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The Effects of Late-Onset Depression on Brain Activity During an Episodic Memory Task

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ABSTRACT

Introduction: Late-onset depression (LOD) has been implicated in irreversible cognitive decline, potentially mirroring early Alzheimer's Disease (AD) pathology. This study aimed to investigate brain activity differences during an episodic memory (EM) task in LOD patients compared to healthy controls (HC).

Methods: We recruited 15 LOD patients and 13 HC matched for age and gender. Participants completed a face-name association task during functional magnetic resonance imaging (fMRI) focusing on both the encoding and retrieval phases of EM.

Results: The statistical contrast between the groups revealed that the HC group showed increased activity in the left visual association cortex (VAC) and left caudate compared to the LOD group during the encoding task. During the face recognition task, the HC group showed increased activity in the right caudate, and during the name recognition task, they showed increased activity in the right frontal eye field (FEF) compared to the LOD group.

Conclusion: The differences observed between the HC and LOD groups in the VAC, caudate, and FEF suggest early changes in maintaining attention, goal-directed learning, EM formation, and coordination of information from storage to retrieval before apparent impairment develops in LOD. Although we did not find statistically significant activations in areas linked to increased vulnerability to AD, our findings of hypoactivation in regions responsible for visual processing and attentional orienting in LOD patients are consistent with hypoactivation patterns observed in AD patients in previous research. These results enhance our understanding of the neural mechanisms underlying memory impairments in LOD and their potential overlap with AD pathology.

Keywords: Alzheimer's Disease, cognitive dysfunction, episodic memory, face-name association, late-onset depression, task-based fMRI

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INTRODUCTION

Major depressive disorder (MDD) is a significant global health concern, ranked as the third leading cause of disease burden worldwide in 2008 by the World Health Organization (WHO) and projected to become the leading cause by 2030 (1). Late-onset depression (LOD), a common subtype of MDD, is often underdiagnosed due to the variability in its definition (different age cut-offs), atypical presentation with prominent somatic complaints and less affective disturbance, and sometimes mistakenly perceived as a normal part of aging (2,3). A missed diagnosis of LOD can lead to a worse prognosis, increased risk of recurrence and disability, and higher fatality rates in suicidal attempts compared to early-onset depression patients (3). Another critical and catastrophic challenge associated with LOD is that, along with the organic changes

Highlights

- **Reduced caudate activity in LOD may signal early encoding and retrieval issues.**
- **Decreased VAC and FEF activity in LOD suggests visual and attentional differences.**
- **Episodic memory tasks may clarify the relationship between LOD and AD.**

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that occur with old age, cognitive dysfunction is more prominent and, to some degree, irreversible (2). This issue has sparked an ongoing debate about whether LOD could be associated with dementia (4). Considering the increasing life expectancy and the fact that aging is the most significant known risk factor for Alzheimer's disease (AD) (5), the most common cause of dementia, it is important to identify the risk factors to diagnose and treat individuals before they develop AD (6). Thus, studies are being conducted to elucidate the association between these two conditions.

While some epidemiological data suggest depression as a risk factor, others propose depression as a progressive prodromal symptom of dementia due to shared neuropathologic processes. In their analysis, Aziz & Steffens (2017) found that late-life depressive symptoms were more predictive of dementia than early-life depressive symptoms. However, in some studies, depression has either a minimal impact on dementia (7) or does not elevate the risk of its development (8). These inconsistencies are thought to be due to the complexity and heterogeneity of the disease, as well as the different methodologies used in these studies (9).

Recent research evidence suggests that LOD contributes to AD pathology through several biological mechanisms, including dysfunction in the hypothalamic-pituitary-adrenal (HPA) axis leading to hippocampal atrophy and ischemia of frontostriatal pathways, increased deposition of β-amyloid plaques, and deficits in neuronal growth factors. These mechanisms are thought to decrease brain reserve and act as both a prodrome and a risk factor by increasing vulnerability to dementia (9).

In structural magnetic resonance imaging (MRI) studies of LOD, decreased cortical thickness in the inferior frontal lobe, hippocampus, superior, inferior temporal, and fusiform gyrus, cingulate cortex, and precuneus is associated with both cognitive dysfunction and AD pathology (10,11). According to Invernizzi et al. (2021), these structural changes could explain decreased episodic memory (EM) performance, which is an important symptom of LOD and the earliest cognitive deficit in AD.

Functional magnetic resonance imaging (fMRI) is a prominent method for identifying abnormal brain activations before structural abnormalities become evident. Most task-based fMRI studies focusing on EM functions in AD patients have consistently revealed hypoactivation in the medial temporal lobe (MTL) during both the encoding and retrieval phases (12). Additionally, some studies have identified compensatory hyperactivation in the prefrontal and cingulate cortices (13,14). In their review, McDonough et al. (2020) investigated the impacts of AD risk factors on brain activation in the elderly. Even though Rashidi-Ranjar et al. (2020) only looked up late-life depression (LLD) and AD, they both reached the same conclusion that LLD patients exhibit hypoactivation in the hippocampus, parahippocampal gyrus, insula, and cingulate cortex, along with hyperactivation in the left inferior frontal gyrus, resembling the pattern of activations seen in Alzheimer's patients during encoding.

Despite recent advancements, earlier studies had limitations when clarifying the association between LOD and AD. These include failure to separate LOD patients from those with early onset within the LLD group, not scanning LOD patients during both encoding and retrieval phases, potentially yielding different activation patterns, and inadequate matching of patients and controls for age. Furthermore, the scarcity of task-based fMRI studies in this context represents an additional limitation in the existing literature. These emphasize the need for more comprehensive studies to understand better the neural correlates of LOD and its implications for cognitive function and dementia risk.

To address this gap, we conducted a task-based fMRI study focusing on both the encoding and retrieval phase of EM to reveal the effect of LOD on brain activation compared to a healthy control (HC) group. We focused on LOD patients with reduced baseline symptoms to minimize the potential confounding effects of severe depression on fMRI task performance. This approach allows us to evaluate ongoing neural alterations associated with LOD, reflecting the chronic nature of the condition and the possibility of continued brain changes even in the absence of severe symptoms. We used a face-name association task that measures associative memory sensitive to early stages of AD (15). We aimed to determine whether the activation patterns observed in the LOD group would be different from the HC group. We hypothesized that there would be activation differences between the groups during the memory task, especially in the core or extended system structures defined by Gobbini & Haxby (2007) and the activation patterns found in the LOD group would be similar to those reported in AD.

METHODS

Participants

Thirty-three participants (16 LOD, 17 HC) were recruited through psychiatry outpatient clinics and community advertisements. One participant from the LOD group was excluded after being assessed with mild cognitive impairment through psychiatric examination and the Clinical Dementia Rating (CDR). From the HC group, one participant was excluded due to a history of head trauma with loss of consciousness, two participants were excluded due to misapplying the instructions during the fMRI scanning, and one participant was excluded due to excessive head motion during scanning. Finally, there were 15 participants (11 female, 4 male) in the LOD group and 13 participants (10 female, 3 male) in the control group. The research was approved by the Ege University Faculty of Medicine Medical Research Ethics Committee (no: 14-12.1/8), and all participants gave their written informed consent.

The inclusion criteria for both groups:

1) being between 45–75 years old,

2) completing at least five years of education,

3) having no history or symptoms of dementia or neurodegenerative disorders,

4) having a null score in CDR,

5) having a Mini-Mental State Examination (MMSE) score above 24.

In addition,

The inclusion criteria for the LOD group are:

1) being diagnosed with MDD defined by DSM IV criteria,

2) being at least 45 years old at the onset,

3) reduction of baseline symptoms ≥50 percent through antidepressants,

4) having a the 17-item Hamilton Depression Rating Scale (HDRS17) score below 16.

The additional inclusion criteria for the HC group:

1) having no MDD diagnosis defined by DSM IV criteria,

2) having a HDRS17 score below 7.

The exclusion criteria for both groups are:

1) a head trauma history with loss of consciousness of more than 3 min,

2) uncontrolled chronic diseases (diabetes, hypertension, etc.),

3) anomalies in structural and functional MRI images,

4) having an Axis I diagnosis other than MDD,

5) contraindications regarding MRI scanning.

All patients and controls were clinically examined by one of our colleagues using the Structured Clinical Interview for DSM (SCID-I). After evaluation, participants who met the inclusion criteria were invited for MRI scanning.

fMRI Task Procedure

Using a block design, the fMRI task consisted of a single session, including a resting state and three memory-related subtasks (Fig. 1). Participants were shown an equal number of unfamiliar faces of both genders and various age groups from the FACES dataset (16), with names selected from the ten-year statistics of the T. C. Ministry of Interior, General Directorate of Population and Citizenship Affairs between 1923 and 2010.

The session began with the encoding task, lasting 288 seconds, comprising alternating 30-second fixation blocks and 42-second encoding blocks. During each encoding block, participants viewed a face-name pair for 6 seconds, followed by 1 second of a black screen, and were asked to remember the face-name association. To ensure they were actively attending to the stimuli, they also indicated the gender of the face by pressing the button. In total, 24 faces were shown.

After a 5-minute resting state with eyes closed, the face-recognition task started, lasting 228 seconds with alternating 15-second fixation blocks and 42-second face-recognition blocks. Participants viewed a face for 6 seconds with "familiar" and "unfamiliar" options, followed by 1 second of a black screen, and were asked to select the appropriate response by pressing the button. Half of the 24 faces shown were from the encoding task.

The session concluded with the name-recognition task, which was also 228 seconds long and followed the same block structure as the face-recognition task. Participants viewed a face with two names below it for 6 seconds, followed by 1 second of a black screen, and were asked to select the correct name by pressing the button. In total, 24 faces were shown.

MRI Acquisition

MRI scanning was performed by a Siemens Magnetom Verio, Numaris/4, Syngo MR B17 MR scanner with a 12-channel head coil (Erlangen, Germany) in 3 Tesla MR unit. T1-weighted images (TR: 1600 ms; TE: 2.21 ms; slice thickness: 1 mm; voxel size: 1×1×1 mm; FOV: 256 mm; matrix: 256×256) were acquired for structural images; T2-weighted Echo-planar imaging (EPI) sequence were acquired (36 slices; TR: 3000 ms; TE: 30 ms; slice thickness: 3 mm; voxel size: 3×3×3 mm; FOV: 192 mm; matrix: 64×64) for functional images.

Preprocessing of fMRI Data

The fMRI data preprocessing and analysis were performed using Statistical Parametric Mapping 12 (SPM12, Wellcome Trust Centre for Human Neuroimaging, London, UK) running under Matlab (MathWorks, Inc). The standard preprocessing steps were applied to the images before statistical analysis (realignment, slice-timing, co-registration, segmentation, normalisation, smoothing with a 8 mm full-width half-maximum Gaussian kernel). In the spatial normalisation step, even though MNI brain template images are widely used, it is recognised that their application may inadequately compensate for brain region discrepancies in special populations, such as older adults (17). Thus, a template specific to these participants was created using the Dartel toolbox (18) to yield optimized results. Then, normalisation was applied to bring the images of all participants into the generated template image. Global Signal Regression (GSR) was not applied, as its use remains debated due to concerns that it may remove meaningful neural signals along with noise, and its effects can vary across groups. For these reasons, we chose not to use GSR in this study.

Statistical Analysis

Data analysis of fMRI images was performed using the General Linear Model (GLM) in SPM12. First-level analysis was conducted to identify individual brain activity during the task. Each participant's head motion parameters were included as regressors in the GLM. Additionally, a high-pass filter (128 s cutoff) was applied to remove low-frequency signal drifts. Three contrasts were defined to compare different conditions: Encoding-Baseline, Face-Baseline, and Name-Baseline. The Encoding-Baseline contrast compares brain activity during the encoding task to the baseline fixation period, while the Face-Baseline and Name-Baseline contrasts serve similar purposes for the face-recognition and name-recognition tasks. In the second-level analysis, a two-sample t-test was used, with age and gender included as covariates to identify differences between the groups. The significance level was set to 0.05 family-wise error (FWE) corrected for group activation and set to 0.001 for group comparison.

Demographic variables, neuropsychological scores, head motion parameters and behavioural data were analysed using Statistical Package for the Social Sciences (IBM Statistical Package for Social Sciences (SPSS) program version 25). Head motion was assessed using mean framewise displacement (FD) calculated from the six motion parameters obtained during preprocessing. Mean FD values were compared between groups. Because of the small sample size in each group, a nonparametric statistical test (Mann-Whitney U test) was used for group comparison.

Sample size calculations were conducted using the G*Power 3.1 software for an independent two-sample t-test. The parameters used

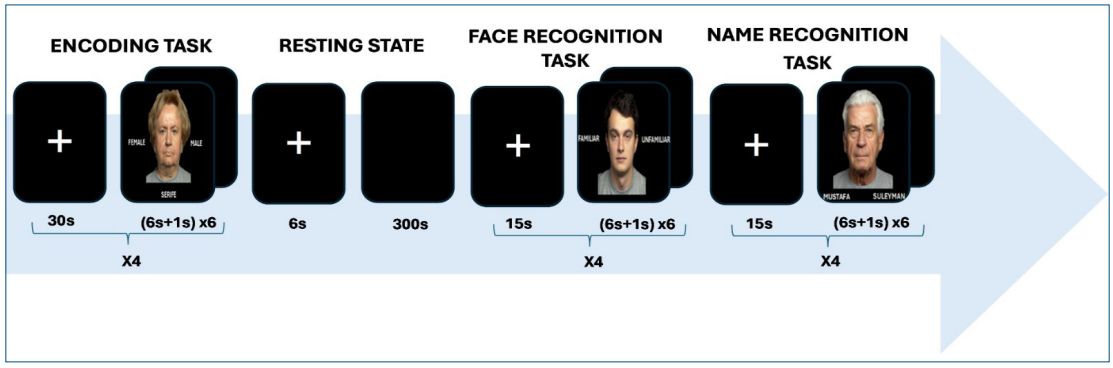

Figure 1. fMRI task design.

for determining the sample size included Cohen's d=0.8 (large effect size), α=0.05 (type I error rate), and 1-β=0.80 (power). Based on these parameters, the required minimum sample size for each group was calculated to be 26. Consequently, our study included two groups (patient and healthy control), each consisting of at least 13 participants as required.

RESULTS

Demographic Variables and Neuropsychological Assessment

The demographic variables and psychometric assessment scores of both groups are shown in Table 1. As expected, the LOD group had significantly higher HDRS17 scores compared to the HC group (z=4.09; p<0.001). There were no significant differences between the groups in age (z=0.60; p=0.548) and MMSE scores (z=1.43; p=0.152). Additionally, the mean FD analysis indicated no significant differences in head motion between the groups (z=-0.83, p=0.46), suggesting that motion artifacts are unlikely to confound the fMRI results.

Behavioural Performances

There was no difference between the groups in the accuracy of the encoding (z=0.78; p=0.435), face-recognition (z=0.72; p=0.471), and name-recognition tasks (z=0.11; p=0.908) (Table 2).

fMRI Results

In this section, we will focus on between-group results, while group activation results are available in the supplements.

The statistical contrast between the groups revealed that the HC group showed increased activity in the left visual association cortex and left caudate compared to the LOD group during the encoding task. During the face recognition task, the HC group showed increased activity in the right caudate and during the name recognition task, they showed increased activity in the right frontal eye field compared to the LOD group (Fig.s 2–4) (Table 3).

DISCUSSION

This study aimed to investigate the impact of LOD on brain activity during an EM task among the elderly and to explore possible associations and resemblances with AD. Contrary to our first hypothesis, the LOD group didn't show prominent differences in core or extended system structures compared to HC group. However, direct between-group comparisons revealed subtle distinctions in the left visual association cortex (VAC) and left caudate during encoding, in the right caudate during face recognition, and in the frontal eye field (FEF) during name recognition subtasks. Our second hypothesis was also not confirmed, which proposed that the LOD group would show activation differences in regions affected early by AD neuropathology. The earliest affected areas by AD neuropathology mentioned by McDonough et al. (2020) and Hantke et al. (2013) include the MTL, frontal cortex, posterior cingulate, and lateral posterior temporoparietal regions. However, the hypoactivation observed in the VAC and FEF in the LOD group might indicate reduced visual processing and attentional orienting. These findings align with those of Li et al. (2015), who demonstrated hypoactivation in the visual and dorsal attention networks in mild cognitive impairment (MCI) patients, with a greater percentage of hypoactivation in AD patients than in the control group. These results extend previous findings by focusing specifically on LOD patients rather than LLD patients and providing more details by analysing each different phase of EM separately.

Our behavioural performance results showed that accuracy rates decreased as task difficulty increased for both groups. Within the LOD group, familiarity was preserved compared to recollection, aligning with previous findings (19).

Within-group activations revealed patterns consistent with previous studies using similar face-name association tasks. In the HC group, the encoding task activated the right fusiform gyrus, inferior frontal gyrus, insula, temporal cortex, hippocampus, precentral gyrus, middle temporal gyrus, and cerebellum (20–24). In the LOD group, similar regions were activated, including additional activation in the dorsolateral prefrontal cortex and cingulate cortex (23,24). During the face-recognition task, the fusiform gyrus, inferior frontal cortex, superior parietal lobule, insula, supplementary motor area, and left pallidum were active (22). For the name-recognition task, activations included the lingual gyrus, prefrontal cortex, hippocampus, left insula, and premotor cortex (22,25,26). These activations, consistent with the literature, confirm the effectiveness of our experimental design and the reliability of our results. Detailed within-group activation results can be found in Supplementary Table 1 and 2.

Table 1. Demographic characteristics and neuropsychological test scores of the groups

	LOD group (N: 15) mean ± SD	HC group (N: 13) mean ± SD	z-score	p-value
Age	56.27±5.31	54.54±4.46	0.60	0.548
HDRS17	4.40±3.31	0.31±0.75	4.09	<0.001
MMSE	27.47±2.13	28.62±1.44	1.43	0.152
FD	0.27±0.03	0.30±0.03	-0.83	0.46

FD: framewise displacement; HC: healthy control; HDRS17: the 17-item Hamilton depression rating scale; LOD: late-onset depression; MMSE: mini-mental state examination.

Table 2. Means and comparisons of tasks accuracy in the groups

fMRI task	LOD group (N: 15) (mean ± SD)	HC group (N: 13) (mean ± SD)	z-score	p-value
Encoding accuracy	20.13±8.36	20.23±8.98	0.78	0.435
Face-recognition accuracy	15.47±6.64	14.00±6.90	0.72	0.471
Name-recognition accuracy	11.47±5.08	11.69±5.79	0.11	0.908

HC: healthy control; LOD: late-onset depression.

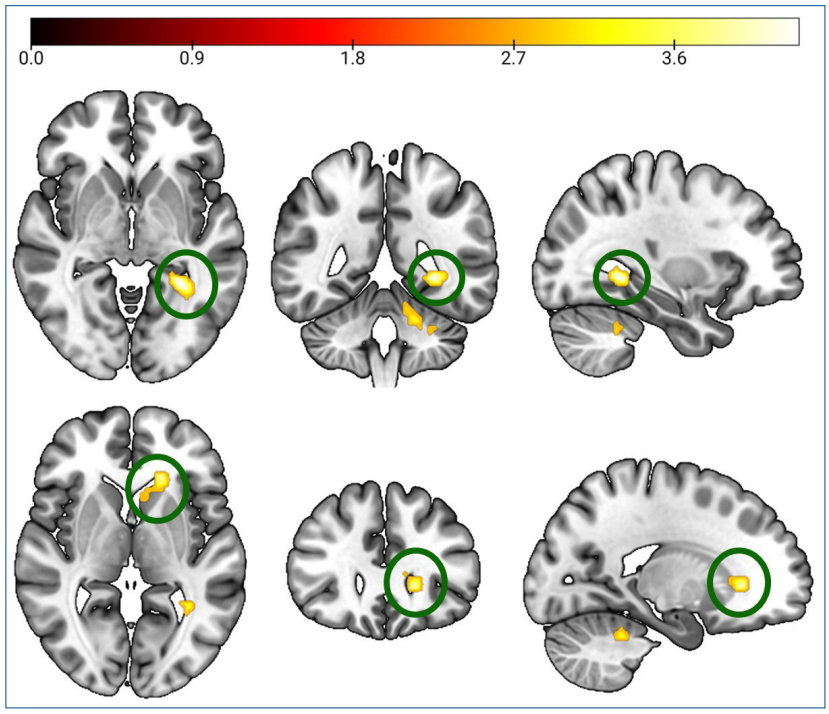

Figure 2. Increased brain activity of the HC group compared to the LOD group during encoding task. (The upper row of brain sections shows increased activation in the left visual association cortex with a voxel size of 20, MNI coordinates of -30, -45, -3, and a t-value of 4.36, while the lower row shows increased activation in the left caudate with a voxel size of 13, MNI coordinates of -18, 27, 3, and a t-value of 4.06. Activations are displayed with an uncorrected threshold of p <0.005 at the voxel level for better visualization).

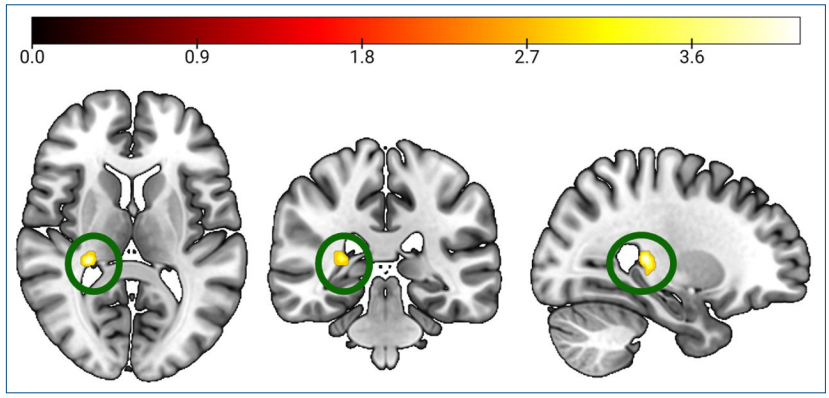

Figure 3. Increased brain activity of the HC group compared to the LOD group during face-recognition task. (Increased activation in the right caudate is observed with a voxel size of 13, MNI coordinates of 27, -33, 9, and a t-value of 4.30. Activations are displayed with an uncorrected threshold of p <0.005 at the voxel level for better visualization).

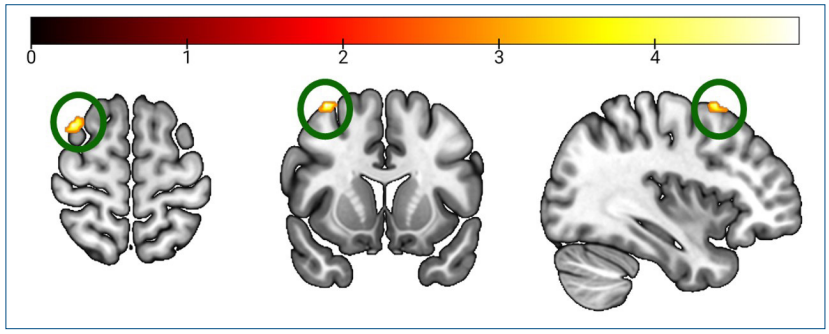

Figure 4. Increased brain activity of the HC group compared to the LOD group during name-recognition task. (Increased activation in the right frontal eye field is observed with a voxel size of 10, MNI coordinates of 36, 12, 63, and a t-value of 5.43. Activations are displayed with an uncorrected threshold of p <0.005 at the voxel level for better visualization).

Table 3. Brain regions exhibiting increased activation during tasks

Region	Voxel	MNI coordinates			t-value
		x	y	z	
Encoding task, HC > LOD					
Left visual association cortex	20	-30	-45	-3	4.36
Left caudate	13	-18	27	3	4.06
Face-recognition task, HC > LOD					
Right caudate	13	27	-33	9	4.30
Name-recognition task, HC > LOD					
Right frontal eye field	10	36	12	63	5.43

HC: healthy control; LOD: late-onset depression; MNI: Montreal neurological institute.

Between-group activations showed subtle distinctions potentially due to the small number of participants per group. During the encoding task, the HC group showed increased left anterior caudate activity, while right posterior caudate activity was increased during the face recognition task compared to the LOD group. Different regions of the caudate display distinct functions. The anterior caudate is involved in executive functioning, whereas the posterior caudate is associated with working memory and helps process visual information (27,28). Additionally, data suggest that different groups of neurons in the anterior caudate guide short-term memory of object values, while those in the posterior caudate guide long-term memory (29). Previous studies also revealed that the caudate, in connection with the hippocampus, supports goal-directed learning and EM formation and the temporal coordination of information from storage to retrieval (30). Furthermore, studies have shown that degeneration of the caudate is linked to EM deficits (31), and smaller volumes of the right anterior caudate in depression patients are associated with diminished learning and memory (32). Considering the caudate's role in depression pathology and these findings, hypoactivation of the caudate in the LOD group compared to the HC might indicate early signals of both encoding and retrieval dysfunction.

The VAC plays a crucial role in integrating visual stimuli with attentional processes, enabling effective memory encoding (33). By processing perceptual and semantic features, the VAC facilitates the formation of stable memory traces, particularly in tasks requiring complex associations. In our study, the LOD group exhibited left VAC hypoactivation during encoding, suggesting reduced engagement of visual processing regions, which may impair the encoding of face-name associations. As part of the extrastriate cortex, the VAC interacts with multiple cortical regions during encoding, particularly the MTL and frontoparietal attention network. The MTL, including the hippocampus and parahippocampal cortex, plays a critical role in episodic memory formation, while top-down modulation from the frontal and parietal regions ensures selective attention to relevant stimuli (34,35). Disruptions in these interactions have been observed in MDD, with studies reporting weakened functional connectivity between the VAC and memory-related structures (36). The observed VAC hypoactivation in LOD may therefore reflect a broader network dysfunction rather than an isolated visual processing deficit. Additionally, depression is frequently associated with impairments in visual perception and attention, which may be linked to VAC dysfunction. Studies suggest that individuals with depression exhibit slower visual processing, abnormal neural filtering of irrelevant information, occipital brain perfusion deficits, and attentional biases (36). Given the VAC's role in integrating visual input with attentional control, its hypoactivation in LOD may contribute not only to memory deficits but also to the broader cognitive impairments observed in these patients (37).

Frontal eye field facilitates memory retrieval by regulating eye movements, shifting attention, and guiding visual search strategies (38,39). In our study, the LOD group displayed right FEF hypoactivation during retrieval, suggesting a reduced ability to efficiently direct attentional resources toward stored information. Dysfunction of the FEF, a key region of the dorsal attention network (DAN), has been linked to attentional control deficits in depression. Moreover, studies have reported impairments in oculomotor control, including unstable fixation, slower saccadic responses, and difficulties in gaze modulation (40). Additionally, excessive activity in the default mode network (DMN) in depression may interfere with the reciprocal antagonism between the DMN and DAN, leading to reduced FEF activation during retrieval (41). Since the DAN facilitates top-down attentional control and is positively coupled with visual regions, its suppression may weaken attentional allocation, impairing memory search. Furthermore, the frontoparietal control network (FPCN), which regulates the balance between the DMN and DAN, may fail to appropriately shift network engagement based on task demands, exacerbating retrieval deficits in LOD (41). Given that successful memory retrieval requires both internal memory search and external visual scanning, FEF hypoactivation may contribute to inefficient recall by limiting the ability to reorient attention toward relevant memory representations.

One of our hypotheses was that LOD patients would show activation patterns similar to those in AD. Studies have reported altered activations during EM tasks in AD, MCI, and asymptomatic individuals with AD risk factors, particularly in regions such as the MTL, frontal cortex, posterior cingulate, and inferior parietal cortices. While these studies reported varying activation changes (42,43), we did not identify similar differences. However, our findings of hypoactivation in the VAC and FEF in the LOD group align with recent meta-analyses showing hypoactivation in visual and dorsal attention networks in MCI patients (44). These findings suggest reduced visual processing and attentional orienting in LOD patients, similar to what is observed in AD.

The current study had several limitations. The sample size in this study was determined based on calculations using the G*Power 3.1 software. Utilising parameters of Cohen's d=0.8 (large effect size), α=0.05, and 1-β=0.80, the minimum required sample size for each group was found to be 26 participants. Although our target was to include 17 participants per group, our study was completed with two groups consisting of 15 and 13 participants. Nevertheless, this is still above the required minimum of 13 participants per group and is adequate to demonstrate the relationship. Moreover, future research should include larger and more diverse samples to verify these findings and enhance the generalisability of the results. Additionally, antidepressant therapy usage by patients may confound the group differences, as previous studies have shown that EM could be influenced by antidepressants (45). Moreover, we did not include patients unresponsive to antidepressants, which may limit the applicability of our findings to all LOD patients. In this study, we used a block design. While this design helps to increase the power of detecting activation patterns, it averages responses across trials, which can obscure differences between correct and incorrect responses (46). Despite this, the EM task was chosen because it is the first cognitive function to be impaired in AD and affected in LOD. Although Hantke et al. (2013) suggest that semantic memory (SM) tasks might offer certain advantages, such as being easier to use across different age groups and potentially detecting early AD pathology, the EM task remains highly relevant. Future studies incorporating various task designs could provide additional insights.

In conclusion, this study contributes to the growing body of evidence on LOD's impact on cognitive decline and its possible association with AD. While we initially hypothesized that LOD patients would exhibit activation patterns resembling those seen in AD, our findings did not fully support this across all regions. However, the observed hypoactivation in the VAC and FEF in LOD aligns with studies showing similar deficits in visual and attentional networks in MCI and AD, suggesting a potential functional overlap in these domains. Despite these similarities and overlapping cognitive symptoms, LOD and AD may involve key differences. Whereas AD is primarily characterized by MTL neurodegeneration, LOD appears to involve network-level dysfunctions (11). Moreover, the absence of significant hippocampal hypoactivation in our study suggests that memory deficits in LOD may stem more from impaired attentional control and sensory integration than from primary episodic memory dysfunction. These findings deepen our understanding of the neural mechanisms underlying memory impairments in LOD and their potential overlap with AD pathology, particularly in terms of disrupted attentional and visual

processing networks. They also highlight the importance of future research in determining how these dysfunctions contribute to cognitive decline and whether they increase vulnerability to AD-related changes over time.

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SUPPLEMENTARY

https://www.noropsikiyatriarsivi.com/uploads/NPA_28903_EN_SUPPL.pdf

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