Altered structure in patients with classical trigeminal neuralgia

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Abstract

Classical trigeminal neuralgia (TN) is a specific type of chronic neuropathic orofacial pain of which the plasticity of brain structure and connectivity have remained largely unknown. Voxel-based morphometry was used to analyze the change of gray matter volume. Resting state functional imaging was used to analyze the connectivity between brain regions. Furthermore, the relation between the duration of TN and changes derived from functional or structural perspective was also examined.

Introduction

Trigeminal Neuralgia (TN) is one of the most common facial pains, characterized by recurrent brief paroxysmal pain. It is most frequently described as a 'stabbing'- or 'electric-shock'-like pain that is localized to the sensory supply area of trigeminal nerve. Neurovascular compression of the trigeminal nerve at root entry zone is the most common cause of idiopathic TN [Love and Coakham, 2001, Maarbjerg et al., 2015]. TN that develops without apparent cause other than neurovascular compression is defined as classical TN [Headache Classification Committee of the International Headache Society (IHS), 2013]. This is distinct from trigeminal neuropathy that has similar clinical presentation. Trigeminal neuropathy is defined as facial pain in the distribution of trigeminal nerve cause by another disorder (such as herpes zoster infection, multiple sclerosis) or trauma and is indicative of neural damage. It is more often a constant orofacial pain and is different from classical TN that presents with recurring and paroxysmal attacks.

Neuroimaging has also been used to investigate the changes in brain structure and function associated with [DeSouza et al., 2014]. Although functional and structural changes in the thalamus, SMC, PFC and basal ganglia were frequently reported, these observed results are heterogeneous. Noticeably, most of these studies enrolled patients with painful trigeminal neuropathy instead of classical TN, which is a specific type of chronic neuropathic orofacial pain with distinct pathophysiology and alteration in brain activity [Gustin et al., 2011]. Furthermore, a majority of these studies evaluated brain responses to experimentally induced pain, which were more likely to reveal the CNS pathways that are involved in pain processing of acute TN.

The plasticity of brain and the alterations of connectivity between pain-associated brain regions in chronic classical TN patients have remained largely unknown. In addition, the lateralization of pain processing on TN has seldom been discussed. The current study uses structural and resting-state functional magnetic resonance imaging (MRI) to achieve three specific aims. The first aim is to analyze regional gray matter (GM) volume changes, and to evaluate the change of connectivity between each brain regions with GM volume change in patients with classical TN. This can help to identify specific brain areas and networks that may be associated with the development and persistence of this specific type of chronic neuropathic orofacial pain. Because brain structure and functional change may be dynamic and progressively pain-driven over time, the third aim of this study is to estimate the correlationsbetween the duration of TN with the amplitude of structural and functional change, which may represent brain plasticity due to pain chronicity.

Methods

Forty-five patients with TN were prospectively enrolled into this study. Thirty-six patients suffered from right TN and 26 suffered from left side TN. Patients presenting with bilateral TN were excluded. All patients were diagnosed with classical TN according to the criteria of the International Headache Society for TN, and underwent MRI. 3D MP-RAGE anatomical images were obtained using a gradient echo sequence (TR = 1900 ms; TE = 2.98 ms; FOV = 230 mm; matrix = 220 X 256; slice number: 160, spatial resolution of 0.9 mm x 0.9 mm x 0.9 mm). The VBM8 toolbox (Gaser, C., http://dbm.neuro.uni-jena.de/vbm/) was used to analyze all anatomical images. Preprocessing steps included bias-field correction and segmentation into GM, white matter, and cerebrospinal fluid. Segmented images were registered to standard Montreal Neurological Institute (MNI) space. The GM images were then modulated by correcting non-linear normalization wrap with nonlinear-only modulation, while correcting for the different brain sizes. Finally, the normalized and modulated images were smoothed with an

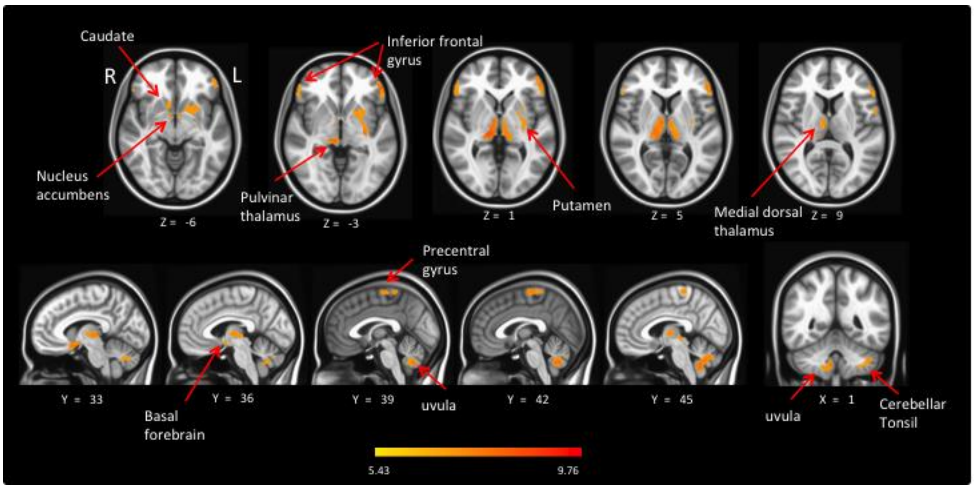

Fig 1: The significant volume reduction of GM which are different between two groups.

8mm Gaussian kernel. The final images can be regarded as relative gray matter volume without any further statistical correction for the total intracranial volume. The linear regression model was performed separately to address the differences between TN group and normal controls. Age and gender are used as covariates. FSL' randomise function was used to conduct the permutation test based on above models. The significant results were thresholded at FWE corrected P< 0.05.

Results

The results showed gray matter volume reduction in components of prefrontal cortex, cerebellar tonsil, thalamus, hypothalamus and nucleus accumbens among right side TN patient and in inferior frontal gyrus, precentral gyrus, cerebellum, thalamus, nucleus accumbens and putamen among TN patients (Fig 1).

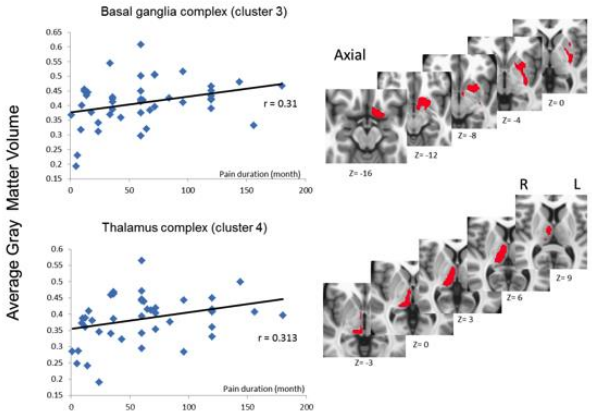

Fig 4: The correlation between GM volume and pain duration. GM volumes in the striatum and the thalamus complex have shown significant positive correlations with pain duration. An outlier with 360 months of pain was removed from this analysis.

In the TN group, significant correlation between averaged GM volume in the left striatum and pain duration (P = 0.0184), and between the thalamus complex and pain duration (P = 0.0190) were observed (Fig. 2).

Conclusion

This study suggests that brain regions such as the thalamus may not only be involved in processing of pain stimuli but also important for the development of TN. The left hemisphere may be dominant in processing and modulation of TN pain signal. Chronification of this specific neuropathic pain induces change in connectivity between brain regions involved in emotional or cognitive modulation of pain.

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