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Neural processing of emotional stimuli before and after cognitive behavioural therapy for insomnia

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ABSTRACT

Background: Previous research has suggested an association between insomnia disorder (ID) and alterations in emotion processing. Therefore, it is crucial to investigate neurobiological changes in emotion processing in patients with ID before and after Cognitive Behavioral Therapy for Insomnia (CBT-I) and to compare them with healthy controls (HC) with task-based functional magnetic resonance imaging (fMRI).
Methods: 20 patients with ID and 20 HC were included in this study to view five different blocks of pictures with varying emotional arousal, valence, and content (sleep-relatedness) in the fMRI scanner.
Results: A significant Group × Session interaction was identified in the amygdala for both the sleep-related negative contrast ($F(1,38) = 4.19$, $p = .048$) and the neutral moderate contrast ($F(1,38) = 5.39$, $p = .026$). Post-hoc tests revealed that patients with ID had a significantly higher average amygdala reactivity to sleep-related stimuli at T0, whereas no significant difference was observed between the groups at T1. However, the analysis of Intraclass Correlation Coefficients (ICC) in the control group suggests a very low retest reliability across all fMRI measures.
Conclusions: CBT-I may normalise amygdala responses to sleep-related negative stimuli, which may reflect a shift toward improved emotional processing. However, the very low retest reliability of fMRI measures warrants cautious interpretation of these results.

1. Introduction

Insomnia disorder (ID) is a prevalent and costly condition associated with substantial personal, societal, and public health consequences [1]. It frequently co-occurs with depression [2] and anxiety disorders [3,4], suggesting that disrupted sleep in ID may contribute to emotion-related alterations. Evidence supporting this idea comes from self-report and physiological research showing that poor sleep quality is linked to heightened negative and reduced positive emotions [5–7]. Recent work has also examined the role of stimulus content in emotional processing among individuals with ID. Findings from this line of research indicate that patients with ID exhibit heightened behavioural and physiological reactivity to sleep-related stimuli [5,8–11]. This increased sensitivity to sleep-related information may reflect an elevated perception of threat associated with poor sleep [12–15].

Given its critical role in emotional processing, the amygdala has been a primary focus of neurobiologically oriented research in ID. For example, a number of resting-state functional magnetic resonance imaging (fMRI) studies have demonstrated altered functional connectivity between the amygdala and various brain regions in individuals with ID

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[16–18], a result that parallels findings in depression and anxiety disorders [19–21]. A more direct approach to investigate the link between amygdala function and emotion processing is to use emotional stimuli during fMRI [22]. Recurrent cortical hyperarousal and sleep fragmentation, as well as abnormal amygdala reactivity during REM sleep, may be driven by hyperactivation or insufficient suppression of the noradrenergic system involved in emotional memory consolidation [22] and a recent study showed increased amygdala activation in patients with ID when viewing negative facial expressions [23]. In addition, several studies used sleep-related emotional images during fMRI recordings [10, 24]. For example, patients with ID exhibited greater amygdala activation in response to insomnia-related stimuli than healthy controls [9].

However, previous neuroimaging investigations may have been underpowered to detect realistic effect sizes in comparisons between patients with ID and healthy good sleepers. To overcome this limitation, the present study implemented a within-subject design, assessing patients with ID both before and after cognitive behavioural therapy for insomnia (CBT-I), the first-line intervention for ID. This design confers greater statistical power and permits a more precise delineation of the neural correlates of emotion processing associated with ID. In this study, five categories of emotional pictures were employed as experimental stimuli to elucidate the amygdala reactivity underlying emotion processing in ID. Patients with ID underwent fMRI assessments at baseline and following four bi-weekly CBT-I sessions. This within-subject longitudinal design enabled the examination of neurobiological changes in emotional reactivity associated with therapeutic improvement. In addition, healthy good sleepers were assessed at both time points as a control cohort to facilitate between-group comparisons and to delineate the disorder-specific neural alterations linked to ID.

2. Methods

2.1. Participants

Twenty-three patients with ID and 21 healthy controls (HC) were recruited in the study, with groups matched for age and sex. All participants were between 18 and 65 years of age. Patients with ID met research diagnostic criteria for ID according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). All participants underwent a structured clinical interview to assess eligibility. Participants meeting any of the following exclusion criteria were excluded: (1) use of sleep medication within two weeks prior to and during study participation; (2) suicidality; (3) psychiatric conditions requiring immediate treatment; (4) alcohol, medication, or illicit substance abuse or dependence within the past year; (5) psychotherapy within the past three years; (6) unstable or progressive medical conditions; (7) acute pain or poorly managed chronic pain temporally linked to insomnia symptoms; (8) intellectual disability; (9) history of brain injury; (10) pregnancy or lactation; (11) contraindications for MRI; (12) insufficient fluency in German to complete the study protocol. Additionally, patients with ID were excluded if they had the presence of sleep disorders other than ID. This study was conducted in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Medical Center – University of Freiburg, and the study was registered in the German Clinical Trials Register (https://drks.de/search/en/trial/DRKS00018839). Based on the preregistered analysis plan, the current analyses focused on amygdala reactivity. Specifically, we tested the preregistered hypothesis that patients would show decreased amygdala reactivity to sleep-related stimuli after CBT-I. All participants provided written informed consent and received financial compensation for their participation.

2.2. Intervention

CBT-I was delivered in person at the Medical Center – University of Freiburg by psychotherapy trainees under the supervision of a specialist in behavioural sleep medicine. The intervention comprised four individual sessions, each lasting 50 min. The manualised CBT-I protocol included psychoeducation, relaxation training, sleep restriction therapy, stimulus control therapy, and cognitive therapy. For sleep restriction therapy, the initial sleep window was determined based on the patient's average sleep duration during the previous week, as recorded in sleep diaries. The placement of the sleep window was adapted to patient preference, with a minimum allowable time in bed of 4.5 h. Adjustments were made weekly: time in bed was increased by 30 min when sleep efficiency exceeded 90%, reduced by 30 min when it fell below 80%, and kept unchanged when it ranged between 80% and 90%. Stimulus control therapy followed Bootzin's standard protocol [25]. Progressive muscle relaxation was employed as the relaxation technique [26]. Cognitive therapy consisted of cognitive restructuring and the "constructive worry" method [27].

2.3. Questionnaires

To characterise the two groups at baseline (T0) and post-treatment (T1), participants completed the following self-report questionnaires: (1) the Insomnia Severity Index (ISI) [28], assessing insomnia severity over the preceding two weeks; (2) the Pittsburgh Sleep Quality Index (PSQI) [29], measuring sleep quality and disturbances over the past month; (3) the Ford Insomnia Response to Stress Test (FIRST) [30], evaluating sleep vulnerability under stressful conditions; (4) the Pre-Sleep Arousal Scale (PSAS) [31], assessing physiological and cognitive arousal before sleep; (5) the Glasgow Sleep Effort Scale (GSES) [32], a measure of sleep effort; (6) the Dysfunctional Beliefs and Attitudes about Sleep Scale (DBAS) [33], an instrument assessing beliefs, attitudes, and expectations about sleep and insomnia; (7) the Epworth Sleepiness Scale (ESS) [34], an instrument measuring daytime sleepiness; (8) the Beck Depression Inventory (BDI) [35], a widely used measure of depressive symptoms; and (9) the Beck Anxiety Inventory (BAI) [36], assessing anxiety levels.

2.4. fMRI emotional task

All participants underwent two MRI recording sessions (T0 and T1). For the ID group, brain MRI was acquired before and after the CBT-I intervention, whereas for the HC group, neuroimaging was obtained before and after a comparable time interval. During these sessions, all participants were instructed to view 80 pictorial stimuli presented in the MRI scanner using the Presentation software (https://www.neurobs.com/). The pictorial stimuli comprised the following categories: 10 insomnia-related negative stimuli with moderate arousal levels (sleep_neg_moderate; e.g., an individual in bed with an impatient expression suggestive of insomnia); 10 negative stimuli with high arousal levels (neg_high); 10 negative stimuli with moderate arousal levels (neg_moderate); 10 neutral stimuli with moderate arousal levels (ntrl_moderate); and 40 neutral stimuli with low arousal levels (ntrl_low) serving as the control condition. Here, the non-sleep pictorial stimuli were collected from the International Affective Picture System (IAPS) [37] and all the pictorial stimuli had been previously validated for valence and arousal [9]. The fMRI task followed a block design, with each block consisting of five stimuli from the same category (sleep_neg_moderate, neg_high, neg_moderate, ntrl_moderate, or ntrl_low). Each stimulus was presented for 5 s, yielding blocks with a total duration of 25 s. Blocks were presented in a randomised order, with the restriction that each ntrl_low block preceded a block from a different category. The experimental procedure is illustrated in Fig. 1.

2.5. MRI data acquisition

Functional and anatomical images were collected using a 3 T MRI scanner (Magnetom TIM-Trio, Siemens, Erlangen, Germany) at the Medical Center – University of Freiburg. Parameters for the T2*-

Fig. 1. The task employed a block design. Each block comprised five pictures from the same stimulus category, with each picture presented for 5 s. Blocks from the ntrl_low condition were always shown first, prior to any other block types. Apart from this constraint, the order of pictures within each block and the overall block sequence were randomised.

weighted echo-planar imaging (EPI) gradient-echo sequences were as follows: repetition time (TR) = 2.62 s; echo time (TE) = 30 ms; flip angle = 90°; field of view = 192 × 192 mm^2; number of slices = 42; voxel size = 3 × 3 × 3 mm^3. The total duration of the task was approximately 5 min. Following task-related image acquisition, T1-weighted structural images were obtained with the following parameters: TR = 2 s; TE = 0.4 ms; flip angle = 12°; field of view = 256 × 256 mm^2; voxel size = 1 × 1 × 1 mm^3.

2.6. Data analysis

Self-report data were analysed using R (version 4.5.1; https://www.r-project.org/). Missing questionnaire data at T1 (<2%) were imputed using the last-observation-carried-forward method. In addition, one HC participant did not complete the BAI at T0; therefore, this participant's BAI score at T1 was also excluded from the dataset.

MRI data was preprocessed and modelled by using Statistical Parametric Mapping 12 (SPM12, Wellcome Department of Cognitive Neurology, London, UK). Two patients with ID were excluded from the final analysis due to missing MRI data at T1. Preprocessing steps included slice-timing, realignment, co-registration, segmentation, normalisation and smoothing. After realignment, one patient with ID and one HC were excluded due to sustained movement (>3 mm translation or > 3° rotation together with framewise displacement (FD) > 0.3 mm in more than 20% of the volumes) during task periods. To control for head movement effects, FD was calculated for each time point. Time points with FD > 0.3 mm were flagged, and the corresponding regressors were included in the first-level general linear model (GLM) as nuisance covariates [38]. A full width at half maximum of 6 mm was chosen for smoothing.

GLM was used by the fMRI model specification function in SPM12. In the first-level GLM, the stimulus onset times were convolved with the canonical hemodynamic response function to predict the preprocessed brain signal. Six head movement parameters and the binary FD regressor for each participant were included as nuisance covariates to control for movement-related artefacts. In this step, four contrasts were calculated:

Contrast 1 = sleep_neg_moderate – ntrl_low = C1_sleep_neg_moderate; Contrast 2 = neg_high – ntrl_low = C2_neg_high; Contrast 3 = neg_moderate – ntrl_low = C3_neg_moderate; Contrast 4 = ntrl_moderate – ntrl_low = C4_ntrl_moderate.

Following the pre-registered protocol, the amygdala was selected as a region of interest (ROI) for the present analysis. For each participant, the left and right amygdala were segmented from individual T1-weighted structural images using FSL's FIRST (FMRIB's Integrated Registration and Segmentation Tool; labels 18 and 54). The left and right amygdala were combined for further analysis. For each participant, the mean β values within the resulting ROI were extracted for each contrast. These values were then used for second-level ROI analysis.

For the second-level analysis, one-sample t-tests for the four contrasts at T0 were conducted, ensuring the appropriateness of the data analysis pipeline. Then, mixed design factorial Group × Session ANOVAs were created for the four contrasts. Besides, following previous work [2,9] (Groups) × 2 (Contrasts) ANOVAs were conducted for arousal (C2_neg_high vs C3_neg_moderate), valence (C3_neg_moderate vs C4_ntrl_moderate) and content (C1_sleep_neg_moderate vs C3_neg_moderate) at T0. Finally, in order to test the reliability of the measurements, Intraclass Correlation Coefficients (ICCs) of mean β values in the amygdala across sessions were computed in the HC group for each contrast. ICC(1,1), derived from a one-way random-effects ANOVA model, was calculated as:

$$ICC(1,1) = \frac{(MS_B - MS_W)}{(MS_B + (k-1)MS_W)}$$

where MS_B and MS_W correspond to the between- and within-subject mean squares, respectively, and k represents the number of sessions. In addition, exploratory whole-brain analyses were also performed for each contrast to identify treatment-related changes in neural activation. In the whole brain Group × Session mixed ANOVA, the statistical threshold was set at an uncorrected $p < .001$ at the voxel level and at $p < .05$ at the cluster level, FWE corrected. For brain regions exhibiting significant main or interaction effects, the average signal across all voxels within each region was extracted for each participant. Post-hoc comparisons between groups and sessions were then performed by using these mean values.

3. Results

3.1. Participants

The analysis included 20 patients with ID (10 women and 10 men) and 20 HC participants (10 women and 10 men). Age at T0 was 40.4 ± 13.3 years in the ID group and 39.0 ± 13.5 years in the HC group (t(38)

= 0.33, p = .74). The T1 assessment was conducted 89.6 ± 10.8 days after T0 in the ID group and 91.0 ± 12.7 days after T0 in the HC group (t(38) = −0.37, p = .71).

3.2. Clinical outcomes

All participants in the ID group completed all four CBT-I sessions. Within this group, ISI scores significantly decreased from T0 to T1 (t(19) = −6.44, p < .001). Similar reductions were observed for PSQI (t(19) = −6.84, p < .001), FIRST (t(19) = −4.06, p < .001), PSAS (t(19) = −5.61, p < .001), GSES (t(19) = −6.33, p < .001), DBAS (t(19) = −3.21, p = .005), ESS (t(19) = −2.26, p = .036), and BDI (t(19) = −3.26, p = .004). In contrast, BAI scores did not differ significantly between T0 and T1 (t(19) = −1.75, p = .097). Means and standard deviations for these variables at both time points are provided in Table 1.

3.3. FMRI data

3.3.1. Validation of the data analysis pipeline

To examine whether the experimental stimuli effectively elicited neural responses, one-sample t-tests were performed for each contrast at T0 across all participants, both within the amygdala and at the whole-brain level. The results revealed that there was a significant amygdala response for C2_neg_high (t(39) = 3.30, p = .002), while none of the other contrasts (C1_sleep_neg_moderate, C3_neg_moderate and C4_ntrl_moderate) was significant. The significant activation clusters of the whole brain analyses are summarised in Table S1.

3.3.2. Analysis focusing on the amygdala

In the Group × Session ANOVA, there was a significant Group × Session interaction for C1_sleep_neg (F(1,38) = 4.19, p = .048). Post-hoc tests revealed that patients with ID had a significantly higher average β value than HC at T0 (estimate = 0.204, SE = 0.095, t(57) = 2.16, p = .035), whereas no significant difference was observed between the groups at T1 (estimate = −0.058, SE = 0.095, t(57) = −0.61, p = .546). However, no significant association was found within the group of patients with ID between treatment-related changes in amygdala reactivity for the contrast C1_sleep_neg_moderate and treatment-related changes in ISI scores (r = −0.189, p = .424). This relationship is illustrated in Fig. S1.

Besides, a significant Group × Session interaction was observed for C4_ntrl_moderate (F(1,38) = 5.39, p = .026). Post-hoc tests showed that patients with ID had a significantly lower average β value than HC at T0 (estimate = −0.165, SE = 0.080, t(57) = −2.06, p = .045), whereas no significant difference was observed between the groups at T1 (estimate = 0.138, SE = 0.080, t(57) = 1.71, p = .092). The average β values for each contrast are presented in Fig. 2.

Table 1
Means and standard deviations of clinical outcome variables at T0 and T1.

	ID group		Control group	
	T0	T1	T0	T1
ISI	15.8 ± 4.7	8.9 ± 4.9	2.1 ± 1.7	2.5 ± 2.4
PSQI	11.0 ± 2.4	6.1 ± 2.7	3.4 ± 1.6	3.1 ± 1.5
FIRST	27.8 ± 4.9	24.9 ± 5.0	20.2 ± 4.8	19.6 ± 4.0
PSAS	37.8 ± 9.0	29.3 ± 8.9	21.0 ± 3.6	20.5 ± 5.4
GSES	7.2 ± 2.6	5.1 ± 2.6	1.7 ± 1.5	1.4 ± 1.2
DBAS	82.4 ± 19.7	70.7 ± 23.8	43.4 ± 21.9	41.3 ± 25.4
ESS	8.9 ± 5.8	6.8 ± 2.8	6.5 ± 3.5	6.3 ± 3.8
BDI	12.9 ± 8.8	8.5 ± 8.4	4.6 ± 3.7	4.6 ± 3.8
BAI	10.0 ± 9.0	6.9 ± 5.8	3.4 ± 3.0	4.2 ± 6.1

Note. BAI: Beck Anxiety Inventory; BDI: Beck Depression Inventory; DBAS: Dysfunctional Beliefs and Attitudes about Sleep Scale; ESS: Epworth Sleepiness Scale; FIRST: Ford Insomnia Response to Stress Test; GSES: Glasgow Sleep Effort Scale; ID: insomnia disorder; ISI: Insomnia Severity Index; PSAS: Pre-Sleep Arousal Scale; PSQI: Pittsburgh Sleep Quality Index.

3.3.3. Effect of the arousal, valence, and content dimensions within the amygdala

Consistent with the analysis of Baglioni and colleagues [9], group differences in the neurobiological responses to arousal, valence, and content at T0 were examined. First, a Group (patients with ID vs HC) × Contrast (C2_neg_high vs C3_neg_moderate) ANOVA was conducted to investigate the neurobiological response to arousal. A significant Contrast main effect was found (F(1,38) = 4.40, p = .043), indicating a higher amygdala activation for C2_neg_high compared with C3_neg_moderate across participants. No significant Group main effect (F(1,38) = 0.50, p = .484) or Group × Contrast interaction (F(1,38) = 0.18, p = .674) were found.

Similarly, a Group (patients with ID vs HC) × Contrast (C3_neg_moderate vs C4_ntrl_moderate) ANOVA was performed to test the neurobiological response to valence. However, no significant main (Contrast main effect: F(1,38) = 0.43, p = .514; Group main effect: F(1,38) = 0.91, p = .346) or interaction effects (F(1,38) = 2.79, p = .103) were observed.

Finally, a Group (patients with ID vs HC) × Contrast (C1_sleep_neg_moderate vs C3_neg_moderate) ANOVA was conducted to investigate the neurobiological response to the content of the stimuli. No significant main (Contrast main effect: F(1,38) = 0.09, p = .76; Group main effect: F(1,38) = 2.44, p = .127) or interaction effects (F(1,38) = 1.42, p = .241) were observed.

3.3.4. ICCs across sessions in the HC group

To assess the reliability of estimates of amygdala reactivity, the ICCs were calculated for all the four contrasts within the HC group. The ICCs were 0.139 (95% CI: −0.305 < ICC <0.537), −0.014 (95% CI: −0.437 < ICC <0.418), −0.205 (95% CI: −0.580 < ICC <0.246), and −0.293 (95% CI: −0.639 < ICC <0.156) for contrasts C1-C4 respectively. To visualise the lack of reliability across sessions, the mean β values from each participant's amygdala in the HC group at T0 and T1 is plotted in Fig. 3.

3.3.5. Explorative analysis for the whole brain

For the whole brain analysis, the same Group × Session mixed ANOVAs were computed for the four contrasts using the flexible factorial function in SPM12. The results indicated that no significant interactions were observed in any of the four contrasts. Significant Session main effects were found for C1_sleep_neg_moderate in three clusters in the right lingual gyrus (MNI coordinate: 6 -84 -6, cluster size = 146, Peak-level T-score = 33.92), left middle occipital gyrus (MNI coordinate: -42 -78 24, cluster size = 55, Peak-level T-score = 19.40), and in the right superior frontal gyrus (MNI coordinate: 18 9 48, cluster size = 91, Peak-level T-score = 27.97). In all three clusters, both the ID and the HC group had a higher activation at T0 compared to T1. These results are illustrated in Fig. 4.

4. Discussion

In the present study, we replicated earlier evidence showing that patients with ID exhibit heightened amygdala reactivity in response to sleep-related stimuli compared to HC. Following CBT-I, which produced a robust improvement in insomnia symptoms, this between-group difference was no longer detectable, thereby supporting the hypothesis outlined in the preregistration. Across all participants, amygdala activation increased in response to stimuli rated as more arousing, indicating that the experimental procedure and analytical pipeline functioned as intended. However, stimulus valence was not associated with amygdala reactivity. Moreover, our repeated-measures design revealed very low retest reliability across all measures, warranting considerable caution when interpreting comparisons between the baseline and post-treatment assessments.

Clinical outcomes indicate that patients with ID experienced meaningful improvements in both sleep and mental health following CBT-I.

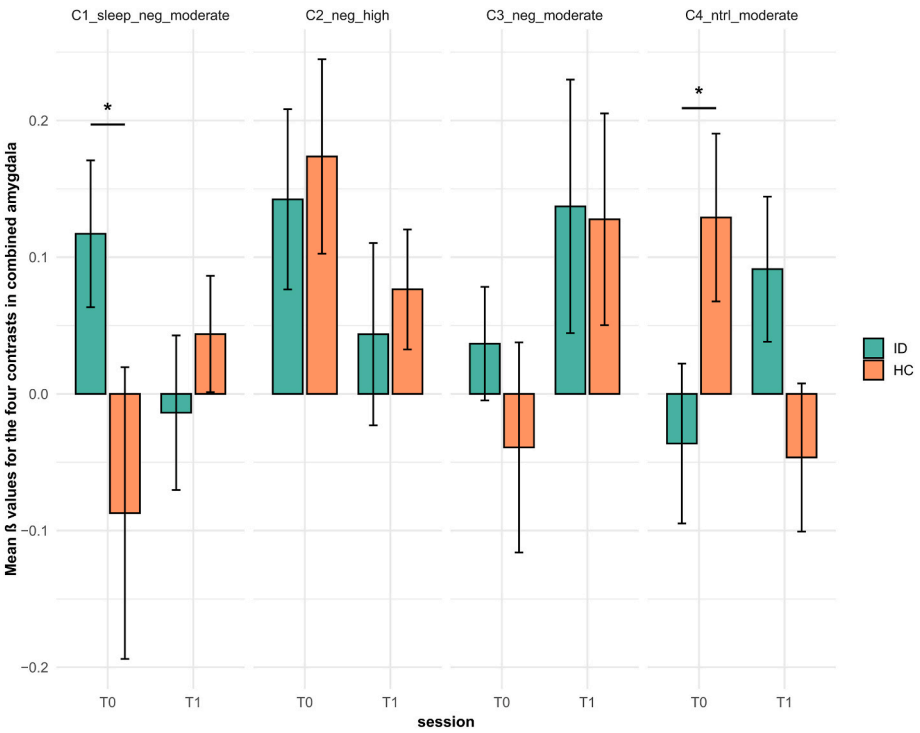

Fig. 2. Amygdala reactivity (means ± standard errors) for the four contrasts (C1_sleep_neg_moderate, C2_neg_high, C3_neg_moderate and C4_ntrl_moderate) in patients with ID and HC at T0 and T1.

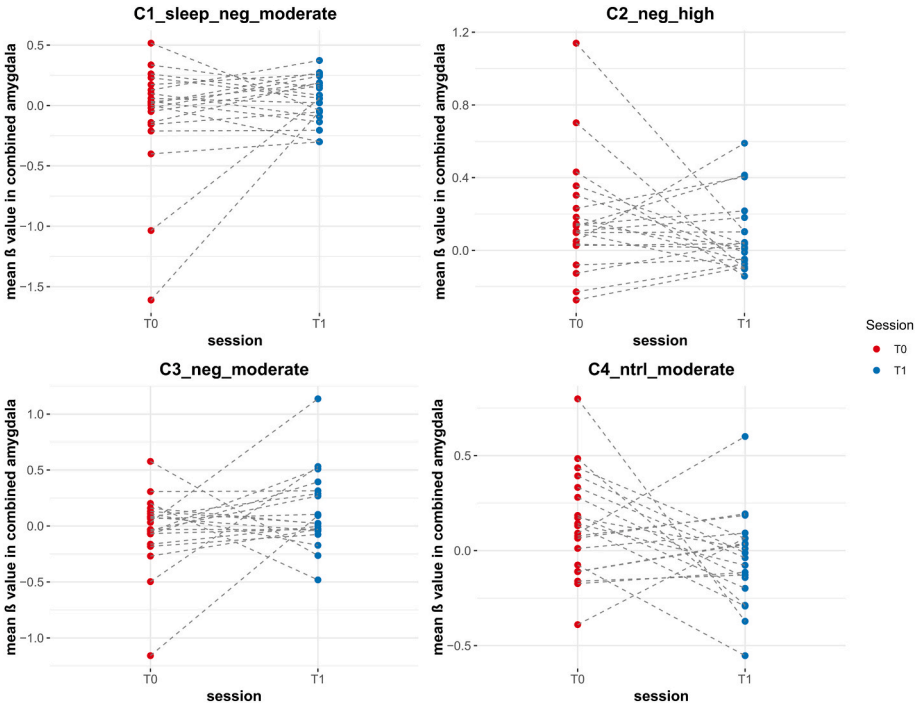

Fig. 3. T0 and T1 amygdala activation (average β values) for each participant in the HC group for the four contrasts. Points are coloured by session (T0 = red, T1 = blue) and connected with dashed lines to indicate individual changes. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

Notable benefits included reductions in insomnia severity, pre-sleep arousal, sleep effort, dysfunctional sleep-related beliefs and attitudes, and daytime sleepiness, along with improvements in depressive symptoms. Overall, these findings suggest that CBT-I demonstrated efficacy comparable to that reported in clinical trials, not only in reducing insomnia symptoms but also in enhancing broader related domains [39–41].

Regarding the brain imaging results, patients with ID showed statistically greater amygdala activation than HC in response to sleep-related stimuli at T0, consistent with previous findings [9]. After

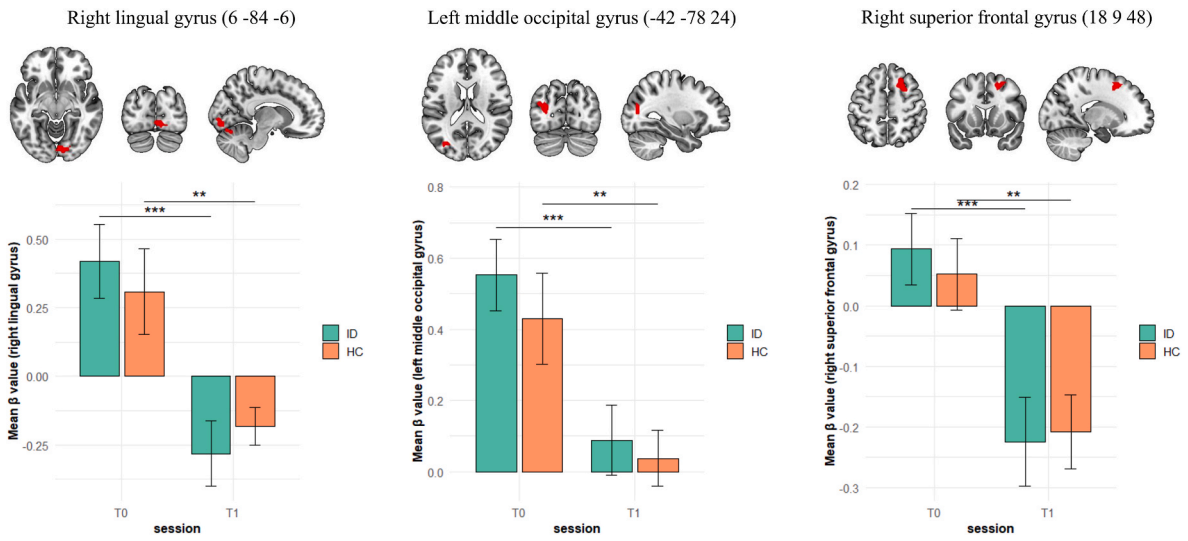

Fig. 4. Mean β values and standard errors of the significant clusters for the Session main effect for C1_sleep_neg_moderate. Post-hoc comparisons showed consistently higher values at T0 than at T1 in all three clusters in both groups: ID group (right lingual gyrus: estimate = 0.701, $p < .001$; left middle occipital gyrus: estimate = 0.464, $p < .001$; right superior frontal gyrus: estimate = 0.318, $p < .001$) and HC group (right lingual gyrus: estimate = 0.491, $p = .005$; left middle occipital gyrus: estimate = 0.393, $p = .004$; right superior frontal gyrus: estimate = 0.261, $p = .003$). In the bar plot, $p < .001$: ***, $p < .01$: **.

CBT-I, this effect was no longer detectable, suggesting that the intervention may have normalised amygdala reactivity to sleep-related information, partially consistent with our preregistered hypothesis. This pattern aligns with the cognitive model and the attention–intention–effort (A-I-E) pathway of insomnia [12,14]. According to the cognitive model, selective attention to and heightened monitoring of sleep-related cues foster worry and rumination, which contribute to the maintenance of insomnia [14]. The A-I-E model further proposes that selective attention to negative sleep-related information increases explicit sleep intention and sleep effort, thereby perpetuating poor sleep [12]. The current study adds to these models by identifying increased amygdala reactivity as a potential neurobiological correlate of disturbed processing of sleep-related information.

An important caveat for interpreting the current study concerns the low ICCs for amygdala reactivity across T0 and T1 in the HC group, indicating very poor test–retest reliability of the employed paradigm. We also examined the correlation between pre- and post-treatment differences in amygdala activation to C1_sleep_neg_moderate stimuli and ISI score changes among patients with ID and did not find any significant association. Consequently, conclusions about the role of amygdala reactivity in ID should be drawn with caution. While the T0 results were largely consistent with our hypotheses, the T1 findings (particularly those for the contrasts C3_neg_moderate and C4_ntrl_moderate) are difficult to interpret. This pattern resembles that of a previous study [9], which also reported discrepancies between neural responses to the first and second presentation of stimuli. One possible explanation lies in the passive viewing paradigm, which does not allow verification that participants consistently attended to the stimuli. Moreover, the whole-brain analyses revealed weaker effects than expected. Taken together, these results suggest that participants may have habituated quickly to the stimulus presentations, thereby reducing the validity of the T1 findings.

Despite the insights provided by this study, several methodological limitations should be noted. First, the relatively small sample size reduces statistical power and may limit the generalisability of the findings. Some results, which just met the threshold for statistical significance, should be interpreted with caution due to the limited sample size and the associated risk of Type I error. Second, the sleep-related stimulus set comprised only moderately emotional images, which may have produced comparatively small differences in neural responses across stimulus categories and it raises concerns regarding the validity of the stimuli and the sensitivity of the experimental task in engaging the target neural circuitry. Third, because the study did not employ a randomised controlled design, any T0-T1 changes observed in the ID group should be interpreted with caution, and causal inferences cannot be drawn. Fourth, emotional processing was not examined during follow-up periods after the completion of CBT-I, and therefore it remains unclear whether the observed neural and behavioral changes are sustained, attenuated, or further evolve after treatment. Fifth, variables like potential variations in emotional state between the two scanning sessions, as well as differences in alertness and attention to pictorial stimuli across sessions in the HC group, were not directly assessed, which may limit the validity of the findings.

In summary, the present study assessed alterations in brain function during emotion processing in patients with ID before and after CBT-I, providing insight into the neural mechanisms of insomnia. It investigated the neural processing of emotional stimuli in patients with ID and HC participants across two sessions. At baseline, patients with ID exhibited heightened amygdala reactivity in response to sleep-related stimuli compared to HC, which was not evident any more after CBT-I. However, due to low ICCs, these findings should be interpreted with caution. Future studies could build on these findings by expanding the sample size and adopting multi-timepoint longitudinal designs to clarify the dynamic changes in emotion-processing brain function during CBT-I. In addition, the incorporation of a broader range of stimuli, together with improved differentiation between moderate and low levels of stimulus arousal, may be crucial for ensuring the validity of the stimuli and the sensitivity of the experimental task in effectively engaging the target neural circuitry. Furthermore, the application of complementary neuroimaging analysis approaches and the integration of neuroimaging markers with clinical symptoms, emotional measures, and treatment response may help identify neural biomarkers that predict CBT-I efficacy. Such efforts would provide important insights for the development of precision, stratified interventions and mechanism-based treatment strategies for ID.

CRediT authorship contribution statement

Ziye Xu: Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Julian E. Schiel:** Resources, Investigation. **Roxana Petri:** Resources, Investigation. **Nikolas Konzen:** Resources, Investigation. **Anahita Davoodabadi:**

Writing – review & editing, Software, Investigation. **Sarah Schmid:** Resources, Investigation. **Bernd Feige:** Software, Methodology. **Simon Maier:** Resources, Investigation. **Ursula Feige:** Methodology. **Lukas Frase:** Writing – review & editing. **Masoud Tahmasian:** Writing – review & editing. **Chiara Baglioni:** Writing – review & editing. **Katharina Domschke:** Writing – review & editing, Supervision. **Kai Spiegelhalder:** Writing – review & editing, Supervision, Software, Resources, Methodology, Investigation, Data curation, Conceptualization. **Florian Holub:** Writing – review & editing, Supervision, Software, Methodology.

Data availability statement

Data generated and/or analysed during the current study are available from the first author upon reasonable request.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process

During the preparation of this manuscript, the authors used ChatGPT to assist with language editing and to improve consistency in academic English. The authors take full responsibility for the content of the published article.

Declaration of competing interest

The authors declare the following financial interests/personal relationships, which may be considered as potential competing interests: Katharina Domschke reports a relationship with the Neurotorium Editorial Board, Lundbeck Foundation, and Janssen-Cilag GmbH that includes: board membership and speaking and lecture fees. The other authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.sleep.2026.108964.

References

[1] Morin CM, Drake CL, Harvey AG, Krystal AD, Manber R, Riemann D, et al. Insomnia disorder. Nat Rev Dis Primers 2015;1:15026. https://doi.org/10.1038/nrdp.2015.26.

[2] Riemann D, Krone LB, Wulff K, Nissen C. Sleep, insomnia, and depression. Neuropsychopharmacology 2020;45:74–89. https://doi.org/10.1038/s41386-019-0411-y.

[3] Chellappa SL, Aeschbach D. Sleep and anxiety: from mechanisms to interventions. Sleep Med Rev 2022;61:101583. https://doi.org/10.1016/j.smrv.2021.101583.

[4] Palagini L, Miniati M, Caruso V, Alfi G, Geoffroy PA, Domschke K, et al. Insomnia, anxiety and related disorders: a systematic review on clinical and therapeutic perspective with potential mechanisms underlying their complex link. Neurosci Appl 2024;3:103936. https://doi.org/10.1016/j.nsa.2024.103936.

[5] Baglioni C, Lombardo C, Bux E, Hansen S, Salveta C, Biello S, et al. Psychophysiological reactivity to sleep-related emotional stimuli in primary insomnia. Behav Res Ther 2010;48:467–75. https://doi.org/10.1016/j.brat.2010.01.008.

[6] Meneo D, Samea F, Tahmasian M, Baglioni C. The emotional component of insomnia disorder: a focus on emotion regulation and affect dynamics in relation to sleep quality and insomnia. J Sleep Res 2023;32:e13983. https://doi.org/10.1111/jsr.13983.

[7] Schiel JE, Holub F, Petri R, Leerssen J, Tamm S, Tahmasian M, et al. Affect and arousal in insomnia: through a lens of neuroimaging studies. Curr Psychiatry Rep 2020;22:44. https://doi.org/10.1007/s11920-020-01173-0.

[8] Akram U, Barclay N, Milkins B, Stevenson J, Gardani M. Sleep-related attentional and interpretive-bias in insomnia: a systematic review and meta-analysis. Sleep Med Rev 2023;67:101713. https://doi.org/10.1016/j.smrv.2022.101713.

[9] Baglioni C, Spiegelhalder K, Regen W, Feige B, Nissen C, Lombardo C, et al. Insomnia disorder is associated with increased amygdala reactivity to insomnia-related stimuli. Sleep 2014;37:1907–17. https://doi.org/10.5665/sleep.4240.

[10] Kim SJ, Lee YJ, Kim N, Kim S, Choi J-W, Park J, et al. Exploration of changes in the brain response to sleep-related pictures after cognitive–behavioral therapy for psychophysiological insomnia. Sci Rep 2017;7:12528. https://doi.org/10.1038/s41598-017-13065-0.

[11] Spiegelhalder K, Baglioni C, Regen W, Kyle SD, Nissen C, Hennig J, et al. Brain reactivity and selective attention to sleep-related words in patients with chronic insomnia. Behav Sleep Med 2018;16:587–600. https://doi.org/10.1080/15402002.2016.1253014.

[12] Espie CA, Broomfield NM, MacMahon KMA, Macphee LM, Taylor LM. The attention–intention–effort pathway in the development of psychophysiologic insomnia: a theoretical review. Sleep Med Rev 2006;10:215–45. https://doi.org/10.1016/j.smrv.2006.03.002.

[13] Harris K, Spiegelhalder K, Espie CA, MacMahon KMA, Woods HC, Kyle SD. Sleep-related attentional bias in insomnia: a state-of-the-science review. Clin Psychol Rev 2015;42:16–27. https://doi.org/10.1016/j.cpr.2015.08.001.

[14] Harvey AG. A cognitive model of insomnia. Behav Res Ther 2002;40:869–93. https://doi.org/10.1016/S0005-7967(01)00061-4.

[15] Morin CM. Insomnia: psychological assessment and management. New York, NY, US: Guilford Press; 1993.

[16] Huang Z, Liang P, Jia X, Zhan S, Li N, Ding Y, et al. Abnormal amygdala connectivity in patients with primary insomnia: evidence from resting state fMRI. Eur J Radiol 2012;81:1288–95. https://doi.org/10.1016/j.ejrad.2011.03.029.

[17] Kweon W, Lee KH, Choi SH, Shin J, Seo M, Jeon JE, et al. Amygdala resting-state functional connectivity alterations in patients with chronic insomnia disorder: correlation with electroencephalography beta power during sleep. Sleep 2023;46. https://doi.org/10.1093/sleep/zsad205. zsad205.

[18] Wang H, Li H, Kou J, Fatemeh NN, Peng Y, Qian Y, et al. Enhanced volume and resting-state functional connectivity of amygdala subregions in patients with insomnia disorder. Neuroscience 2025;586:154–62. https://doi.org/10.1016/j.neuroscience.2025.09.018.

[19] Dresler T, Guhn A, Tupak SV, Ehlis A-C, Herrmann MJ, Fallgatter AJ, et al. Revise the revised? New dimensions of the neuroanatomical hypothesis of panic disorder. J Neural Transm 2013;120:3–29. https://doi.org/10.1007/s00702-012-0811-1.

[20] Pace-Schott EF, Zimmerman JP, Bottary RM, Lee EG, Milad MR, Camprodon JA. Resting state functional connectivity in primary insomnia, generalized anxiety disorder and controls. Psychiatry Res Neuroimaging 2017;265:26–34. https://doi.org/10.1016/j.pscychresns.2017.05.003.

[21] Ye Y, Wang C, Lan X, Li W, Fu L, Zhang F, et al. Abnormal amygdala functional connectivity in MDD patients with insomnia complaints. Psychiatry Res Neuroimaging 2023;328:111578. https://doi.org/10.1016/j.pscychresns.2022.111578.

[22] Wassing R, Lakbila-Kamal O, Ramautar JR, Stoffers D, Schalkwijk F, Someren EJWV. Restless REM sleep impedes overnight amygdala adaptation. Curr Biol 2019;29:2351–2358.e4. https://doi.org/10.1016/j.cub.2019.06.034.

[23] Leerssen J, Aghajani M, Bresser T, Rösler L, Winkler AM, Foster-Dingley JC, et al. Cognitive, behavioral, and circadian rhythm interventions for insomnia alter emotional brain responses. Biol Psychiatry Cogn Neurosci Neuroimaging 2024;9:60–9. https://doi.org/10.1016/j.bpsc.2023.03.007.

[24] Lee MH, Lee KH, Oh SM, Seo MC, Lee H, Jeon JE, et al. The moderating effect of prefrontal response to sleep-related stimuli on the association between depression and sleep disturbance in insomnia disorder. Sci Rep 2022;12:17739. https://doi.org/10.1038/s41598-022-22652-9.

[25] Bootzin RR. Stimulus control treatment for insomnia: (465522008-198). https://doi.org/10.1037/e465522008-198; 1973.

[26] Jacobson E. Progressive relaxation. second ed. Oxford, England: Univ. Chicago Press; 1938.

[27] Jansson-Fröjmark M, Norell-Clarke A. The cognitive treatment components and therapies of cognitive behavioral therapy for insomnia: a systematic review. Sleep Med Rev 2018;42:19–36. https://doi.org/10.1016/j.smrv.2018.05.001.

[28] Bastien CH, Vallières A, Morin CM. Validation of the Insomnia Severity Index as an outcome measure for insomnia research. Sleep Med 2001;2:297–307. https://doi.org/10.1016/S1389-9457(00)00065-4.

[29] Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213. https://doi.org/10.1016/0165-1781(89)90047-4.

[30] Drake C, Richardson G, Roehrs T, Scofield H, Roth T. Vulnerability to stress-related sleep disturbance and hyperarousal. Sleep 2004;27:285–91. https://doi.org/10.1093/sleep/27.2.285.

[31] Nicassio PM, Mendlowitz DR, Fussell JJ, Petras L. The phenomenology of the pre-sleep state: the development of the pre-sleep arousal scale. Behav Res Ther 1985;23:263–71. https://doi.org/10.1016/0005-7967(85)90004-X.

[32] Broomfield NM, Espie CA. Towards a valid, reliable measure of sleep effort. J Sleep Res 2005;14:401–7. https://doi.org/10.1111/j.1365-2869.2005.00481.x.

[33] Morin CM, Vallières A, Ivers H. Dysfunctional beliefs and attitudes about sleep (DBAS): validation of a brief version (DBAS-16). Sleep 2007;30:1547–54. https://doi.org/10.1093/sleep/30.11.1547.

[34] Johns MW. A new method for measuring daytime sleepiness: the epworth sleepiness scale. Sleep 1991;14:540–5. https://doi.org/10.1093/sleep/14.6.540.

[35] Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–71. https://doi.org/10.1001/archpsyc.1961.01710120031004.

[36] Beck AT, Epstein N, Brown G, Steer RA. An inventory for measuring clinical anxiety: psychometric properties. J Consult Clin Psychol 1988;56:893–7. https://doi.org/10.1037/0022-006X.56.6.893.

[37] Bradley MM, Lang PJ. International affective picture system. Encycl. Personal. Individ. Differ. Cham: Springer; 2017. p. 1–4. https://doi.org/10.1007/978-3-319-28099-8_42-1.

[38] Power JD, Barnes KA, Snyder AZ, Schlaggar BL, Petersen SE. Spurious but systematic correlations in functional connectivity MRI networks arise from subject motion. Neuroimage 2012;59:2142–54. https://doi.org/10.1016/j.neuroimage.2011.10.018.

[39] Benz F, Knoop T, Ballesio A, Bacaro V, Johann AF, Rücker G, et al. The efficacy of cognitive and behavior therapies for insomnia on daytime symptoms: a systematic review and network meta-analysis. Clin Psychol Rev 2020;80:101873. https://doi.org/10.1016/j.cpr.2020.101873.

[40] Trauer JM, Qian MY, Doyle JS, Rajaratnam SMW, Cunnington D. Cognitive behavioral therapy for chronic insomnia. Ann Intern Med 2015;163:191–204. https://doi.org/10.7326/M14-2841.

[41] van Straten A, van der Zweerde T, Kleiboer A, Cuijpers P, Morin CM, Lancee J. Cognitive and behavioral therapies in the treatment of insomnia: a meta-analysis. Sleep Med Rev 2018;38:3–16. https://doi.org/10.1016/j.smrv.2017.02.001.