Bioceramic Material Stimulation Affects Perceptual Consciousness: A Study Combining Descriptive Observation and Functional MRI Connectivity Analysis

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Abstract

There is still no clear explanation of the process of perceptual consciousness that connects our body with brain. Innovation on the technology of bioceramic has now advanced towards clinical applications, including rehabilitation of brain infarction, therapies of insomnia and migraine. To demonstrate how ‘resonant energy transfer through the bioceramic material with tempo sound and visible light spectrum’ (bioceramic material stimulation, BMS) non-invasively affects perceptual consciousness, we investigated the responses of participants to BMS on perceptual consciousness by questionnaire of subjective descriptions and analyzed resting state fMRI during BMS. There were 61.3% participants who were categorized as positive group with various types of perceptual consciousness. By setting a threshold value at ‘p<0.001’, enhanced connections of ‘parahippocampal gyrus to cerebellar lobule V’ and ‘angular gyrus to precuneus’ were found. However, decreased connection of ‘caudate nucleus to cerebellar lobule VIIb’ was found. We conclude that the most affected brain functions by BMS including somatosensory, audio-visual perception and social cognition. The analysis of functional connectivity during BMS may help us gain more knowledge of consciousness and related division of neuroscience in humans.

Introduction

To date, there is no clear explanatory link connecting ‘consciousness’ to the human body and brain. Thus, many studies have been designed to account for subjective conscious experiences in terms of different features of brain states and neural interactions [1]. Current knowledge of neurophysiological approaches revealed that different states of consciousness are mainly brought about by a compromised brain anatomy, transient changes in connectivity, and neurochemical and metabolic processes. Altered states of consciousness could be evoked by: (1) physical and physiological stimulation (such as transcranial brain stimulation) [2]; (2) chemical drugs (such as alcohol and hallucinogen) [3]; (3) psychological means (such as hypnosis) [4]; (4) physical diseases (such as sleep deprivation or brain tumor) [5]; and (5) spontaneously (mythology or religion) [6,7].

To investigate different state of consciousness noninvasively, we used BMS to generate biological field in this study. The advantage of BMS as based on the characteristics of bioceramic material which emits non-ionized radiation that can be amplified by sound. It produces a weak biological field effect and has been hypothesized as a new concept in physics [8,9]. Research results show remarkable effects both physically and physiologically. Weakening of hydrogen bonds, improved microcirculation, better absorption of water-treated with bioceramic material, speeding up the healing mechanisms in tissue damage, enhanced plant growth, and many more physical-biological effects [10–14] have been observed in the laboratory and preliminary clinical trials [15–17]. In our previous research, BMS treatment significantly improved sleep quality in insomnia patients [18]. BMS causes a significant elevation in the beta spectrum of the EEG (at 15–27 Hz), in contrast to non- BMS group of participants [18]. Our clinical studies have shown that BMS attenuated symptoms in somatization disorder, obsessive-compulsive disorder, interpersonal sensitivity, schizophrenia, depression and anxiety[19].

In the present study we examined whether BMS enhanced various types of perception through certain parts of the body with no actual direct physical stimulation to the corresponding parts of the sense organs. We have designed a questionnaire in this study based on a previous research on electrical stimulation of the human brain induced various sensations and defined it as a 'perceptual and behavioral phenomena' [2]. It is suggested that the perceptual consciousness are beyond the usual five senses of external stimulation by sight, sound, smell, taste, and touch. In other words, there is no direct stimulation of the peripheral nervous receptors on the sensory organs of tongue, eye, skin, nose, and ear, but it is sensed by the central nervous system or mind that may be related to high level of consciousness[3,20]. In our previous study, activation of various brain areas during BMS were detected by fMRI [18]. Moreover, during BMS participants that was monitored by blood oxygenation level dependent (BOLD) functional magnetic resonance imaging (fMRI) imaging, participants were recorded with increase activations in areas of the left temporal pole, left parahippocampal gyrus, left rolandic operculum, left inferior frontal gyrus, left precentral gyrus, left hippocampus, left middle frontal gyrus, left insula, left thalamus, and left cerebellum [18]. However, the functional connectivity between different brain areas during BMS was unknown. Through literature review, stimulating different locations of the human brain with specific parameters produced variability of the perceptual consciousness[2,20].

In this study, we categorized the subjective responses of the participants with different types of 'perceptual consciousness' during BMS. In addition, resting-state fMRI was used to explore the possible activation of functional connectivity in the human brain during BMS.

Methods

Bioceramic material stimulation (BMS)

The bioceramic powder used in this study (obtained from the Bioenergy laboratory, Taoyuan, Taiwan) was composed of micro-sized particles produced from several ingredients mainly different elemental oxides. The 10% bioceramic powder [13,16], mixed with silicone rubber, produces sheet membrane with characteristics of spongy density (capable of sound transmission). Bioceramic is a kind of material with an energy field that can be enhanced by sound waves and visible light spectrum[18,19]. Bioceramic treatment also facilitates the breakup of large clusters of water molecules by weakening the hydrogen bond; this is one of the key mechanisms of bioceramic treatment on biological-physical and physical-chemical processes [10–12]. In this study, two types of BMS were used, including (i) For questionnaire assessment: participates lying on a platform with head contact with bioceramic silicon rubber sheet enhanced by a tempo sound system setting at 1-12 Hz with about 70dB and visible light spectrum range from 400 to 760 nm with level of illumination at about 200 lux.[21](Figure 1) and (ii) For fMRI analysis: participates lying on MRI scanner with bioceramic silicon rubber sheet placed on bilateral temporal scalp regions, which enhanced by acoustic noise of pulse sequence at about 100 dB during fMRI imaging [22]. All methods were carried out in accordance with relevant guidelines and regulations

Study participants.

The human volunteers that participated in the clinical trials were sourced using poster advertisements placed on bulletin boards near practice waiting rooms. There were 155 (female: 91; male: 64) volunteers. Participants were screened and none were found with neurological/psychiatric disorders, any indications of drug abuse, or sleep deprivation. The study was conducted at the Taoyuan General Hospital, Taiwan and the Human Study protocol was approved by the Medical Ethics and Institutional Review Board of the Taoyuan General Hospital, Ministry of Health and Welfare,Taiwan (approval no.: TYGH106015, see APPENDIX 1). Prior to participating in this study, the participants were all required to sign informed consent forms (see APPENDIX 2).

Questionnaire Assessment Of Subjective Descriptions Of The Bms

In the beginning, volunteer participants sat alone in the experimental room for about 5 minutes (as control condition). Then, the control and the experimental groups received the experiment protocol using the usual sound and BMS system for 20 minutes, respectively. Participants were asked to pay attention and record any change and all sensations that they may experience before and after the BMS xperiment. A questionnaire (Table 1) was designed to quantify the different types of 'perceptual consciousness' (level 0-3) by referring to a previous brain stimulation research [2] that our participants experienced in their subjective response to the BMS system. The participants were then categorized as positive for 'perceptual consciousness' if they belonged to levels 1 to 3 (Table 1).

fMRI data acquisition and preprocessing.

With reference to the previous resting state fMRI study [23], our protocol was designed by the following three steps: (1) MRI acquisition and preprocessing; (2) Network construction and functional module parcellation graph construction; and (3) Differences in effects without and with BMS on the functional connectivity of the brain.

For imaging data collection, the participants were scanned using a 1.5T Philips MRI/MRS system with a 20-channels array head coil. Resting state fMRI involved generating a series of 4 mm axial slices of the region of interest which were acquired using a gradient echo planar imaging (EPI) with the following parameters: time to repetition = 2500 ms, echo time = 30ms, flip angle = 78°, in-plane field of view = 210 × 210 mm, and acquisition matrix = 64 × 64 × 26 to cover whole cerebrum. After all the resting state fMRI scans, one turbofield echo (TFE) 3D T1-weighted imaging (TR/TE = 7.468/3.453 ms) with spatial resolution of 0.64 × 0.64 × 1.2 mm^3 was acquired.

The first five volumes were discarded to allow the magnetization to approach a dynamic equilibrium. The preprocessing of images was performed with SPM12 (Wellcome Trust Centre for Neuroimaging; http://www.fil.ion.ucl.ac.uk/spm) and Resting-State fMRI Data Analysis Toolkit (REST) [24]. For motion correction, aligning each volume to a reference base volume was performed across the functional dataset. Each functional dataset was filtered using a low-pass Chebyshev Type II filter with a frequency range of 0 to 0.1 Hz (in MATLAB; MathWorks, Inc., Natick, MA, USA). After filtering, linear trends were removed to eliminate signal drift induced by system instability. The individual functional images were normalized to the corresponding Montreal Neurological Institute (MNI) space by applying transferred parameters, which calculated from the whole-brain-coverage EPI images and MNI template, and linearly resampled to an isotropic resolution (2 × 2 × 2 mm3). Finally, all datasets were smoothed using a 6 mm FWHM Gaussian kernel to minimize inter-individual variances and to enhance SNR.

Analysis for functional connectivity.

To objectively and comprehensively study the fluctuations in brain activity during BMS, we computed the regional pairwise correlation coefficients (RPCC) between the fMRI activity from ROIs selected based on the 'Automated Anatomical Labeling' (AAL) map template [25]. Altogether, 116 brain regions were used as node ROIs in the RPCC analysis, and each pixel of RPCC matrices shows the correlation between a node ROI and the other one. The MATLAB software was used in all the data analysis and result presenting.

Results

Outcome based on various types of 'perceptual consciousness'

There were 155 questionnaires (n=155) gathered for the experiments using the BMS, and we found that 60 (38.7%) participants were categorized as "none" perceptual consciousness and belonged to the negative group. The remaining 95 (61.3%) participants were positive group and categorized as various perceptual consciousness types (described in Table 1) such as 73 (47.1%) with cutaneous, 13 (8.4%) with motion or rotation, 8 (5.2%) with visual audio-visual and 1(0.6%) with social cognition type of perceptual consciousness (Figure 2). By using 'the Chi Square Goodness of fit' test, a significant statistical difference was found between negative and positive groups (as $p<0.05^{*}$).

Analysis of Brain Connectivity Networks.

After using the regional pairwise correlation coefficients (RPCC) method for variation of resting-state fMRI study between without BMS and with BMS on the 18 participants, it was then compared with the differences in brain connectivity of networks of without BMS and with BMS (Figure 3). By setting a threshold value at '$p<0.001$', enhanced connections of 'parahippocampal gyrus to cerebellar lobule V' and 'angular gyrus to precuneus' were found. On the contrary, decreased connection of 'caudate nucleus to cerebellar lobule VIIb' was found (Figure 4).

Discussion

Comparison with direct electrical stimulation of the brain.

Comparing our results of bioceramic treatment with direct electrical stimulation of the brain [2], we found that some forms of subjective experiential phenomena and behavioral changes evoked by both direct electrical stimulation of the brain and BMS are similar: auditory and visual hallucinations; feeling of being somewhere else or even someone else; dream-like states; gustatory sensations; vestibular effects; feeling of unreality; recitation of lyrics and singing; simple movements; oroalimentary automatisms; epigastric sensations, nausea, urge to cry, and motor response (e.g. locomotion, eye and head turning, body swinging, olfactory sensation and thrusting) [2]. Although the effect of BMS as a technique for induction of perceptual consciousness is weaker than direct electrical stimulation of the brain, it has the advantage of being non-invasive and is free from clinical risk.

Functional connectivity of BMS effect on neuropsychiatric problems.

Our previous preclinical or clinical studies on BMS included positive outcomes of migraine [17], rehabilitation of brain infarction [14], autonomous nervous system disorders, and insomnia[18,19]. With respect to mental illness, BMS has proved its achievements of alleviating the drug withdrawal symptoms of amphetamine and hypnotic-drug addictions [19]. There were also reported cases of clinical improvement from psychological illness of depression [19], anxiety, schizophrenia [19] and suicidal attempts[19].

Our study on BMS showed positive functional connectivity of resting state fMRI including ‘parahippocampal gyrus to cerebellar lobule V’ and ‘angular gyrus to precuneus’ and negative functional connectivity on ‘caudate nucleus to cerebellar lobule VIIb’. It has been reported that finger tapping (movement) activated cerebellar lobules IV-V and VIII. In addition to motor function, cerebellar lobules VI and VII is involved in more cognitively demanding task [26]. Also, caudate nucleus is engaged in numerous functions apart from movements [27], including procedural learning [27], associative learning [28], inhibitory control of action [27], reward functions [29]. Therefore, altered functional connectivity between these brain regions may affect cognition as well as motor function.

Combining our previous study on BOLD fMRI [18] and the present study, the change in brain area activation and connectivity during BMS of the brain detected by fMRI with the corresponding brain function of anatomy, is shown in the table. Based on neuro-anatomical analysis, we speculate the most affected brain functions include memory retrieval, language and speech, social cognition, and affection and attention.

To interpret our results of resting-state fMRI, we further reviewed literature and found that positive functional connectivity on the parahippocampal gyrus, angular gyrus, and precuneus, are related to status of depression [30,31]. Similar studies on patients with insomnia showed functional connectivity on the parahippocampal gyrus and precuneus [32]. Change in functional connectivity was also found on the parahippocampal gyrus, angular gyrus, and posterior lobe of cerebellum in young adult suicide attempter [33]. In adolescents with internet gaming addiction, another fMRI study of functional connectivity had shown locations on the anterior lobe of cerebellum, precuneus and parahippocampus [34]. A study on drug addiction of a heroin-dependent individual showed location on the parahippocampal region and caudate nucleus [35]..

The possible clinical application of resting-state fMRI and non-invasive brain stimulation.

In the past, diagnosis of mental disorders was based on neuropsychological evaluations from subjective professional opinions of psychiatrist that lacked reliable biomarkers to monitor the response to treatment [36]. Comparison of the healthy control and the psychotic depression group by resting-state fMRI analysis showed that psychotic depression was consistently associated with significantly decreased specific functional connectivity[37]. Patients with psychological disorders such as schizophrenia, epilepsy, depression, autism, attention deficit hyperactivity disorder (ADHD), and Alzheimer's disease, were also found to be associated with abnormal activity of fMRI-related brain connectivity network [36]. In the future, combined evidence-based study of fMRI with qualitative neuroanatomical detection and non-invasive BIOCERAMIC stimulation may be applied to abnormal functions related to memory retrieval, language and speech, social cognition, and affection and attention. In addition, this platform may also be applied to psychological disorders of insomnia, drug addictions, and psychological illness of depression, anxiety, schizophrenia and suicidal attempts.

The limitations of this study.

The limitation of this study is that it is a study with small number participants; however, it provides promising preliminary results not yet found in the literature. Second,

Conclusion

This study presented subjective observation data on BMS and achieved alteration of perceptual consciousness accordingly. Using resting state fMRI, it also found that BMS has an association with increased resting-state functional connectivity between parahippocampal gyrus to cerebellar lobule V' and 'angular gyrus to precuneus', but decreased connectivity between 'caudate nucleus to cerebellar lobule VIIb'. These recent findings may help further research on BMS with a larger sample size and for potential clinical applications. BMS compared to direct electrical stimulation of brain, has the advantage of being non-invasive and is free from clinical risk.

Declarations

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Author contributions

T.K.L. contributed substantially to study design, data interpretation and manuscript draft. C.W.L. performed the experiments and analyzed the data. Y.C.L analyzed data and edited P.Y.T searched the literature and edited the manuscript. J.Y.W contributed to the study design, data interpretation, manuscript draft, and manuscript revision. All authors reviewed the manuscript

Competing interests

The authors declare no conflict of interests.

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Tables

Table1: Subjective descriptions of categories of perceptual consciousness induced by BMS

Categories of 'perceptual consciousness'	Change of perceptual consciousness	Possible brain regions involved
None	No significant change of 'perceptual consciousness'	None
Cutaneous	Perception of the skin, such as increased vibration, itching, and slight inductance runs through the surface of the body (without real skin irritation)	Somatosensory Cortex
Motion or rotation	A deeper sense of motion or rotation, moving back and forth,	Somatosensory Cortex (Parietal cortex,Thalamus)
Visual or audio-visual phenomena	Visual phenomena such as seeing one or more specific colors or light (without real visual stimulation) More audio-visual phenomena, such as 'lucid dream like experience';	Occipital & temporal Lobe
Social cognition	'sensation of consciousness leaving your body' feeling or 'interaction or communication with a person of consciousness', but candidates were left alone in the laboratory room.	Hippocampus Amygdala

Appendix

Appendix is not available with this version.

Figures

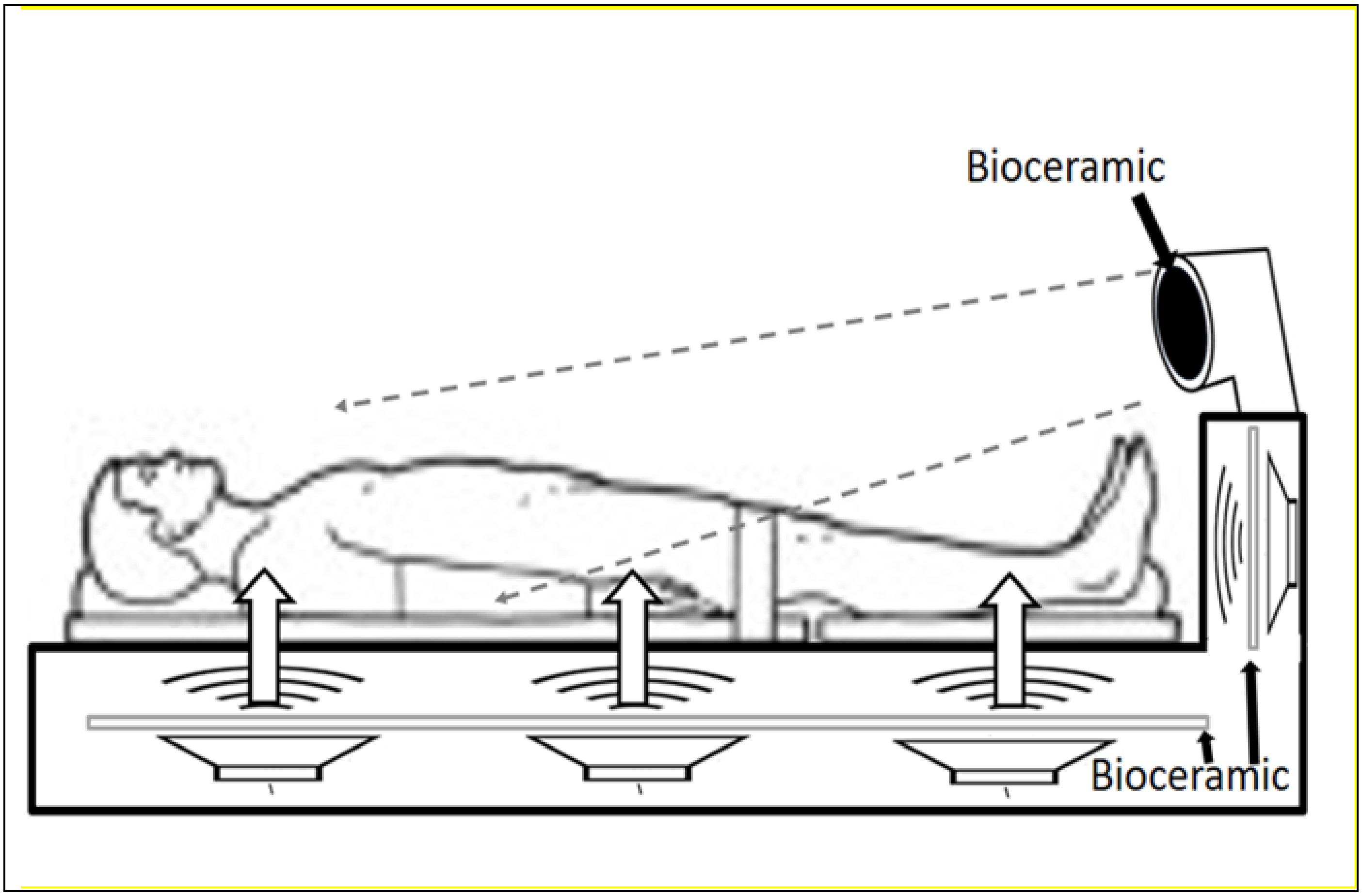

Figure 1

Conceptual drawing of bioceramic stimulation on each participant included resonant energy transfer through the bioceramic material with tempo sound (white arrows) and visible light spectrum (dotted black lines).

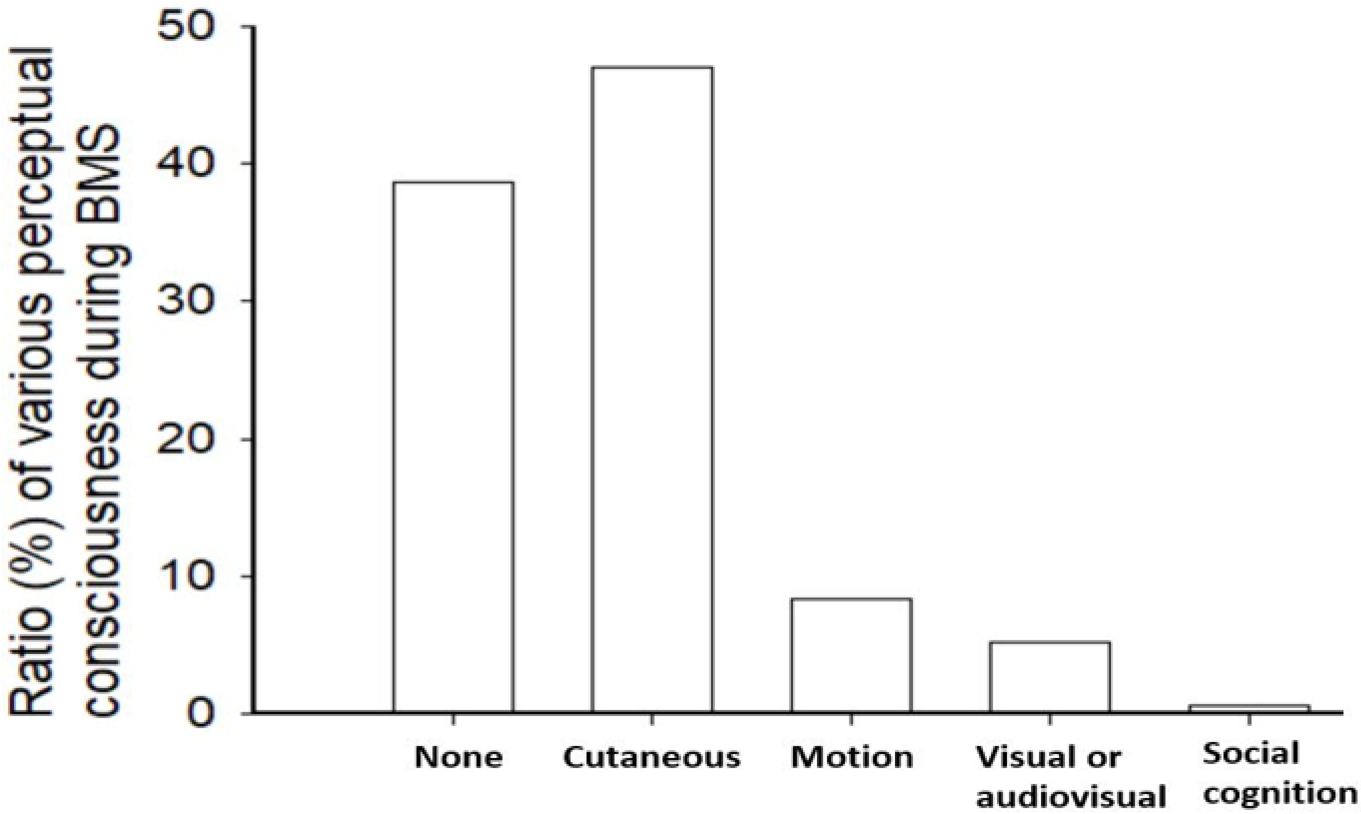

Figure 2

Ratio of various types of perceptual consciousness of subjective responses to BMS from 155 questionnaires

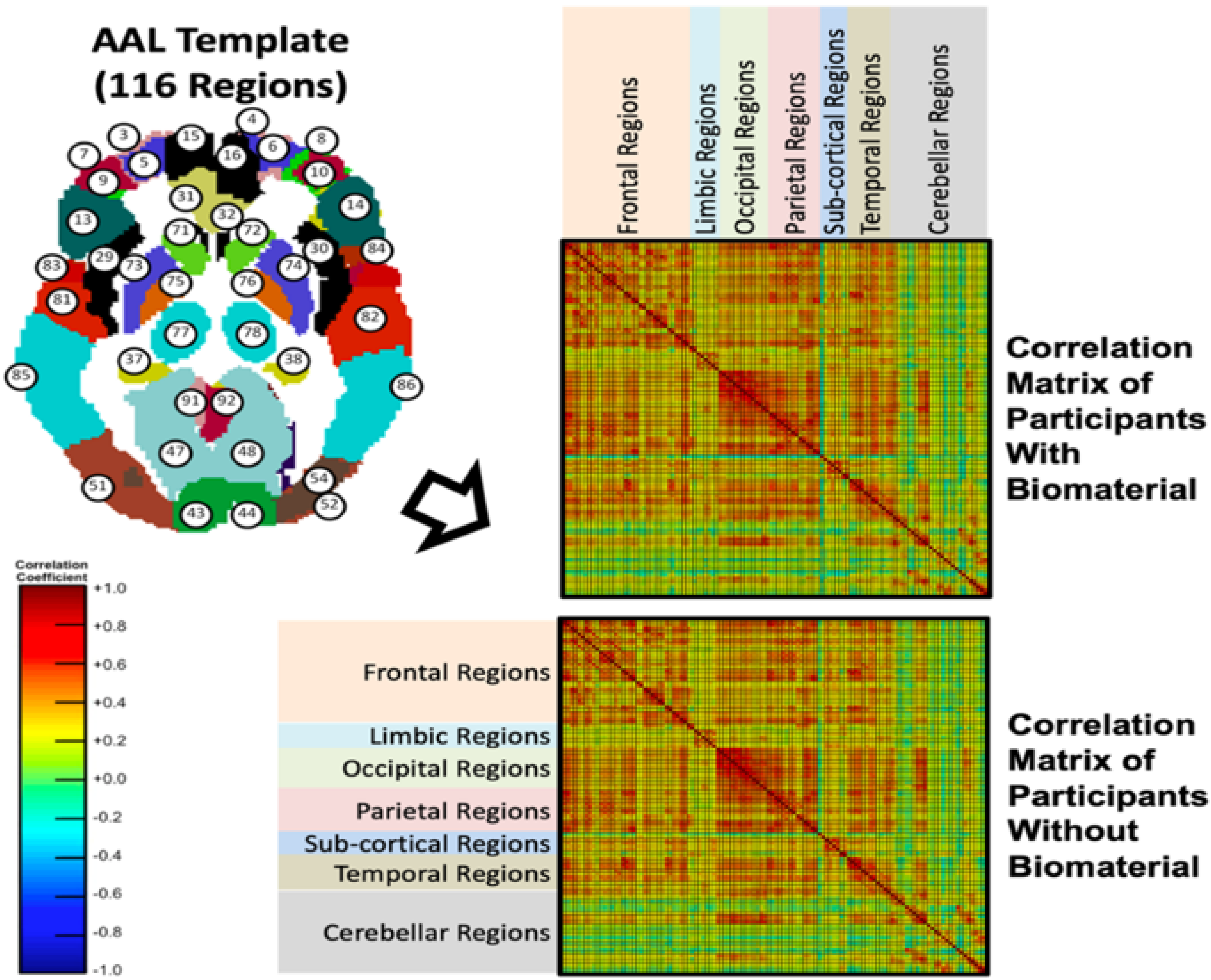

Figure 3

Edgewise connectivity matrices, averaged by subject group. The symmetric 116×116 connectivity matrices (as measured by Pearson correlations), averaged over the with/without BMS conditions. Edges are shown grouped by their module membership. Red edges indicate positive connectivity, while blue edges indicate negative connectivity.

AAL template, Automated Anatomical Labeling template.

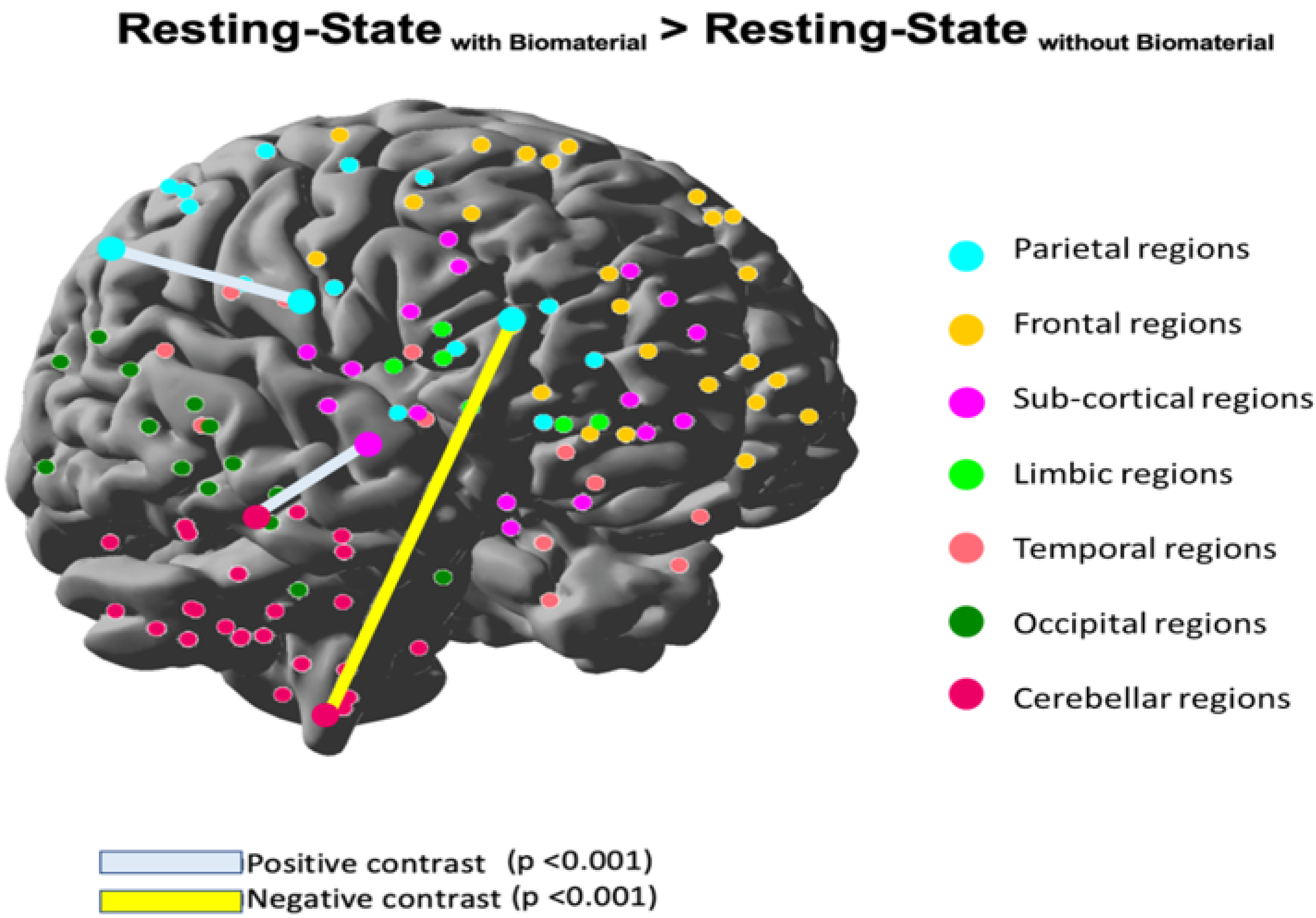

Figure 4

Positive (light blue) and negative (yellow) connections difference between without and with BMS. The threshold was p<0.001.