Coordinate-Based fMRI Meta-Analyses of Episodic Memory Encoding and Retrieval in Depression

Raphaela Schöpfer[1,2,3,4], Reut Zabag[5], Florian Wüthrich[1,3], Romy Lorenz[4], Jutta Joormann[5], Sina Straub[1,3], Jessica Peter[1,3]

1 University Hospital of Old Age Psychiatry and Psychotherapy, University of Bern, Bern, Switzerland

2 Graduate School for Health Sciences, Faculty of Medicine, University of Bern, Bern, Switzerland

3 Translational Imaging Centre, sitem-insel, Bern University Hospital, Bern, Switzerland

4 Max Planck Institute for Biological Cybernetics, Tübingen, Germany

5 Department of Psychology, Yale University, New Haven, USA

Corresponding author:

Raphaela Schöpfer
University Hospital of Old Age Psychiatry and Psychotherapy
Bolligenstrasse 111
3000 Bern
Switzerland
Email: raphaela.schoepfer@unibe.ch

Abstract

Background

Depression is a mood disorder frequently associated with episodic memory impairment. However, it remains unclear whether functional brain activity differs between depressed and non-depressed individuals during encoding or retrieval of autobiographical or non-autobiographical memories. Clarifying these differences is important for refining theoretical models of memory impairment in depression and, potentially, for developing targeted interventions.

Methods

We conducted three coordinate-based meta-analyses examining encoding and retrieval of autobiographical and non-autobiographical memory in control participants and individuals with current, remitted, or subthreshold depression, or those at risk for depression. Studies were identified via database searches and analysed using Seed-based d Mapping.

Results

We included coordinates from 21 fMRI studies. During encoding, depression was associated with reduced activity in the thalamus, the caudate, the salience network, the frontoparietal executive control network, and motor-related areas (ten studies, N = 506). During non-autobiographical retrieval, depression was associated with higher activity in the right inferior frontal gyrus (six studies, N = 332). During autobiographical retrieval, depression was associated with reduced activity in the right insula and fusiform gyrus, alongside increased activity in the left anterior cingulate cortex and the left middle frontal gyrus (ten studies, N = 423). Between-study heterogeneity was low and no evidence for publication bias was found.

Discussion

Our results indicate that depression may be associated with impaired salience integration during encoding and autobiographical retrieval. In contrast, during non-autobiographical

retrieval, increased frontal activity suggests a more vigilant or self-monitoring retrieval mode. Functional brain activity changes in depression therefore appear stage- and content-specific.

Introduction

In addition to negative affect or loss of interest in nearly all activities, depression is characterized by another important component - cognitive symptoms. Memory dysfunction is common [1, 2], affecting both autobiographical and non-autobiographical (i.e., non-self-referential) episodic memory. Both types of episodic memory rely on successful encoding, during which information is selected, integrated, and bound into a durable memory trace [3]. As retrieval depends on the integrity of these initial representations, disturbances at the encoding stage may compromise later retrieval. Hence, encoding may be the earliest stage at which depression-related cognitive alterations emerge, making it critical for understanding downstream episodic memory dysfunction.

Behaviourally, however, the quality of encoding can only be inferred from retrieval outcomes. For instance, patients with depression often retrieve fewer items than non-depressed participants in non-self-referential tasks, such as word lists, and tend to retrieve overgeneralized, less detailed, and less emotionally rich autobiographical memories [4, 5]. While such findings indicate episodic memory impairment in depression, they do not directly reveal *how* information is processed during encoding and retrieval. Investigating the functional activation patterns underlying these stages may therefore provide a more precise characterization of memory-related alterations in depression.

Successful encoding relies on coordinated brain activity in the prefrontal cortex and medial temporal lobe [6], whereas retrieval - autobiographical and non-autobiographical – engages a largely left-lateralized fronto-parietal network with additional involvement of the temporal cortex, the precuneus, the posterior cingulate cortex, and the hippocampal formation [7, 8]. Encoding and retrieval activity therefore appear to converge in overlapping regions, consistent with the cortical reinstatement framework, which posits that successful retrieval depends on reactivation of cortical patterns engaged during encoding [9, 10]. Several studies have reported that similar brain regions show altered activity in individuals with depression

during encoding [11–20], autobiographical retrieval [21–30], and non-autobiographical retrieval [13–16, 31]. These findings indicate that depression alters brain regions and networks involved in encoding and retrieval. Yet, whether these alterations are stage-specific (encoding vs. retrieval) or type-specific (autobiographical vs. non-autobiographical) has not been systematically examined. A very recent meta-analysis investigated autobiographical memory in depression [33] but did not consider stage- or type-specific differences. Clarifying these distinctions is important to develop a mechanistic understanding of depression-related memory dysfunction and to identify potential therapeutic targets. In addition, comparing functional brain activity across encoding and both autobiographical and non-self-referential retrieval allows a process-oriented examination of whether depression-related alterations emerge early during memory formation, persist during content-general retrieval, or become amplified in self-referential contexts.

Importantly, memory impairment in depression is not restricted to individuals meeting full diagnostic criteria for Major Depressive Disorder. They have been observed in individuals with subclinical depressive symptoms, in those at risk for developing depression, and in patients with remitted depression [4, 34–38]. We therefore included studies in patients with current or remitted depression as well as in individuals with subclinical depressive symptoms or those at risk of developing depression due to familial risk.

Methods

Search Strategy

We conducted three coordinate-based meta-analyses in accordance with the PRISMA guidelines [39]. Two pre-registered analyses (OSF: https://doi.org/10.17605/OSF.IO/T54Y2; https://doi.org/10.17605/OSF.IO/U24DS) examined group differences in memory encoding and autobiographical retrieval across the depression continuum. A third, non-pre-registered analysis investigated whether depression-related changes in brain activity during retrieval are

specific to autobiographical memory or extend to non-autobiographical memory more broadly.

We systematically searched PubMed, PsycINFO, Embase, and Elicit AI (an AI-assisted literature search tool) to identify studies that compared encoding or retrieval processes between the depression continuum and control participants. We included studies published up to March 2025 that were available in English, with no restriction on the earliest publication date. We used the following search strings:

((((neuronal[Title/Abstract] OR fMRI[Title/Abstract] OR "functional magnetic resonance imaging"[Title/Abstract] OR neuroimaging[Title/Abstract] OR "brain function"[Title/Abstract] OR "neural mechanism"[Title/Abstract] OR hippocampus[Title/Abstract] OR “prefrontal cortex”[Title/Abstract] OR amygdala[Title/Abstract] OR "functional connectivity"[Title/Abstract])) AND ("episodic memory"[Title/Abstract] OR “memory encoding” [Title/Abstract] OR “memory retrieval”[Title/Abstract] OR “recognition memory”[Title/Abstract] OR "autobiographical memory"[Title/Abstract])) AND (depression[Title/Abstract] OR MDD[Title/Abstract] OR “depressive episode” [Title/Abstract] OR "major depressive episode"[Title/Abstract]))

We adapted the search strings for each database if needed. We also screened reference lists of all included studies to identify additional eligible studies.

Inclusion and exclusion criteria

We included univariate task-based fMRI studies that reported whole-brain activation contrasts related to encoding, non-autobiographical retrieval, or to autobiographical retrieval and that provided peak voxel coordinates in standard stereotactic space (MNI or Talairach). The studies needed to compare control participants with patients with current or remitted depression, individuals with subclinical depressive symptoms, or with individuals at risk for depression. At risk for depression was defined as individuals with no current or past

depressive disorder but with elevated vulnerability due to familial risk (i.e., having a parent or twin with a history of depression).

We excluded studies if they:

(a) used a region-of-interest (ROI) analysis and no whole-brain analysis;

(b) examined resting-state fMRI rather than task-based fMRI;

(c) focused only on structural MRI;

(d) focused on depression with psychotic symptoms or on other psychiatric disorders;

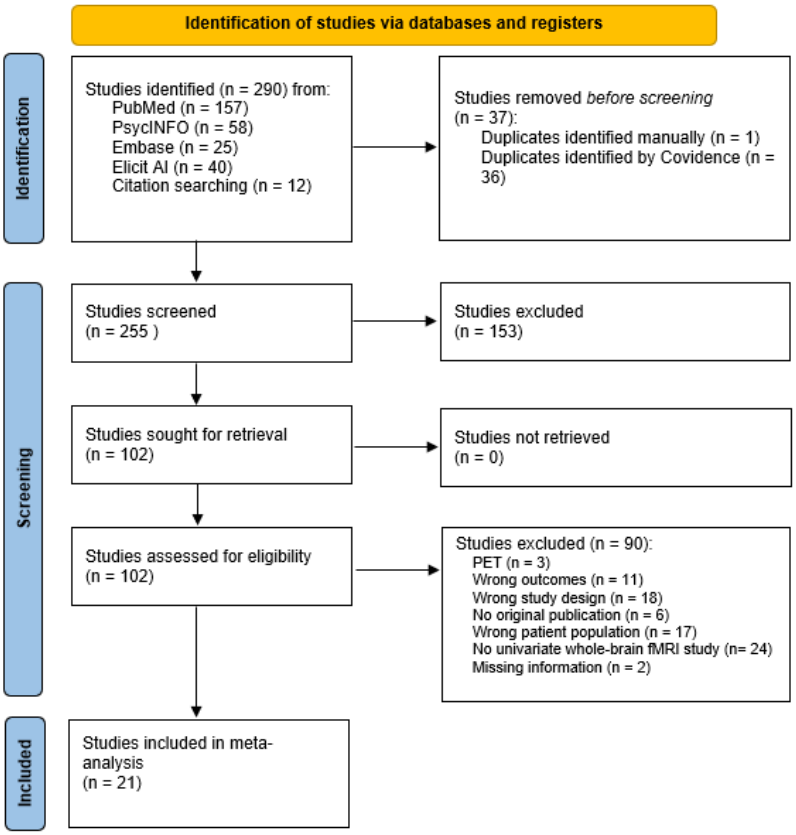
(e) reported centre of mass coordinates instead of peak voxel coordinates;

(f) did not provide sufficient information (e.g., no *t*- or *z*-values, or no coordinates)

Two independent raters (RS, RZ) checked studies for inclusion using Covidence systematic review software (Veritas Health Innovation, Melbourne, Australia). Any discrepancies were discussed and resolved by consensus. Interrater agreement was moderate during title and abstract screening (Cohen's κ = 0.59; agreement = 80%) and substantial during full-text screening (Cohen's κ = 0.64; agreement = 83%).

We identified 290 studies and finally included 21 studies (Figure 1) comprising N = 982 participants. Of these 21 studies, 10 examined encoding, 10 autobiographical memory retrieval, and 6 non-autobiographical memory retrieval.

Figure 1. PRISMA flowchart of the study.



Data Extraction

For each study, two authors (RS, SS) independently extracted MNI or Talairach coordinates, effect sizes (*t*-values), and statistical thresholds. One author (RS) extracted participant information and task descriptions. We contacted authors of studies when information was missing. For one study we received no response, for another study, requested information was unavailable. Hence, these studies had to be excluded. If studies reported *z*-values rather than *t*-values, we converted them using the converter provided on the Seed-based d Mapping website (https://www.sdmproject.com/utilities/?show=Statistics).

Three studies compared three groups (e.g., control participants vs. patients with depression vs. individuals at risk for depression) but did not provide whole-brain, voxel wise pairwise comparisons with extractable peak coordinates or *t*/*z*-maps. If regional summary statistics were available, we combined clinical subgroups into one group using weighted means and pooled standard deviations. We then compared this combined clinical group with control participants using Welch's *t*-tests to estimate effect sizes. When multiple studies reported results from the same participant sample, only one was included in the meta-analysis to prevent double counting and inflation of effect sizes.

Seed-Based d Mapping analysis

We performed three coordinate-based meta-analyses using Seed-based d Mapping (SDM) with permutation of subject images (SDM-PSI; version 6.23; www.sdmproject.com) [40]. Preprocessing included the conversion of peak coordinates into standard MNI space and the recreation of whole-brain maps of Hedges' *g* effect sizes using an anisotropic Gaussian kernel (FWHM = 20 mm, voxel size = 2 mm, anisotropy = 1), restricted to grey matter, following standard SDM procedures for modelling spatial uncertainty of reported peak coordinates [41]. We then calculated mean meta-analytic maps using a random-effects model weighted by study size and variance, and determined statistical significance using permutation tests within the SDM-PSI framework. In line with recommendations for SDM meta-analyses, we used the default threshold for statistical significance (voxel-level $p < .005$ uncorrected, two-sided, minimum cluster extent 10 contiguous voxels). While this threshold does not correct for multiple comparisons, it provides an optimal compromise between sensitivity and specificity [42]. We evaluated between-study heterogeneity using Cochran's Q statistic and its z-transformed value (Q–Z), τ^2 (between-study variance), H^2 (ratio of total to within-study variance), and I^2 (percentage of true heterogeneity). In addition, we used Egger's statistic to test for publication bias. Heterogeneity and bias estimates were done using SDM-PSI.

In addition, we conducted three exploratory meta-regressions to examine whether age or sex moderated encoding- or retrieval-related brain activation differences between groups. These analyses were performed as we did not restrict studies to a specific age range, and we aimed to rule out potential confounding effects of age or sex on observed activity differences.

Results

Encoding of new information

We included 10 studies comprising N = 506 participants (252 control participants and 254 individuals across the depression continuum). The participants were 34.07 ± 14.60 years old, and 65.8 % of them were female. Encoding tasks focused on words, faces, pictures, or on associative learning (Supplementary Table S1).

We found higher activity in control participants compared to individuals across the depression continuum in the right thalamus/right caudate, the bilateral insula, the right precentral gyrus, the left superior frontal gyrus and the left inferior parietal lobe (Table 1, Figure 2A). Effect sizes were small to medium (Hedges' *g* ranging from -.449 to -.314). Heterogeneity was low ($\tau^2 \leq .023$; $I^2 \leq 17$ %) and not significant (Q–Z < 1.96), indicating consistency between studies. We found no evidence to suggest publication bias (Egger's regression tests, all $p > .203$; Supplementary Table S4). The reverse contrast (i.e., depression > health) did not yield any significant results.

We then examined whether age or sex moderated the observed group differences in brain activity. Age did not significantly moderate these effects. In contrast, sex significantly moderated the observed group differences in right precentral gyrus activity. Studies with a higher proportion of female participants showed greater differences in encoding-related right precentral gyrus activity between both groups (Supplementary Table S5).

Retrieval of non-autobiographical memories

For non-self-referential retrieval, we included six studies comprising N = 332 participants (170 control participants and 162 individuals across the depression continuum). They were 32.28 ± 8.82 years old and 64.8 % of them were female. Five studies used a recognition task and one study used a cued-recall task (Supplementary Table S2).

We found higher activity in the right inferior frontal gyrus in the depression group compared to control participants (Table 2, Figure 2B). The effect size was small to medium (Hedges' g = .474). Between-study heterogeneity was low (τ^2 = 0.014; I^2 = 9.881 %), and not significant (Q–Z < 1.96), indicating consistency between studies. We found no evidence to suggest publication bias (i.e., Egger's p = .898; Supplementary Table S6). The reverse contrast (i.e., health > depression) did not lead to any significant results.

We then examined whether age or sex moderated the observed group difference in brain activity. We found no significant moderating effect for age or sex.

Retrieval of autobiographical memories

For autobiographical retrieval, we included 10 studies comprising 423 participants (199 control participants and 224 individuals across the depression continuum). They were 31.3 ± 7.6 years old and 67.0 % of them were female. The studies used different paradigms, including cue-word recall, autobiographical memory recognition, script listening, and photo-based recall (Supplementary Table S3). We found higher activity in the left anterior cingulate and in the left middle frontal gyrus in the depression continuum compared to control participants. There was also lower activity in the right insula and the right fusiform gyrus in the depression group compared to control participants (Table 3; Figure 2C). Effect sizes were small to medium (Hedges' g ranging from -.405 to .539). Between-study heterogeneity was low ($\tau^2 \leq 0.030$; $I^2 \leq 18\%$) and not significant (all Q–Z < 1.96). We found no evidence to suggest publication bias (Egger's regression test, all p > .229; Supplementary Table S7).

We then examined whether age or sex moderated the observed group differences in brain activity. Age significantly moderated the group difference in the left superior frontal lobe activity. Increasing age was associated with a reduction in the difference in activity between control participants and individuals across the depression continuum. In other words, group differences became smaller with increasing age (Supplementary Table S8). Sex significantly moderated group differences in activity in the left middle frontal gyrus. Studies with a higher proportion of female participants showed greater differences in recall-related left middle frontal gyrus activity between both groups (Supplementary Table S9).

Conjunction analysis of all memory processes

As an exploratory analysis, we then created a conjunction map to identify differences in brain activity that are shared between memory processes (i.e., overlaying thresholded maps from all meta-analyses; voxel-level $p < .005$, uncorrected; cluster extent ≥ 10 voxels). We found no direct voxel overlap. However, clusters located within the right insula were in close proximity, indicating consistent hypoactivation across the depression continuum during both encoding and autobiographical memory retrieval (Figure 2D).

Discussion

The goal of the present study was to characterize changes in functional brain activity across the depression continuum during episodic memory, and to explore how these changes vary by memory stage and type. Successful retrieval depends on the quality of initial encoding, during which incoming information is evaluated for relevance, prioritized, and integrated into a coherent representation. Effective encoding relies on executive control that supports elaboration and organization as well as on attention to prioritize information for enhanced processing [43, 44].

Across the depression continuum, we observed reduced brain activity during encoding in the thalamus, right caudate, bilateral insula, left superior frontal gyrus, left inferior parietal lobule, and right precentral gyrus. These regions span key components of the salience network and frontoparietal control network that support the allocation of cognitive resources during encoding. The insula, a core node of the salience network, responds to salient information and supports subsequent memory by flagging important events and by promoting executive resources during encoding [45, 46]. In addition, the dorsal part of insula subregions may be important for relevance evaluation of a stimulus to then directly influence hippocampal activity [47] as proposed by a recent intracranial EEG study. Lower activity in the insula across the depression continuum may therefore reflect a reduced capacity to detect and prioritize relevant information, limiting the engagement of integrative processes necessary for forming strong memory traces. Reduced activity in frontoparietal regions and the thalamus may further reflect impaired attentional regulation and sensory gating, reducing the ability to focus on relevant information while filtering out distractions [48]. Alternatively, this pattern may reflect reduced task engagement or effort, as several identified regions (e.g., the insula and frontoparietal regions) overlap with the multiple-demand network, a domain-general system supporting cognitive control and responses to task demands [49]. Lower activity in the right caudate may reflect reduced goal relevant processing, including the selection and organization of task relevant information [50, 51]. Together, these findings indicate that depression is associated with reduced salience processing, executive engagement, and sensory gating already at the earliest stage of memory processing, potentially leading to weaker memory traces and less detailed and emotionally salient representations.

During autobiographical retrieval, reduced activity in the right insula persisted across the depression continuum and extended to the right fusiform gyrus. During retrieval, the insula may contribute to the evaluation of personally meaningful experiences by processing interoceptive signals [8, 45, 46]. The fusiform gyrus may support the reactivation of details

that underlie a vivid recollection of personal events [52]. Lower activity in these regions during autobiographical retrieval may therefore compromise a detailed, specific memory reactivation. This, in turn, may lead to overgeneralized autobiographical memories that are less vivid and personally salient. Besides reduced activity in the insula and the fusiform gyrus, we found increased activity in the left anterior cingulate cortex and the left middle frontal gyrus across the depression continuum, pointing to a functional imbalance within the salience network of which the anterior cingulate cortex and the insula are core nodes. This imbalance may alter the coordination of network nodes or may lead to unstable network dynamics. As the retrieval of autobiographical memories mostly involved a silent free recall, an increase in activity may also indicate increased regulatory demands during the reconstruction of autobiographical memories. Free recall, even when silent, requires strategic reconstruction when there are no cues that prompt retrieval. Individuals across the depression continuum may need more prefrontal control and monitoring to retrieve even when memories are not very specific (i.e., overgeneralised). Another explanation may be that greater top-down control is needed to reconstruct memories while managing competing negative thoughts.

In contrast to autobiographical retrieval, non-autobiographical retrieval was not associated with reduced activity in the insula or fusiform gyrus but rather with increased activity in the right inferior frontal gyrus, a brain region related to executive control, monitoring, and response selection. Similar to autobiographical retrieval, higher activity in frontal brain regions may indicate increased regulatory demands during the reconstruction of memories. However, non-autobiographical retrieval was largely recognition-based and therefore less demanding than free recall as cues prompt retrieval. In addition, recognition tasks usually lead to *weaker* functional brain activity than, say, free recall tasks. Hence, task difficulty or increased regulatory demands may not be the only reason for an increase in brain activity. Instead, stronger inhibition or monitoring needs, for example, to suppress intrusive thoughts,

may play an important role. Hence, depression may alter control dynamics even when memory demands are low [53].

Together, our study highlights the salience network – particularly the insula - as a hub in depression, consistent with previous reports of structural and functional dysfunctions [54–61] or even network reorganisation [62]. An imbalance in the salience network, or in the insula in particular, may contribute to less efficient switching between the default mode network and the executive control network, impairing the brain's ability to mark memories as important during encoding. This may lead to weaker, less distinct memory traces, contributing to overgeneralized autobiographical memories, in line with previous reports in depression [5, 34]. Depression may therefore not erase memories but instead reduce their emotional richness and vividness. Importantly, during autobiographical and non-autobiographical retrieval, regions supporting cognitive control were more active across the depression continuum. This may reflect greater effort to manage interference from negative thoughts to retrieve memory details despite a known tendency towards overgeneralisation.

Our study has some limitations. First, the number of eligible studies was relatively small, and participants were drawn from across the depression continuum, including individuals with current or remitted depression, those with subthreshold symptoms, or individuals at risk for depression. As a consequence, we were not able to perform subgroup analyses to examine whether activity changes were specific to particular stages or severities of depression. Second, the included studies used similar but not identical tasks. However, we did not find evidence of significant heterogeneity in our results, indicating that the observed effects were relatively consistent across task variations. Third, not all studies fully matched groups on education, IQ, or general cognitive abilities, and task engagement was not controlled for. Therefore, reduced activity during encoding may reflect differences in cognitive abilities or cognitive effort,

rather than encoding-specific deficits. Fourth, medication may have influenced the observed patterns of brain activity. Fifths, since we used group-level coordinate data, we could not determine exactly which large-scale networks each identified region belonged to in individual participants. Hence, we can not be certain that these regions are part of specific networks.

Our study demonstrates that depression-related functional activity changes vary across memory encoding and retrieval, with convergent insula hypoactivation pointing to disrupted salience processing as a potential mechanism underlying episodic memory dysfunction in depression. These findings highlight potential targets for interventions aimed at improving memory functions. For encoding-related changes in the salience network or frontoparietal regions, attention or memory training may be beneficial. The insula also represents a promising target for addressing memory dysfunction, for example by using non-invasive brain stimulation. Although direct modulation of the insula remains challenging, interventions that enhance its functional connectivity with other regions, such as the right superior temporal gyrus [63], may hold promise. Another potential approach is real-time fMRI neurofeedback designed to increase insula engagement during episodic memory formation. Future studies may evaluate the efficacy and feasibility of these interventions. In addition, precision functional mapping may characterize network alterations in individuals across the depression continuum and guide targeted interventions.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Data Availability

The metadata underlying this meta-analysis, including peak coordinates and associated t-values extracted from all included studies, are openly available on the Open Science

Framework (OSF) repository at: https://osf.io/wyx76/overview and https://osf.io/mqj3y/overview

Funding

This project has been funded by the Swiss National Science Foundation (grant number 218252 to JP).

References

1. Rock PL, Roiser JP, Riedel WJ, Blackwell AD. Cognitive impairment in depression: a systematic review and meta-analysis. *Psychol Med* 2014; 44:2029–2040.

2. Weiss-Cowie S, Verhaeghen P, Duarte A. An updated account of overgeneral autobiographical memory in depression. *Neurosci Biobehav Rev* 2023; 149:105157.

3. Eichenbaum H. Memory: Organization and Control. *Annu Rev Psychol*. 2017; 68:19–45.

4. James TA, Weiss-Cowie S, Hopton Z, Verhaeghen P, Dotson VM, Duarte A. Depression and episodic memory across the adult lifespan: A meta-analytic review. *Psychol Bull*. 2021; 147:1184–1214.

5. Williams JMG, Barnhofer T, Crane C, Hermans D, Raes F, Watkins E, et al. Autobiographical Memory Specificity and Emotional Disorder. *Psychol Bull*. 2007; 133:122-148.

6. Kim H. Neural activity that predicts subsequent memory and forgetting: A meta-analysis of 74 fMRI studies. *Neuroimage*. 2011; 54:2446–2461.

7. Henson RNA, Rugg MD, Shallice T, Josephs O, Dolan RJ. Recollection and Familiarity in Recognition Memory: An Event-Related Functional Magnetic Resonance Imaging Study. *J Neurosci*. 1999; 19:3962-3972.

8. Svoboda E, McKinnon MC, Levine B. The functional neuroanatomy of autobiographical memory: A meta-analysis. *Neuropsychologia*. 2006; 44:2189-2208.

9. Johnson JD, McDuff SGR, Rugg MD, Norman KA. Recollection, Familiarity, and Cortical Reinstatement: A Multivoxel Pattern Analysis. *Neuron*. 2009; 63:697–708.

10. Rugg MD, Johnson JD, Park H, Uncapher MR. Encoding-retrieval overlap in human episodic memory: A functional neuroimaging perspective. *Prog Brain Res*. 2008; 169:339–352.

11. Kassel MT, Rao JA, Walker SJ, Briceño EM, Gabriel LB, Weldon AL, et al. Decreased Fronto-Limbic Activation and Disrupted Semantic-Cued List Learning in Major Depressive Disorder. *J Int Neuropsychol Soc*. 2016; 22:412–425.

12. Weisenbach SL, Kassel MT, Rao J, Weldon AL, Avery ET, Briceno EM, et al. Differential prefrontal and subcortical circuitry engagement during encoding of semantically related words in patients with late-life depression. *Int J Geriatr Psychiatry*. 2014; 29:1104–1115.

13. Werner NS, Meindl T, Materne J, Engel RR, Huber D, Riedel M, et al. Functional MRI study of memory-related brain regions in patients with depressive disorder. *J Affect Disord*. 2009; 119:124–131.

14. Wolfensberger SPA, Veltman DJ, Hoogendijk WJG, De Ruiter MB, Boomsma DI, de Geus EJC. The neural correlates of verbal encoding and retrieval in monozygotic twins at low or high risk for depression and anxiety. *Biol Psychol*. 2008; 79:80–90.

15. Dietsche B, Backes H, Stratmann M, Konrad C, Kircher T, Krug A. Altered neural function during episodic memory encoding and retrieval in major depression. *Hum Brain Mapp*. 2014; 35:4293–4302.

16. Holt RJ, Graham JM, Whitaker KJ, Hagan CC, Ooi C, Wilkinson PO, et al. Functional MRI of emotional memory in adolescent depression. *Dev Cogn Neurosci*. 2016; 19:31–41.

17. Arnold JF, Fitzgerald DA, Fernández G, Rijpkema M, Rinck M, Eling PATM, et al. Rose or black-coloured glasses?: Altered neural processing of positive events during memory formation is a trait marker of depression. *J Affect Disord*. 2011; 131:214–223.

18. Van Eijndhoven P, van Wingen G, Fernández G, Rijpkema M, Verkes RJ, Buitelaar J, et al. Amygdala responsivity related to memory of emotionally neutral stimuli constitutes a trait factor for depression. *Neuroimage*. 2011; 54:1677–1684.

19. Roberson-Nay R, McClure EB, Monk CS, Nelson EE, Guyer AE, Fromm SJ, et al. Increased Amygdala Activity During Successful Memory Encoding in Adolescent Major Depressive Disorder: An fMRI Study. *Biol Psychiatry*. 2006; 60:966–973.

20. Van Wingen GA, van Eijndhoven P, Cremers HR, Tendolkar I, Verkes RJ, Buitelaar JK, et al. Neural state and trait bases of mood-incongruent memory formation and retrieval in first-episode major depression. *J Psychiatr Res*. 2010; 44:527–534.

21. Gillard J, Werner-Seidler A, Dalgleish T, Stretton J. Script-driven imagery of socially salient autobiographical memories in major depressive disorder. *Sci Rep*. 2023; 13:1–10.

22. Joormann J, Cooney RE, Henry ML, Gotlib IH. Neural correlates of automatic mood regulation in girls at high risk for depression. *J Abnorm Psychol*. 2012; 121:61–72.

23. Parlar M, Densmore M, Hall GBC, Lanius R, McKinnon MC. Neural and behavioural correlates of autobiographical memory retrieval in patients with major depressive disorder and a history of trauma exposure. *Neuropsychologia*. 2018; 110:148–158.

24. Whalley MG, Rugg MD, Brewin CR. Autobiographical memory in depression: an fMRI study. *Psychiatry Res*. 2012; 201:98–106.

25. Wu D, Chen T, Huang X, Chen L, Yue Y, Yang H, et al. The Role of Old Photos in Reminiscence Therapy in Elderly Women With Depressive Symptoms: A Functional Magnetic Resonance Imaging Study. *Biol Res Nurs*. 2020; 22:234–246.

26. Young KD, Bodurka J, Drevets WC. Functional neuroimaging of sex differences in autobiographical memory recall in depression. *Psychol Med*. 2017; 47:2640–2652.

27. Young KD, Erickson K, Nugent AC, Fromm SJ, Mallinger AG, Furey ML, et al. Functional anatomy of autobiographical memory recall deficits in depression. *Psychol Med*. 2012; 42:345–357.

28. Young KD, Bodurka J, Drevets WC. Differential neural correlates of autobiographical memory recall in bipolar and unipolar depression. *Bipolar Disord*. 2016; 18:571–582.

29. Young KD, Bellgowan PSF, Bodurka J, Drevets WC. Neurophysiological correlates of autobiographical memory deficits in currently and formerly depressed subjects. *Psychol Med*. 2014; 44:2951–2963.

30. Young KD, Bellgowan PSF, Bodurka J, Drevets WC. Functional Neuroimaging Correlates of Autobiographical Memory Deficits in Subjects at Risk for Depression. *Brain Sci*. 2015; 5:144–164.

31. van Wingen GA, van Eijndhoven P, Cremers HR, Tendolkar I, Verkes RJ, Buitelaar JK, et al. Neural state and trait bases of mood-incongruent memory formation and retrieval in first-episode major depression. *J Psychiatr Res*. 2010; 44:527–534.

32. Miskowiak KW, Larsen JE, Harmer CJ, Siebner HR, Kessing L V., Macoveanu J, et al. Is negative self-referent bias an endophenotype for depression? An fMRI study of emotional self-referent words in twins at high vs. low risk of depression. *J Affect Disord*. 2018; 226:267–273.

33. Cheng CCC, Tsang MHL, Han M, Zhang J, Maes M, Klugah-Brown B, et al. Neural systems underlying autobiographical memory dysregulations in depression: A neuroimaging meta-analysis. *Psychol Med*. 2025; 56:e1.

34. Hallford DJ, Rusanov D, Yeow JJE, Barry TJ. Reduced specificity and increased overgenerality of autobiographical memory persist as cognitive vulnerabilities in remitted major depression: A meta□analysis. *Clin Psychol Psychother*. 2022; 29:1515-1529.

35. Hammar Å, Ronold EH, Rekkedal GÅ. Cognitive Impairment and Neurocognitive Profiles in Major Depression—A Clinical Perspective. *Front Psychiatry*. 2022; 13:764374.

36. Rawal A, Rice F. Examining overgeneral autobiographical memory as a risk factor for adolescent depression. *J Am Acad Child Adolesc Psychiatry*. 2012; 51:518–527.

37. Sumner JA, Griffith JW, Mineka S. Overgeneral autobiographical memory as a predictor of the course of depression: A meta-analysis. *Behav Res Ther*. 2010; 48:614–625.

38. Van Vreeswijk MF, De Wilde EJ. Autobiographical memory specificity, psychopathology, depressed mood and the use of the Autobiographical Memory Test: A meta-analysis. *Behav Res Ther*. 2004; 42:731–743.

39. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021; 372: n71.

40. Albajes-Eizagirre A, Solanes A, Fullana MA, Ioannidis JPA, Fusar-Poli P, Torrent C et al. Meta-analysis of voxel-based neuroimaging studies using seed-based d mapping with permutation of subject images (SDM-PSI). *J Vis Exp*. 2019; 153: e59841.

41. Radua J, Rubia K, Canales-Rodríguez EJ, Pomarol-Clotet E, Fusar-Poli P, Mataix-Cols D. Anisotropic Kernels for Coordinate-Based Meta-Analyses of Neuroimaging Studies. *Front Psychiatry*. 2014; 5:13.

42. Radua J, Mataix-Cols D, Phillips ML, El-Hage W, Kronhaus DM, Cardoner N, et al. A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps. *Eur Psychiatry*. 2012; 27:605–611.

43. Uncapher MR, Wagner AD. Posterior parietal cortex and episodic encoding: Insights from fMRI subsequent memory effects and dual-attention theory. *Neurobiol Learn Mem*. 2009; 91:139–154.

44. Craik FIM, Lockhart RS. Levels of processing: A framework for memory research. *J Verbal Learning Verbal Behav.* 1972; 11:671–684.

45. Craig AD. How do you feel -- now? The anterior insula and human awareness. *Nat Rev Neurosci*. 2009; 10:59–70

46. Menon V, Uddin LQ. Saliency, switching, attention and control: a network model of insula function. *Brain Struct Funct*. 2010; 214:655.

47. Huang W, Lyu D, Stieger JR, Gotlib IH, Buch V, Wagner AD, et al. Direct interactions between the human insula and hippocampus during memory encoding. *Nat Neurosci*. 2025; 28:1763-1771

48. Kastner S, Arcaro MJ. The thalamus in attention. in The Thalamus 324–339 (Cambridge University Press, 2022).

49. Duncan J. The multiple-demand (MD) system of the primate brain: mental programs for intelligent behaviour. *Trends Cogn Sci*. 2010; 14:172–179.

50. Grahn JA, Parkinson JA, Owen AM. The cognitive functions of the caudate nucleus. *Prog Neurobiol*. 2008; 86:141–155.

51. Delgado MR, Stenger VA, Fiez JA. Motivation-dependent Responses in the Human Caudate Nucleus. *Cereb Cortex*. 2004; 14:1022–1030.

52. Wheeler ME, Petersen SE, Buckner RL. Memory's echo: Vivid remembering reactivates sensory-specific cortex. *Proc Natl Acad Sci U S A.* 2000; 97:11125–11129.

53. Song X, Long J, Wang C, Zhang R, Lee TMC. The inter-relationships of the neural basis of rumination and inhibitory control: neuroimaging-based meta-analyses. *Psychoradiology*. 2022; 2:11-22.

54. Sprengelmeyer R, Steele JD, Mwangi B, Kumar P, Christmas D, Milders M, et al. The insular cortex and the neuroanatomy of major depression. *J Affect Disord*. 2011; 133:120–127.

55. Schnellbächer GJ, Rajkumar R, Veselinović T, Ramkiran S, Hagen J, Shah NJ, et al. Structural alterations of the insula in depression patients – A 7-Tesla-MRI study. *Neuroimage Clin*. 2022; 36:103249.

56. Yan F, Zan S, Xu J, Zhao S, Wang Z, Yang F. Cognitive and clinical dimensions of structural and functional insula alterations in patients with depression: a resting-state fMRI study. *Int J Neurosci*. 2024; 136:67-76.

57. Guo W, Liu F, Xiao C, Zhang Z, Liu J, Yu M, et al. Decreased insular connectivity in drug-naive major depressive disorder at rest. *J Affect Disord*. 2015; 179:31–37.

58. Wang C, Wu H, Chen F, Xu J, Li H, Li H, et al. Disrupted functional connectivity patterns of the insula subregions in drug-free major depressive disorder. *J Affect Disord*. 2018; 234:297–304.

59. Liu Z, Xu C, Xu Y, Wang Y, Zhao B, Lv Y, et al. Decreased regional homogeneity in insula and cerebellum: A resting-state fMRI study in patients with major depression and subjects at high risk for major depression. *Psychiatry Res Neuroimaging*. 2010; 182:211–215.

60. Hwang JW, Egorova N, Yang XQ, Zhang WY, Chen J, Yang XY, et al. Subthreshold depression is associated with impaired resting-state functional connectivity of the cognitive control network. *Transl Psychiatry*. 2015; 5:e683.

61. Reed E, Ji L, Beeghly M, Majbri A, Bhatia T, Duffy M, et al. Fetal functional connectivity: Examining the role of prenatal maternal depression symptoms using graph theory. *Dev Cogn Neurosci*. 2025; 74:101585.

62. Lynch CJ, Elbau IG, Ng T, Ayaz A, Zhu S, Wolk D, et al. Frontostriatal salience network expansion in individuals in depression. *Nature.* 2024; 633:624–633.

63. Wu CL, Lu TH, Chang WH, Wang TY, Tseng HH, Yang YK, et al. Role of the insula in rTMS response for depression. *J Affect Disord*. 2025; 370:538–546.

Tables

Table 1. Significant differences in brain activity between control participants and the depression continuum during encoding of new information.

Region	MNI coordinate (x,y,z)	Cluster size	SDM-Z	*p*-value	Direction	Hedges' g
Right thalamus/Right caudate	14,-6,14	126	-3.722	<.001	control > depression	-.449
Right insula	38,16,-4	124	-3.601	<.001	control > depression	-.420
Right precentral gyrus	30,-6,56	96	-3.615	<.001	control > depression	-.436
Left insula	-40,-14,4	40	-3.033	.001	control > depression	-.359
Left superior frontal gyrus	-2,46,-6	20	-2.841	.002	control > depression	-.349
Left inferior parietal lobe	-30,-58,42	14	-2.865	.002	control > depression	-.314

Abbreviations: MNI = Montreal Neurological Institute, SDM-Z = Seed based d mapping z value.

Table 2. Significant differences in brain activity between control participants and the depression continuum during retrieval of non-autobiographical memories.

Region	**MNI coordinate (x,y,z)**	**Cluster size**	**SDM-Z**	***p*-value**	**Direction**	**Hedges' g**
Right inferior frontal gyrus	48,28,24	47	3.086	.001	depression > control	.474

Abbreviations: MNI = Montreal Neurological Institute, SDM-Z = Seed based d mapping z value.

Table 3. Significant differences in brain activity between control participants and the depression continuum during autobiographical retrieval.

Region	MNI coordinate (x,y,z)	Cluster size	SDM-Z	*p*-value	Direction	Hedges'g
Left anterior cingulate	0,22,30	276	4.116	<.001	depression > control	0.539
Left middle frontal gyrus	-28,18,54	33	3.084	.001	depression > control	0.454
Right insula	36,10,4	122	-3.330	<.001	control > depression	-0.470
Right fusiform gyrus	26,-44,-12	46	-3.194	<.001	control > depression	-0.405

Abbreviations: MNI = Montreal Neurological Institute, SDM-Z = Seed based d mapping z value.

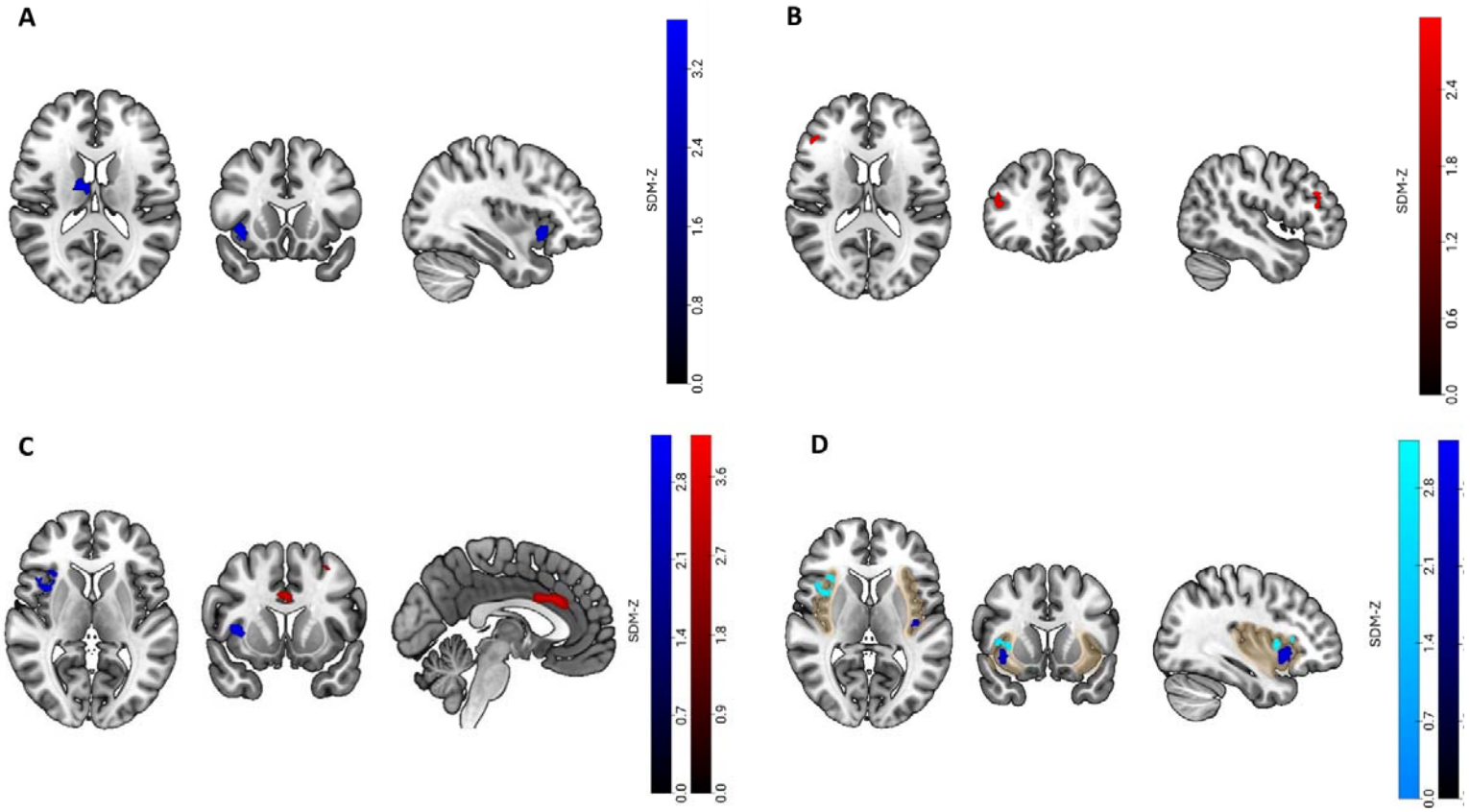



Figure 2. Functional brain activity differences in individuals across the depression continuum compared to control participants during (A) encoding of new information, (B) non-autobiographical memory retrieval, or (C) autobiographical memory retrieval. (D) Conjunction of adjacent clusters in the right insula during encoding (dark blue) and autobiographical retrieval (light blue). The statistical threshold was set at $p < .005$, uncorrected, with a minimum cluster extent of 10 voxels. Colour bars represent Seed based d Mapping z-values. Red denotes increased activity in depression, blue reduced activity.