Regional Average Brain Cortical Thickness and Cognitive Exams in ALS

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Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease that generally destroys the motor neurons responsible for voluntary muscle control. An increasing body of evidence supports the theory that ALS is not simply a motor neuron disease, but a more widespread neurodegenerative disorder [1-3]. Recently, we studied the relationship between verbal associative fluency, verbal abstract reasoning, and judgment in ALS using a 20-minute screening evaluation. Deficiencies in these measures were found in a large percentage of patients with both limb-onset and bulbar-onset ALS [4]. In this study we measured average thickness in cortical brain regions and correlated these measurements to a modification of this cognitive screen sensitive to the three recognized frontotemporal dementia (FTD) syndromes. It was hypothesized that a deficient score on measures of frontal and temporal dysfunction would show a negative correlation with thickness; that is, a direct association with cortical thinning.

Methods

Twelve ALS subjects (8 male and 4 female, average age 51.1 years) received a whole brain T1-weighted MDEFT (TE=3.14ms, TR=10.55ms, TI=680ms, SENSE factor=2, 20° flip angle) scan on a Philips Intera 3.0 T system with isotropic 1mm voxel size. Mean symptom duration for ALS subjects was 39 months (range: 15 – 76). Images were segmented into gray matter (GM), white matter (WM), and cerebrospinal fluid (CSF) using SPM5 [5]. GM thickness was calculated from the segmented GM images using a novel method based on the Euclidian distance filter developed at our institution [6]. Automatic whole brain labeling was performed using HAMMER [7, 8]. Subjects were administered the Penn State Screen Exam of Frontal and Temporal Dysfunction Syndromes (PSSFTS), a refinement of our recently published screen of frontal dysfunction [4]. Multiple regression analysis of average thickness and age to cognitive exam scores was performed in Excel for select brain regions that included the lateral orbital frontal gyrus, medial frontal gyrus, inferior frontal gyrus, precentral gyrus, superior temporal gyrus, medial temporal gyrus, inferior temporal gyrus, superior occipital gyrus, superior parietal lobule, angular gyrus, middle occipital gyrus, inferior occipital gyrus, and lateral occipitotemporal gyrus.

Table 1. Cortical Thinning in Association with PSSFTS Subtest Deficiencies in an ALS Sample

PPSFTS Subtest	ROI				
	LITG	LMTG	RSPL	RIOG	RMOG
CF (N=5)	**p=.029**	p=.088			
COGNISTAT					
CONST (N=10)				**p=.055**	
VisM (N=9)		p=.106	p=.090		p=.107

PSSFTS=Penn State Screen of Frontal and Temporal Dysfunction Syndromes, CF=category fluency, COGNISTAT=Neurobehavioral Cognitive Status Examination, CONST=2-D constructions, VisM=visual memory, LITG=left inferior temporal gyrus, LMTG=left middle temporal gyrus, LIOG=left inferior occipital gyrus, RIOG=right inferior occipital gyrus, RMOG=right middle occipital gyrus, RSOG=right superior occipital gyrus, RSPL=right superior parietal lobule.

Results

Cognitive deficiencies in association with cortical thinning are depicted in Table 1.

Discussion

Consistent with recent imaging literature [9, 10], evaluation of the association between cognitive deficiencies in ALS and cortical thinning evidenced significant relationships for temporal and occipital cortical mediated capacities. Category fluency demonstrated a statistically significant association with the left inferior temporal region, approaching significance for association with the left medial temporal region. The COGNISTAT subtest of 2-D constructions approached significance for association with the right inferior occipital region. Trends were further evident for a drawing task of visual memory in association with the left medial temporal, right inferior occipital, and right medial occipital regions (Table 1). The latter is consistent with the recent work of Jeannerod and co-workers [10].

To date, no known study has attempted to examine the relationships between a clinically practical cognitive screen in ALS, brief while sensitive enough to identify FTD sub-types, and quantitative imaging data. This study provides pilot data upon which to base larger studies that will validate the PSSFTS as a diagnostic tool for use in ALS Multidisciplinary Outpatient Clinics. Brain imaging validation of this screen exam of FTD sub-types will contribute to the success of approaches to facilitate ALS-FTD patient decision making during discussions of treatment planning and end-of-life issues.

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