maximal summed statistic. A similar sta- $^{\scriptscriptstyle 139}$ 67 tistical procedure was followed to compare TFRs between large and $^{\mbox{\tiny 140}}$ 68 small N2 trials. 69

Source localization

We created realistic 3-shell boundary element models (BEM) based on individual T1 MRIs. Each BEM consisted of 3 closed, nested compartments with conductivities .33 S/m, .0042 S/m and .33 S/m corresponding to skin, skull, and brain, respectively. To obtain the models, skull and brain binary images were obtained using Fieldtrip segmentation routine. Scalp voxels were first identified with the SPM8's "New Segment" algorithm (Ashburner and Friston, 2005) combined with an extended tissue probability map (eTPM) that includes eyeballs, the whole head and the neck (for more details, see procedure and code provided by Huang et al., 2013). Resulting scalp probability maps (including eyeballs) were smoothed and binarized. All binary images were manually corrected using MRI visualization software to fit better the anatomy and make them suitable for BEM computation (i.e., remove overlaps and irregularities). It was particularly critical to correct the scalp masks because EEG sensors were automatically classified as scalp tissue and would have produced bumpy models otherwise. Binary masks were used to create boundary meshes in Fieldtrip using iso2mech method with 10000 vertices, which were smoothed afterwards. Real EEG sensor coordinates were determined by hand from rendered models of raw scalp masks using MRI visualization software (ITK-SNAP). This was possible because EEG sensors were visible in the T1s and appeared as small bumps on the rendered models. TP9 and TP10 sensors (behind the ears) were often difficult to identify and were excluded from source localization analyses to reduce localization errors. A grid of source locations was defined in individual's brain space but corresponding to 1-cm grid MNI coordinates that were consistent across participants. To obtain individual coordinates, MRIs were normalized to the standard T1 template, using non-linear transformations in SPM12. The inverse of this transformation was then applied to the template source grid obtained in Fieldtrip. The leadfields were computed with OpenMEEG v2.4 (Gramfort et al., 2010) called from Fieldtrip, using international units (i.e., EEG amplitudes in Volts and electrode and source-grid coordinates in meters).

To localize ERP and TFRs effects, we employed linearly constrained minimum variance (LCMV) beamformer (Van Veen et al., 1997). To enhance the detection of N2 sources from less superficial brain areas such as those in dACC, we first subtracted the trialaveraged data (0.5-30 Hz) of Think from No-Think condition. This method is called subtraction of epoch-averaged sensor data (SAD), and is one of the subtraction techniques recommended to reduce interference from dominant sources common to two experimental conditions (Mills et al., 2012). The spatial filters were first computed within the time window showing significant amplitude differences at sensor-level (300-570 ms), and then applied to the N2 and baseline time windows to obtain a power distribution map per participant. Participants' power distribution maps entered a group-level one-sample T-test against zero. To correct for multiple comparisons, we applied the maximal statistic method using 5000 Monte Carlo randomizations implemented in Fieldtrip (Oostenveld et al., 2011). We used a similar procedure to localize the sources within the time window of maximal amplitude differences in dACC ROI (548-708 ms). To determine whether source activity differences were task-related, power distribution maps were contrasted with baseline power maps using pairedsample T-tests and cluster-based statistics with 5000 randomizations. To determine the time window of maximal amplitude differences within dACC ROI, dipole momentum time-courses were extracted for each cartesian direction and averaged across trials for each condition. Think and No-Think amplitudes were compared with paired-sample T-tests and cluster-based statistics as described for sensor-level ERP analyses, to correct for multiple comparisons across time points, source locations and orientations. To localize TFR effects, the spatial filters were computed over the whole epoch (-500-3000 ms) without averaging. For each pre-defined source location, dipole momentum timecourses were extracted for each cartesian direction and collapsed into a single trace after determining the principal component. TFRs were computed and z-transformed as described for sensor-level. For statistical analyses, power values within the time-frequency window of interest were averaged and translated to brain maps. Contrasts were performed with paired-sample T-tests and cluster-based statistics as for ERP analyses. For ROI analysis, TFRs from all voxels within an ROI were identified and averaged across trials for each condition. Think

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and No-Think amplitudes were compared with paired-sample T-tests
and cluster-based statistics, to correct for multiple comparisons across
time-frequency bins and source locations. The regularization param eter was set at 0.001 % of the largest eigenvalue of the covariance
matrices.

6 **ROIs definition**

To test our a-priori hypotheses, some analyses were restricted to the dACC, rDLPFC and bilateral hippocampus. dACC, and rDLPFC masks 8 only included subregions that are commonly activated during action 9 cancellation and memory inhibition, revealed by meta-analyses using 10 fMRI data from stop-signal and TNT tasks (Apšvalka et al., 2020; Guo 2018). Each mask comprised the cluster of voxels revealed by conjunction analyses combining the contrasts No-Think>Think and 13 Stop>Go (e.g., Figure 3.2 of Guo et al., 2018). Left and right hip-14 pocampal masks were constructed from a probabilistic map based on cytoarchitectonic delimitations derived from 10 post-mortem human 16 17 brains warped to the MNI template brain (Amunts et al., 2005). These maps contain the relative frequency with which a cerebral structure 18 was present on each voxel of the anatomical MNI space. A binary 19 mask was built from the region having a probability of 0.1 or higher to 20 be labelled as hippocampal (CA, DG, Subc) or entorhinal cortex (EC). 21 00

Granger causality analyses

To investigate the effective connectivity and directionality of the infor-23 mation flow between our a-priori selected ROIs, we performed Granger 24 25 causality (GC) analyses on EEG source activity. We computed spectral GC (Geweke, 1982) estimates within the 1-s time window right 26 after the N2 (450-1450 ms) using the Fourier-based nonparametric ap-27 proach (Dhamala et al., 2008) as implemented in Fieldtrip (Oostenveld 28 et al., 2011). We chose the nonparametric instead the autoregressive 29 approach because it does not require to determine the optimal model 30 order for each participant. The window width was defined to be rela-31 tively short as to fulfil the stationarity assumption and have some temporal resolution, long enough to include sufficient data, and has been 33 used in a previous application of the nonparametric approach in a simi-34 lar context (Popov et al., 2018). To further approximate stationarity, we 35 subtracted the event-related potential from the data before computing 36 the Fourier transform for the whole spectrum (frequency smoothing 37 38 of 2 Hz). Thereafter, the Fourier coefficients were used to compute the cross-spectral density matrix. This matrix was then factorized into 39 the noise covariance matrix and the spectral transfer matrix which are 40 necessary for calculating GC (see Dhamala et al., 2008 for more de-41 tails). To determine the statistical significance of the directionality of 42 information flow between each pair of sources, we compared the mag-43 nitude of Granger coefficients (2-30 Hz) for both possible directions 44 (from source 1 to source 2 and vice versa) and trial types (e.g., Think 112 45 and No-Think) using cluster-based permutation ANOVAs and T-tests. 46 In addition, to confirm that the observed differences in GC values were 47 caused by true directed relationships and not by differences in signal-48 to-noise ratio (SNR), we computed GC on the time-reversed source 49 activities. After doing this control analysis, true causal interactions 50 should show an inversion in the directionality of the information flow, 51 118 whereas spurious interactions would appear as unchanged. 119

53 fMRI data preprocessing

FMRI data were preprocessed using SPM12 software (Henson et al., 122 54 2019). Standard preprocessing steps were applied, including: (i) spa-123 55 tial realignment to correct for head movements, (ii) slice timing, (iii) 124 56 coregistration of the structural to the functional images, (iv) segmenta-125 tion of the coregistered structural image (which performs spatial nor-126 58 malization to MNI space and generates a deformation field file), (v) 127 59 normalization of the functional images applying the deformation field, 128 60 and (vi) spatial smoothing with a three-dimensional 6 mm full-width 129 61 at half maximum Gaussian kernel. As an additional control for head-130 62 movement artifacts, we excluded two data blocks in a participant be-131 63 cause its mean head-movement regressors exceeded 4 mm in one of $^{\scriptscriptstyle 132}$ 64 the orthogonal directions. 134

fMRI data analysis

FMRI data acquired during the TNT phase was analysed through general linear models (GLMs) in SPM12. Each data block for a given participant was modelled separately at the first level using a fixed-effects model. Then, each group analysis used a random-effects model. To identify the regions that were engaged or downregulated during retrieval suppression, we constructed a GLM containing three regressors of interest and one regressor of no interest. Regressors of interest were built with the onset times of the words presented in the three experimental conditions (Think, No-Think and Perceptual Baseline). fMRI analyses were conditionalized, so Think and No-Think onset times corresponding to word pairs that participants failed to learn at study (Misses) were excluded from the main regressors and grouped in the regressor of no interest. Six further regressors contained the head-movement parameters obtained during spatial realignment and were included as covariates. First-level analyses calculated the main effects between the three conditions. For group-level analyses, contrasts between No-Think and Think, each relative to Perceptual baseline, were compared by means of paired-sample T-tests. For whole brain analyses, activations were considered significant if formed by clusters of at least 20-voxels with an uncorrected p-value smaller than 0.001. For dACC ROI analysis, a paired-sample t-test was applied to averaged contrast-values (p<0.05).

ERP-informed fMRI analyses

To determine whether and how (e.g., positive or negative modulation) ROI's BOLD responses covaried with the EEG measures across trials, we chose a parametric design approach (Debener et al., 2006). For each EEG measure, we built a separate GLM. Each GLM extended the previously described GLM by including two additional regressors of interest and one of no interest. The regressors of interest were parametric modulator vectors for No-Think and Think conditions containing single-trial values of the corresponding EEG measure. The regressor of no interest gathered the onset times of all trials that were classified as artifacts during EEG pre-processing or that showed EEG measures larger or smaller than 3 standard deviations (i.e., these onset times were removed from the original main regressors). One of the parametric modulators was built from single-trial N2 amplitude values from the pooled frontocentral channel in the selected time window. To extract single-trial N2 amplitudes, an individual search window was first limited to participants P2 and P3 waveforms of the pooled channel ERP. Then, N2 latencies were defined as the minimum peak found within the individual search window for each trial. To help the peak detection algorithm, data were low pass filtered at 8 Hz. However, single-trial N2 amplitudes were obtained from the 0.5-30 Hz data, by averaging 100-ms windows centred on the N2 latencies. A second parametric modulator was built from mean theta (4-8 Hz) power values extracted from dACC ROI in the N2 time window. Other parametric modulators (i.e., hippocampal ROIs theta power) were built from mean power values across all voxels within a cluster. We computed other GLMs for control purposes. In one case, we extracted the mean dipole momentum from dACC ROI within the N2 effect time window. To control for the sign of the source time-courses and the correlation with BOLD, we run three separated GLMs, one for each cartesian direction, and the resulting contrasts were averaged. The signs of the source time-courses followed the same convention of the frontocentral channel in that window (i.e., more negative for larger N2 amplitudes, compared to small N2 amplitudes). For group-level analyses, contrasts of parameter estimates were averaged across all voxels within each ROI for each condition and subject. Within-condition and between-condition contrasts were assessed using one-sample and paired-sample and independent-sample T-tests, respectively. Wholebrain statistical maps were corrected for multiple comparisons using a cluster-based permutation approach. For each permutation, we used the same original GLM, but the order of the values in the parametric modulator (i.e., amplitude or latency) was randomized. As a result, the new parametric modulators contained the same values than the original regressor, but each value was assigned to an onset time of a different trial. This procedure was repeated 100 times in all participants (first-level fixed effects), which yielded 100 second-level fixed effects analyses. We recorded the sizes of all clusters obtained from the resulting statistical maps after applying an initial threshold at |Z|-

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score>2.57 (uncorrected p<0.005). Then, we generated a distribution 63 1 with the cluster sizes, which enabled us to determine the largest clus- 64 ter size leading to a significance level of p<0.05. This cluster size was used as a threshold to correct the original statistical maps (Fouragnan 66 et al., 2017).

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Author Contributions

M.C.A. and X.L. conceived the experiment. Y.W. performed the exper-21 iment. M.C.G., Y.W., X.L. and M.J. analysed the data. M.C.G. and M.C.A wrote the manuscript. M.C.A., X.L., Y.W. and M.J. discussed 23 the results and contributed to the manuscript. 24

Declaration of Interests

The authors declare no competing interests. 26

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