Altered cortical activation in ALS differs in motor and extra-motor regions

B. R. Stanton[1], A. Simmons[1], V. Williams[1], C. Blain[1], P. N. Leigh[1]
[1]MRC Centre for Neurodegeneration Research, Institute of Psychiatry, King's College London, London, United Kingdom

Background

Amyotrophic Lateral Sclerosis (ALS) is a devastating neurodegenerative disorder, which principally targets the motor system. PET and functional MRI (fMRI) studies in ALS have demonstrated increased cortical activation extending outside the primary sensorimotor cortex during motor tasks[1-3]. However, failure to control for weakness has hampered the interpretation of these findings since increased activation in ALS may simply be an artefact of task difficulty[3]. We tested the hypothesis that patients with ALS show more extensive cortical activation during a motor task when compared to both healthy controls and patients with muscle weakness due to lower motor neurone (LMN) syndromes.

Methods

Data were acquired using a 1.5T GE NV/*i* MR system and a conventional transmit and receive birdcage head coil. 100 near axial T2* weighted images were acquired using a gradient echo EPI pulse sequence over a period of 5 minutes (TR =3s, TE=40ms, 20 slices, 5mm thickness/0.5mm slice gap, 24cm field of view, 64x64 matrix). A block design activation paradigm was used contrasting blocks of 30s of right hand movements against 30s of rest in sixteen patients with ALS, seventeen healthy controls and nine patients with LMN disorders. The groups were matched for age and gender and the two patient groups were matched for their degree of upper limb weakness. After correction for head movement and transformation to the space of Talairach and Tournoux statistical analysis used a non-parametric approach[4] to perform a 3 way hypothesis-driven comparison between the groups.

Results

During the motor task, patients with ALS showed increased cortical activation bilaterally, extending from the sensorimotor cortex (Brodmann Areas (BA) 1, 2, 4) posteriorly into the inferior parietal lobule (area 40) and inferiorly to the superior temporal gyrus (BA 22) when compared to LMN patients and controls (Figure 1). In addition, ALS patients showed reduced activation in the dorsolateral pre-frontal cortex (DLPFC) extending to anterior and medial frontal cortex (BA 8, 9, 10, 32) compared to both LMN patients and controls (Figure 2).

Figure 1: Map of increased cortical activation in ALS patients compared to controls and LMN patients

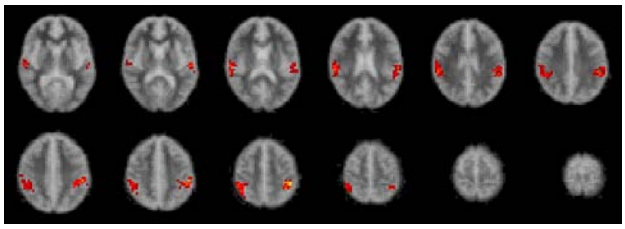
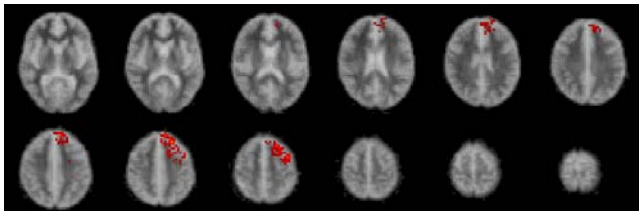


Figure 2: Map of decreased cortical activation in ALS patients compared to controls and LMN patients



Discussion

Patients with ALS show an altered pattern of cortical activation during motor tasks compared to both healthy controls and patients with lower motor neurone syndromes. Importantly, we have shown that these changes are not simply an artefact of weakness or task difficulty, but relate specifically to upper motor neurone pathology in ALS. Increased activation around motor areas may result from cortical plasticity in response to selective neuronal loss. Alternatively, it may be explained by the loss of intrinsic inhibitory neurones[5] which may contribute to excitotoxicity in this disease. In contrast, activity in the DLPFC related to the free selection component of this task is reduced in ALS patients (as in previous studies[6]) despite the similar pattern of cell loss in this area. We conclude that alterations in cortical function in ALS are complex and differ in sensorimotor and pre-frontal regions.

References

1. Kew JJ et al. Cortical function in amyotrophic lateral sclerosis. A positron emission tomography study. *Brain* 1993;116 (Pt 3):655-80.
2. Kew JJ et al. Cortical function in progressive lower motor neuron disorders and amyotrophic lateral sclerosis: a comparative PET study. *Neurology* 1994;44:1101-10.
3. Schoenfeld MA et al. Functional motor compensation in amyotrophic lateral sclerosis. *J.Neurol.* 2005.
4. Brammer MJ et al. Generic brain activation mapping in functional magnetic resonance imaging: a nonparametric approach. *Magn Reson.Imaging* 1997;15:763-70.
5. Maekawa S et al. Cortical selective vulnerability in motor neuron disease: a morphometric study. *Brain* 2004;127:1237-51.
6. Abrahams S et al. Word retrieval in amyotrophic lateral sclerosis: a functional magnetic resonance imaging study. *Brain* 2004;127:1507-17.ljklkjljlkjlj