

RESTING STATE FUNCTIONAL CONNECTIVITY ALTERATIONS OF THE SENSORIMOTOR AND EXTRA-MOTOR NETWORKS IN PRIMARY LATERAL SCLEROSIS

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Introduction. Primary lateral sclerosis (PLS) is a rare, slowly progressive disorder characterized by an isolated degeneration of the upper motor neurons (UMN). During its progression, the disease involves both motor and extra-motor systems. Resting state functional MRI (RS fMRI) has the potential to provide an *in vivo* assessment of the motor and extra-motor brain alterations in PLS.

Objective. To investigate RS functional connectivity within the sensorimotor and extra-motor brain networks in patients with PLS, and to explore whether the RS changes are related to patient clinical features and white matter (WM) structural connectivity.

Methods. RS fMRI and diffusion tensor (DT) MRI were obtained from 24 PLS patients and 26 healthy controls. Clinical and neuropsychological data were available. RS fMRI data were analyzed using a model free (MELODIC) approach in FSL. Multiple regression models were performed to assess the association between RS connectivity, clinical variables and WM tract fractional anisotropy values.

Results. Compared with controls, PLS patients showed an increased connectivity in the right precentral gyrus of the sensorimotor network, bilateral superior frontal and supramarginal gyri of the fronto-parietal networks, and anterior cingulate cortex (ACC) of the executive network (**Figure 1**). In PLS, the enhanced sensorimotor connectivity was associated with more severe disability, more rapid rate of progression, and WM damage to the corticospinal tracts and corpus callosum (**Figure 2**). The increased connectivity of the fronto-parietal networks was related with worse executive/language performances and WM damage to the superior longitudinal fascicule (**Figure 2**). Conversely, the enhanced connectivity of the ACC in the executive network correlated with a better performance at a frontal cognitive test and WM integrity of the genu of the corpus callosum (**Figure 2**).

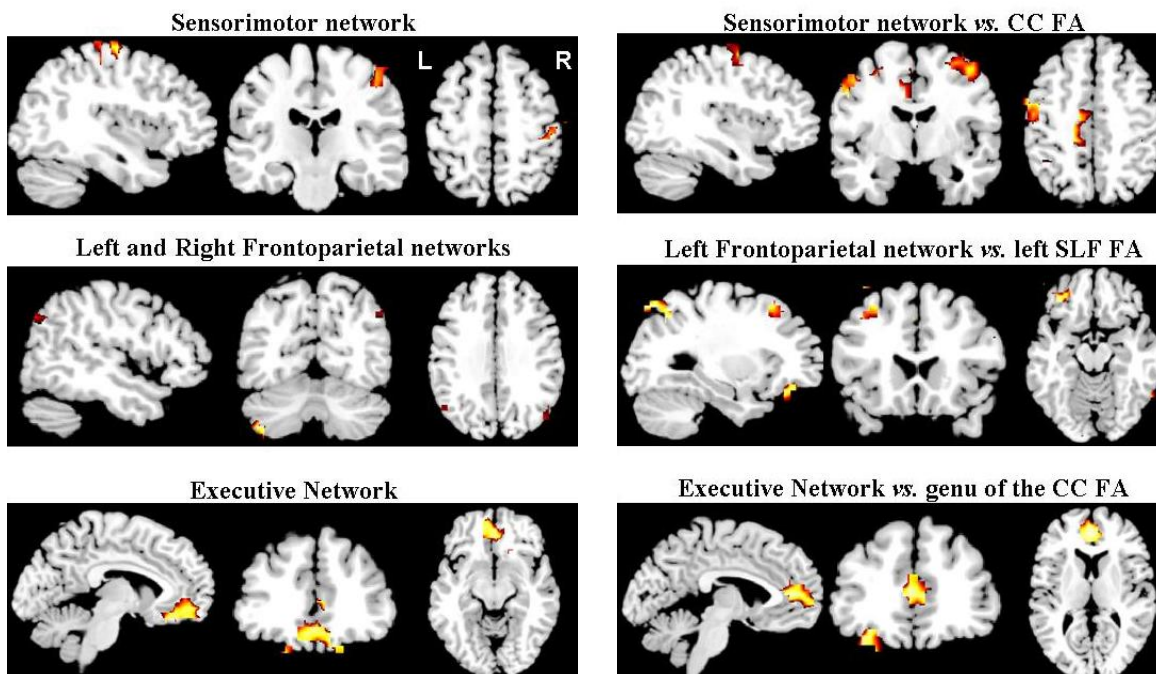


Figure 1. Increased connectivity in PLS patients compared with controls within the sensorimotor and extra-motor networks ($p < 0.05$ corrected FWE).

Figure 2. Relationship between RS connectivity and fractional anisotropy (FA) of the corpus callosum (CC) and the left superior longitudinal fasciculus (SLF) in PLS patients ($p < 0.05$ uncorrected).

Conclusion. Cerebral network breakdown in PLS is characterized by functional connectivity increases. The observation that PLS patients with more severe disability, cognitive impairment and WM damage had the greatest sensorimotor and fronto-parietal functional connectivity lends support to a pathogenic loss of local inhibitory circuitry, rather than only compensatory recruitment.