P 3-86

Increased Brain White Matter Diffusivity Associated with Phantom Limb Pain

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Introduction

We used diffusion tensor imaging (DTI) to evaluate the phantom limb pain-related changes of cerebral white matter in unilateral arm amputation patients whose cerebral blood volume (CBV) changes was proved to be associated with emotion in the cerebral pain network in our previous paper (DOI: https://doi.org/10.1016/j.apmr.2017.03.010).

Methods

Ten patients with phantom limb pain (43.8±3.4 years, 1 woman) and 16 age- and sex-matched healthy controls (41.7±2.2 years, 7 women) participated in the study. The patients (i) were aged less than 50 years, (ii) underwent the amputation of the unilateral upper limb after electrical injury, (iii) suffered from the phantom limb pain longer than 12 months, and (iv) had uncontrolled pain despite medication and physical therapy. DTI data were obtained using a MAGNETOM Sonata 1.5 T system (Siemens AG, Erlangen, Germany). Preprocessing and diffusion tensor modeling were performed using FDT v3.0 included in FSL (http://fsl.fmrib.ox.ac.uk/fsl/). At each voxel within the whole-brain mask created by excluding non-brain tissue, a diffusion tensor was modelled and diffusion tensor-derived parameters, including fractional anisotropy (FA), mean diffusivity (MD), axial diffusivity (AD), and radial diffusivity (RD), were computed. We flipped the images of the diffusion tensor-derived parameters around the midsagittal axis for the patients who underwent the amputation of the left upper limb, such that the amputated upper limb could be uniformly connected to the left hemisphere in all patients. Then, for voxel-wise statistical analyses of the diffusion tensor-derived measures, we utilized a tract-based spatial statistics approach implemented in FSL. For each diffusion tensor-derived measure, the images projected onto the mean FA skeleton were fed into voxel-wise analyses to examine differences in values between the patients and healthy controls. In addition, associations between the values of each diffusion tensor-derived measure and VAS scores across the patients were assessed. Because HDRS scores were much higher in the patients than in the healthy controls and individual differences in the severity of depression may affect white matter microstructure as well as pain, HDRS scores were included as a nuisance covariate in the statistical models.

Results

The patients showed higher AD values compared to the healthy controls. White matter structures of the altered AD values in the patients comprised the internal capsule, posterior thalamic radiation, sagittal striatum, corona radiata, external capsule, superior longitudinal fasciculus, superior fronto-occipital fasciculus, and fornix in both hemispheres (Fig 1). The RD values of patients were positively correlated with VAS scores, specifically across white matter structures in the hemisphere associated with missing hand (Fig 2).

Conclusion

The increase of diffusivity in phantom limb pain patients reflects white matter alteration associated with pain intensity.

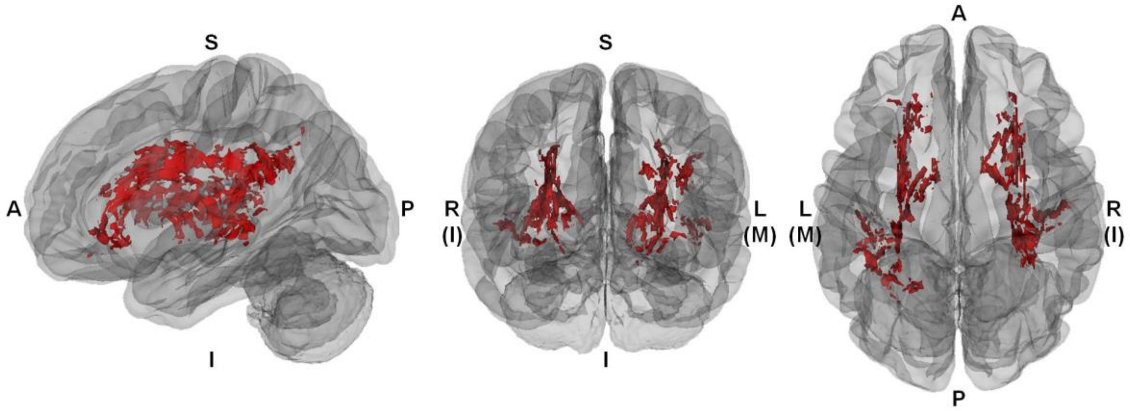

fig1. Mapping of patient versus control AD as adjusted for depressive symptoms. The distribution of white matter structures in which the values of AD were higher in patients with phantom limb pain than in healthy controls. Abbreviations: M, hemisphere associated with missing hand; I, hemisphere associated with intact hand; A, anterior; P, posterior.

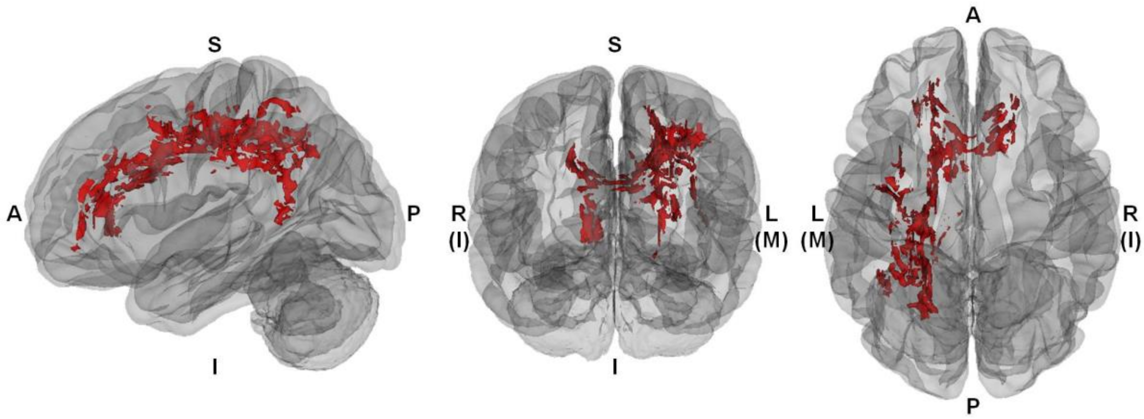

fig2. Mapping of RD correlations with severity of phantom limb pain in the patient group. When the HDRS scores were included as a nuisance covariate, the distribution of white matter structures in which the values of RD were positively correlated with VAS scores in patients with phantom limb pain. Abbreviations: M, hemisphere associated with missing hand; I, hemisphere associated with intact hand; A, anterior; P, posterior.