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SPONTANEOUS NEURAL ACTIVITY ALTERATIONS IN TEMPOROMANDIBULAR DISORDERS: A CROSS-SECTIONAL AND LONGITUDINAL RESTING-STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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Abstract—The involvement of the central nervous system in the pathophysiology of temporomandibular disorders (TMD) has been noticed. TMD patients have been shown dysfunction of motor performance and reduced cognitive ability in neuropsychological tests. The aim of this study is to explore the spontaneous neural activity in TMD patients with centric relation (CR)–maximum intercuspation (MI) discrepancy before and after stabilization splint treatment. Twenty-three patients and twenty controls underwent clinical evaluations, including CR–MI discrepancy, Helkimo indices and chronic pain, and resting state functional magnetic resonance imaging scans at baseline. Eleven patients repeated the evaluations and scanning after the initial wearing (T1) and 3 months of wearing (T2) of the stabilization splint. The fractional amplitude of low-frequency fluctuation (fALFF) was calculated to compare the neural functions. At baseline, the patients showed decreased fALFF in the left precentral gyrus, supplementary motor area, middle frontal gyrus and right orbitofrontal cortex compared with the controls ($P < 0.05$, AlphaSim corrected). Negative correlations were found between the fALFF in the left precentral gyrus and vertical CR–MI discrepancy of bilateral temporomandibular joints of patients ($P < 0.05$, two-tailed). At T2, the symptoms and signs of the patients were improved, and a stable condylar position on the CR was recovered, with increased fALFF in the left precentral gyrus and left posterior insula compared with pretreatment. The fALFF decrease in the patients before treatment was no longer evident at T2 compared with the controls. The results suggested that TMD patients with CR–MI discrepancy showed significantly decreased brain activity in their frontal cortexes. The stabilization splint elicited functional recovery in these cortical areas. These findings provided insight into the cortical neuroplastic processes underlying TMD with CR–MI discrepancy and the therapeutic mechanisms of stabilization splint.

Key words: temporomandibular disorders, centric relation, chronic pain, functional magnetic resonance imaging, neuronal plasticity, occlusal splints.

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Abbreviations: Ai, anamnestic dysfunction index; BOLD, blood oxygen level-dependent; CR–MI discrepancy, centric relation–maximum intercuspation discrepancy; Di, clinical dysfunction index; DPARSF, Data Processing Assistant for Resting-State fMRI; fALFF, fractional amplitude of low-frequency fluctuation; fMRI, functional magnetic resonance imaging; GCPS, Graded Chronic Pain Scale; MRI, magnetic resonance imaging; RDC/TMD, Research Diagnostic Criteria for Temporomandibular Disorders; rfMRI, resting state functional magnetic resonance imaging; TMD, temporomandibular disorders; TMJ, temporomandibular joint.

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INTRODUCTION

Temporomandibular disorders (TMD) are defined as a subgroup of craniofacial pain problems involving the temporomandibular joint (TMJ), masticatory muscles and associated head and neck musculoskeletal structures. TMD patients most frequently suffer from fairly localized pain, limited or asymmetric mandibular movements and TMJ noises and other common associated symptoms include ear pain and stuffiness, tinnitus, dizziness, neck pain, and headache. (Scrivani et al., 2008). TMD is a common reason for chronic facial pain and the prevalence of TMD has been reported to vary from 7% to 84% in different studies (Luther, 2007). The signs and symptoms could be chronic and difficult to manage and thus the oral health-related quality of life was negatively affected in TMD patients (John et al., 2007; Dahlstrom and Carlsson, 2010). Besides, there is a marked comorbidity of TMD with fibromyalgia and other chronic pain syndromes and stress-related disorders

(Eze-Nliam et al., 2011). The etiologies and pathogenesis of TMD are poorly understood and are considered multifactorial including systemic, physiological and structural factors (Scrivani et al., 2008). Recently it is considered that TMD may share a common pathophysiology involving the central nervous system similar to disorders such as fibromyalgia and chronic fatigue syndrome (Scrivani et al., 2008). TMD patients have been shown to have abnormal cortical response to tactile stimulation, exhibit dysfunction of motor performance and have reduced cognitive ability in neuropsychological tests (Shibukawa et al., 2007; Nebel et al., 2010; Weissman-Fogel et al., 2011). Although structural and functional neural changes have been reported by a few studies, suggesting an important role of the central nervous system in TMD, further studies are needed to characterize pattern of neural alterations in TMD regarding the complex representations of TMD symptoms and signs (Younger et al., 2010; Moayedi et al., 2011; Weissman-Fogel et al., 2011; Ichesco et al., 2012).

Centric relation (CR)–maximum intercuspation (MI) discrepancy, which refers to the shift of condyle between two important physical mandibular positions – CR and MI during mandibular movement, is often observed in TMD patients (He et al., 2010; Weffort and de Fantini, 2010; Barrera-Mora et al., 2012; Padala et al., 2012). CR describes the position of condyles articulating with the thinnest avascular portion of their respective disks with the condyle in the anterior–superior position against the slopes of the articular eminence, which is a position independent of tooth contact. MI describes the complete intercuspation of the opposing teeth independent of the condylar position, and the condylar position in MI is subject to tooth contact. The relationship between the CR–MI discrepancy and TMD is not clearly understood. The current evidences have not excluded the potential relevance of condylar positions to TMD (Rinchuse and Kandasamy, 2005; Mohlin et al., 2007; Scrivani et al., 2008). Functional occlusal theory believes that achieving CR–MI harmony after orthodontic treatment reduces the risk of developing TMD (Williamson, 1976; Roth, 1981; Cordray, 1996). Our previous experiment found that the degree of CR–MI discrepancy has a positive correlation with the severity of the signs and symptoms of TMD, and might serve as a reliable indicator of the presence and severity of TMD (He et al., 2010). A few studies have also suggested displacement between CR and MI may play a significant role in signs and symptoms of TMJ disorders (Weffort and de Fantini, 2010; Barrera-Mora et al., 2012; Padala et al., 2012). Mandibular movement conducted by masticatory systems is of great importance not only for oral-related functions such as food taking and speech, but also for the systematic, mental and physical functions of the body, especially the cognitive function of the brain (Ono et al., 2010). The peripheral sensory inputs from the tooth, oral muscles and TMJ could modulate the mandibular movements, which are generated and dominated by the central nervous system (Onozuka et al., 2002). However, the spontaneous neural function of TMD patients with CR–MI discrepancy has not previously been explored.

Functional magnetic resonance imaging (fMRI) is a non-invasive technique to demonstrate brain functional activity by using blood oxygen level-dependent (BOLD) signals (Biswal et al., 1995). Previous fMRI studies have revealed abnormal motor and cognitive functions in TMD patients during specific tasks (Nebel et al., 2010; Weissman-Fogel et al., 2011; Ichesco et al., 2012). Resting state fMRI (rfMRI) investigates brain function and is considered to be physiologically meaningful and related to spontaneous neural activity (Fox and Raichle, 2007). The fractional amplitude of low-frequency fluctuation (fALFF) of BOLD signals measures the power of a given time course within a specific frequency range (e.g., 0.01–0.08 Hz) divided by the total power in the entire detectable frequency range, providing a specific measure of intrinsic low-frequency oscillatory phenomena and effectively suppressing non-specific signal components. Therefore, this factor significantly improves the sensitivity and specificity involved in detecting regional spontaneous brain activity (Zou et al., 2008).

To our best knowledge, rfMRI has not been used previously to examine brain functions in TMD patients with CR–MI discrepancy. Furthermore, the stabilization splint has been found to be effective in alleviating TMD symptoms and signs, although little evidence has been shown to illustrate the mechanisms of action (Dawson, 2006; Scrivani et al., 2008). Thus, the aims of the present study were to explore intrinsic neural function in TMD patients with CR–MI discrepancy before and after stabilization splint treatment using rfMRI. We hypothesized the following that: (i) TMD patients would show abnormal spontaneous neural activity at baseline, which would be associated with CR–MI discrepancy, and (ii) the altered brain activity would become more normal after the treatment.

EXPERIMENTAL PROCEDURES

Participants

This study was approved by the ethics board of Sichuan University, and written informed consent was obtained from all subjects. The inclusion criteria for the patient group (P) were the following: full permanent dentition; no history of orthodontic or prosthetic treatment, injury to the face or jaw, chewing side preference, or rheumatic arthritis; the presence of TMD diagnosed by the Research Diagnostic Criteria for Temporomandibular Disorders (RDC/TMD) (Dworkin and LeResche, 1992); with CR–MI discrepancy according to the criteria of discrepancy > 1 mm in the horizontal or vertical planes and/or > 0.5 mm in the transverse plane. (Crawford, 1999); and being right-handed. No patients took any drugs for TMD before the first rfMRI scanning, and no patients took any other treatments except stabilization splint during the whole follow-up. The inclusion criteria for the healthy control group (N) were the following: full permanent dentition; no history of orthodontic or prosthetic treatment, injury to the face or jaw, chewing side preference, parafunction or rheumatic arthritis; no signs and symptoms of TMD according to RDC/TMD criteria; CR–MI in harmony; and being right-handed. All