A Functional MRI Study of Social Cognition in Amyotrophic Lateral Sclerosis

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INTRODUCTION

Varying degrees of frontal lobe dysfunction are present in patients with ALS1,2. About 49% of patients with sporadic ALS1, and 62% of patients with familial ALS2 (in review), present with cognitive changes that may only be apparent via neuropsychological testing. Dysfunction ranges from mild to frank frontotemporal dementia (FTD). Apathy, executive dysfunction and disinhibition are behavioral changes reported by family members in approximately 29% of ALS patients (unpublished data).

Neuropathological and imaging studies have shown fronto-temporal atrophy and changes reported by family members in approximately 29% of ALS patients (unpublished data).

Frontal involvement might cause the changes in social cognition described in ALS patients, or this may be due to alterations in other brain regions involved in social cognition. To investigate this further, we administered a test of social behavior called the “trust game” to pairs of ALS patients and controls (people without ALS). They interacted while undergoing simultaneous functional magnetic resonance imaging (fMRI).

Prior studies with the trust game have shown activation of the middle cingulate gyrus in controls playing as investors and activation of the anterior cingulate gyrus in controls playing as trustees3. We tested whether the same areas are activated in patients with ALS and whether controls behave similarly when playing with a physically challenged person.

RESULTS

Regional Blood oxygenation level–dependent (BOLD) response patterns were analyzed to identify activation of different brain areas

Fig. 1 Trust game3

Fig. 2. Behavior: Average Investments and Repayments. The control experiment (in blue) and the ALS experiment (in red) show that ALS pts and controls return, on average, a similar percentage of earnings. However, their pattern of return, round-to-round, differs (Fig 3).

Additional Results

- The ALS trustees from Fig. 2 were separated into cognitively intact (n=12) and cognitively impaired (n=4) groups. Investment returns were the same for the 2 groups.
- 16 pairs was not enough to determine whether there is a difference in the caudate or cingulate gyrus activation in controls vs ALS patients. We estimate that about 14 more pairs will need to be tested before a difference might be demonstrated.

CONCLUSIONS

While the ALS trustees had a similar average return to the Control trustees (Fig. 2), they respond to their partners behaviors differently than Controls (Fig. 3).

- ALS patients actively penalize investors when trust would be expected.
- The better the score on a neuropsychological measure of attention, the VSAT, the higher the activity in the parahippocampal gyrus (PPA, parahippocampal place area) and performance on a measure of attention and concentration (VSAT) when the investment was revealed to the Trustee.

Fig. 3  Behavior: Round-to-round differences. ALS trustees do not show a typical reciprocity response to control investments over the previous 2 rounds (<0.31 vs -0.03, bold= significant). Control investment also differed significantly: their behavior is more positively correlated with the ALS trustee responses than observed between controls (0.65 vs 0.45).

Table 1. Demographics

<table>
<thead>
<tr>
<th></th>
<th>ALS</th>
<th>Controls</th>
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<tbody>
<tr>
<td>Male gender (%)</td>
<td>75</td>
<td>75</td>
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<tr>
<td>Age (years)</td>
<td>46.62</td>
<td>44.75</td>
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<tr>
<td>No cognitive impairment (%)</td>
<td>68.75</td>
<td>100</td>
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</tbody>
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Table 1. Demographics

REFERENCES