Confrontation Naming and Morphometric Analyses of Structural MRI in Frontotemporal Dementia

Corey McMillana James Geeb Peachie Moorea Kari Dennisa Chris DeVitaa Murray Grossmana
Departments of aNeurology and bRadiology, University of Pennsylvania, Philadelphia, Pa., USA

Abstract
We studied the neural basis for confrontation naming difficulty in 29 patients with frontotemporal dementia (FTD) by correlating naming with voxel-based morphometric analyses of gray matter volume in structural MRI. We found that naming is significantly impaired in FTD, including patients with semantic dementia (SD), progressive nonfluent aphasia (PNFA), and nonaphasic patients (NON-APH) with a disorder of social and executive functioning. Significant cortical atrophy was found in the left anterior temporal cortex in all three FTD subgroups relative to healthy seniors. We also found significant cortical atrophy in unique anatomic distributions in each FTD subgroup. This included: lateral, ventral, and parahippocampal regions of the left temporal lobe in SD; inferior, orbital, dorsolateral, and premotor regions of the left frontal lobe in PNFA, and bilateral frontal regions in NON-APH. Direct correlations between confrontation naming and gray matter volume revealed distinct patterns in each FTD subgroup. SD patients showed a significant correlation in the left lateral temporal cortex, PNFA patients in several left frontal regions, and NON-APH patients in the right dorsolateral prefrontal cortex. These findings suggest that confrontation naming is supported by a large-scale neural network, and that naming is compromised in FTD due to interruption of the network in several different ways.

Introduction
Naming difficulty is common in frontotemporal dementia (FTD). Behavioral studies of naming in subgroups of patients with FTD have reported quantitative differences in naming accuracy, with semantic dementia (SD) patients being more impaired than patients with progressive nonfluent aphasia (PNFA) and non-aphasic FTD patients (NON-APH) with a disorder of social and executive functioning [1, 2]. Nevertheless, naming difficulty is present in PNFA and NON-APH subgroups as well [2, 3]. The cause of this impairment has proven elusive since failure to produce a word – the most common manifestation of naming difficulty – reveals little about the qualitative basis for impaired naming. Different patterns of cortical disease have been demonstrated in patients with SD [4–6], PNFA [7, 8], and NON-APH [9, 10]. We investigated whether confrontation naming difficulty in FTD is due in part to different impairments by direct correlations
of confrontation naming with voxel-based morphometric analyses of volumetric structural MRI in SD, PNFA, and NON-APH patients.

**Methods**

**Subjects**

We studied 29 right-handed patients with FTD. One subgroup included 7 SD patients with fluent, circumlocutory speech and frequent word-finding pauses [mean age = 65.5 years; mean education = 15.4 years; mean disease duration = 41.5 months; mean Mini-Mental State Examination (MMSE) score = 23.8]. Another subgroup included 8 PNFA patients with effortful speech that was dysarthric or contained grammatical errors (mean age = 68.8 years; mean education = 14.9 years; mean disease duration = 39.0 months; mean MMSE score = 21.9). The NON-APH subgroup (n = 14) presented with social and behavioral difficulties and a limitation of executive functioning (mean age = 63.1 years; mean education = 15.1 years; mean disease duration = 42.4 months; mean MMSE score = 18.0). The subgroups were matched for age [F(2, 26) = 0.52; n.s.], education [F(2, 26) = 0.10; n.s.], disease duration [F(2, 26) = 0.03; n.s.], and MMSE score [F(2, 26) = 2.40; n.s.]. Naming was assessed relative to 25 age- and education-matched healthy seniors. Cortical atrophy was assessed relative to 12 age-matched healthy seniors.

**Materials**

To assess visual confrontation naming, we used an abbreviated version of the Boston Naming Test [11]. Each subject was asked to name each test stimulus. All visual stimuli were black-and-white line drawings. There were 15 stimuli: 5 high-frequency, 5 mid-frequency and 5 low-frequency items. Patients were given as much time as they needed to respond.

**Imaging Procedure**

All images were acquired by a GE Horizon Echospeed 1.5-tesla MRI scanner (GE Medical Systems, Milwaukee, Wisc., USA). Each study began with a rapid sagittal T1-weighted 3-dimensional spoiled gradient echo images were acquired with a repetition time of 35 ms, an echo time of 6 ms, a slice thickness of 0.9 mm. Normalization of naming difficulty and cortical volume that corresponded to areas of gray matter atrophy are indicated by arrows in figure 1. This included: in SD, the lateral region of the left temporal lobe; in PNFA, anterior, orbital, insula, and dorsolateral regions of the left frontal lobe. Areas of cortical atrophy in NON-APH were also seen in anterior, inferior, orbital, insula, and dorsolateral regions of the left frontal lobe. Additional areas of cortical atrophy in SD (fig. 1A) were seen in anterior, posterolateral, ventral, and parahippocampal regions of the left temporal lobe. Cortical atrophy in PNFA (fig. 1B) also included inferior, orbital, insula, and dorsolateral regions of the left frontal lobe. Areas of cortical atrophy in NON-APH were also seen in anterior, dorsolateral, and insula regions of the right frontal lobe, the insula region of the left frontal lobe, and the left parahippocampal region.

**Results**

**Naming**

All three FTD subgroups were significantly impaired in their confrontation naming relative to the performance of healthy seniors at least at the p < 0.01 level, according to the z score distribution (SD: z score = –4.87; PNFA: z score = –3.67; NON-APH: z score = –3.55). Although FTD patient subgroups did not differ in their confrontation naming [F(2, 26) = 0.48; n.s.], the SD subgroup was most impaired.

**Imaging**

Significant cortical atrophy in subgroups of patients with FTD is illustrated in figure 1. All FTD patient subgroups showed significant cortical atrophy in the left anterior temporal cortex. Direct correlations of naming difficulty and cortical volume that corresponded to areas of gray matter atrophy are indicated by arrows in figure 1. This included: in SD, the lateral region of the left temporal lobe; in PNFA, inferior, orbital, dorsolateral, and premotor regions of the left frontal lobe, and in NON-APH, the right dorsolateral prefrontal cortex and left anterior temporal cortex.

**Discussion**

All three FTD subgroups had significant naming difficulty. They did not differ in the severity of their naming impairment, and one cortical region was significantly atrophic across all FTD subgroups. One possible account of naming difficulty in FTD consistent with these findings...
Fig. 1. Significant atrophy relative to healthy seniors in SD (A), PNFA (B), and NON-APH patients with a social and executive disorder (C) [1]. Arrows indicate clusters of significant cortical atrophy where there was also a significant correlation between confrontation naming difficulty and gray matter volume.

attributes impaired naming to a deficit in a single, crucial component of naming. Any differences between FTD subgroups, from this perspective, are attributable to differing extents of disease affecting the cortical region – left anterior or temporal cortex – that is responsible for this crucial process.

Several observations of this study are inconsistent with this hypothesis. First, cortical atrophy in SD extends beyond the left anterior temporal cortex to affect other left temporal brain regions. This is also evident in previously published studies of cortical atrophy in SD [4–6]. Moreover, we found significant cortical atrophy in other brain regions in PNFA and NON-APH patients who also had impaired naming. Finally, when we examined the neural basis for naming difficulty directly by correlating naming performance with gray matter volume, we found a distinct naming-volume correlation profile in each subgroup of FTD patients. This pattern of results is most consistent with the hypothesis that a large-scale neural network undererves naming. Despite the superficial appearance of a single pattern of impaired naming – failure to retrieve a word – this approach suggests that a large-scale naming network underlying naming may be interrupted in several different ways in subgroups of patients with FTD.

Acknowledgment

This work was supported in part by the US Public Health Service (AG17586, AG15116, and NS35867).
References