Behavioural Brain Research 503 (2026) 116060

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research article

An exploration of the association between sub bands of gamma and individual symptoms of melancholia

Christopher F. Sharpley *, Ian D. Evans, Vicki Bitsika, G.Lorenzo Odierna

Brain-Behaviour Research Group, University of New England, Queen Elizabeth Drive, Armidale, New South Wales 2351, Australia

ARTICLE INFO

Keywords:
Depression
Melancholia
Gamma
Sub bands

ABSTRACT

Melancholia is often found to be unresponsive to standard antidepression medication. In the search for biomarkers that may also suggest possible treatment options, some attention has been given to EEG data. However, this research has largely ignored the gamma band of electrical activity in the brain (30–130 Hz). In an exploratory investigation of the association between melancholia and gamma wave activity, a standardized 8-item scale was completed by 100 community participants, who also underwent eyes-open and eyes-closed EEG data collection from 30 brain sites. There was a significant association between severity of depression, melancholia, and gamma. Individual melancholia symptoms were found to have meaningful correlations with specific EEG sites, which were then further explored via source localization (*eLORETA*). Most associations between gamma and melancholia items as measured via *eLORETA* were direct, indicating that, as gamma increased, so did participants' severity of particular melancholia symptoms, implying that depressed participants utilized increased neurocognitive activity as a possible strategy for coping with aspects of melancholia. Although these results are exploratory, they address a gap in the literature and suggest several hypotheses for future research.

1. Introduction

1.1. Melancholia

Melancholia is described in the DSM-5-TR [1] as a specifier of Major Depressive Disorder (MDD), although it may also be a separate category of depression [2]. Notwithstanding this debate, melancholia has been associated with elevated metabolic syndrome, lower physical activity, and smoking [3], all of which are independent risk factors for a wider range of diseases. In terms of its diagnostic features, Melancholic depression is usually characterized by: anhedonia, despair/empty mood, psychomotor agitation or depression, lack of reactivity to usually pleasant events, early waking, weight problems, and excessive guilt [1]. Although these (and other) symptoms are generally accepted to be present in melancholia, there has been some debate as to the precise core aspects of melancholia [4,5]. Parker and colleagues [6,7] developed a scale ("CORE") for reporting melancholia, which has been confirmed in multiple research studies (for a review, see: [8]), and which was further developed into the Sydney Melancholic Prototype Index (SMPI), able to distinguish melancholic from non-melancholic participants in a community sample [9]. Parker et al. [9] also noted that melancholia was positively correlated with the severity of general depression. The SMPI focusses upon symptoms of: anhedonia, low energy, loss of interest, impaired concentration, lack of improvement in mood or being able to be cheered up, and thoughts of death or suicide [9]. This model of melancholia represents an evidence-based process for identifying and assessing the severity of melancholia in community samples, particularly when depressed and non-depressed participants are included, and allows for valid and reliable exploration of the nature and correlates of melancholia.

1.2. Biomarkers of melancholia

Despite ongoing calls for the establishment of diagnostic biomarkers for mental disorders [10,11], a review of potential endocrinological, neurological and immunological biomarkers of melancholia concluded that, due to the diversity and inconsistency in definition of melancholia, definitive conclusions were limited, and that further investigation of possible biomarkers of melancholia might be facilitated by adopting a standardized and evidence-based index of melancholia, such as the SMPI

* Correspondence to: School of Science & Technology, University of New England, Armidale, New South Wales 2351, Australia.
E-mail addresses: csharpl3@une.edu.au (C.F. Sharpley), ievans3@une.edu.au (I.D. Evans), Vicki.Bitsika@une.edu.au (V. Bitsika), godierna@une.edu.au (G.Lorenzo Odierna).

https://doi.org/10.1016/j.bbr.2026.116060
Received 27 October 2025; Received in revised form 13 December 2025; Accepted 23 January 2026
Available online 25 January 2026

[12]. Of the many potential biomarkers that might be investigated, neural correlates present a large range of possible metrics that could be relevant and have the advantage of relating directly to brain function.

1.3. Neural correlates of melancholia

1.3.1. Alpha asymmetry

Although some previous research applying electroencephalography (EEG) has identified alpha asymmetry (AA) across the left and right frontal brain sites as being indicative of MDD [13–15], relatively little has been reported regarding the association between AA and melancholia [16]. It has been suggested that this may be due to the lack of consistency in methodologies across AA studies [17]. One recent report that did focus on AA and melancholia [18] found that one of the two subcomponents of the scale measuring melancholia was inversely correlated with frontal AA, but the other subcomponent of melancholia was directly correlated with parietal-occipital AA. As well as providing some support for the AA-melancholia association and its possible variability across the brain regions, these results argue for consideration of melancholia in greater detail than as a simple total score on a melancholia inventory such as the SMPI. Similarly, although alpha has been commonly examined as a possible correlate of melancholia, there are other wavelengths of scalp-measured electrical cortical activity that may repay investigation for their association with melancholia. For example, in their discussion paper, Fitzgerald and Watson [19] raised a number of potential advantages of using gamma oscillations when investigating the associations between depression and brain activity, although they did not focus on melancholia *per se*.

1.3.2. Gamma oscillations, disorder, and melancholia

Gamma refers to the relatively high frequency electrical oscillations in the 30 Hz to 200 Hz range [19], although Buzsaki and Draguhn [20] described gamma as between 30 and 90 Hz, Buzsáki, Wang [21] extended this to 30 Hz to 140 Hz, and Fernandez-Ruiz et al. [22] referred to the 30 Hz to 150 Hz range as gamma. Buzsáki, Wang [21] further named the 90–140 Hz as 'fast' gamma or the 'epsilon' band. For the purposes of this study, gamma was defined as occurring between 30 Hz and 130 Hz so as to incorporate the most common of these ranges in terms of the slowest frequency (i.e., 30 Hz), while also including high-frequency gamma (i.e., 130 Hz), and also allowing for the definition of five separate 20-Hz sub bands (i.e., 30–50 Hz, 50–70 Hz, 70–90 Hz, 90–110 Hz, 110–130 Hz). This definition was therefore maximally comprehensive across the accepted gamma band range, thus allowing for identification of sub band effects.

Buzsaki and Wang (2004; 2012) explained the gamma oscillatory process as priming neurons to integrate information by bringing inputs into synchrony, adding that gamma's oscillations may have been modulated by slower brain rhythms (called 'cross-frequency coupling'). In a major review of the principles of cortical rhythms, [23] reported on the role of gamma "as a fingerprint of attention", largely via its association with the integration of sensory information. When that integration is interrupted by dysfunction of synchronization, deficits in information integration, working memory, and selective attention may be observed, as in mental illnesses such as schizophrenia and depression [23]. As evidence of that, abnormalities in gamma have been previously associated with a range of brain disorders that involve impaired sensory or cognitive processing, such as MDD, schizophrenia, and Alzheimer's disease [24]. For example, Arikan et al. [25] found that gamma of 40–50 Hz at F4, Fz, C4, Cz, O2, F8, T5 and T6 regions was significantly higher in patients who reported suicidal ideation.

However, none of that research also focused on melancholia, leaving the hypothetical association between melancholia and gamma as worthy of attention. This is particularly important because, although Fitzgerald and Watson [19] noted that there are initial indications that gamma oscillations can be different between depressed patients versus healthy control participants, they did not comment on gamma and melancholia specifically. Regardless of this lack of previous attention, there is a *prima facie* case for investigation of gamma in melancholia because melancholia is, as noted by Parker (2019), correlates with general depression, which shares some common symptoms with melancholia. As an indicator of the need to focus on the gamma-melancholia relationship, a recent review that updated the field since 2018 reported 31 studies of the association between gamma and depression, but none of those examined melancholia specifically (Coleman, in press).

1.4. Aims of this study: gamma and melancholia

Based upon the absence of previous research on gamma and melancholia specifically, the current study explored that association, using the definition of melancholia given by Parker et al. [9]. In order to provide as detailed an account of that relationship as possible, and because it has been established that there are many forms of melancholia [26], all of the eight individual diagnostic criteria for melancholia that are included in the SMPI were examined individually as well as the total melancholia score. In terms of gamma, the relationship with melancholia was examined at several sub band levels as well as the 30–130 Hz range because of Hudson and Jones' [24] comment that this procedure may assist in deciphering the specific functions of narrow bands of gamma activity. Due to the current study's largely exploratory nature, firm directional hypotheses could not be posited, but it was expected that gamma would be directly correlated with melancholia, based upon the comments made by Fitzgerald and Watson [19] about general depression.

2. Methods

2.1. Participants

A community sample consisting of both depressed and non-depressed participants was recruited. *A priori* power analysis indicated that sample sizes of at least 33 participants in each of these categories was sufficient to test for the presence of a moderately powered correlation of at least $r = .3$ with alpha $< .05$ and at least.80 power [27] within each subsample. This study used the same sample as reported in the previous investigation of AA and melancholia [18], consisting of 100 adults (44 males, 56 females at least 18 yr of age), 33 of whom met the criteria for clinically significant depression [28], who had no previous medical history of severe physical brain injury, previous brain surgery, or past or current history of epilepsy or seizure disorder, and who were recruited from the New England region of New South Wales, Australia. Right-handed participants are sometimes recruited for EEG studies because handedness may be linked to hemispheric dominance, but 60–70 % of left-handed people also have left hemisphere dominance [29]. Further, meta-analytic data based on 35,000 individuals across 87 studies did not find any meaningful effect of handedness on depression [30], and so handedness was not included in the selection criteria here.

2.2. Instruments

2.2.1. Background questionnaire. Participants gave information about their age in years, and their identified sex

The Self-rating Depression Scale (SDS) [31] is a 20-item self-report scale based on the Diagnostic Criteria and Associated Features of MDD [1]. Participants are invited to indicate the level of severity of their experience of these 20 items during the last two weeks, and these responses provide a raw score ranging from 20 to 80. [28] defined raw scores of 40 or more as indicative of "clinically significant depression". The SDS has demonstrated split-half reliability of between 0.79 [32] and 0.94 [33], and internal consistency (alpha) of 0.88 for depressed and 0.93 for non-depressed individuals [34].

Melancholia scale. Following Parker et al.'s (2019) recommendations the item 'I do not feel much better even when good things happen',

plus relevant SDS items, were included to form an 8-item Melancholia scale using the items shown in Table 1. Scores for melancholia were calculated from these items using the procedures described by Parker et al. [9].

2.3. EEG data

Participants fasted from caffeine and other substances likely to influence their concentration or psychophysiological state for 12 hr prior to the EEG recording. Thirty channel EEG data (Fig. 1) were collected with a Digital EEG Amplifier (NuAmps) and a *Quick Cap* with electrodes during a 3 mins Eyes Closed resting condition and a 3 mins Eyes Open resting condition. Participants' hair had been washed with conditioner-free shampoo before the EEG session, and electrode sites were cleaned with *Nuprep* gel plus an alcohol swab. Electrodes were applied with the cap, ensuring that the Cz electrode was halfway between the glabella and inion. Participants sat in an experimental booth while their EEG signals were collected and recorded using the *Curry 7* software. The average of the A1/A2 electrodes was used as the reference, and EOG was measured using four electrodes above and below the left eye as well as adjacent to both outer canthi. Data were collected at a sampling rate of 1 KHz and a 400 Hz lowpass filter. The allowable impedance level was < 10 kΩ for each electrode.

After recording, data were processed using a band pass filter with a low filter (high pass) frequency of 1 Hz and a slope of 2 Hz; a high filter (low pass) with frequency of 150 Hz and a slope of 8 Hz; a notch filter of 50 Hz (including harmonics) with a slope of 1.5 Hz. Data tapering was done using a Hann window with 10 % width to prevent data loss. Artifact rejection was conducted using the FASTER algorithm [35] which uses independent component analysis to automatically identify components associated with common types of artefact such as (but not limited to) eye movement/blink, jaw clenching, EMG, electrode popoff and EKG measured at the scalp. Following this procedure, EEG data were visually examined to identify any remaining bad portions of data. Back-to-back epochs of 1 s duration were then created from the cleaned EEG data, excluding epochs with bad blocks. Spectral analysis using FFT was conducted on the generated epochs to calculate absolute power values within multiple gamma frequency bands: 30–50 Hz, 50–70 Hz, 70–90 Hz, 90–110 Hz, and 110–130 Hz.

2.4. Procedure

Participants all confirmed that they had refrained from caffeine and other substances that may have influenced their concentration or psychophysiological state for the previous 12 hr, and then they read an Explanatory Statement and completed a Consent Form; any questions they had were answered. They also completed the Background Questionnaire and the SDS plus the extra Melancholia item. Their scalps were prepared and they had the electrode cap fitted. They were taken to the experimental booth to minimize external stimuli, and had headphones placed upon their ears to allow them to hear a pre-recorded transcript of instructions free from auditory distraction. They were asked to relax and, after 15 min of sitting quietly (Adaptation), they listened to the pre-recorded experimental protocol for 3 min eyes closed followed by 3 mins eyes open. After the end of the protocol, participants were led from the booth, and had the headphones and electrode cap removed, and were thanked for their participation. This protocol and all other aspects of the study were approved by the Human Research Ethics Committee of the University of New England, Australia (Approval No. HE14–051).

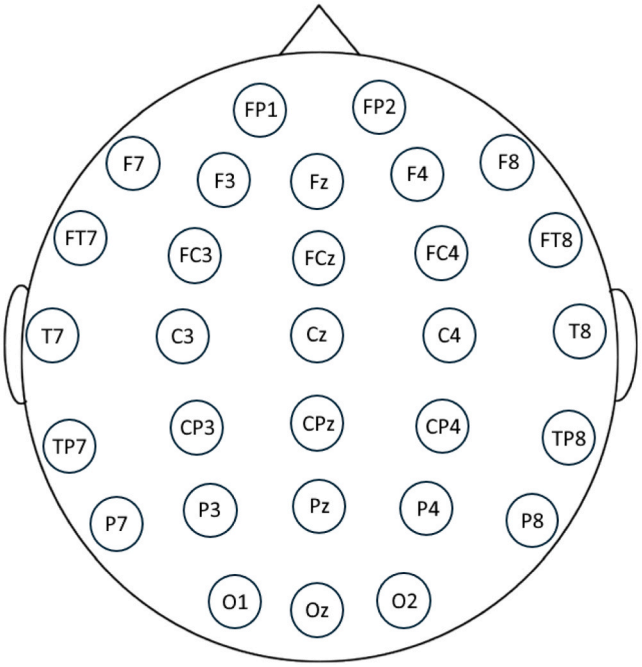

Fig. 1. EEG sites used in this study.

2.5. Statistical analyses

Data were analyzed with SPSS 27 for SDS internal consistency, normality, and sex differences; depressed versus non-depressed participants were also compared with ANOVA. EEG data were not normalized because it has been demonstrated that this can lead to bias in statistical outcomes [36]. Because there is an inherent limitation to statistical power by dichotomizing continuous data [37], the advice of Kołodziej et al. [38] to use correlational analysis was followed to test for the association between gamma and melancholia at the total scale level and the individual item level. Following [39], p. 41 statement that the Pearson correlation coefficient is "robust" to the presence of non-normality, and Norris and Aroian's [40] finding that data transformation is neither necessary nor advisable when analyzing skewed data, Pearson's Product Moment correlation procedures were used to calculate the associations between gamma and melancholia raw data. These analyses were conducted for the entire sample, the depressed, and the non-depressed subsamples.

Because this is an exploratory study due to the lack of previous research on the associations between various gamma sub bands and the symptoms of melancholia, consideration was given to the appropriate balance between Type I and II error rates [41]. Applying the $p < .05$ threshold for Type I error rates and 80 % power as the major criteria for detecting a 'significant' result may be disadvantageous in detecting the kind of moderate but real effects that emerge from exploratory research [42]. Therefore, results of the tests for correlation between melancholia

Table 1
Melancholia symptoms and items used in Melancholia scale.

Melancholia symptoms[a]	Item
Anhedonia	I still enjoy sex[b] (R)
Low energy	I get tired for no reason[b]
Loss of interest	I still enjoy doing the things I used to do[b] (R)
Impaired concentration	My mind is as clear as it used to be[b] (R); I find it hard to make decisions[b]
Thoughts of death/suicide	I feel that others would be better off if I was dead[b] I feel that I am useful and needed[b] (R)
Lack of improvement in mood/able to be cheered up	I do not feel much better even when good things happen[c]

[a] Based on Parker, et al. [7,9]
[b] SDS item
[c] Item derived from Parker, et al. [7,9] and framed in SDS item format; R = reverse-worded item in SDS.

and gamma EEG data were primarily examined for their 'meaningfulness' by reference to their effect size, applying Cohen's [27] definition of a medium effect size (appropriate for an exploratory study) (i.e., $r \geq .3$). Family-wise error corrections were not applied because this may increase the likelihood of a Type II error, and there are arguments against this kind of correction in exploratory studies such as these [43,44]. Therefore, the effect size of $r \geq .3$ was used as the indicator of a meaningful association between EEG site gamma power and melancholia severity suitable for further hypothesis testing in larger samples.

As well as the main testing for meaningful correlation between gamma power at specific EEG sites and melancholia, a further exploration was undertaken of the precise brain regions in which a meaningful correlation between gamma power and melancholia was observed. This was performed by source localization using *eLORETA* [45]**.** Fortunately, *eLORETA* overcomes the multiple comparisons problem by employing nonparametric permutation testing [46]. To summarize this approach, *eLORETA* calculates a single significance threshold for the entire brain (all 6239 voxels) instead of a separate threshold for each individual voxel being compared across the sample.

3. Results

3.1. Data

Internal consistency (Cronbach alpha) was acceptable for the SDS (.921) and the 8-item Melancholia scale (.894). Normal Q-Q plots for both scales approached straight lines, indicative of a normal distribution, allowing raw data from both these scales to be used in parametric analysis. Means and standard deviations for the two scales for the entire sample, the 33 depressed participants identified by applying the 40-point cutoff on the SDS, and the 67 participants who did not reach this score [28], and for males and females, are shown in Supplementary Table 1. MANOVA (Type II Sums of Squares, Pillai's Trace, used because of the difference in subsample sizes) indicated that the clinically significantly depressed subsample had significantly higher SDS total scores than the participants whose SDS score was < 40 $F(1,99) = 257.645$, $p < .001$, $\mu^2 = .729$, and also significantly higher Melancholia scores $F(1,99) = 195.329$, $p < .001$, $\mu^2 = .670$, and significantly higher univariate scores on all 20 SDS items and all 8 Melancholia scale items, confirming Parker et al.'s (2019) contention that melancholia is associated with depression severity. There were no significant sex differences for the SDS or Melancholia total scales, or for any of the items from these scales.

3.2. Gamma and melancholia: EEG site data from surface electrodes

As a first step in the analysis of the association between gamma and melancholia, correlations were calculated between gamma oscillations broken into 20 Hz sub bands and the (a) Melancholia total score, and (b) Melancholia individual scale items.

3.2.1. Melancholia total score

Total sample. None of the correlations between various EEG sites and gamma sub bands and the Melancholia total score for the total sample under the eyes closed or eyes open conditions met the criterion for a meaningful association between gamma and melancholia total score as defined above.

Depressed participants. There were four meaningful ($r \geq .300$) correlations between various gamma bands and Melancholia total score under the eyes closed condition. In fact, all these correlation coefficients were $> .316$, thus accounting for at least 10 % of the variance. These were: for CPZ in the 70–90 Hz sub band ($r = .373$), the 90–110 Hz sub band ($r = .405$), and for the 110–130 Hz sub band ($r = .371$); and for CZ in the 110–130 Hz sub band ($r = .348$). There were two meaningful correlations under the eyes open condition: these were in the 70–90 Hz sub band ($r = .355$), and the 90–110 Hz sub band ($r = .370$). These meaningful correlations were only in the upper ranges of gamma (i.e., 70–130 Hz) and represented only three separate EEG sites (CPZ, CZ, and FCZ), all of which are in the central brain region. CZ is collocated with Brodmann areas 24, 32, and 33, located in the anterior cingulate cortex (ACC) and associated with attention, reward anticipation, and decision-making; FCZ is also located in the anterior cingulate cortex, associated with a range of cognitive processes (attention, working memory, emotional regulation); and CPZ (Brodmann area 5) is in the posterior parietal cortex and is associated with somatosensory processing and movement.

Non-depressed participants. None of the correlations between gamma sub bands and melancholia were meaningful under eyes open or eyes closed conditions for these 67 participants. These results further confirm the suggestion made by Parker et al. [9] that severity of depression is a factor in melancholia.

3.2.2. Melancholia symptoms

Although the melancholia total score is a valuable target variable for investigation of its association with gamma, the eight symptoms of Melancholia shown in Table 1 vary a great deal in their content and cognitive/emotional associations. Therefore, the corresponding eight items also depicted in Table 1 were analyzed for their correlations with gamma in the range 30 Hz to 130 Hz, again using the depressed and the non-depressed subsamples.

3.2.2.1. Depressed vs non-depressed participants. Fig. 2 shows only those melancholia items that had meaningful correlations with gamma in the wavelengths 30–130 Hz for the depressed participants under the eyes open and eyes closed conditions at specific EEG sites (complete numerical data are presented in Supplementary Table 2). These data reflect the number of associations between Melancholia symptoms when gamma is defined as 30 Hz to 130 Hz, and according to depression state. Clearly, from these data, depressed participants exhibited many more meaningful correlations between EEG sites and overall gamma than non-depressed participants. Moreover, with only two exceptions (P3: 'My mind is not as clear as it used to be'; FP2: 'I find it hard to make decisions') all the meaningful associations between melancholia symptoms and gamma for the depressed participants were in a uniform direction according to eyes closed/open condition (eyes closed = mostly direct correlation coefficients; eyes open = mostly inverse correlations). Both correlations between gamma and 'I feel that others would be better off if I were dead' for the non-depressed participants were direct.

3.2.2.2. Depressed vs non-depressed participants, eyes open vs eyes closed, gamma sub bands. Fig. 3 shows the data presented in Fig. 2 broken down according to gamma sub bands of 20 Hz for both depressed and non-depressed participants under the eyes open and eyes closed conditions. (Complete data are presented in Supplementary Table 3.) Several major characteristics are apparent. First, there was variability in the rate of meaningful correlations between Melancholia items and different gamma sub bands, ranging from 11 in the 30–50 Hz sub band to 22 in the 110–130 Hz band. Second, some of the correlations recorded at lower gamma levels were also repeated at higher gamma levels. For example, for the melancholia item 'I don't enjoy sex' for the depressed participants the correlation with gamma at EEG site FCZ was found at 30–50 Hz, 50–70 Hz, 70–90 Hz, and 110–130 Hz. Similar multiple-gamma sub band correlations occurred for FT8 and FCZ for the item 'I don't enjoy doing the things I used to', and for FTZ, FCZ, T8, FT7 and CPZ for 'My mind is not as clear as it used to me'. Other examples were found for the next three melancholia items, but not for the two items 'I get tired for no reason' and 'I don't feel better even when good things happen." Third, many different EEG sites were involved in those meaningful correlations, with Fig. 3 showing those EEG sites that were meaningfully correlated with gamma more than once. Fourth, for the depressed participants, all correlations with gamma of any sub band

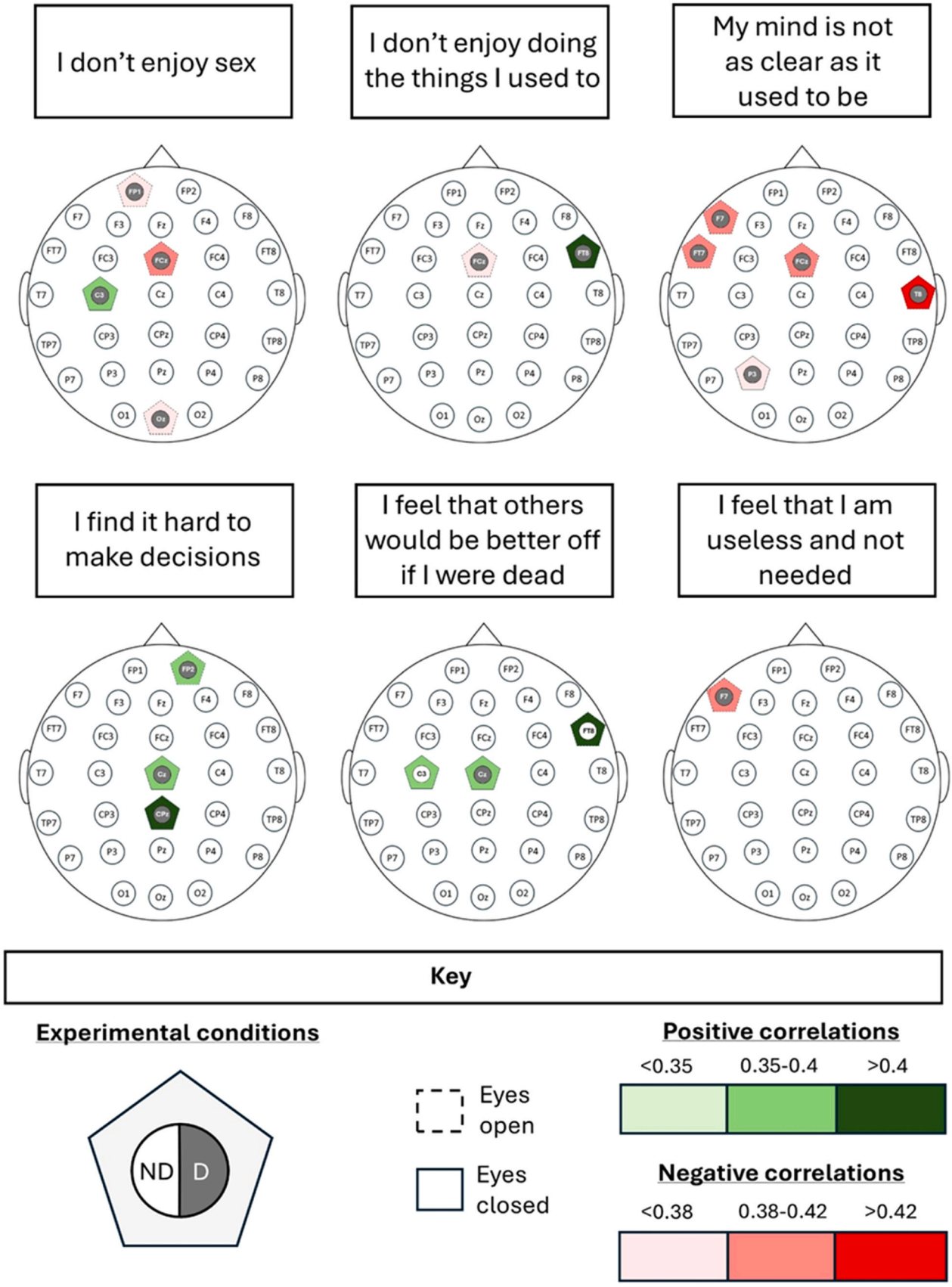

Fig. 2. Meaningful correlations between Melancholia items and EEG gamma frequency (30–130 Hz) across EEG sites. Grey circle indicates this site was correlated for depressed (D) individuals; white circle for non-depressed (ND) individuals. Broken border indicates this site was correlated for the eyes open condition; solid border for eyes closed. Green colour indicates positive correlation; red colour indicates negative correlation (shading represents strength of correlation).

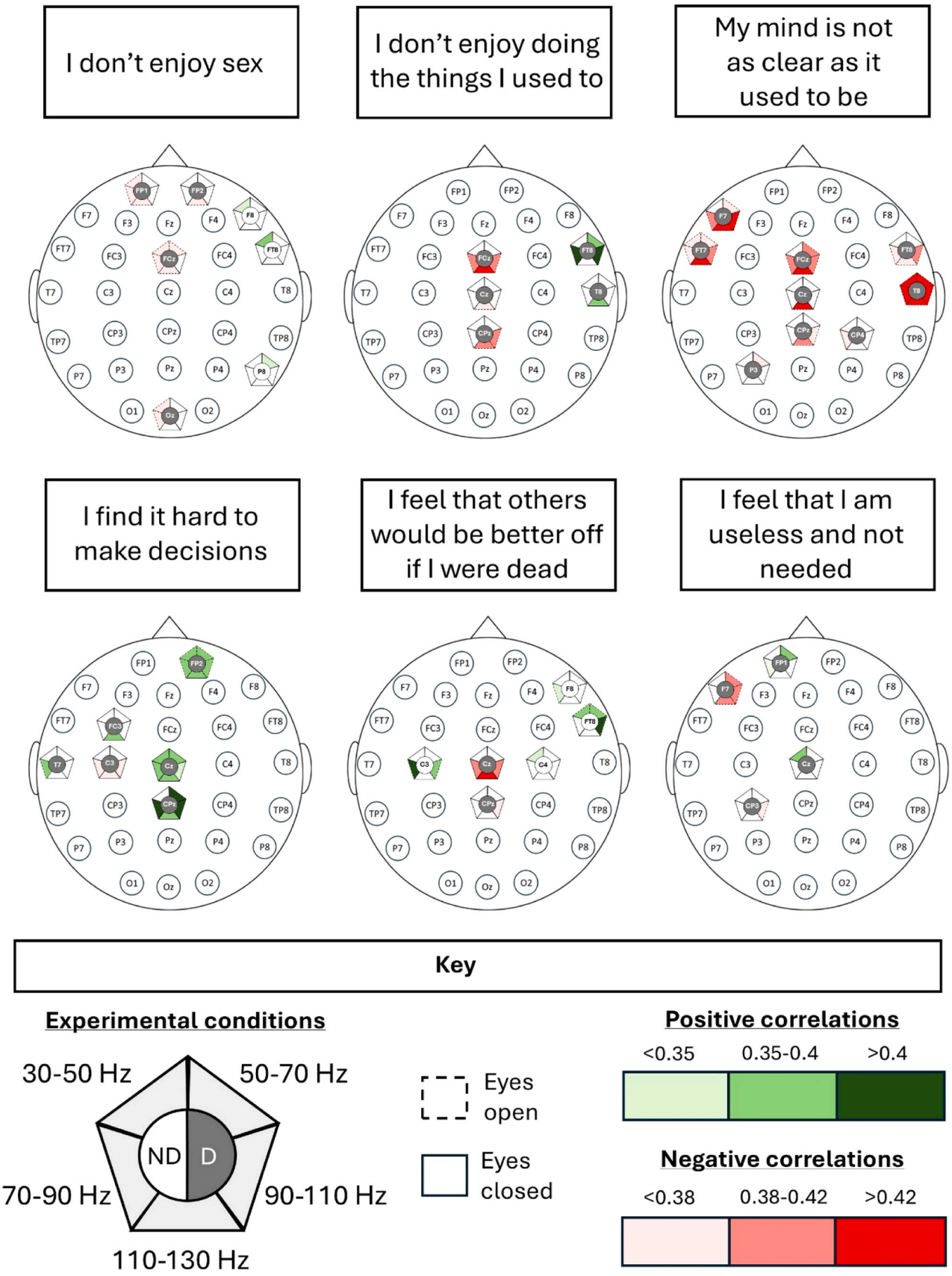

Fig. 3. Meaningful correlations between Melancholia items and EEG gamma frequency sub bands across EEG sites. Grey circle indicates this site was correlated for depressed (D) individuals; white circle for non-depressed (ND) individuals. Sub bands of gamma are displayed as wedges surrounding the EEG site (frequency band split shown in the key). Broken border indicates this site was correlated for the eyes open condition; solid border for eyes closed. Green colour indicates positive correlation; red colour indicates negative correlation (shading represents strength of correlation).

were uniformly inverse for the melancholia items 'I don't enjoy sex' and 'My mind is not as clear as it used to be', whereas correlations with gamma for the melancholia items 'I find it hard to make decisions' and 'I feel that others would be better off if I were dead' were all were almost all direct. Fifth, all the correlations between gamma and the melancholia items 'I don't enjoy sex', 'I don't enjoy doing the things I used to', 'My mind is not as clear as it used to be', 'I feel that I am useless and not needed', and 'I don't feel better even when good things happen' were inverse under the eyes open condition but direct under the same condition for the items 'I find it hard to make decisions', and 'I feel that others would be better off if I were dead'. Sixth, for the depressed participants, 24/28 (85.7 %) of correlation coefficients under the eyes closed condition were direct, across all eight melancholia items. By contrast, under the eyes open condition, 46/51 (90.2 %) of correlation coefficients with gamma were inverse for the depressed participants. These results suggest a complex multi-level association between gamma and melancholia symptoms that may defy simplification, especially by sole reference to surface EEG data. To enhance that finding, source localization analysis was undertaken to identify brain regions associated with melancholia symptoms and gamma activity.

3.3. Gamma and melancholia: eLORETA analysis

As mentioned above, a further exploratory analysis was undertaken to identify which specific brain regions exhibited meaningful correlations with melancholia using source localization via *eLORETA*. Because of the acknowledged ultra conservative *p* values produced *by eLORETA's* statistical analysis procedures [46,47], the cut off for a meaningful association between gamma power and melancholia severity was set at Cohen's [27] 'small' effect (i.e., $r \geq .2$) which he described as "not so small as to be trivial" [48], p. 281.

Fig. 4 presents only those correlations identified by *eLORETA* that were meaningfully correlated at $r \geq .2$ with the melancholia items. Some items had more than one such correlation with gamma (yellow shading indicates a meaningful positive correlation, blue shading indicates a meaningful negative correlation). Although the 'small' correlation value of $r \geq .2$ was set as the cut off for consideration of these exploratory data, 11 of the 13 coefficients found by *eLORETA* met the $r \geq .3$ level of strength, with the remaining two coefficients being $r = .296$.

I don't enjoy sex: Fig. 4(a): In the eyes closed condition, higher scores were associated with maximally increased 30–50 Hz band power in the right orbital and inferior frontal gyrus ($r = .304$).

My mind is not as clear as it used to be: Fig. 4(b): In the eyes closed condition, higher scores were associated with maximally increased gamma power in the left superior frontal gyrus in multiple frequency bands: 30–50 Hz ($r = .316$), 50–70 Hz ($r = .314$), 70–90 Hz ($r = .296$), and 90–110 Hz ($r = .296$). In contrast, Fig. 4(c) shows higher scores related to maximally decreased gamma power in the left middle/inferior temporal gyrus in the 90–110 Hz band ($r = -.312$), and the 110–130 Hz band ($r = -.324$). For the same question in the eyes open condition, (Fig. 4(d)) higher scores correlated with increased gamma power in the right parahippocampal gyrus for the 30–50 Hz band ($r = .317$), the 50–70 Hz band ($r = .330$), the 70–90 Hz band $r = .338$) and the 90–110 Hz band ($r = .320$).

I feel that others would be better off if I were dead: Fig. 4(e): In the eyes open condition, higher scores were liked to maximally increased 30–50 Hz band power in the left insula ($r = .304$).

I feel that I am useless and not needed: Fig. 4(f): In the eyes closed condition, higher scores correlated with maximally increased 30–50 Hz band power in the left middle frontal gyrus ($r = .302$).

I don't feel better even when good things happen: Fig. 4(g): In the eyes open condition, higher scores correlated with maximally increased 70–90 Hz band power in the left parahippocampal gyrus ($r = .305$).

4. Discussion

4.1. Overall results

These results indicate that meaningful associations existed between melancholia as a total score on Parker et al.'s (2019) scale and gamma activity in several specific brain sites. The initial results reported here argue for a complexity in that relationship that varies with gamma band and melancholia symptoms. These data therefore imply that melancholia might not be a unitary disorder but, like MDD, quite heterogeneous [49], a concept that has some current value [26,50]. The combination of the EEG site results (Figs. 2 and 3) plus the exploratory *eLORETA* data (Fig. 4), suggest some initial hypothetical explanations as to the reasons why specific melancholia symptoms might be linked with gamma activity in certain regions of the brains of depressed individuals.

4.2. Specific melancholia symptoms and gamma in select brain areas

The majority of meaningful results showed positive correlations between gamma band power and scores on multiple melancholia items. If it follows that increased gamma is associated with increased cognitive symptoms relating to attention, memory and learning, it also follows that these findings indicate increased active thinking about the item content/symptom that gamma is positively correlated with. For example, an increased belief that someone feels better off dead correlating with increased gamma power in the insula (a key structure in the interaction between the executive control and salience networks) indicates that suicidal ideation may result from an active decision-making process or an over-focus on suicide rather than the absence of a motivating reason to continue living. This finding challenges the perspective that melancholia is associated with cognitive deficits by suggesting that elevated gamma may reflect the melancholic individual's urgent attempts to adjust to/solve environmental challenges that appear to be beyond the individual's control or ability. Under this perspective, elevated gamma may represent anxiety in dealing with major mood challenges rather than an increase in higher-level cognitive activity that is associated with effective problem solving. This perspective is referred to below when discussing association between gamma and anxiety. The distinction between thoughts like "I wish I were dead" and "I don't see any reason to go on" reflects the difference in agency shown by those with melancholic depression compared to those with more anhedonic forms of depression. This distinction is worth noting as melancholia is often overgeneralized as anhedonic or indicative of a lack of affect or engagement.

Increased reports that "my mind is not as clear as it used to be" were found to link primarily with gamma in the left but also the right superior frontal gyrus in Brodmann area 8 in the eyes closed condition. At first this seems unusual as this region is primarily known as the frontal eye fields, which would be less active when no visual stimuli are available. However, increased activity in BA 8 has also been found when people report a sense of uncertainty and difficulty making decisions [51]. As above, this indicates some symptoms of melancholic depression may be products of active cognitive processes rather than a deficit in cognitive function.

Emotional aspects of gamma activation were also observed in these results: increased reports of "feeling useless" or "feeling not needed" meaningfully correlated with increased 30–50 Hz gamma in the left middle frontal gyrus area of Brodmann area 9, a region known to be active during attention to negative emotions and self-criticism [52,53]. Similarly, "not enjoying sex" was associated with increased 30–50 Hz gamma in the right orbital/inferior frontal gyrus, a region typically associated with language processing and also emotional recognition. A review by Goodkind et al., [54] reported that this area is vital for the ability to track dynamically changing emotions, while the reduced volume of the entire orbitofrontal area in patients with MDD (but no reduction in neural activity: [55]) also implicates this region.

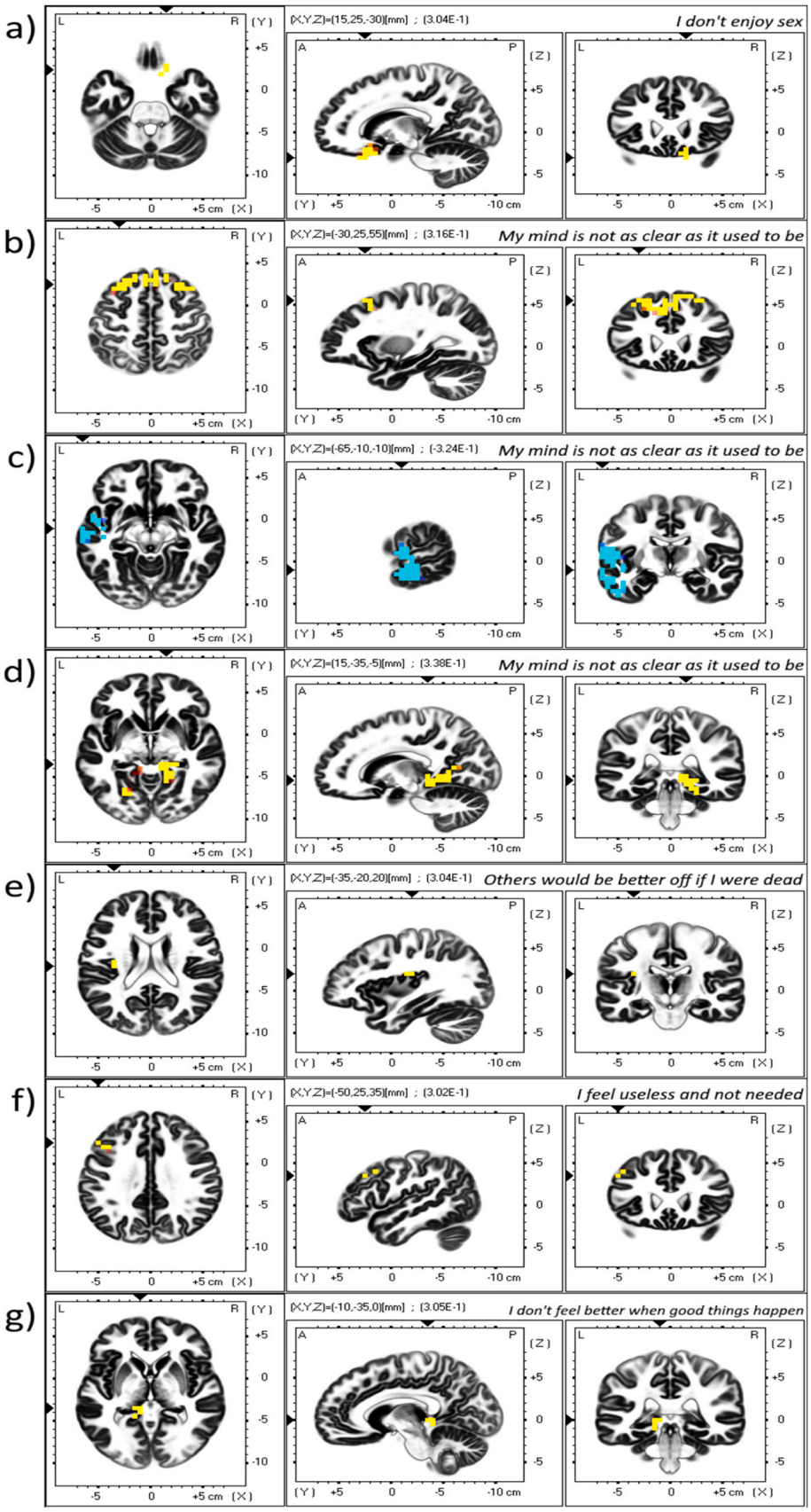

Fig. 4. Five Melancholia items with meaningful correlations with specific brain sites (from eLORETA source localization). Yellow shading indicates a meaningful positive correlation; blue shading indicates a meaningful negative correlation.

Similar to the results above, this indicates that patients with melancholic depression show an increase in emotional processing rather than suppressing their feelings.

Two lateralized correlations were found in the parahippocampal gyrus: 70–90 Hz gamma increased in the left hemisphere as responses to "I don't feel better even when good things happen" increased, and 30–110 Hz gamma (especially 70–90 Hz) increased in the right hemisphere as responses to "My mind is not as clear as it used to be" increased. While the parahippocampus is known to be active when episodic memory is being called upon for the semantic and social aspects of visual scene processing [56], these results are more likely to be the outcome of activity in the hippocampus itself where high frequency gamma activity has an established role in memory processing [19,57]. Previous findings implicating the left hippocampus' involvement in autobiographical or context-dependent episodic memory align well with the correlation between increased gamma activation and stronger feelings that "good things never happen" [58,59].

The sole negative correlation in the *eLORETA* results showed a fall in the 90–130 Hz gamma band power in the left middle temporal lobe as responses to "My mind is not as clear as it used to be" increased. Typically associated with language processing, high frequency gamma oscillations in this region have been reported as increased during speech production and co-speech gestures [60]. The results from this study may indicate that patients scoring high on a lack of mental clarity may be suppressing gamma in their language centers in an attempt to avoid self-talk or their own internal narrative.

Overall, the majority of associations between gamma and melancholia items were direct, indicating that, as gamma increased, so did participants' scores on the particular melancholia items. This may be interpreted as representing the situation where a participant is experiencing melancholia to a high degree of severity, and gamma also increases as a potential method for increasing neurocognitive activity aimed at managing the melancholia symptom and its causes. This hypothesis is supported by findings that, in autistic boys, gamma correlated directly with elevated anxiety due to social interaction demands [61], perhaps representing neurocognitive effort extended to manage the source of social anxiety or the individual's over-reaction to that source, which is a major defining diagnostic criteria for autism [1]. This hypothesis is congruent with the 'neurocognitive compensation' hypothesis that suggests that factors such as lifestyle, metabolism, and neural plasticity may produce a form of cognitive resilience by enlisting brain regions to process particular information that they usually are not involved with [62,63].

If this interpretation is to be considered, it challenges the traditional notion that melancholia is majorly characterized by pervasive anhedonia, psychomotor retardation, and unreactive mood [64,65] due to lowered neurocognitive activity. That view remains in place [66], but may repay further investigation in terms of the relative amounts of high frequency electrical activity that accompany melancholia symptoms, and the direction of the correlation between the two variables.

4.3. Clinical implications

Several suggestions for clinical practice arise from these exploratory data. First, in terms of diagnosis, consideration of melancholia as a multi-faceted heterogeneous disorder (like MDD) means that using total scores from inventories such as Parker et al.'s SMPI might be as unreliable in understanding the kind of melancholia that an individual is experiencing as is using a single score or dichotomous rating scale for MDD as a basis for treatment decisions. Much has been written about the need to individualize treatment for depression based on symptom profiles [10,11,67,68], and this holds true for the melancholia subtype of MDD. Second, as a consideration regarding treatment, if melancholic patients exhibit over-active cognitive processing in specific brain regions rather than simply an overall apathetic attitude, then this has implications for the kind of therapy that might be applied to patients exhibiting melancholia. Although Brown [69], Taylor, Fink [70], and Thase, Friedman [71] suggested that melancholia was traditionally considered to be biological in origin, and therefore reliant upon medication, ECT, and similar non-talk therapies, some other data from that period also indicated that treatment of melancholia with antidepressants (especially SSRIs) led to deterioration, but ECT, antipsychotics and mood stabilisers were effective in reducing melancholia severity [72]. By contrast, a more recent evaluation of the efficacy of ECT for melancholia reported no significant difference between the outcome for melancholia and non-melancholic depressed patients [73]. Far less invasive than ECT and relatively free from ethical challenges, electrical stimulation of the brain via repetitive transcranial magnetic stimulation (rTMS) has been used successfully with melancholic patients. For example, theta burst stimulation (TBS) mimics rhythmic bursts of 3 Hz to 8 Hz endogenous brain activity, and has been demonstrated to be a successful treatment for depression (see a systematic review and meta-analysis of 23 studies: [74]). When applied to the left dorsolateral prefrontal cortex (DLPFC) [75], TBS was reported to lead to significant reductions in melancholia symptoms.

4.4. Limitations

Spoelma, Serafimovska, and Parker [12] examined neurological markers of depression, including results from EEG studies, but none of those studies reported on gamma sub bands, preventing comparison with the current data. The limitations of sample size (although sufficient for the analyses carried out here, this was very close to the minimum acceptable size for correlational analyses), geographical and cultural restrictions, and the use of a community sample rather than hospitalized patients, restrict the generalizability to some other settings and populations. Psychiatric medication, sleep quality, and anxiety may affect gamma. Data were collected at a single point in time, and so no developmental variability in symptoms was apparent. Resting state gamma may be influenced by mind wandering or muscle tension, and collection of electromyographic data would add to the validity of the results.

Measurement of depression and melancholia were performed with valid and reliable self-report scales, but collection of clinician interviews would add strength to the diagnostic process used here. The further investigation of what neurocognitive processes accompany gamma sub bands must be a future research target, building upon some initial work in that field [76–78]. Finally, in terms of the statistical analyses, the application of an effect size metric rather than a p value that would have biassed results towards a too-conservative Type I error rate enabled a balanced approach to be taken regarding the trade-off between Type I and Type II error rates, which was considered to be vital in an exploratory study that utilized small effects. However, with larger sample sizes in confirmatory studies of these findings, reference to both effect size and Type I error values would enhance the strength of results.

4.5. Conclusion

Notwithstanding these limitations, these are the first gamma sub band data to be correlated with melancholia, at either total scale score or individual item levels. By including the entire brain, a comprehensive picture of how melancholic symptoms relate to specific brain site activity has been initially compiled. From these exploratory data, it is possible to derive directional hypotheses for formal testing with larger samples and greater statistical power.

CRediT authorship contribution statement

Evans Ian: Writing – review & editing, Writing – original draft, Formal analysis, Data curation, Conceptualization. **Sharpley Christopher:** Writing – review & editing, Writing – original draft, Project administration, Investigation, Formal analysis, Conceptualization. **Vicki Bitsika:** Writing – review & editing, Writing – original draft, Project

administration, Methodology, Conceptualization. **G Lorenzo Odierna:** Writing – review & editing, Writing – original draft, Visualization, Resources.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declaration of Competing Interest

None of the authors has any conflict of interest to declare.

Acknowledgements

The authors express their gratitude to the volunteers who participated in this study.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.bbr.2026.116060.

References

[1] APA, Diagnostic and Statistical Manual of Mental Disorders 5th Ed Text Revision, American Psychiatric Association, 2022, https://doi.org/10.1176/appi.books.9780890425787.
[2] G. Parker, M.J. Spoelma, Melancholia defined with the precision of a machine, J. Affect. Disord. 282 (2021) 69–73, https://doi.org/10.1016/j.jad.2020.12.112.
[3] C.V. Day, A.J. Rush, A.W. Harris, P.M. Boyce, W. Rekshan, A. Etkin, C. DeBattista, A.F. Schatzberg, B.A. Arnow, L.M. Williams, Impairment and distress patterns distinguishing the melancholic depression subtype: an iSPOT-D report, J. Affect Disord. 174 (2015) 493–502, https://doi.org/10.1016/j.jad.2014.10.046.
[4] K. Fletcher, G. Parker, A. Paterson, M. Fava, D. Iosifescu, D. Pizzagalli, Anhedonia in melancholic and non-melancholic depressive disorders, J. Affect. Disord. 184 (2015) 81–88, https://doi.org//10.1016/j.jad.2015.05.028.
[5] L. Tondo, G. Vázquez, R. Baldessarini, Melancholic versus nonmelancholic major depression compared, J. Affect. Disord. 266 (2020) 760–765, https://doi.org//10.1016/j.jad.2020.01.139.
[6] G. Parker, D. Hadzi-Pavlovic, P. Boyce, K. Wilhelm, H. Brodaty, P. Mitchell, I. Hickie, K. Eyers, Classifying depression by mental state signs, Br. J. Psychiatry 157 (1) (1990) 55–65.
[7] G. Parker, D. Hadzi-Pavlovic, K. Wilhelm, I. Hickie, H. Brodaty, P. Boyce, P. Mitchell, K. Eyers, Defining melancholia: properties of a refined sign-based measure, Br. J. Psychiatry 164 (3) (1994) 316–326.
[8] G. Parker, S. McCraw, The properties and utility of the CORE measure of melancholia, J. Affect. Disord. 207 (2017) 128–135.
[9] G. Parker, G. Tavella, D. Hadzi-Pavlovic, Identifying and differentiating melancholic depression in a non-clinical sample, J. Affect. Disord. 243 (2019) 194–200, https://doi.org//10.1016/j.jad.2018.09.024.
[10] T. Insel, Transforming diagnosis, National Institute of Mental Health, 2013. ⟨www.nimh.nih.gov/about/director/2013/transforming-diagnosis-shtml⟩. Retrieved May 27 from.
[11] M.J. Kas, B.W. Penninx, G.M. Knudsen, B. Cuthbert, P. Falkai, G.S. Sachs, K. J. Ressler, E. Bałkowiec-Iskra, F. Butlen-Ducuing, M. Leboyer, Precision psychiatry roadmap: towards a biology-informed framework for mental disorders, Mol. Psychiatry (2025) 1–10.
[12] M. Spoelma, A. Serafimovska, G. Parker, Differentiating melancholic and non-melancholic depression via biological markers: a review, World J. Biol. Psychiatry (2023) 1–107 (just-accepted).
[13] J. Henriques, R. Davidson, Regional brain electrical asymmetries discriminate between previously depressed and health control subjects, J. Abnorm. Psychol. 1 (1990) 22–31.
[14] J. Henriques, R.J. Davidson, Brain electrical asymmetries during cognitive task performance in depressed and nondepressed subjects, Biol. Psychiatry 42 (1997) 1039–1050.
[15] E. Jesulola, C. Sharpley, V. Bitsika, L. Agnew, P. Wilson, Frontal alpha asymmetry as a pathway to behavioural withdrawal in depression: research findings and issues, Behav. Brain Res. 292 (2015) 56–67.
[16] G.E. Bruder, J.W. Stewart, P.J. McGrath, Right brain, left brain in depressive disorders: clinical and theoretical implications of behavioral, electrophysiological and neuroimaging findings, Neurosci. Biobehav. Rev. 78 (2017) 178–191.
[17] C. Bruun, C. Arnbjerg, L. Kessing, Electroencephalographic parameters differentiating melancholic depression, non-melancholic depression, and healthy controls. A systematic review [Systematic Review], Front. Psychiatry 12 (2021), https://doi.org/10.3389/fpsyt.2021.648713.
[18] C.F. Sharpley, V. Bitsika, S.M. Shadli, E. Jesulola, L.L. Agnew, Alpha wave asymmetry is associated with only one component of melancholia, and in different directions across brain regions, Psychiatry Res. Neuroimaging 334 (2023) 111687.
[19] P.J. Fitzgerald, B.O. Watson, Gamma oscillations as a biomarker for major depression: an emerging topic, Transl. Psychiatry 8 (1) (2018) 177, https://doi.org/10.1038/s41398-018-0239-y.
[20] G. Buzsaki, A. Draguhn, Neuronal oscillations in cortical networks, Science 304 (5679) (2004) 1926–1929.
[21] G. Buzsáki, X.-J. Wang, Mechanisms of gamma oscillations, Annu. Rev. Neurosci. 35 (1) (2012) 203–225.
[22] A. Fernandez-Ruiz, A. Sirota, V. Lopes-dos-Santos, D. Dupret, Over and above frequency: gamma oscillations as units of neural circuit operations, Neuron 111 (7) (2023) 936–953.
[23] X.-J. Wang, Neurophysiological and computational principles of cortical rhythms in cognition, Physiol. Rev. 90 (3) (2010) 1195–1268.
[24] M.R. Hudson, N.C. Jones, Deciphering the code: identifying true gamma neural oscillations (Article), Exp. Neurol. 357 (2022) 114205, https://doi.org/10.1016/j.expneurol.2022.114205.
[25] M.K. Arikan, M.G. Gunver, N. Tarhan, B. Metin, High-gamma: a biological marker for suicide attempt in patients with depression, J. Affect. Disord. 254 (2019) 1–6.
[26] E.I. Fried, F. Coomans, L. Lorenzo-Luaces, The 341 737 ways of qualifying for the melancholic specifier, Lancet Psychiatry 7 (6) (2020) 479–480.
[27] J. Cohen, Statistical power for the behavioural sciences, Erlbaun, 1988.
[28] W. Zung, From art to science: The diagnosis and treatment of depression, Arch. Gen. Psychiatry 29 (1973) 328–337.
[29] S. Segalowitz, M. Bryden, Individual differences in hemispheric representation of language, in: In.S.J. Segalowitz (Ed.), Language Functions and Brain Organization, Academic Press, 1983, pp. 341–372, https://doi.org//10.1016/B978-0-12-635640-3.50024-2.
[30] J. Packheiser, J. Schmitz, C. Stein, L. Pfeifer, G. Berretz, M. Papadatou-Pastou, J. Peterburs, S. Ocklenburg, Handedness and depression: a meta-analysis across 87 studies, J. Affect. Disord. 294 (2021) 200–209, https://doi.org//10.1016/j.jad.2021.07.052.
[31] W. Zung, A self-rating depression scale, Arch. Gen. Psychiatry 12 (1965) 63–70.
[32] J. DeJonge, J. Baneke, The Zung self-rating depression scale: a replication study on reliability, validity and prediction, Psychol. Rep. 64 (1989) 833–834.
[33] J. Gabrys, K. Peters, Reliability, discriminant and predictive validity of the Zung Self-Rating Depression Scale, Psychol. Rep. 57 (1985) 1091–1096.
[34] A. Schaefer, J. Brown, C. Watson, D. Plenel, J. DeMotts, M. Howard, N. Petrik, B. Ballweg, Comparison of the validities of the Beck, Zung and MMPI depression scales, J. Consult. Clin. Psychol. 53 (1985) 415–418.
[35] H. Nolan, R. Whelan, R.B. Reilly, FASTER: fully automated statistical thresholding for EEG artifact rejection, J. Neurosci. Methods 192 (1) (2010) 152–162.
[36] C.F. Sharpley, W. Arnold, I. Evans, V. Bitsika, E. Jesulola, L. Agnew, Studies of EEG asymmetry and depression: to normalise or not? Symmetry 15 (9) (2023) https://doi.org/10.3390/sym15091689.
[37] J. Cohen, The cost of dichotomization, Appl. Psychol. Meas. 7 (1983) 249–253.
[38] A. Kołodziej, M. Magnuski, A. Ruban, A. Brzezicka, No relationship between frontal alpha asymmetry and depressive disorders in a multiverse analysis of five studies, eLife 10 (2021) e60595.
[39] J. Cohen, P. Cohen, S. West, L.S. Aiken, Applied multiple regression/correlation analysis for the behavioral sciences, Lawrence Erlbaum Associates, 2003.
[40] A. Norris, K. Aroian, To transform or not transform skewed data for psychometric analysis: that is the question!, Nurs. Res. 53 (2004) 67–71.
[41] Z.T. Haile, Power analysis and exploratory research, J. Hum. Lact. 39 (4) (2023) 579–583.
[42] M. Maier, D. Lakens, Justify your alpha: a primer on two practical approaches, Adv. Methods Pract. Psychol. Sci. 5 (2) (2022) 25152459221080396, https://doi.org/10.1177/25152459221080396.
[43] K. Rothman, No adjustments are needed for multiple comparisons, Epidemiology 1 (1990) 43–46.
[44] D. Streiner, G. Norman, Correction for multiple testing, Chest 140 (2011) 16–18.
[45] R.D. Pascual-Marqui, M. Esslen, K. Kochi, D. Lehmann, Functional imaging with low-resolution brain electromagnetic tomography (LORETA): a review, Methods Find. Exp. Clin. Pharmacol. 24 (C) (2002) 91–95.
[46] T. Nichols, A. Holmes, Nonparametric permutation tests for functional neuroimaging: a primer with examples, Hum. brain Mapp. 15 (1) (2002) 1–25.
[47] T. Nichols, S. Hayasaka, Controlling the familywise error rate in functional neuroimaging: a comparative review, Stat. Methods Med. Res. 12 (5) (2003) 419–446.
[48] G.M. Sullivan, R. Feinn, Using effect size—or why the P value is not enough, J. Grad. Med. Educ. 4 (3) (2012) 279–282.
[49] S. Ostergaard, S. Jensen, P. Bech, The heterogeneity of the depressive syndrome: when numbers get serious, Acta Psychiatr. Scand. 124 (2011) 495–496, https://doi.org/10.1111/j.1600-0447.2011.01744.x.
[50] P.R. Regonia, M. Takamura, T. Nakano, N. Ichikawa, A. Fermin, G. Okada, Y. Okamoto, S. Yamawaki, K. Ikeda, J. Yoshimoto, Modeling heterogeneous brain dynamics of depression and melancholia using energy landscape analysis, Front. Psychiatry 12 (2021) 780997.
[51] K.G. Volz, R.I. Schubotz, D.Y. von Cramon, Variants of uncertainty in decision-making and their neural correlates, Brain Res. Bull. 67 (5) (2005) 403–412.
[52] R. Kerestes, C.D. Ladouceur, S. Meda, P.J. Nathan, H.P. Blumberg, K. Maloney, B. Ruf, A. Saricicek, G.D. Pearlson, Z. Bhagwagar, Abnormal prefrontal activity subserving attentional control of emotion in remitted depressed patients during a working memory task with emotional distracters, Psychol. Med. 42 (1) (2012) 29–40.

[53] O. Longe, F.A. Maratos, P. Gilbert, G. Evans, F. Volker, H. Rockliff, G. Rippon, Having a word with yourself: neural correlates of self-criticism and self-reassurance, NeuroImage 49 (2) (2010) 1849–1856.
[54] M.S. Goodkind, M. Sollberger, A. Gyurak, H.J. Rosen, K.P. Rankin, B. Miller, R. Levenson, Tracking emotional valence: the role of the orbitofrontal cortex, Hum. brain Mapp. 33 (4) (2012) 753–762.
[55] J. Scheuerecker, E.M. Meisenzahl, N. Koutsouleris, M. Roesner, V. Schöpf, J. Linn, M. Wiesmann, H. Brückmann, H.-J. Möller, T. Frodl, Orbitofrontal volume reductions during emotion recognition in patients with major depression, J. Psychiatry Neurosci. 35 (5) (2010) 311–320.
[56] E.M. Aminoff, K. Kveraga, M. Bar, The role of the parahippocampal cortex in cognition, Trends Cogn. Sci. 17 (8) (2013) 379–390.
[57] L.L. Colgin, E.I. Moser, Gamma oscillations in the hippocampus, Physiology 25 (5) (2010) 319–329.
[58] J. Lisman, G. Buzsáki, A neural coding scheme formed by the combined function of gamma and theta oscillations, Schizophr. Bull. 34 (5) (2008) 974–980.
[59] N. Burgess, E.A. Maguire, J. O'Keefe, The human hippocampus and spatial and episodic memory, Neuron 35 (4) (2002) 625–641.
[60] L. Marstaller, H. Burianová, P.F. Sowman, High gamma oscillations in medial temporal lobe during overt production of speech and gestures, PLOS One 9 (10) (2014) e111473.
[61] V. Bitsika, C.F. Sharpley, I.D. Evans, C.B. Watson, R.J. Williams, K.A. Vessey, Low-level social demand is associated with anxiety-related gamma wave responses in autistic male youth, Brain Sci. 15 (1) (2025) 40. ⟨https://pmc.ncbi.nlm.nih.gov/articles/PMC11763477/⟩.
[62] Y. Stern, C.A. Barnes, C. Grady, R.N. Jones, N. Raz, Brain reserve, cognitive reserve, compensation, and maintenance: operationalization, validity, and mechanisms of cognitive resilience, Neurobiol. Aging 83 (2019) 124–129, https://doi.org/10.1016/j.neurobiolaging.2019.03.022.
[63] N. Bunzeck, T.K. Steiger, U.M. Krämer, K. Luedtke, L. Marshall, J. Obleser, S. Tune, Trajectories and contributing factors of neural compensation in healthy and pathological aging, Neurosci. Biobehav. Rev. 156 (2024) 105489, https://doi.org/10.1016/j.neubiorev.2023.105489.
[64] K.S. Kendler, The genealogy of major depression: symptoms and signs of melancholia from 1880 to 1900, Mol. Psychiatry 22 (11) (2017) 1539–1553, https://doi.org/10.1038/mp.2017.148.
[65] A.J. Rush, J.E. Weissenburger, Melancholic symptom features and DSM-IV, Am. J. Psychiatry 151 (4) (1994) 489–498.
[66] D.J. Martino, A.G. Szmulewicz, M.P. Valerio, G. Parker, Melancholia: an attempt at definition based on a review of empirical data, J. Nerv. Ment. Dis. 207 (9) (2019) 792–798.
[67] H. de Kluiver, R. Jansen, B.W. Penninx, E.J. Giltay, R.A. Schoevers, Y. Milaneschi, Metabolomics signatures of depression: the role of symptom profiles, Transl. Psychiatry 13 (1) (2023) 198.
[68] E.I. Fried, R.M. Nesse, Depression is not a consistent syndrome: an investigation of unique symptom patterns in the STAR* D study, J. Affect. Disord. 172 (2015) 96–102.
[69] W.A. Brown, Treatment response in melancholia, Acta Psychiatr. Scand. 115 (s433) (2007) 125–129, https://doi.org/10.1111/j.1600-0447.2007.00970.x.
[70] M.A. Taylor, M. Fink, Melancholia Diagn. Pathophysiol. Treat. Depress Illn. (2006) (New York, NY: Cambridge).
[71] M.E. Thase, E.S. Friedman, Is psychotherapy an effective treatment for melancholia and other severe depressive states? J. Affect. Disord. 54 (1-2) (1999) 1–19.
[72] A. Koukopoulos, G. Sani, A. Koukopoulos, G. Manfredi, I. Pacchiarotti, P. Girardi, Melancholia agitata and mixed depression, Acta Psychiatr. Scand. 115 (2007) 50–57.
[73] S. Waite, P.C. Tor, T. Mohan, D. Davidson, S. Hussain, V. Dong, C.K. Loo, D. M. Martin, The utility of the Sydney Melancholia Prototype Index (SMPI) for predicting response to electroconvulsive therapy in depression: a CARE Network study, J. Psychiatr. Res. 155 (2022) 180–185, https://doi.org/10.1016/j.jpsychires.2022.08.011.
[74] T. Kishi, T. Ikuta, K. Sakuma, M. Hatano, Y. Matsuda, J. Wilkening, R. Goya-Maldonado, M. Tik, N.R. Williams, S. Kito, Theta burst stimulation for depression: a systematic review and network and pairwise meta-analysis, Mol. Psychiatry (2024) 1–7.
[75] G. Parker, G. Tavella, M.J. Spoelma, V. Sazhin, Does theta burst stimulation have differential benefit for those with melancholic or non-melancholic depression? J. Affect. Disord. 350 (2024) 847–853.
[76] X. Jia, A. Kohn, Gamma rhythms in the brain, PLoS Biol. 9 (4) (2011) e1001045.
[77] M.T. Kucewicz, B.M. Berry, V. Kremen, B.H. Brinkmann, M.R. Sperling, B.C. Jobst, R.E. Gross, B. Lega, S.A. Sheth, J.M. Stein, Dissecting gamma frequency activity during human memory processing, Brain 140 (5) (2017) 1337–1350.
[78] P.J. Uhlhaas, G. Pipa, S. Neuenschwander, M. Wibral, W. Singer, A new look at gamma? High-(> 60 Hz) γ-band activity in cortical networks: function, mechanisms and impairment, Prog. Biophys. Mol. Biol. 105 (1-2) (2011) 14–28.