Impaired Effective Functional Connectivity of the Sensorimotor Network in Interictal Episodic Migraineurs Without Aura

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Abstract

**Background:** Resting-state functional magnetic resonance imaging (Rs-fMRI) has confirmed sensorimotor network (SMN) dysfunction in migraine without aura (MwoA). However, the underlying mechanisms of SMN causal functional connectivity in MwoA remain unclear. We aimed to explore the association between clinical characteristics and effective functional connectivity in SMN, in interictal patients who have MwoA.

**Methods:** We used Rs-fMRI to acquire imaging data in forty episodic patients with MwoA in the interictal phase and thirty-four healthy controls (HCs). Independent component analysis was used to profile the distribution of SMN and calculate the different SMN activity between the two groups. Subsequently, Granger causality analysis was used to analyze the effective causal connectivity between the SMN and other brain regions.

**Results:** Compared to the HCs, MwoA patients showed higher activity in the bilateral postcentral gyri (PoCG) and supplementary motor areas, but lower activity in left Rolandic operculum/insula. Moreover, MwoA patients showed significantly causal connectivity from the SMN to the left calcarine sulcus, left middle temporal gyrus, right angular gyrus and right precuneus. There was also significant causal connectivity from the left calcarine sulcus, left inferior orbitofrontal cortex, right cuneus, right putamen and left inferior parietal lobule to the SMN. In the interictal period, there was positive correlation between the activity of the left PoCG and headache frequency ($r = 0.410, p = 0.013$), but negative correlation between the activity of the right PoCG and the impact of headache ($r = -0.397, p = 0.016$). In addition, the disease duration was directly proportional to the connectivity strength from the left PoCG to the right angular gyrus ($r = 0.418, p = 0.011$), and from the right PoCG to the left calcarine sulcus ($r = 0.377, p = 0.023$).

**Conclusions:** These differential, resting-state functional activities of the SMN in episodic MwoA may contribute to the understanding of migraine-related intra- and internetwork imbalances associated with nociceptive regulation and chronification.

Introduction

Migraine is an incapacitating neurological disorder, typically characterized by unilateral, throbbing or pulsating headaches, and the second-largest contributor to global neurological disorders, after stroke[1]. It affects more than 10% of the general population, thus causing enormous individual and social burden. Patients with migraine often experience anxiety, depression and sleep disturbances, which enhances the mental disorder and significantly impair the quality of daily life[2]. In order to explore effective treatment options for migraine headaches, it is imperative to understand the neuropathological mechanisms of migraine.
A migraine attack is not only a somatic perturbation, but also a sensory dysfunction that amplifies light, sound or touch perceptions in both ictal and interictal phases[3]. These characteristics make migraine a somatosensory disorder that eventually induce aberrant neuroplastic alterations in the central nervous system (CNS). In the last decades, neuroimaging has greatly contributed to the understanding of the neurological diseases involved in migraine pathophysiology. The neuroimaging data have shown that the disorder is associated with microstructural and functional alterations in various brain regions including the sensory motor network (SMN)[4]. The SMN, previously implicated in migraine, is a crucial region that is a multipurpose high-order cognitive processing center[5], which encompass the primary somatosensory cortex, primary motor cortex, premotor cortex and supplementary motor area (SMA)[6]. Previous migraine resting-state functional magnetic resonance imaging (Rs-fMRI) studies have demonstrated functional alterations in some SMN subregions associated with pain and cognition[7,8]. Besides, the migraine attack is a paroxysmal dysfunctional alteration or inflow-outflow dysfunctional modulation of multiple sensory systems[9]. Various neuroimaging outcomes have demonstrated correlation of functional connectivity between the subregions in SMN, and the central executive network (CEN) [6], salience network (SN)[10] as well as default mode network (DMN)[11] in patients with MwoA. The functional connectivity strength of SMN has been shown to significantly illuminate the perception of pain intensity and therapeutic effect in MwoA[12].

Whereas many studies have found that MwoA is associated with changes in functional connectivity between the SMN and other regions, it has been difficult to discern the directionality or specificity of the disrupted connections. Here, we selected the independent component analysis (ICA) method, a data-driven method that requires no prior experience, to separate the spatiotemporal component from the whole brain and extract the distribution of the SMN in a standard template. Using the Granger causality analysis (GCA), we identified differences in the direction of the SMN functional connectivity between patients with MwoA and healthy controls (HCs). Taken together, we observe that, akin to other pain disorders, migraineurs without aura would exhibit abnormal functional alterations within the SMN and the disruptions might define nociceptive transmission pathway related to the SMN in the interictal resting state. Moreover, the disruptions of the SMN effective connectivity would be associated with specific migraine characteristics.

**Methods**

**Participants**

All episodic patients with MwoA were screened and classified following the criteria outlined by the third edition of the International Classification of Headache Disorders (ICHD-3; Code 1.1)[13]. By reviewing family medical history, we enrolled age- and gender-matched HCs, who were headache-free and whose family members did not suffer from any form of headache. We excluded patients who had brain organic disorders, other mental diseases, family history of mental retardation, dementia or physical disease, history of alcohol abuse, and any MRI contraindications. MwoA patients were headache-free and drug-free for at least three days prior to and after scanning to ensure that the patients were in the interictal...
periodand avoidpharmacological interferences on signal fluctuation. For female participants, the data was recorded at mid-cycle to avoid hormonal influences on cortical excitement. Clinical characteristicssuch as age at onset, frequency of attacks, pain intensity (visual analogue scale (VAS)), and headache impact (Headache Impact Test (HIT)-6) were collected. Additionally, for all the participants, psychiatric assessments including Self-rating Anxiety Scale (SAS) and Self-rating Depression Scale (SDS), were also conducted to assess depression and anxiety state. This study was approved by the Medical Ethics Committee of Nanjing Medical University. Informed written consent was obtained from all the participants.

Data acquisition

All data were acquired using a 3.0 Tesla MRI scanner (Ingenia, Philips Medical Systems, Netherlands) with an 8-channel head coil. Head motion and scanner noise were reduced by custom-fit foam pads and earplugs. The Rs-fMRI images were obtained axially using a gradient echo-planar imaging sequence as follows: repetition time (TR) 2000 ms, echo time (TE) 30 ms, flip angle (FA) 90°, number of slices 36, field of view (FOV) 220×220 mm², matrix size 64×64, slice thickness 4 mm, and total 230 volumes. Structural images were acquired by a three-dimensional turbo fast echo (3D-TFE) sequence. The parameters were as follows: TR/TE8.1/3.7 ms; slices170; thickness1 mm; gap0 mm; FA8°; acquisition matrix256×256; FOV256 mm×256 mm. None of the subjects recorded any discomfort or fell asleep during scanning. No obvious structural damage was observed based on the conventional MR images.

Data preprocessing

Using an automated preprocessing pipeline, we preprocessed the data using the Rs-fMRIData Analysis Toolkit plus (RESTplus, http://restfmri.net/forum/). In the functional data pipeline, we discarded the first 10 time-point resting-state data due to the instability of the initial MRI signals. Then the remaining images were corrected for slice-timing and realigned to the middle volume using a six-parameter rigid body transformation. The generated images underwent spatial normalization into the Montreal Neurological Institute standard space at a resolution of a 3×3×3mm³ and then smoothed using anisotropic Gaussian kernel (fullwidth at half maximum = 4). After removal of the linear trend of the time courses, the temporal band-pass filtering (0.01–0.08 Hz) was performed to reduce the effects of low- and high-frequency physiological noise. Besides, to further reduce the effects of confounding factors unrelated to specific regional correlation, we used linear regression to remove several sources of spurious variance. The sources include six head motion parameters and average signals from cerebrospinal fluid (CSF) and white matter (WM). To avoid the risk of obtaining spurious negative correlations, we did not remove the global signal. Subjects with maximum head translation or maximum rotation that exceeded 2 mm or 2° respectively, were excluded.

Voxel-based morphometry (VBM) analysis was performed to segment the cerebral tissues into gray matter (GM), WM or CSF using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm), as previously described.[14]. Subsequently, GM segments were modulated (with linear components) in order to preserve
the absolute regional amount of GM from distortions. Finally, the modulated GM volumes were smoothed with a Gaussian kernel of 8 mm FWHM. We reported surviving clusters of voxels exceeding a voxel-level threshold of \( p < 0.001 \) (uncorrected) or a cluster size threshold of \( p < 0.05 \), family-wise error (FWE) correction for multiple comparisons.

**ICA processing**

To investigate the independent components in MwoA and HCs, the smoothed data were analyzed using the Group ICA of fMRI Toolbox (GIFT, [http://mialab.mrn.org/software/gift/](http://mialab.mrn.org/software/gift/)). On the other hand, the preprocessed functional images for all the subjects were temporally concatenated to create a single four-dimensional data set, while the independent components were automatically estimated against consistent time-dependent functional activity. We then selected the SMN from these components as the best-fit component as previous studies[15,16]. After estimating the group spatial maps, we performed back reconstruction of participant-specific spatial maps using the GICA method and then created output images for the components normalized with Fisher’s z-transformation. One-sample \( t \)-tests were utilized to extract principal component images per group with the FWE correction (\( p < 0.001 \)). Subsequently, two-sample \( t \)-tests were conducted on the sensorimotor component with the false discovery rate (FDR) correction (\( q < 0.001 \)). Age, sex, GM and education were used as covariates.

**GCA processing**

We used GCA to detect the effective connectivity between the reference time series of the regions of interest (ROIs) defined above in SMN and those of each voxel within the rest of the brain. GCA estimates the causal effects of the ROIs of SMN (X) on every other voxel in the brain (Y). A positive coefficient from X to Y indicates that activity in region X exerts a causal influence on the activity region Y, while, a negative coefficient from X to Y shows that the activity of region X exerts an adverse influence on the activity of region Y. The generated voxel-wise GCA model maps were transformed and normalized into z scores. For group-level comparison, clusters passing a threshold of \( p < 0.001 \) (uncorrected) were deemed significant ROIs with the consideration of age, sex, GM or education as covariates.

**Correlation analysis**

To investigate the association between abnormal activity or effective connectivity strength of the SMN and clinical characteristics, the ICA values within the significant ROIs and the strength of connectivity were extracted and correlated with the clinical features using partial correlation analysis. Age, sex, GM and education were used as covariates. Statistical analyses were performed in SPSS 24.0 and the threshold was set at \( p < 0.05 \).

**Results**

**Demographic and clinical information**
Compared with the HCs, MwoA patients showed no significant differences in the age, sex, educational level or brain volumes, as shown in Table 1. However, migraineurs demonstrated higher scores in psychiatric tests than the HCs.

ICA findings

The SMN for all the participants was extracted and reconstructed to group-level maps by ICA. The spatial positional distribution of the resting-state SMN is shown in Figure 1. Inter-group comparison within the SMN revealed four significant ROIs: the bilateral postcentral gyri (PoCG) and SMA with increased activity, and the left Rolandic operculum/insula (ROL/insula) with decreased activity (Table 2).

GCA findings

Two-sample t-test findings of resting-state effective connectivity from the SMN to the rest of the brain are illustrated in Figure 2 (first row, \( p < 0.001 \) uncorrected). Compared with the HCs, MwoA patients showed significantly increased connectivity from the left PoCG to ipsilateral middle temporal gyrus (MTG), but decreased connectivity to contralateral angular gyrus and precuneus. On the other hand, the right PoCG showed a lower causal influence on the contralateral calcarine sulcus.

In addition, the two-sample t-test findings of resting-state effective connectivity from the whole brain to SMN is illustrated in Figure 2 (second row, \( p < 0.001 \) uncorrected). Here, our data showed as significantly increased causal connectivity from left inferior orbitofrontal cortex (IOFC), left calcarine sulcus and right cuneus to the right PoCG, and from the right putamen to the left ROL/insula as well as bilateral SMA. Furthermore, the left inferior parietal lobule (IPL) showed decreased causal influence on ipsilateral ROL/insula.

Correlation analysis results

The activity of regions in SMN significantly correlated with headache features, as shown in Figure 3. There was positive correlation between the activity of the left PoCG and the frequency of headache (\( r = 0.410, p = 0.013 \)), but negative correlation between that of the right PoCG and headache impact intensity (\( r = -0.397, p = 0.016 \)). In addition, the disease duration was positively correlated with abnormal effective connectivity from the left PoCG to the right angular gyrus (\( r = 0.418, p = 0.011 \)), and from the right PoCG to the left calcarine sulcus (\( r = 0.377, p = 0.023 \)).

Discussion

There are numerous challenges in discerning the directionality or specificity of the changes in functional connectivity between the SMN and other regions, especially in patients with MwoA. In this study, we extracted the distribution of SMN and identified abnormal neural activity of bilateral PoCG, left ROL/insula, and bilateral SMA unique to patients with MwoA. Specifically, the SMN in episodic patients with MwoA exhibited abnormal inflow or outflow influence on multiple functional networks and headache dysregulation related to clinical characteristics (e.g., headache impact and duration). Our
findings are in agreement with prior evidence of a disrupted SMN functional connectivity in migraineurs without aura[6], thus providing new insights into multi-sensory modulation in migraine processing. Moreover, we demonstrate that these effective functional abnormalities are independent of structural and microstructural changes.

In the current study, we found higher neural activity in bilateral PoCG, decreased functional connectivity from the right PoCG to the contralateral calcarine sulcus, as well as increased connectivity intensity from the visual cortex (left calcarine sulcus and right cuneus) to the right PoCG. The calcarine sulcus and cuneus are core regions of the primary visual network in the brain, and therefore, the present findings suggest that functional abnormalities between the SMN and visual network are specifically altered in patients with MwoA. Indeed, previous migraine studies have showed that altered activity within the sensory-related cortex, including SMN and visual cortex, results in dysfunction associated with affective, cognitive or pain processing[17,18]. Our findings also show increased brain activity of the right PoCG, which negatively regulate the headache impact intensity, and functional deficits that fail to compensate recurrent endogenous and exogenous pain stimuli or inhibit nociceptive signals in the interictal period. Previous longitudinal investigation[19] showed that the morphological alteration of the visual cortex was significantly associated with migraine progression, especially in the calcarine sulcus and cuneus. In agreement, our results demonstrate functional influences from the right PoCG to the left calcarine sulcus positively correlated with disease course and prior structural plasticity.

However, Wang et al. reported opposite neural activity of the bilateral PoCG by low-frequency oscillations approach to reflect the spontaneous neural function of the brain[8]. In addition, an electroencephalography-related study[20] demonstrated higher desynchronization and power overlying the primary sensorimotor cortex in the preictal phase compared to the interictal phase, with no significant differences between interictal migraineurs and HCs. The heterogeneity of the migraineurs phase and the use of different neuroimaging methods might explain the discrepancy between the studies. Therefore, the abnormal effective functional connectivity between the SMN and visual cortex may be part of the pathological mechanism of failure to filter the unpleasant signals or lower the threshold to somatosensory stimuli in the visual pathway. Furthermore, our resting-state fMRI study also showed the abnormal effective connectivity from the left inferior OFC to the right PoCG in migraineurs without aura compared to HC. The OFC, a segment of the advanced processing center and a key function to the regulation of negative feedback[21], might constitute the cognitive function, regulation of emotions, psychiatric disorders and inhibitory control. The heightened effective connectivity might be interpreted as a dysfunctional inhibitory response to malaise signals. Our demonstration of positive functional coupling between the primary somatosensory cortex and the OFC may also infer the possible role of the OFC in migraine.

Compared with the HCs, migraineurs without aura showed changed effective connectivity from the left PoCG to many pain-related areas, such as the MTG, angular gyrus, precuneus, and IPL[5,22]. These regions have been demonstrated to be crucial in the default mode network (DMN)[23]. The DMN, one of the core brain networks that is activated when at a rest state, plays a pivotal role in discriminative, cognitive and
perceptive functions of pain\[18,24-26\]. Previous studies have shown altered function associated with nociceptive processing and cognitive impairment, within the angular gyrus and MTG in migraineurs\[26\]. Moreover, the precuneus participates in the discrimination of sensory perception of pain\[27\] and the brainstem-thalamus-cortex circuit which modulates pain intensity\[28\] in the migraineurs. Our data found that the increased brain function in the left PoCG has a negative modulatory effect in the frequency of headache attacks. Thus, our results indicated that the dysfunction between the primary somatosensory cortex and DMN may disrupt the neural transmission pathway of discrimination and intensity involved in sensory perception of pain. Besides, long-term and repetitive migraine headache attacks may lead to somatosensory cortex compensatory or dysfunctional changes. These observations agree with our data which showed that influence from the left somatosensory cortex to DMN play a role in functional adaption along migraine progressing.

The current study also observed that, in resting state, there is decreased activity of the left ROL/insula, near to the limbic system, subcortical network and anterior DMN, which may trigger pain processing adjustments in multiple instinct brain networks. The insula is a component of the salient network (SN, a pivotal large-scale intrinsic network associated with perceiving) which process and integrate internal and external stimuli\[29\]. Similarly, a resting-state fMRI study reported that insular cortex demonstrated abnormal functional connectivity to DMN encoding headache severity in migraineurs\[30\]. Whereas, high SN function occurs when the mind is engaged in specific tasks, rise in DMN activity does not depend on external stimulation. Hence, the ROL/insula-DMN functional connectivity modulates the switching between self-monitoring and task processing. In addition, the operculum, which contains the secondary sensory cortex, is another key region involved in the processing of sensory information\[31\]. Previous studies have shown that the secondary sensory cortex and insula could provide information about the intensity, cognition and spatial discriminative pain pathways of nociceptive stimulus in migraine\[8,18\]. The ROL/insula has been proposed to be involved in the multi-network sensory integration of pain. It predominantly mediates the intensity and signals ascending the spinothalamic tracts of the pain processing system\[32-34\]. Furthermore, the decreased effective connectivity from the left IPL to the left ROL/insula may support the impaired function and lower inhibition power of DMN, and hypersensitive responses to external sensory inputs. Since the SMN and DMN are key regions of the trigeminovascular modulatory system, a pain inhibiting system, disrupted activity of these regions may lead to a dysfunctional pain inhibition pathway, thus contributing to the hypersensitivity of pain and migraine.

In addition, we observed that the SMN subregions could be influenced by abnormal inputs from the putamen and the caudate nucleus, components of the striatum. Literature has shown that the striatum affects the neuronal pathways underlying the inhibition effect of nociceptive stimulation. These effects are mediated by the striatal dopamine D2 receptors which are associated with pain inhibitory circuitry of the caudal trigeminal nucleus\[35\]. The abnormal interaction of the putamen has been shown to trigger many independent components\[33\], justifying the hypothesis that transmission of pain is complex and multidimensional\[36\]. Moreover, the SMA contributes to response selection and nociceptive generation in MwoA\[7,9\]. Furthermore, since the cortico-striato-thalamo-cortical loop affects many
neurological disorders [37], we speculated that perturbation of the striato-cortical circuit may suppress the inhibitory function on the nociceptive reflex. Together with the previous evidence, we highlight the importance of stratum and SMA in pain- and movement-related processing as well as in the regulation of migraine and other chronic pain syndromes[38,39]. The information transformation and transmission pathway corresponds to both ventral and dorsal streams specialized in processing the intensity of painful stimuli[27]. This pattern of increased effective connectivity indicates that the putamen may influence the activity of somatosensory cortex in discriminating pain experience, thus, its potential and vital role in shaping of the pain perception. Our findings explain the dysregulation between the putamen and sensory cortex in migraine headaches.

Our study, however, used a small sample size. Therefore, a large sample size might be needed to enhance our data repeatability and reliability. In addition, the heterogeneity of the participants, such as the etiology, headache severity, disease duration, or neuropsychiatric comorbidity could result in neural activity biasness. Besides the functional alterations, more studies are required to investigate the possibility of structural connectivity involved in SMN.

**Conclusions**

In conclusion, we have explicited the abnormal interactions between the SMN and other networks in MwoA patients. Our data demonstrates that SMN plays a crucial role in pain modulation and chronification, as well as dissecting the neuropathologic mechanisms underlying episodic MwoA patients in headache-free phase.

**Abbreviations**

CSF: Cerebrospinal fluid; GM: Gray matter; HCs: Healthy controls; HIT: Headache impact test; ICA: Independent component analysis; IOFC: Inferior orbitofrontal cortex; IPL: Inferior parietal lobule; MwoA: Migraine without aura; MTG: Middle temporal gyrus; Rs-fMRI: Resting-state functional magnetic resonance imaging; SAS: Self-rating Anxiety Scale; SDS: Self-rating Depression Scale; SMN: Sensorimotor network (SMN); SMA: Supplementary motor area; VAS: Visual analogic scale; WM: White matter.

**Declarations**

**Ethics approval and consent to participate**

The ethical committee of Nanjing Medical University approved the study. Informed consent was obtained from each participant.
Consent for publication

Not applicable.

Availability of data and materials

Clinical, neuroimaging and statistical data will be available upon request from any qualified investigator.

Competing interests

The authors declare that they have no competing interests.

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Authors’ contributions

WHL and CJ designed and drafted the manuscript. CYC, YYS and GX analyzed the data and drafted the manuscript. ZGP and ZQQ performed the experiments. HZZ and YL contributed to the acquisition of fMRI data and analyzed them. YX, LJ and ZH revised the manuscript. All authors read and approved the final manuscript.

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**Tables**
|                          | MwoA         | HCs          | p value |
|--------------------------|--------------|--------------|---------|
| Age (year) \(^a\)       | 35.15±10.18  | 35.50±8.59   | 0.875   |
| Sex (male/female)        | 6/34         | 5/29         | 0.758   |
| Education (year) \(^a\) | 12.15±3.02   | 13.41±3.16   | 0.084   |
| Disease duration (year) \(^b\) | 5.5 (2,10.75) | /            | /       |
| Frequency (days/month) \(^b\) | 3 (3,5)     | /            | /       |
| HIT-6 score \(^a\)      | 58.45±9.32   | /            | /       |
| VAS score \(^b\)        | 6 (5,7)      | /            | /       |
| SAS score \(^b\)        | 35 (29,47)   | 23(22,26)    | < 0.001 |
| SDS score \(^b\)        | 35 (29,50)   | 24(23,26)    | < 0.001 |
| Gray matter (mm\(^3\)) \(^a\) | 633.25±56.72 | 619.48±54.18 | 0.292   |
| White matter (mm\(^3\)) \(^a\) | 492.47±44.35 | 499.94±55.22 | 0.521   |
| Cerebrospinal fluid (mm\(^3\)) \(^a\) | 215.83±19.42 | 217.90±27.75 | 0.708   |
| Brain parenchyma (mm\(^3\)) \(^a\) | 1125.72±92.20 | 1119.42±92.48 | 0.771   |

Data are presented as mean ± SD (a) or medians and interquartile ranges (25th–75th percentiles) (b). HIT-6: Headache Impact Test-6; SAS: Self-rating Anxiety Scale; SDS: Self-rating Depression Scale; VAS: visual analogue scale; MwoA: migraine without aura; HCs: healthy controls.
### Table 2
Significant differences in the SMN in patients with MwoA compared with HCs

| Brain regions                        | X  | Y   | Z  | K  | T score |
|--------------------------------------|----|-----|----|----|---------|
| R postcentral gyrus                  | 48 | -18 | 60 | 22 | 8.9687  |
| L postcentral gyrus                  | -48| -42 | 60 | 23 | 9.5054  |
| L Rolandic operculum/insula         | -42| -6  | 15 | 91 | -6.9314 |
| B supplementary motor area           | 6  | 6   | 66 | 42 | 6.5761  |

Significant thresholds were corrected by false discovery rate correction ($q< 0.001$). SMN: sensorimotor network; MwoA: migraine without aura; HCs: healthy controls; L: left; R: right; B: bilateral.

### Table 3
Altered effective connectivity between SMN and rest of brain in MwoA compared with HCs

| From SMN                                      | X  | Y   | Z  | K  | T score |
|-----------------------------------------------|----|-----|----|----|---------|
| R postcentral gyrus → L calcarine sulcus      | -21| -60 | 3  | 16 | -4.3319 |
| L postcentral gyrus → L middle temporal gyrus| -63| -48 | -3 | 11 | 4.7747  |
| R angular gyrus                               | 54 | -51 | 24 | 15 | -4.2479 |
| R precuneus                                   | 6  | -63 | 24 | 28 | -3.9978 |

| To SMN                                        | X  | Y   | Z  | K  | T score |
|-----------------------------------------------|----|-----|----|----|---------|
| R postcentral gyrus ← L calcarine sulcus      | -21| -60 | 6  | 24 | 5.1605  |
| L inferior orbitofrontal cortex               | -24| 33  | -12| 24 | 4.6069  |
| R cuneus                                      | 18 | -69 | 30 | 20 | 3.8579  |
| L ROL/insula ← R putamen                      | 27 | 12  | 9  | 12 | 4.0865  |
| L inferior parietal lobule                    | -42| -36 | 42 | 10 | -4.1561 |
| B supp motor area ← R putamen                | 27 | 9   | 9  | 10 | 4.1487  |

ROL: Rolandic operculum; SMN: sensorimotor network; supp: supplementary; MwoA: migraine without aura; HCs: healthy controls; L: left; R: right; B: bilateral; ($p< 0.001$, uncorrected).
Figures

Figure 1

Group-level sensorimotor network in migraineurs without aura (MwoA) and healthy controls (HCs). Significant thresholds were corrected by family-wise error correction (p< 0.001).
Figure 2

Altered effective connectivity from the SMN to the other brain regions and vice versa, in migraineurs without aura compared with the healthy controls. Thresholds were set at a p<0.001 (uncorrected). SMN: sensorimotor network; PoCG: postcentral gyrus; ANG: angular gyrus; PCUN: precuneus; MTG: middle temporal gyrus; CAL: calcarine sulcus; ROL: Rolandic operculum; SMA: supplementary motor area; PUT: putamen; IOFC: inferior orbitofrontal cortex; CUN: cuneus; L: left; R: right; B: bilateral.
Figure 3

Significant correlations between clinical characteristics and abnormal connectivity in migraineurs. There was positive correlation between the ICA values of the left PoCG and the frequency of attacks (a); and negative correlation between the ICA values of the right PoCG and headache impact (b). There was positive correlation between the disease duration and the abnormal effective connectivity from the left PoCG to the right angular gyrus (c), as well as from the right PoCG to the left calcarine sulcus (d). ICA: independent component analysis; PoCG: postcentral gyrus; ANG: angular gyrus; CAL: calcarine sulcus; HIT: headache impact test; L: left; R: right.