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Longitudinal qEEG changes correlate with clinical outcomes in patients with somatic symptom disorder

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ABSTRACT

Objective: The quantitative electroencephalography (qEEG) of patients with somatic symptom disorder (SSD) was not yet thoroughly studied. This study aimed to investigate qEEG of SSD patients compared with those of normal controls (NCs), and changes therein after treatment.

Methods: SSD patients currently without treatment and age- and sex-matched NCs were recruited. Spectral analysis of 64-channel EEG recording was performed and somatization, anxiety, and depression were evaluated via self-rating scales at baseline. After six months of treatment as usual, SSD patients were longitudinally followed up for assessments.

Results: At baseline, the SSD group ($n = 44$) had higher alpha ($p = 0.047$) and lower beta 2 ($p = 0.027$) and gamma power ($p = 0.001$) compared with NCs ($n = 29$). After 6-month treatment, SSD patients showed improvement in symptoms, as well as increased beta 1 ($p = 0.032$), beta 2 ($p = 0.012$), and gamma power ($p = 0.009$) compared with baseline. A significant correlation was observed between the change in somatization score and temporal gamma power ($r = -0.424$, $p = 0.031$), and between the change in anxiety score and beta 2 power in the frontal ($r = -0.420$, $p = 0.033$) and central ($r = -0.484$, $p = 0.012$) regions.

Conclusions: EEG findings in this study may provide neurophysiological features of SSD. The alpha enhancement and reduced fast wave activity may reflect attentional dysfunction in patients with SSD. Decreased fast wave activity is reversible and may serve as a state marker of SSD.

1. Introduction

Somatic symptom disorder (SSD) is characterized by one or more distressing somatic symptoms accompanied by excessive thinking, feelings, or behaviors associated with those symptoms [1]. SSD was previously referred to as somatoform disorders with more emphasis on medically unexplained symptoms. In the fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM–5), the term SSD was introduced to include people with somatic complaints who are excessively concerned about their symptoms, regardless of whether they have a diagnosed medical condition. The core feature of SSD remains a reaction disproportionate to the physical state.

SSD is heterogeneous and complex, and symptoms vary widely. The prevalence of SSD was estimated at 5–7% in the general adult population [1]. Despite the high prevalence and cost of treatment of SSD, the underlying mechanism remains unclear. Individuals with SSD apparently perceive and interpret somatic information differently than those without the condition [2]. SSD patients focus more on their own bodies and are quicker to label bodily complaints as indicative of illness than healthy people, i.e., they demonstrate "somatosensory amplification" [3]. Along with sensitization [4], changes in attention also prolong and augment symptoms. Somatic hypervigilance refers to heightened and sustained attention on bodily sensations and symptoms. The "signal-filtering model" emphasizes that "faulty filtering" leads to bodily sensations that are usually outside of conscious awareness being perceived consciously [5]. A similar model emphasizes the role of attention in medically unexplained symptoms. Increased attention on symptom-related information and somatic representations is hypothesized to contribute to the development and maintenance of somatic symptoms [6]. A previous study reported that attention intensifies, and distraction ameliorates, physical symptoms [2].

Quantitative electroencephalography (qEEG) is a useful tool to assess

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Table 1
Demographic comparison between patients with SSD and healthy controls.

	SSD ($n = 44$)	NC ($n = 30$)	p
Age, year	47.4 ± 11.3	45.7 ± 9.4	0.498
Female, n (%)	31 (70.5%)	21 (70%)	0.966
Married, n (%)	32 (72.7%)	24 (80%)	0.474
Education, year	15.1 ± 3.0	15.4 ± 2.0	0.654
BMI, kg/m2	22.0 ± 3.3	23.2 ± 2.8	0.094
SCL-SOM, score	13.6 ± 7.8	3.1 ± 3.3	< 0.001***
BDI-II, score	15.6 ± 8.3	3.9 ± 3.8	< 0.001***
BAI, score	20.6 ± 13.4	3.0 ± 3.0	< 0.001***

Pearson χ^2 test for differences between categorical variables and Student's t-test for differences between means. *SSD* Somatic symptom disorder, *NC* Normal controls, *BMI* Body mass index, *SCL-SOM* the somatization subscale of the Symptom Checklist-90-Revised, *BDI-II* Beck depression inventory-II, *BAI* Beck anxiety inventory. *** $p < 0.001$.

the neurophysiological characteristics of individuals with various disorders. Spontaneous brain activity in the resting state may shed light on cognition and behavior [7–9]. In normal subjects, alpha EEG activity predominates during eye-closed resting. Increased slow-frequency waves may reflect sleepiness or cortical dysfunction, whereas increased high-frequency waves indicate an attentive state, heightened vigilance, or anxiety. Associations between brainwave activity and mental disorders have been repeatedly reported; qEEG can aid diagnosis of mental disorders and prediction of treatment responses. An increased theta/beta ratio is a well-known biomarker for attention deficit and hyperactivity disorder (ADHD), and alpha asymmetry on EEG is typically seen in patients with depression [9]. Increased slow-wave EEG activity is common in subjects with brain dysfunction, including various diseases associated with impaired cognition (i.e., schizophrenia, dementia, and depression) [9,10]. The qEEG findings of psychiatric disorders have been reviewed [9]. In terms of prognosis, the slow-wave rhythm predicts improvement of depression in patients receiving electroconvulsive therapy, and alpha and theta activity is associated with a better response to selective serotonin reuptake inhibitors [11]. Given the high test-retest reliability, qEEG may be useful to evaluate longitudinal changes and treatment efficacy. Also, qEEG is non-invasive and less expensive than many other brain imaging modalities, so is readily applicable in a wide range of clinical settings [12].

While neural correlates of somatic symptoms have been proposed, qEEG has been applied in only a few studies [13]. Furthermore, because the DSM–5 is relatively new, its SSD criteria have been applied in only one qEEG study [14]. Ahn et al. compared theta coherence among SSD patients, major depressive disorder (MDD) patients and healthy subjects, and observed lower functional connectivity in the patient groups. Both the SSD and MDD groups showed decreased connectivity in the left temporoparietal region, which is associated with cognitive-attentional processing. Theta coherence in the frontotemporal and parietal areas, which is associated with perception, emotion, and somatosensory sensations, was lower in the SSD group compared with the controls and MDD patients. The authors suggested that dysfunction in frontotemporal and parietal circuits is a neuropathological marker of SSD. However, spectral power analysis was not performed. Another qEEG study on somatoform pain disorder reported decreased power in the 21–30 Hz frequency range in patients compared with healthy controls, for many brain regions including the primary and secondary somatosensory cortices (SI and SII, respectively) [15]. The lower beta activity differentiated somatoform pain disorder from neuropathic pain, which is characterized by overactivation of the pain matrix and heightened beta activity.

To the best of our knowledge, spectral power analysis of resting-state EEG data has not been performed in SSD patients. We compared baseline EEG activity between normal controls (NCs) and SSD patients, and aimed to identify neurophysiological markers for SSD. A longitudinal design was used to determine if EEG activity changes after treatment, and to evaluate the association between symptom improvement and EEG changes. We hypothesized that patients with SSD would show different qEEG patterns to NCs, such as increased alpha power and decreased power of fast waves due to attentional dysfunction. We postulated that EEG dysfunction would be reversible and thus recover after treatment.

2. Methods

2.1. Participants

Patients with SSD were enrolled from the psychiatric clinic of Seoul National University Bundang Hospital between December 2017 and July 2019. The Structured Clinical Interview for DSM-5 Disorders-Clinician Version (SCID-5-CV) was used to diagnose SSD and screen for other possible psychiatric comorbidities [16]. The inclusion criteria were as follows: 1) aged between 19 and 65 years, 2) diagnosed with SSD according to the DSM-5, and 3) specified as severe, as defined by the DSM-5. Subjects with the following conditions were excluded: 1) neurological or medical conditions associated with their somatic symptoms, 2) a major mental illness (e.g., a psychotic, cognitive, or bipolar disorder, or a severe major depressive disorder accompanied by significant suicidal ideation), 3) a history of head trauma accompanied by loss of consciousness or any cerebral disease, 4) psychotropic drug use within the past 3 months, or 5) use of any non-pharmaceutical treatment potentially affecting EEG. The NC group consisted of age- and sex-matched healthy volunteers who were recruited by placing advertisements in the hospital and local newspapers. All healthy volunteers also underwent screening using the SCID-5-CV; none had a psychiatric disorder.

All participants underwent an initial assessment to acquire demographic data, psychological scale scores, and qEEG (visit 1; V1). For patients with SSD, treatment was provided after the baseline assessment. Treatment included pharmacological and non-pharmacological therapy, such as supportive psychotherapy and psychoeducation. After 6 months of treatment, follow-up assessments of the patient group were performed to evaluate symptom and qEEG changes at visit 2 (V2). Participants in the NC group did not receive any specific intervention or undergo a follow-up assessment.

All procedures were conducted in accordance with the ethical standards of the Institutional Review Board of Seoul National University Bundang Hospital (B1710426302) and the 1964 Helsinki declaration and its amendments. Written informed consent was obtained from all participants.

2.2. Measurements

2.2.1. Questionnaires

The somatization subscale of the Symptom Checklist-90-Revised (SCL-SOM) was used to assess the distress caused by somatic symptoms [17,18]. Each item is rated on a five-point Likert scale of distress (none = 0, extreme = 4). The somatization subscale comprises 12 items and focuses on complaints associated with the cardiovascular, gastrointestinal, respiratory, and neurological systems, and any other autonomically mediated systems. An earlier validation study reported that the Korean version of the SCL-SOM had good internal consistency (0.87) [19]. In the present study, Cronbach's alpha was 0.84 for the SSD group and 0.71 for the NC group.

Depression and anxiety were assessed using the Beck Depression Inventory-II (BDI-II) [20] and Beck Anxiety Inventory (BAI) [21], respectively. The Korean versions of the BDI-II and BAI showed good internal consistency (0.89 and 0.91, respectively) and test-retest reliability (0.90 and 0.84, respectively) [22,23]. Cronbach's alpha of the BDI-II was 0.92 and that of the BAI was 0.96 in this study.

2.2.2. EEG recording and data analysis

The waking EEG was recorded in a sitting position for 15 min after

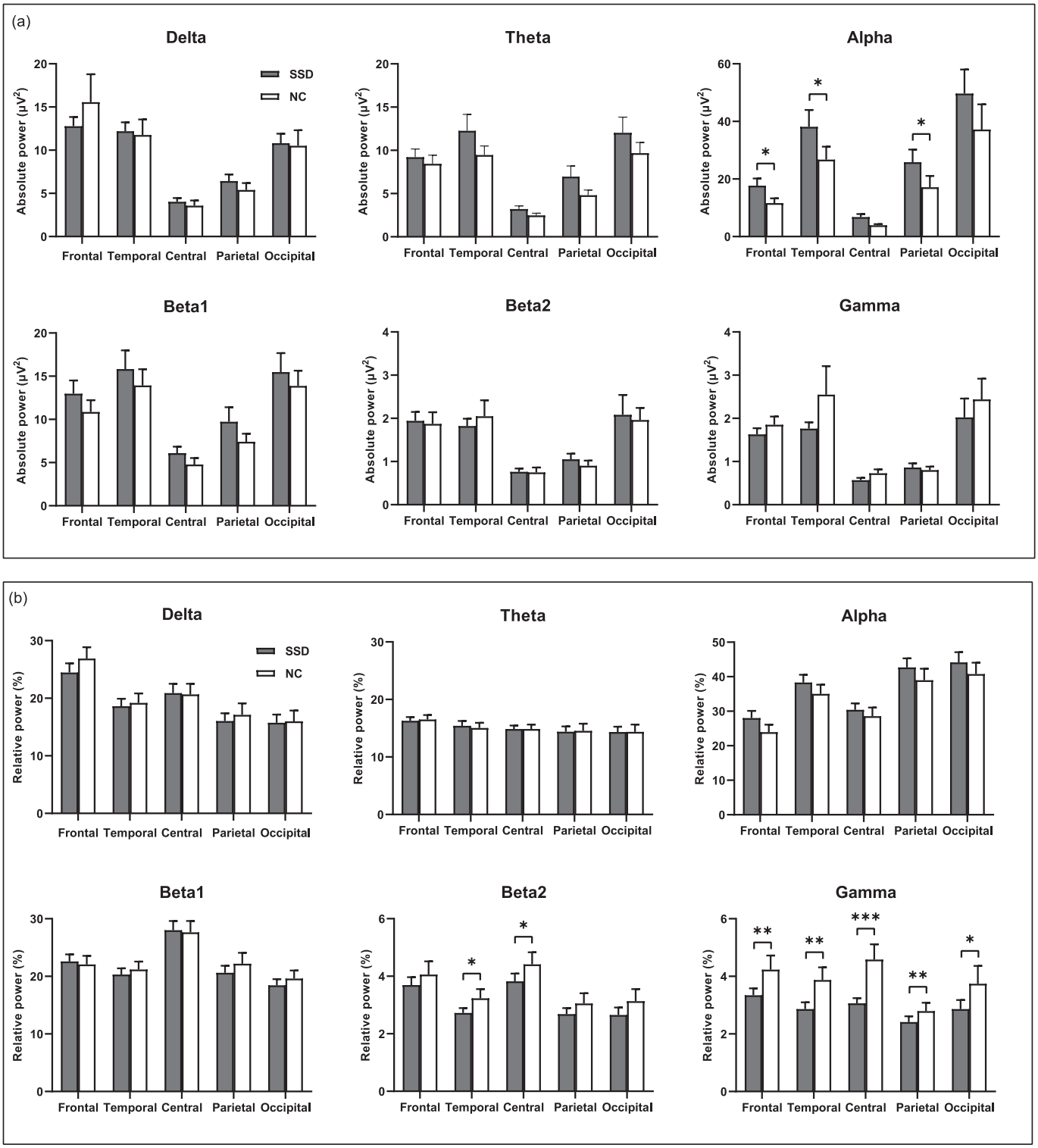

Fig. 1. Comparison of electroencephalogram between patients with SSD and NCs: (a) absolute power and (b) relative power. Vertical bars represent standard errors. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, adjusted for age, sex, body mass index, scores of Beck Depression Inventory-II and Beck Anxiety inventory. *SSD* Somatic symptom disorder, *NCs* Normal controls.

participants had been instructed to close their eyes and relax. Electrodes were placed according to the extended international 10–20 system. The EEG signals were amplified and digitalized using the 64-channel NeuroScan SynAmps device (Compumedics, Charlotte, NC, USA) at a sampling rate of 1 kHz.

The EEG data were processed using NeuroGuide (Applied Neuroscience, Inc., St. Petersburg, FL, USA). The high and low pass filters were set to 100 and 0.3 Hz, respectively. Each EEG was conducted in a blinded manner and visually inspected for artifacts due to muscle activity, small body movements, eyelid movements, and micro-sleep; an artifact-free 90-s EEG recording was selected for analysis. Then, spectral analysis was performed with fast Fourier transform (FFT) to compute the absolute power values among six bands (delta: 1.0–4.0 Hz, theta: 4.0–8.0 Hz, alpha: 8.0–12.0 Hz, beta 1: 12.0–25.0 Hz, beta 2: 25.0–30.0 Hz, and

Table 2
Comparison of symptom scales before and after treatment in patients with SSD.

	Visit 1 (n = 26)	Visit 2 (*n* = 26)	*p*
SCL-SOM, score	14.1 ± 7.7	9.3 ± 5.2	0.001**
BDI-II, score	16.9 ± 8.0	12.5 ± 8.8	0.016*
BAI, score	22.7 ± 12.6	14.2 ± 10.8	< 0.001***

Paired sample t-test for differences between means. *SSD* Somatic symptom disorder, *SCL-SOM* the somatization subscale of the Symptom Checklist-90-Revised, *BDI-II* Beck depression inventory-II, *BAI* Beck anxiety inventory. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

gamma: 30.0–80.0 Hz). Relative power values, i.e., the percentage of the total power of each band, were also calculated. The electrodes were grouped into five cerebral regions, and both the mean absolute and relative powers of various regions were calculated, similar to a previous EEG study: frontal (FP1, FP2, F3, F4, F7, and F8), temporal (T3, T4, T5, and T6), central (C3 and C4), parietal (P3 and P4), and occipital (O1 and O2) [24].

2.3. Statistical analysis

Results are reported as means ± standard deviations. Comparisons of demographic, clinical, and EEG power data between the SSD and NC groups were performed using the independent *t*-test or chi-square test. Analysis of covariance (ANCOVA) was used to analyze the variables with adjustment for covariates. EEG activity was analyzed using generalized estimating equations (GEEs) [25,26]. The regional distribution of each baseline EEG band was compared between the SSD and the NC groups. In the SSD group, symptom scale scores were compared between visits (i.e., baseline (V1) and follow-up (V2)) using the paired *t*-test. EEG activity in SSD patients was also compared between V1 and V2 using GEEs. Correlations between the score difference (V2 − V1) of each questionnaire and the difference in EEG power between visits (V2 − V1) were evaluated by calculating Pearson correlation coefficients for data that were normally distributed, and Spearman correlation coefficients otherwise. All significance tests were two sided and a *p*-value <0.05 was considered statistically significant. SPSS for Windows software (version 25.0; SPSS Inc. Chicago, IL, USA) was used for all the analyses.

3. Results

3.1.1. Demographic and clinical data

In total, 44 patients with SSD and 30 age- and sex-matched healthy adults were recruited to this study. The mean age of the SSD patients was 47.4 years and that of NCs was 45.7 years ($p = 0.498$). Approximately 70% of the participants were female in both groups ($p = 0.966$). There was no significant differences in age, sex distribution, marital status, years of education, or body mass index (BMI) between the two groups (Table 1). As expected, the questionnaire scores were significantly different between the two groups. Compared with the NC group, the SSD group had higher SCL-SOM ($p < 0.001$), BDI-II ($p < 0.001$), and BAI scores ($p < 0.001$), indicating that they were more depressed and anxious.

3.1.2. EEG activity

In the EEG analyses, age, sex, BMI, and BDI-II and BAI scores were included as covariates. Fig. 1 shows the absolute and relative EEG power of each band in each region, for both groups, at V1. For the absolute power analysis, a significant group × region interaction effect was observed in the gamma band ($\chi^2 = 11.11$, $p = 0.025$). However, there was no group difference in the post hoc test. In the alpha band, the group × region interaction effect was nonsignificant; however, a significant group effect was observed ($\chi^2 = 3.96$, $p = 0.047$). The SSD group had stronger absolute alpha power than the NC group in the frontal ($p = 0.039$), temporal ($p = 0.043$) and parietal ($p = 0.047$) regions. In the other bands (delta, theta, beta 1, and beta 2), there were no statistically significant group × region or group effects.

Regarding relative power, there was no significant group × region interaction in any of the six bands. However, a main effect of group was observed in the beta 2 ($\chi^2 = 4.90$, $p = 0.027$) and gamma bands ($\chi^2 = 11.07$, $p = 0.001$). SSD patients showed lower beta 2 power in the temporal ($p = 0.016$) and central ($p = 0.018$) areas, and lower gamma power in all five brain regions (frontal: $p = 0.005$, temporal: $p = 0.002$, central: $p < 0.001$, parietal: $p = 0.008$, and occipital: $p = 0.017$) compared with the NCs.

3.1.3. Longitudinal follow-up

After 6 months of treatment, 26 patients (59.1%) underwent follow-up assessments; 5 received only non-pharmacological treatment and 21 received both pharmacological and non-pharmacological treatments. Table 2 shows the baseline (V1) and follow-up (V2) symptom scale scores. The mean SCL-SOM ($p = 0.001$), BDI-II ($p = 0.016$), and BAI ($p < 0.001$) scores had significantly decreased at the 6-month follow-up assessment.

Significant changes in EEG activity were also observed after 6 months of treatment, as shown in Fig. 2. A significant time × region interaction was seen for the absolute power of the alpha ($\chi^2 = 11.30$, $p = 0.023$), beta 2 ($\chi^2 = 9.87$, $p = 0.043$), and gamma ($\chi^2 = 10.32$, $p = 0.035$) bands. In the post hoc test, no significant change in the absolute alpha or beta 2 power was found in any brain region; however, a significant increase of the absolute gamma power was observed in the frontal and temporal areas at V2 compared with V1 ($p = 0.014$ and $p = 0.021$, respectively). Regarding the delta, theta, and beta 1 bands, there were no significant time × region or time effects.

A significant time × region interaction effect was observed only in the alpha band ($\chi^2 = 12.05$, $p = 0.017$) for relative EEG power; however, there was no significant between-visit difference according to the post hoc test. A main effect of time was observed in the beta 1 ($\chi^2 = 4.58$, $p = 0.032$), beta 2 ($\chi^2 = 6.26$, $p = 0.012$), and gamma ($\chi^2 = 6.83$, $p = 0.009$) bands. In the beta 1 band, the SSD patients showed a significant increase of power at V2 compared with V1 in the temporal, central, and parietal areas ($p = 0.041$, $p = 0.022$, and $p = 0.015$, respectively). In the beta 2 band, a significant increase of power at V2 was observed in the frontal, central, and occipital areas ($p = 0.018$, $p = 0.012$, and $p = 0.049$, respectively). In the gamma band, the relative power at V2 was significantly higher than at V1 in the frontal, temporal, central, and parietal areas ($p = 0.010$, $p = 0.026$, $p = 0.010$, and $p = 0.049$, respectively). There were no statistically significant time × region or time effects in the delta and theta bands.

Correlation analyses were performed to examine the association between the degree of symptom improvement in the scores (V2 − V1) for each questionnaire (SCL-SOM, BDI-II, and BAI) and the difference of EEG power (V2 − V1). The significant results are presented in Fig. 3. The change in SCL-SOM score correlated with the change in absolute gamma power in the temporal region ($r = -0.424$, $p = 0.031$); the lower the SCL-SOM score, the greater the gamma power. Regarding the relative power, significant correlations were observed between the change in BAI and beta 2 power in the frontal ($r = -0.420$, $p = 0.033$) and central ($r = -0.484$, $p = 0.012$) regions. There was no significant association between the score difference and change of beta 1 power.

4. Discussion

In the current study, the EEG characteristics of SSD patients, and changes therein after treatment, were compared with NCs. At baseline, the SSD group had higher absolute alpha power and lower beta 2 and gamma power compared with the NC group. After 6 months of treatment, the patients with SSD not only showed improvement of symptoms,

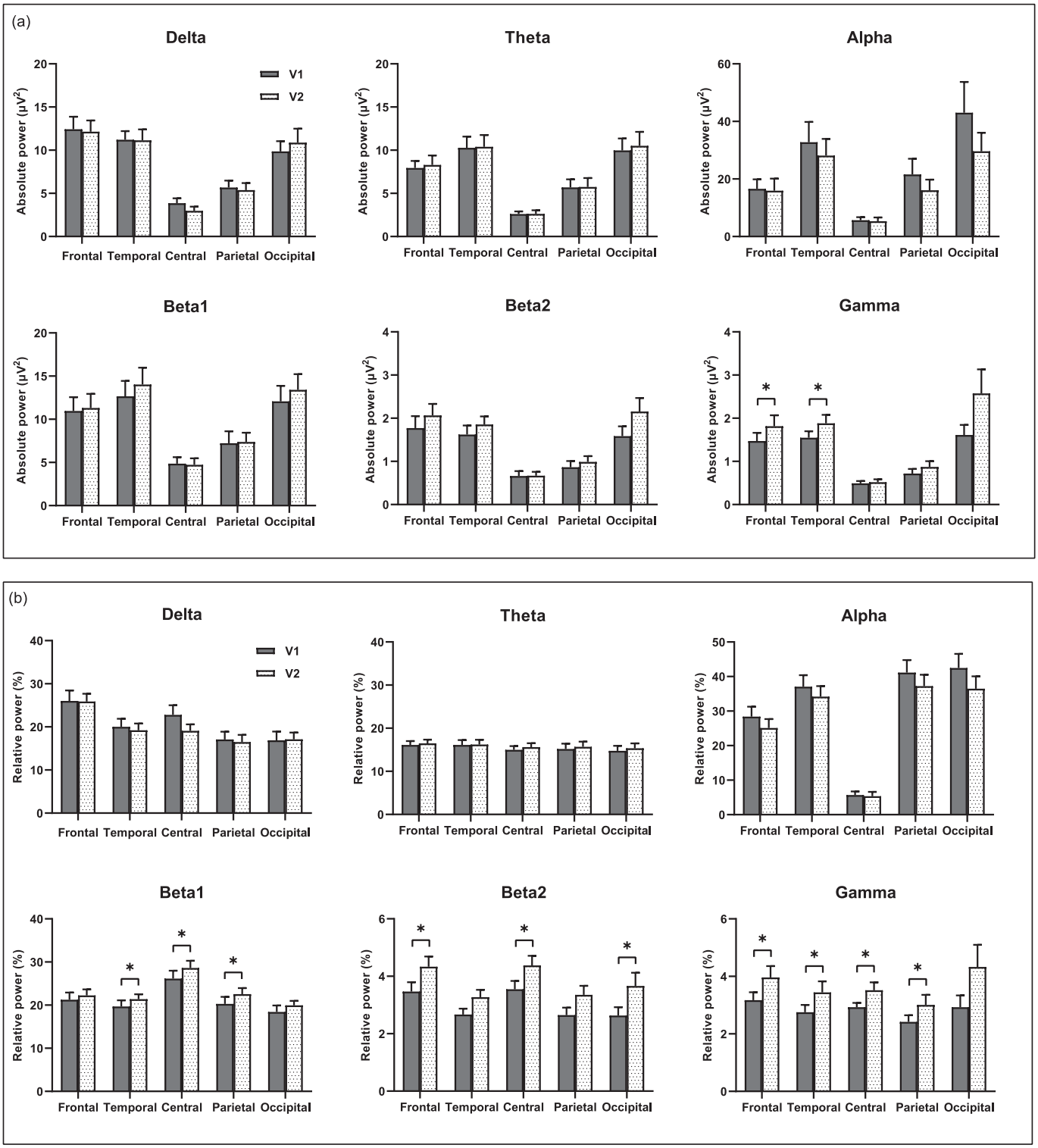

Fig. 2. Comparison of electroencephalogram before and after treatment in SSD: (a) absolute power and (b) relative power. Vertical bars represent standard errors. * $p < 0.05$, adjusted for scores of Beck Depression Inventory-II and Beck Anxiety inventory. *SSD* Somatic symptom disorder.

but also significantly increased beta 1, beta 2, and gamma band power compared with baseline. Furthermore, a reduced SCL-SOM score was significantly associated with increased absolute gamma power, and the between-visit BAI score difference was significantly associated with increased beta 2 power.

Compared to the NC group, greater frontal, temporal, and parietal alpha power was exhibited by the SSD group. The alpha rhythm predominates during rest with the eyes closed; an increased alpha power is commonly taken to indicate restfulness. However, alpha power does not merely reflect the resting state, rather, it is a complicated form of brain activity that varies depending on whether the focus is on external or internal stimuli. The power across the alpha band is negatively associated with regional cortical activity; increased alpha activity indicates local inhibition [27]. When processing external stimuli, the corresponding brain regions become active (blocked alpha activity) while others are inhibited (enhanced alpha activity) [28,29]. Conversely,

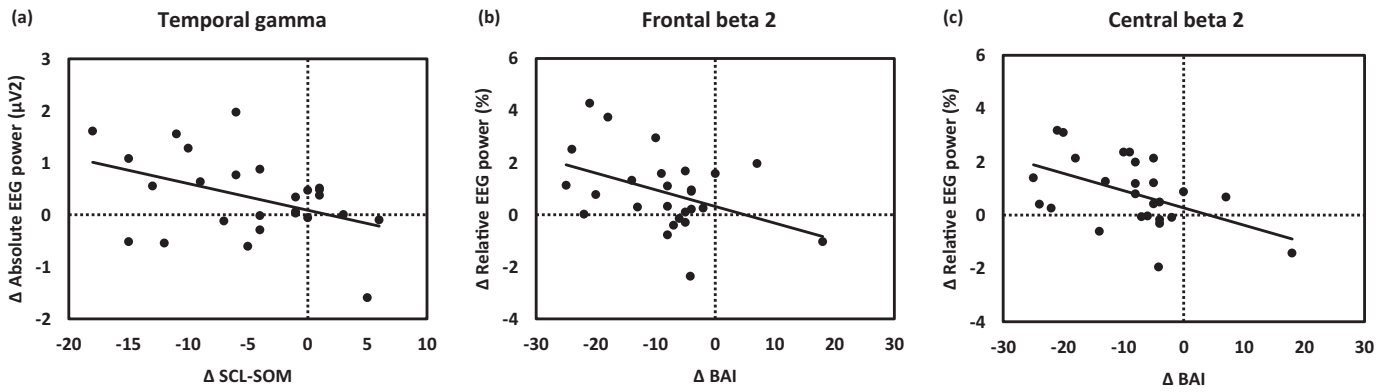

Fig. 3. Correlation between the between-visit differences (visit 2 − visit 1) in questionnaire scores and electroencephalographic power. (a) Correlation between the change in SCL-SOM and absolute gamma power in the temporal region. (b) and (c) Correlations between the change in BAI and relative beta 2 power in the frontal and central regions, respectively. *SCL-SOM* the somatization subscale of the Symptom Checklist-90-Revised, *BAI* Beck anxiety inventory.

when the focus is on internal stimuli, i.e., mental imagery, imagination, and internal attention, alpha activity increases [28]; this has been interpreted as the active inhibition required for "internally driven mental operations" [28,30]. Therefore, we suggest that the global enhancement in alpha power evident in the SSD group may reflect over-selective attention to internal body signals and related thoughts, and thus a decreased response to the external world. This is consistent with previous reports showing that patients with SSD tend to concentrate more on bodily sensations and inner stimuli, and have difficulty switching their attention to external stimuli [3,6]. In addition, the alpha power exhibited particularly strong negative correlations with resting brain activity in frontal and parietal areas [31] which are associated with attentional processing [32]. This suggests that the higher alpha powers in these areas may reflect decreased attention.

Our results showing that SSD patients had reduced beta 2 (25–30 Hz) power in the temporal and central areas are consistent with a previous study in terms of the EEG frequency affected and the spatial overlap. Stefani et al. investigated patients with somatoform disorder, and observed decreased spectral power in the 21–30 Hz range in many brain regions, including the SI, SII, supplementary motor cortex (SMC), prefrontal cortex (PFC), anterior cingulate cortex (ACC), amygdala, hippocampus, insula and posterior parietal cortex (PPC), and occipital areas [15]. Beta power is positively correlated with cortical activity, and a decrease therein may reflect neural deactivation. In addition, we found that SSD patients exhibited lower gamma power in all five cerebral regions than the NCs. Gamma activity plays a key role in the mediation of local sensory and attentional-processing signals [33,34]. Lower gamma activity may suggest an altered response to sensory stimuli. Clinically, reduced fast wave (including beta and gamma wave) power has been reported in various populations with attentional problems. Reduced beta power has been consistently observed in children with ADHD [9,35], whereas decreased gamma power has been reported in both children and adults with ADHD [36,37]. Among patients with MDD, those with inattention showed lower beta and gamma power than both those without inattention and NCs [38]. Furthermore, a negative correlation between inattention and gamma power was observed in children with ADHD [36], and with beta and gamma power in MDD patients [38]. The cited findings support an association between decreased fast wave activity and attentional impairment. Similarly, the increased beta and gamma powers evident in our patients with SSD may reflect their attentional problems; attentional deficits in SSD subjects [39] were considered integral to SSD development. Additionally, recent studies have reported that SSD patients may exhibit multiple cognitive dysfunctions (i.e., in memory, executive function and information processing) in addition to attentional deficit [40]. Beta and gamma activities have been also implicated in executive function and memory processing [41,42]. Therefore, the altered beta and gamma activities of SSD patients may reflect defects in other cognitive functions as well. Future studies should explore the relationships between specific cognitive functions and neurophysiological activity in SSD patients.

Notably, after 6 months of treatment, including medication and supportive psychotherapy, the SSD patients showed not only a significant reduction in symptom scale scores, but also increased power of the beta 1, beta 2, and gamma bands compared with baseline. The EEG change after treatment may reflect a reversal of EEG dysfunction and improved disease status. Specifically, the beta 2 and gamma powers of the patients was significantly lower at baseline compared with controls, despite their high levels of anxiety, but were restored after treatment. The correlations between the difference in SCL-SOM score and absolute gamma power, and between anxiety reduction and beta 2 enhancement, further indicated that increased fast wave activity was associated with clinical improvement. This may be an unexpected result because beta enhancement is commonly assumed to be associated with hyperarousal and anxiety. Indeed, anxiety, which is a diagnostic criterion for SSD, is one of the characteristic symptoms of the disorder, with which anxiety disorders frequently co-occur [43]. Anxiety may weaken cognitive control and thus enhance SSD development and persistence [44]. The initially reduced beta power in SSD patients may not be a finding against the high level of anxiety in SSD; it seemed more likely to be associated with the cognitive aspects of SSD rather than hyperarousal. Overall, our findings imply a possible connection between the courses of anxiety and SSD symptoms. We suggest that the decreased fast waves observed at baseline, which recovered after treatment and symptom relief, might serve as a marker for SSD severity. In particular, decreased fast waves in patients with SSD may reflect a state that is likely reversible with appropriate treatment.

The effects of drugs on EEG should also be considered. The drugs most frequently prescribed in the current study were serotonin re-uptake inhibitors, which generally decrease alpha power and increase beta power in the 12.5–25-Hz range [45,46]. The increased beta 1 activity at V2 may be at least partially explained by such drugs. However, no significant change in alpha power was observed after treatment. Although the significant time × region interaction may indicate a difference in alpha power pre- versus post-treatment, the difference between time points was not significant in any region.

To the best of our knowledge, this is the first study in which the EEG activity of patients with SSD was investigated and compared with healthy controls. In addition, this is the first longitudinal follow-up study of patients with SSD to investigate EEG changes after treatment. We recruited SSD patients who were drug-naïve and recently diagnosed. Therefore, effects of psychiatric drugs on EEG, which is the major obstacle when investigating psychiatric disorders using EEG, could be excluded in the baseline comparison with the NC group. Furthermore, common comorbidities of SSD, such as anxiety and depression, were

thoroughly evaluated in interviews, and mood symptom scores were adjusted for to minimize confounding effects. The longitudinal comparison and correlation analyses further elucidated the association between clinical symptom improvement and EEG recovery.

The present study had several limitations. First, we calculated nominal *p*-values; they were not corrected for multiple testing. Given that we considered 30 EEG power variables (six bands in each of five regions), we were concerned that alpha adjustment using the Bonferroni correction might increase the risk of type 2 error [47]. Thus, our findings should be taken as preliminary and exploratory; confirmation is required. Second, following the DSM-5 revision, SSD now includes heterogeneous patients with diverse somatic symptoms affecting various organ systems. Although these patients all show severe distress and an excessive response to their somatic symptoms, different types of symptoms may have different effects (i.e., activate or deactivate) on various neural pathways. In the present study, 44 patients with SSD were recruited, which was insufficient for subgroup analysis based on somatic complaints. Whether brain activity differs by symptom phenotypes should be evaluated in future studies. Third, although the association of EEG alterations with attentional dysfunction in SSD was presumed, attention was not explicitly measured in the present study. Lastly, only 59.1% of patients participated in the follow-up evaluation; the loss to follow-up may have caused a bias.

In conclusion, higher alpha activity and lower power of fast waves (ranging from 25 to 80 Hz) were observed in patients with SSD. The reversibility of decreased beta 2 and gamma activity after treatment, and its association with the degree of symptom improvement, further indicate the potential of reduced beta 2 and gamma activity as a state marker for SSD. These neurophysiological findings are in accordance with the biological and objective features of SSD.

Declaration of Competing Interest

The authors have no competing interests to report.

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