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- Body dysmorphic disorder (BDD) patients show reduced startle-evoked N100 amplitude
- Potentially impaired attention processes in BDD patients
- Global field power of the EEG at the N100 predicts BDD severity
- Neural responses in prepulse inhibition are lower than in prepulse facilitation

Early Auditory-Evoked Potentials in Body Dysmorphic Disorder: An ERP/sLORETA Study

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Abstract

Body dysmorphic disorder (BDD) is characterized by excessive preoccupation with imagined or slight physical defects in appearance. BDD is associated with cognitive impairments (attention, visual processing). Our study aims to evaluate the early neural responses (N100, P200) to prepulse inhibition (PPI) and prepulse facilitation (PPF), to investigate attentional processing of BDD in the auditory domain. Fifty-five adults took part: 30 BDD patients and 25 healthy controls. We compared their brain responses to PPI and PPF by analyzing global field power (GFP), event-related potentials (ERPs) and their respective sources. BDD exhibited reduced N100 amplitudes compared to healthy controls in response to the startle tone elicited by

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both PPI and PPF, potentially suggesting impaired allocation of attention. Interestingly, the lower the GFP at the N100, the higher the BDD severity. Source reconstruction analysis showed reduced activation for BDD during the N100 time window in PPI. Scalp responses and source activations in PPI were decreased overall compared to PPF, confirming the gating effect of PPI. We provided evidence that the N100 may serve as an electrophysiological marker of BDD, predicting its severity. Our study demonstrated the potential of using ERPs combined with behavioural PPI and PPF protocols to advance our understanding of BDD pathophysiology.

Keywords: Body Dysmorphic Disorder; EEG; N100 component; Prepulse Inhibition; sLORETA.

1. Introduction

Body dysmorphic disorder (BDD) is a psychiatric disorder characterized by distress and excessive preoccupation with perceived flaws in appearance that are not observable to others (DSM-5: American Psychiatric Association, 2013). Its recent classification within the Obsessive-Compulsive and Related Disorders (OCD) is attributed to constant preoccupations that trigger repeated acts (Buhlmann et al., 2002). Importantly, BDD patients exhibit impairments in memory and attention, as demonstrated in the digit span, story memory recall, and Stroop interferences tasks (Toh et al., 2017), suggesting executive dysfunction. Both BDD and OCD groups exhibit substantially poorer immediate memory and sustained attention compared to healthy controls, as evaluated by the Repeatable Battery for the Assessment of Neuropsychological Status (Toh, Castle, & Rossell, 2015). Furthermore, during processing of inverted faces on a screen, BDD show reduced inversion effect compared to healthy controls, which might be attributed to greater focus on detail ("over-attention") and reduced holistic processing (Feusner et al., 2010).

A promising way to investigate the neurophysiological markers of BDD patients would be to consider their underlying cognitive deficits. However, most scientific research on BDD to date has investigated its symptomatology in isolation from its neural correlates. The present study aims to fill this crucial gap by directly investigating the relationship between neural and behavioural measures of BDD. Specifically, here we examine the neural correlates of auditory prepulse inhibition (PPI) and facilitation (PPF) in BDD patients, as well as investigate how those can predict BDD severity, in order to reveal specific neural measures as electrophysiological markers of BDD. In a recent study, our group found reduced alpha power at left temporo-parietal areas in BDD compared to healthy controls, attributed to impaired resource allocation (Kapsali et al., 2020). Following up from this, we aim to investigate the neural correlates of BDD by analysing event-related

potentials (ERPs) and global field power (GFP), which offer a higher temporal resolution compared to brain oscillations.

Early ERPs have been systematically linked to early selective attention processes (e.g., N100: Fujiwara et al., 1998; Hillyard et al., 1973; Mangun & Hillyard, 1991; P200: Carretié et al., 2004; Yuan et al., 2009). In an EEG study, participants were instructed to attend to a series of tones presented independently to either ear (Hillyard et al., 1973). The authors found that the N100 was enhanced in the attended compared to the unattended ear. The N100 was increased to validly-cued, compared to invalidly-cued, visual stimuli in a Posner-type paradigm (Mangun & Hillyard, 1991). The P200 component has also been associated with attention allocation, reflecting task-relevant stimulus salience (Yuan et al., 2009). Notably, decreased amplitude of auditory evoked potentials (e.g., P50, N100) has been previously found in OCD patients, potentially linked to increased serotonergic tone in OCD (Molina et al., 1995). Increased N100 latency was observed in compulsive checkers, interpreted as subcortical dysfunction (Sher et al., 1983).

In this study, PPI of the acoustic startle response is used as a measure of attention linked to inhibitory function and sensorimotor gating (Braff & Geyer, 1990). PPI occurs when a pulse tone (startle) is presented 30-500 ms after a prepulse tone, and the latter inhibits the response to the former (Braff & Geyer, 1990). Subjects with low PPI present lower attention levels, worse strategy formation, and slower execution times than subjects with high PPI (Larrauri & Schmajuk, 2006). In contrary, when the time interval between the prepulse and the startle is large (>500 ms), the startle response is facilitated (prepulse facilitation, PPF: Graham, 1975). In PPF, the prepulse orients the individual's attention towards an upcoming stimulus, thus leading to an increased startle response (Wynn et al., 2004).

The aforementioned research led to the primary interest in this study: whether attention processes in the auditory domain would be differentiated between BDD patients relative to healthy controls, as evidenced from their neural responses in a PPI and PPF paradigm. PPI and PPF constitute an ideal paradigm to study attention processes and sensorimotor gating. We have already noted that inhibition and facilitation of the auditory startle response are automatic and that they may be assessed through neurophysiological measures. In addition, previous psychophysiological research has demonstrated the stability of the PPI and PPF measures over time in healthy participants (Abel et al., 1998; Braff et al., 1978; Cadenhead et al., 2013; Schwarzkopf et al., 1993).

We examined this question by presenting BDD and healthy controls with PPI and PPF trials, while recording their electroencephalogram (EEG). Participants also completed a number of questionnaires assessing BDD symptomatology. In contrary to previous studies focusing on visual processing, we investigated attentional processing in the auditory domain. Specifically, we conducted a comprehensive analysis by evaluating the spatiotemporal neural correlates of BDD associated with PPI and PPF. To that end, we analyzed two early time windows (N100 and P200) which showed predominant responses to the startle tone. We computed the following measures: a reference-independent, whole-scalp measure (GFP: Lehmann & Skrandies, 1980), the

ERP components, as well as their respective source generators. We further used the aforementioned neural measures to predict BDD severity.

Considering the previously demonstrated impairments in executive function and, in particular, attention in OCD and BDD (Toh et al., 2015), as well as the role of N100 in controlling directed attention (Hillyard et al., 1973), we hypothesized that BDD patients would exhibit lower amplitudes in early neural responses. Importantly, Molina and colleagues (1995) showed decreased auditory-evoked N100 in OCD patients, attributed to altered serotonergic neurotransmission, while Richter and colleagues (2012) reported evidence for inhibitory dysregulation in OCD. We also expected that these effects would be reflected in reduced cortical activation for BDD, potentially linked to deficits in sensory gating and attention orienting (Hu, Jansen, & Boutros, 2005). Consequently, we expected that the aforementioned effects would be reflected in reduced activation of cortical sources. Therefore, to the extent that BDD affects perceptual responses as well as cognitive performance, BDD might show reduced attention-related brain responses. With regards to between-conditions contrasts, we aimed to replicate the previous results of PPF eliciting enhanced neurophysiological responses compared to PPI. We were also interested in identifying the brain sources of the neural responses to PPI and PPF. Finally, we explored what brain signatures might predict BDD degree of symptomatology.

2. Methods

2.1. Participants

Fifty-five human adults (BDD patients and healthy controls) took part in the experiment. The BDD group consisted of 30 patients: 19 women (mean ± SD age of 32.53 ± 8.30 years) and 11 men (mean ± SD age of 27.55 ± 5.77 years). Similarly, 25 healthy controls were matched for age and biological sex: 16 women (mean ± SD age of 32.25 ± 9.07 years) and 9 men (mean ± SD age of 27.55 ± 5.65 years). The two groups were also balanced in terms of handedness (3 vs. 4 left-handed participants in control vs. BDD group, respectively) and smoking (6 vs. 5 smokers, respectively). Independent samples *t*-tests confirmed the absence of significant differences between the two groups in age ($t(53) = .153$, $p = .439$) and educational level ($t(53) = 1.389$, $p = .171$). Exclusion criteria included active drug or alcohol abuse, history of neurological disorders, and current pregnancy. Six patients were under SSRI medication and 3of them were also under medication with antipsychotics.

All participants underwent clinical interviews by two psychiatrists. BDD was diagnosed according to DSM-5 criteria. The following questionnaires confirmed the diagnosis: Body Dysmorphic Disorder Examination (BDDE), BDD-YBOCS Questionnaire, Dysmorphic Concern Questionnaire (DCQ) and Brown Assessment of belief scale (BABS). The study was performed in the psychophysiology laboratory of the University Mental Health, Neurosciences and Precision Medicine Research Institute “Costas Stefanis”, and was approved by the local ethics committee. All subjects gave written consent for their participation.

2.2. EEG recording and procedure

EEG recording were conducted in a Faraday cage. Evoked biopotential activity was digitalized at a sampling frequency of 1 kHz from 30 uniformly placed (active) electrodes mounted on an elastic cap according to the International 10-20 System. Electrode impedance was kept constantly below 5kΩ. EEG online reference was the average of earlobes, while the ground electrode was placed on the left mastoid.

Participants were informed that they would hear 51 pairs of tones (first tone at 60 dB = prepulse, second tone at 140 dB = startle) via headphones. The session comprised of 51 randomly presented trials from two conditions, based on the time interval between the prepulse and the startle tone. Specifically, there were 26 prepulse-pulse "short" intervals (30-500 ms, corresponding to prepulse inhibition, PPI) and 25 prepulse-pulse "long" intervals (500-2000 ms, corresponding to prepulse facilitation, PPF). Both tones had a duration 40 ms and a frequency of 2 kHz. EEG was recorded from -2 to 2 seconds, time-locked to the startle tone.

2.3. EEG preprocessing

First, EEG signals were down-sampled to 250 Hz and then band-pass filtered at 1-40 Hz (roll-off -6dB/octave) to remove baseline drifts and line noise. Electrodes showing abnormal time-course were excluded and interpolated Then, each electrode activity was re-referenced to the whole-scalp common average. An independent samples t-test confirmed the absence of significant differences in the number of rejected channels between groups ($t(53) = 0.598$, $p = 0.553$; 2.80±1.06 channels in BDD; 2.48±0.87 channels in controls). Electrodes located close to eyes (FP1, FP2 or FPz) were the most frequently rejected channels in the whole population (removed from 83% of the subjects). Subsequently, Independent Component Analysis (ICA) was run to correct eye-blinks and saccades. Artifactual components were removed in a semi-automatic manner by visual inspection along with simultaneous consideration of the SASICA suggestions (Chaumon et al., 2015). Continuous data were then segmented from -0.1 to 0.8 sec around the startle tone, and baseline corrected from -.05 to 0 sec. This narrow baseline correction was selected to avoid possible contaminations in PPI trials with prepulse-pulse intervals close to 50 ms. All datasets were preprocessed using EEGLAB (Delorme & Makeig, 2004).

2.4. Psychometric ratings

We analyzed the scores of the following questionnaires, in order to investigate potential correlations between BDD symptomatology and EEG measures (see also Supplementary material for all screening measures):

Yale-Brown Obsessive-Compulsive Scale for BDD (BDD-YBOCS): This psychometric questionnaire is a modified version of the original YBOCS, useful in evaluating the severity of BDD symptoms (Phillips et al., 1997). We used a 12-item version translated, adapted and validated in Greek (Kapsali et al., 2019). Items 1-5 assess obsessional preoccupation with the perceived defect in appearance, while items 6-10

assess compulsive behaviours. Item 11 measures the degree of insight, and item 12 avoidance. It is rated on a 0 (not at all) to 4 (every day) Likert scale.

Dysmorphic Concern Questionnaire (DCQ): This questionnaire is a 7-item self-report measure that assesses cognitive and behavioural symptoms of physical overconcern without seeking to establish a "diagnosis" of BDD (Oosthuizen et al., 1998). Respondents rate their concern on their physical appearance on a 4-point scale, ranging from 0 (not at all) to 3 (much more than most people).

There were significant differences ($p < .001$) between groups in both scales, with BDD showing 14.167 ± 0.815 (in DCQ) and 29.400 ± 1.039 (in BDD-YBOCS), while controls scored 6.040 ± 0.654 (in DCQ) and 3.800 ± 0.465 (in BDD-YBOCS). It is also worth noting that the BABS and BDDE measures were obtained only for the BDD group, scoring a Mean ± SD of 18.80 ± 2.80 (in BABS) and 117 ± 27 (in BDDE).

BDD group exhibits also intra-group homogeneity on delusional scales, namely on the (i) BABS, (ii) SCL-90-R Psychoticism dimension and (iii) Eysenck Personality Psychoticism dimension, with z-score-transformed values not exceeding ± 3 (as presented in Supplementary material).

2.5. Spatiotemporal computations of scalp and source data

2.5.1. Preliminary considerations

Initially, to visually inspect the "when-and-where" of predominant early ERP peaks elicitation, the grand-averaged ERPs and the Global Field Power curve (GFP; standard deviation across electrode ERPs at each time point) were calculated. Based on previous literature reporting PPI-related N100 and P200 evoked potentials (De Pascalis et al., 2013; De Pascalis & Russo, 2013), visual inspection of the ERPs, as well as the GFP (Fig.1), the N100 and the P200 were analyzed in the post-startle windows of 60-160 ms and 161-260 ms, respectively. Both components showed peak activity at fronto-central sites (Fig.1). Due to the absence of significant differences between groups and conditions in latencies, all groups and conditions were investigated in the same time windows.

Fig. 1. A. Butterfly plot of grand-average ERPs (over subjects and conditions; collapsed localizer). **B.** Global Field Power (GFP) curve with color-coded N100 (red) and P200 (blue) areas. **C.** Scalp topographies for N100 and P200 components.

2.5.2. Global Field Power (GFP) Analysis

First, we analyzed ERP responses in terms of a global map descriptor, namely the GFP. This metric constitutes a single, reference-independent measure of the whole-scalp response strength (Lehmann & Skrandies, 1980). GFP is a non-linear transformation, meaning that GFP of the grand-averaged ERPs is not equal to the average GFP of the single-subject ERPs. Computing the time-series of GFP enables the determination of time-points with high signal-to-noise ratios, presumably

corresponding to moments of high global neuronal synchronization (Michel et al., 1993), thus indicating the latency of ERP components. Our main goal was to evaluate the neural activity based on a single, global, and reference-free indicator of auditory startle response. Single-subject GFP waveforms were extracted separately for each group and condition. Two GFP measures (mean amplitudes and peak latencies) were then calculated within the N100 (60-160 ms) and P200 (161-260 ms) time windows.

2.5.3. Event-Related Potentials (ERP)

To more precisely localize effects, N100 and P200 components were analyzed. Both components were extracted over a fronto-central region of interest (ROI) where they exhibited maximal activity (Fig.1): AFz, Fz, F3, F4, FCz, FC3, and FC4. For the selected ROI, the mean ERP amplitude of the N100 (60-160 ms) and P200 (161-260 ms) components was calculated.

2.5.4. Statistical Analyses of GFP and ERP

For each dependent variable (GFP and ERP measures), separate mixed ANOVAs were conducted with the following factors: *condition* (PPI, PPF) and *group* (control, BDD). Greenhouse-Geisser corrections were applied for sphericity violations and Bonferroni corrections were used for the post-hoc pairwise *t*-tests. Kolmogorov-Smirnov normality tests were applied to confirm the validity of comparisons (all $p > .05$). For the group differences, a Levene's test was also conducted prior to the ANOVA to confirm the equality of variances between BDD and controls. All statistical thresholds were set at the significance level of 0.05.

2.5.5. Identifying ERP brain sources with sLORETA

ERP responses were exported for further analysis using the sLORETA software (Pascual-Marqui, 2002). sLORETA inverse-problem solution algorithm has been established as a reliable estimator of (sub)cortical sources, useful for the analysis of different time segments of ERPs (De Pascalis et al., 2013; De Pascalis & Russo, 2013). For each subject, the 30-channel ERPs of each condition was transformed to 6239-voxel sLORETA images, containing the 3D cortical current source density vectors (magnitudes) of each voxel. Finally, the source localization of the N100 and P200 components were calculated as the mean sLORETA activations.

2.5.6. Statistical mapping of source differences

To find significant effects of component activations, a voxel-by-voxel statistical approach was performed by juxtaposing PPF vs. PPI conditions and control vs. BDD, separately for N100 and P200. Source comparisons were performed only for the significant effects revealed by scalp-domain analyses. To control for multiple comparisons, all statistical tests were conducted using non-parametric testing (Nichols & Holmes, 2002), derived from 5000 randomizations. Finally, significant voxels are grouped according to their localization information (lobe, region, Brodmann area).

2.5.7. Predicting the psychometrics scores with EEG measures

In order to evaluate the predictive strength of the EEG measures (GFP and ERP amplitudes) for the psychometric scores (DCQ and Y-BOCS), we constructed two separate multiple linear regression (MLR) models using stepwise regression. The dependent variables involved in the MLRs were the psychometric scores, while the GFP-N100, GFP-P200, ERP-N100 and ERP-P200 amplitudes were considered as predictors. Each model contained an intercept, linear terms for each predictor, and all products of pairs (or interactions) of distinct predictors (no squared terms).

3. Results

3.1. Global Field Power (GFP) responses

3.1.1. Time window 60-160 ms

A mixed ANOVA revealed a significant main effect of *condition* ($F(1,53) = 6.7, p = .012, \eta_p^2 = .112$), as PPF ($M \pm SE = 2.10 \pm .09$) exhibited higher GFP amplitudes than PPI ($M \pm SE = 1.85 \pm .09$). Additionally, the BDD group ($M \pm SE = 1.77 \pm .11$) showed reduced amplitudes compared to the control group ($M \pm SE = 2.19 \pm .12$) (main effect of *group*: $F(1,53) = 6.76, p = .012, \eta_p^2 = .113$). There was no significant interaction between the variables. Finally, there were no significant main effects or interaction between the variables with regards to the GFP latencies (all $p's > .05$). Control analyses showed that the same effects survive either when 3 patients (under SSRI and psychotics medication) are excluded from the BDD sample, or 6 patients (under only SSRI medication) are excluded (as presented in Supplementary material).

3.1.2. Time window 161-260 ms

GFP amplitudes during the second time window revealed a significant main effect of *condition* ($F(1,53) = 12.85, p = .001, \eta_p^2 = .195$), with PPF ($M \pm SE = 2.04 \pm .19$) showing higher GFP values compared to PPI ($M \pm SE = 1.63 \pm .15$). No significant effect of group or interaction between the variables was detected ($p's > .28$). Similar to the first time window, no significant effects were observed on GFP latencies (all $p's > .05$).

The grand-averaged GFP waveforms for each group (Fig. 2A) and condition (Fig. 2B) are illustrated, accompanied with the corresponding descriptive statistics (error bars).

Fig. 2. Grand-averaged global field power (GFP) waveforms for BDD (purple) vs. control (green) groups (panel **A**) and PPI (blue) vs. PPF (red) conditions (panel **B**). The two shaded time windows indicate the N100 and P200 ranges, respectively. Below each panel, the corresponding scatter box-plots are depicted for each time window. Symbol '*' denotes statistically significant differences.

3.2. Scalp-domain ERP analysis

3.2.1. N100 component

A mixed ANOVA revealed a main effect of *condition* ($F(1,53) = 7.31, p = .009, \eta_p^2 = .121$), as PPF elicited significantly enhanced N100 ($M \pm SE = -1.33 \pm .15$) compared to PPI ($M \pm SE = -1.01 \pm .13$). Furthermore, the N100 was reduced for BDD ($M \pm SE = -.88 \pm .17$) compared to the control ($M \pm SE = -1.46 \pm .19$) group (main effect of *group:* $F(1,53) = 5.2, p = .027, \eta_p^2 = .089$). No significant interaction was obtained ($p = .46$).

3.2.2. P200 component

PPF ($M \pm SE = .92 \pm .19$) elicited higher P200 amplitudes compared to PPI ($M \pm SE = .34 \pm .13$) (main effect of *condition:* $F(1,53) = 19.16, p < .001, \eta_p^2 = .265$). There were no group or interaction effects ($p's > .33$).

The grand-averaged group- (Fig.3A) and condition-specific (Fig.3B) ERP waveforms are presented, along with the corresponding error bars of the grand means.

Fig. 3. Grand-averaged, fronto-centrally distributed ERPs for BDD (purple) vs control (green) groups (panel **A**) and PPI (blue) vs. PPF (red) conditions (panel **B**). The two shaded time windows indicate the N100 and P200 ranges, respectively. Below each panel, the corresponding scatter box-plots are depicted for each time window. Symbol '*' denotes statistically significant differences between the means.

3.3. Source reconstruction of ERP components

Source localization analysis of N100 and P200 was performed to find the responsible generators that produce the GFP/ERP alterations. Non-parametric voxel-wise tests were conducted (i) to compare N100 and P200 sources between PPF and PPI, separately for the two groups, and (ii) to compare N100 sources between controls and BDD, separately for the two conditions.

3.3.1. Contrasts between PPI and PPF

Both groups revealed significantly higher activation in PPF than PPI condition. Tables 1 and 2 detail the spatial information of significant voxels for N100 and P200, respectively. Fig.4 shows the LORETA x-, y- and z-slices around the maximum (t-score) condition differences. No significantly higher activations in PPI than PPF were observed.

Table 1. Source localization contrasts for the N100 component between PPF and PPI, separately for control and BDD group. From left to right column, the primary lobe, region, cluster size (the number of significant voxels), Brodmann areas, peak voxel (voxel that corresponds to the highest t-score inside the cluster) and its MNI coordinates are tabulated.

Critical t-scores for control and BDD group are 3.89 and 3.77, respectively, defined by 5000 randomizations, corresponding to p = .05.

The control group exhibited significantly higher N100 activations in PPF than PPI in a total of 18 voxels, with the largest cluster (size = 9) located at the postcentral gyrus (parietal lobe) and the peak difference occurring at BA-3. Regarding the BDD group, a total of 167 voxels were more active in PPF than PPI, with the largest cluster (size = 78) located at the cingulate gyrus (limbic lobe) and peaking at BA-24.

Table 2. Source localization contrasts for the P200 component between PPF and PPI, separately for control and BDD group. From left to right, the primary lobe, region, cluster size (the number of significant voxels), Brodmann areas, peak voxel (voxel that corresponds to the highest t-score inside the cluster) and its MNI coordinates are presented. Critical t-scores for control and BDD group are 3.8 and 3.94, respectively, corresponding to p = .05.

The source comparisons of P200 activations revealed that control group showed significantly higher activations in PPF than PPI in a total of 10 voxels (largest cluster: size = 6; frontal lobe; cingulate gyrus; peak at BA-32), while BDD exhibited the same effect in a total of 736 (largest cluster: size = 104; superior temporal gyrus; peak at BA-21).

Fig. 4. XYZ LORETA slices on the most significant condition differences. Red voxels indicate areas where PPF activation > PPI activation.

3.3.2. Contrasts between BDD and controls

Source localization contrasts of N100 between BDD patients and controls revealed differences only in the PPI condition. Controls showed higher activation in the N100 time window in several areas, as detailed in Table 3. Fig.5 shows the LORETA images in x-, y- and z-slices around the maximum (*t*-score) group differences for the PPI condition. No significant voxels were observed in the PPF condition (all $p's >$ .05).

Table 3. Source localization of N100 contrasts for PPI condition between control and BDD group. From left to right, the primary lobe, region, cluster size (the number of significant voxels), Brodmann areas, peak voxel (voxel that corresponds to the highest t-score inside the cluster) and its MNI coordinates are illustrated. Critical t-score of comparisons was 3.48, defined by 5000 randomizations, corresponding to p = .05.

Fig. 5. N100 sources in XYZ LORETA slices at the neighborhood of most significant group differences in PPI condition. Green voxels indicate areas where control activation > BDD activation.

3.4. Predicting BDD psychometric scores from EEG measures

We tested whether the two psychometric scores accounted for BDD symptomatology (Y-BOCS, DCQ) could predict EEG measures (GFP and ERP amplitudes in N100 and P200 time windows). The control group did not reveal any significant (linear or quadratic) predictor. Interestingly, the regression model for BDD group revealed that the GFP amplitudes in the 60-160 ms time window is a significant linear predictor of Y-BOCS scores ($\beta = -5.56, p = .009$). The model showed a significant overall fit of: $R^2 = .22, p = .009$. No predictors were identified for DCQ ratings. Fig.6 illustrates the scatter plot of Y-BOCS and GFP N100 variables, accompanied with the best-fitting line (Pearson's coefficient $r = -.47$).

Fig. 6. Linear term predicting Y-BOCS ratings of BDD patients from their GFP amplitudes within 60-160 ms in response to the startle tone.

In further investigating the relations between psychometrics and electrophysiological data, we computed the Pearson's correlation coefficients between N100 LORETA activations and body-related obsession scales, namely the BDD-YBOCS and BABS scores. No significant correlations were observed (all p's > .18).

4. Discussion

To review, our main purpose here was to investigate the neural correlates of auditory prepulse inhibition (PPI) and facilitation (PPF) in body dysmorphic patients (BDD) relative to healthy controls. Our study was the first to examine the EEG responses of BDD in a comprehensive way, by performing global field power (GFP), ERP analysis, and source reconstruction in response to PPI and PPF. BDD exhibited significantly reduced N100 amplitudes in response to the startle tone compared to healthy controls, potentially suggesting impaired allocation of attention. This was also reflected in reduced source activation for BDD during the N100 time window. Importantly, GFP at the N100 was predictive of BDD symptomatology. Finally, in line with previous studies, neural responses and source activations in PPI were decreased overall compared to PPF, confirming the gating effect of the PPI condition.

First of all, the BDD group showed significantly reduced neural responses in the 60-160 ms time window relative to healthy controls. This was evidenced at the frontocentral N100 component and at the GFP at the same time window. Previous studies have associated N100 with attentional processes (Fujiwara et al., 1998; Lijffijt et al., 2009; Näätänen & Picton, 1987). For example, in an MEG study, participants were presented with tone sequences, and were asked to attend or to not attend to the tones (Fujiwara et al., 1998). Results showed that the N100 was reduced in the non-attended condition compared to the attended condition, suggesting that N100 might index early selective attention. It has been suggested that the N100 elicited by auditory stimuli in passive listening tasks might orient attention to the stimuli,

improving discrimination between signal and noise (Näätänen & Picton, 1987), and thus allowing for more efficient cognitive functioning (Lijffijt et al., 2009). Importantly, although in our study the medication effects did not significantly influence the N100 effect, it should be noted that future studies are needed to systematically investigate the effects of medication on the electrophysiological correlates of PPI and PPF in BDD.

Decreased amplitude of auditory evoked potentials has been previously found in several psychiatric disorders, such as OCD (Molina et al., 1995) and schizophrenia (Rosburg et al., 2008). In particular, OCD patients show reduced early auditory evoked potentials, potentially linked to increased serotonergic tone (Molina et al., 1995). On the contrary, schizophrenic patients lack an increase in N100 during allocation of attention, which provides corroborating evidence for reduced N100 associated with impaired attention processes (Rosburg et al., 2008). Notably, BDD patients exhibit impairments in memory and attention, as demonstrated in the digit span, story memory recall, and Stroop interferences tasks (Toh et al., 2015, 2017). Our sLORETA findings also suggested decreased activations for BDD, therefore providing additional evidence for impaired attention. However, the absence of significant correlations between attention-related LORETA activations and body-related obsession scores might suggest that the early selective attention mechanisms in response to PPI are not directly linked to body-related obsessions. This may constitute evidence that the identified electrophysiological markers are not necessarily differentiated between BDD and OCD, given also their inherently overlapping features. This is also in line with the DSM-5 taxonomy, which highlights that BDD is dominated by OCD.

Interestingly, we found that GFP at the N100 was negatively correlated with BDD severity. Previous neurophysiological research has found neural indices of perceptual distortions in BDD (Feusner et al., 2010, 2007). In an EEG study (Li et al., 2015), results showed reduced amplitude in the N170 component during visual processing of faces and houses. Noteworthy, the lower N170 amplitude was associated with poor insight with regards to their psychiatric condition. Furthermore, in an fMRI study (Feusner et al., 2010), frontostriatal hyperactivity was associated with obsessive thoughts and compulsive behaviours. The brain anatomical characteristics of BDD also revealed correlations between BDD symptom severity and volumes of the left inferior frontal gyrus and right amygdala, potentially contributing to the involvement of these regions in pathological face processing (Feusner et al., 2009). Importantly, GFP constitutes a reference-free metric, allowing to expect that our findings would be confirmed in future studies, independently of the reference method used. Our study might add to the previous findings by proposing N100 amplitude as a novel electrophysiological marker of BDD to be used in clinical practice.

Regarding the group differences, we found reduced activation in BDD, predominantly located over the precuneus, inferior parietal lobule, fusiform and parahippocampal gyrus. Previous studies demonstrated that the auditory N100 is mainly generated in the primary and secondary auditory cortices (Giard et al., 1994;

Pantev et al., 1995; Thoma et al., 2003). However, several studies proposed additional sources in the dorsal anterior cingulate cortex, the inferior parietal, ventrolateral prefrontal cortices (Grau et al., 2007), as well as the hippocampus, dorsolateral prefrontal cortex, and thalamus (Boutros et al., 2008). Furthermore, these sources partially overlapped with the Posterior Cingulate Cortex (PCC), a central node in the default mode network (DMN: Giard et al., 1994; Pantev et al., 1995). The combined functionality of DMN and PCC is highly reactive and quickly deactivates during tasks with externally directed attention (Leech & Sharp, 2014).

Since N100 has been associated with sensory gating and attention orienting (Hu et al., 2005), these findings might suggest impaired sensory gating in BDD. Indeed, the N100 has been proposed to be elicited in early perceptual processes following sudden stimulation in a PPI paradigm (De Pascalis et al., 2013). The extent to which PCC is activated influences the preparation for coping with a physical threat (Bremner, 2002). Therefore, reduced PCC activity in BDD may reflect enhanced avoidance or deficits in sensorimotor gating systems in response to excitement-related stimuli. Most generators appeared around parahippocampal gyrus, a brain region that is believed to be involved in goal-directed attention processes. Indeed, Annic and colleagues (2016) found enhanced activation in parahippocampal regions for *to-be-attended* stimuli vs. *unexpected* stimuli. Therefore, reduced parahippocampal activity may reflect that BDD patients did not successfully orient their attention to the startle tone, thus processing the startle tone as *unexpected*.

As predicted, neural responses in PPI were decreased overall compared to PPF. Specifically, we observed reduced GFP, ERP amplitudes, as well as source activations in PPI compared to PPF. This is in line with previous neurophysiological research that showed PPI in various evoked potentials (for a review see Ford & Roth, 1999), as well as brain oscillations (Kapsali et al., 2020, 2006). This is in line with converging evidence suggesting that PPI and PPF are differently affected by prepulse intensity (Plappert et al., 2004; Reijmers & Peeters, 1994). This is also stressed by Mansbach and Geyer (1991) who found that the NMDA antagonist ketamine blocked PPI but increased PPF. Swerdlow and colleagues (2002) also demonstrated that PPF is mediated by the D1-dopamine receptor, while PPI is mediated by the D2-dopamine receptor. In this framework, sLORETA analysis revealed distributed sources of activation mainly at fronto-temporal and parieto-occipital networks. In line with previous studies (sLORETA: De Pascalis et al., 2013; De Pascalis & Russo, 2013; fMRI: Bremner, 2002; Hu et al., 2005; Leech & Sharp, 2014), these findings suggest that the co-operation of the aforementioned areas might contribute to the modulation of startle responses (Angrilli, Bianchin, Radaelli, Bertagnoni, & Pertile, 2008; Knight, Staines, Swick, & Chao, 1999; Neuner et al., 2010). Therefore, enhanced brain activation in PPF may suggest that the influence of the prepulse on the pulse tone is mitigated.

Our present findings need to be interpreted with the following limitations in mind. First, we have not registered the hormonal status of women that took part in our experiment. There is evidence that PPI may vary depending on the phase of menstrual cycle in females (Jovanovic et al., 2004). Indeed, sex differences have been

previously demonstrated in acoustic startle response paradigms (see Hantsoo, Golden, Kornfield, Grillon, & Epperson, 2018 for a review). For instance, females exhibit lower PPI in the luteal phase of the menstrual cycle, where hormonal levels are elevated (Jovanovic et al., 2004), while test-retest reliability in PPI and PPF is reduced in females compared to males (Stachtea et al., 2020). Furthermore, we do not know the potential impact of family history of psychiatric/neurological disorders and premorbid IQ on the neural responses under investigation, due to the absence of the relevant data. However, our groups were matched with regards to gender, therefore gender-related effects should be minimized. Second, future studies are recommended to take into account genetic information (genetic differences were related to low PPI in healthy subjects (Quednow et al., 2009)), as well as nicotine levels (P50 suppression changes induced by nicotine (Millar et al., 2011)). Third, muscular responses were not analyzed in this paper. The reason lies in the antisymmetric approach required for simultaneous consideration of neural and muscular PPI. Specifically, epochs with strong eye blinks reinforce muscular PPI, but, contradictorily, are removed from neural PPI, thus reducing the power of parallel comparison of these measures, since they are not evaluated over the same trials. On the other hand, most studies failed to confirm correlational relationships between neural and muscular PPI responses (Ford & Roth, 1999; Kedzior et al., 2006), supporting that inhibition in EMG and ERPs is controlled by different mechanisms. Finally, the generalizability of the sLORETA results need to be interpreted with cautions, since inverse-problems are inherently ill-posed.

CONCLUSION

Our study examined the neural correlates of BDD in a comprehensive way, by investigating the electrophysiological measures in an auditory prepulse inhibition and facilitation paradigm. Extending previous studies on BDD patients' visual deficits, we found that BDD exhibit attentional impairments in the auditory domain as well. This was evidenced from reduced amplitude and source activation in the N100 time window relative to healthy controls. Importantly, analyses revealed a differentiated neural signature of BDD patients in relation to sensorimotor gating performance, especially in the time-window of N100 where the amount of neural resources (GFP amplitudes) were shown to be negatively correlated with the BDD severity (Y-BOCS scores). Overall, these results demonstrate the potential of using EEG measures in combination with BDD behavioural protocols, allowing a dimensional approach to symptomatology and circumventing illness-related epiphenomena, such as medication effects.

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Disclosure statement

The authors declare no conflict of interest.

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Anastasios E. Giannopoulos: Formal Analysis, Writing – Original Draft, Visualization, Software. **Ioanna Zioga:** Investigation, Formal Analysis, Writing – Original Draft. **Panos C. Papageorgiou:** Writing - Review and Editing. **Fotini Kapsali:** Data curation. **Sotirios T. Spantideas:** Validation, Visualization. **Nikolaos C. Kapsalis:** Writing - Review and Editing. **Christos N. Capsalis:** Supervision, Conceptualization, Writing - Review and Editing. **Konstantinos Kontoangelos:** Writing - Review and Editing. **Charalabos C. Papageorgiou:** Conceptualization, Methodology, Validation, Investigation.

Conflict of interest

The authors declare no conflict of interest.

Lobe	Region	Cluster size	Brodmann areas	Peak voxel (t-score)	MNI (X Y Z)
Control group					
Frontal	Precentral Gyrus	7	4	4,34	-35 -20 45
	Postcentral Gyrus	1	**3**	**4,56**	-35 -25 40
Parietal	Sub-Gyral	1	2	4,16	-35 -30 40
	Postcentral Gyrus	9	2,3	4,36	-40 -25 40
BDD group					
Temporal	Fusiform Gyrus	3	20	3,94	40 -25 -30
	Sub-Gyral	1	20	3,84	40 -20 -25
Limbic	Parahippocampal Gyrus	6	20,35,36	3,89	30 -30 -25
	Cingulate Gyrus	78	23,**24**,32	**5,01**	5 0 40
Frontal	Middle Frontal Gyrus	19	6	4,57	-25 0 50
Occipital	Cuneus	3	7,19	3,98	-20 -80 30
Parietal	Postcentral Gyrus	3	2,3	3,81	50 -25 30
	Precuneus	22	7,19	4,4	-25 -80 35
	Supramarginal Gyrus	4	40	4,08	-60 -45 35
	Inferior Parietal Lobule	11	7,39,40	4,41	-40 -70 45
	Angular Gyrus	2	39	3,95	-30 -65 35
	Superior Parietal Lobule	15	7	4,29	-35 -70 45

Lobe	Region	Cluster size	Brodmann areas	Peak voxel (t-score)	MNI (X Y Z)
Control group					
Limbic	Cingulate Gyrus	6	32	4,11	5 20 35
Frontal	Cingulate Gyrus	4	**32**	**4,21**	5 20 40
BDD group					
Temporal	Inferior Temporal Gyrus	30	20,21,37	5,85	50 -25 -25
	Middle Temporal Gyrus	95	20,21,22,37,39	6,02	50 -30 -5
	Superior Temporal Gyrus	104	13,**21**,22,39,41,42	**6,05**	50 -25 -5
	Fusiform Gyrus	58	20,36,37	5,96	50 -30 -25
	Sub-Gyral	5	20,21,37	4,82	40 -20 -25
	Transverse Temporal Gyrus	13	41,42	5,86	55 -25 10
	Supramarginal Gyrus	6	40	4,63	60 -50 20
Limbic	Parahippocampal Gyrus	63	19,20,27,28,30,35-37	5,4	40 -25 -20
	Posterior Cingulate	16	23,30,31	4,54	10 -70 15
	Cingulate Gyrus	19	31	5,15	5 -50 40
Frontal	Paracentral Lobule	3	5	4,21	5 -45 50
Occipital	Middle Temporal Gyrus	3	19,22	4,13	55 -65 15
	Fusiform Gyrus	11	18,19,37	4,66	20 -95 -20
	Inferior Occipital Gyrus	16	17,18,19	4,78	20 -95 -15
	Lingual Gyrus	28	17,18,19	4,88	25 -95 -10
	Middle Occipital Gyrus	34	18,19	4,74	25 -90 5
	Cuneus	38	7,17,18,19,23,30	4,82	20 -80 10
	Precuneus	18	18,23,31	4,62	5 -65 25
Sub-lobar	Insula	36	13,40,41	5,4	50 -25 15
Parietal	Postcentral Gyrus	10	40,43	5,51	55 -25 15
	Precuneus	93	7,31	5,21	15 -50 45
	Supramarginal Gyrus	1	40	4,04	60 -55 25
	Inferior Parietal Lobule	17	7,39,40	4,83	60 -45 20
	Angular Gyrus	5	39	4,26	35 -65 35
	Superior Parietal Lobule	14	7	4,57	25 -55 45

Lobe	Region	Cluster size	Brodmann areas	Peak voxel (t-score)	MNI (X Y Z)
		N100 component			
Temporal	Middle Temporal Gyrus	13	19,39	3,73	35 -65 25
	Superior Temporal Gyrus	9	39,41	3,6	35 -60 25
	Fusiform Gyrus	36	**20**,36,37	**4,65**	-35 -40 -25
	Transverse Temporal Gyrus	1	41	3,65	-35 -35 10
	Postcentral Gyrus	1	39	3,5	35 -80 30
	Precuneus	1	39	3,5	40 -80 30
Limbic	Parahippocampal Gyrus	88	19,27,28,30,35,36,37	4,58	-30 -40 -15
	Sub-Gyral	1	19	4,16	-15 -45 -10
Occipital	Fusiform Gyrus	21	18,19,37	4,43	-35 -45 -15
	Parahippocampal Gyrus	6	17,18	4,1	-25 -90 -20
	Orbital Gyrus	40	17,18,19	4,02	-15 -45 -5
	Rectal Gyrus	5	18,19	3,98	-25 -85 -15
	Sub-Gyral	16	7,18,19	3,83	25 -85 35
	Inferior Frontal Gyrus	5	31	3,65	15 -75 25
	Superior Frontal Gyrus	4	19	3,77	35 -75 25
Parietal	Postcentral Gyrus	1	40	3,59	55 -35 50
	Precuneus	31	7,19,31	3,76	25 -80 35
	Supramarginal Gyrus	3	40	3,6	55 -40 35
	Inferior Parietal Lobule	32	7,39,40	3,82	60 -40 45
	Superior Occipital Gyrus	3	39	3,52	50 -65 30
	Cingulate Gyrus	2	7	3,5	50 -65 30