Brain and Cognition 72 (2010) 423–429

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Sound naming in neurodegenerative disease

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ARTICLE INFO

Article history:
Accepted 11 December 2009
Available online 20 January 2010

Keywords:
Corticobasal degeneration
Progressive supranuclear palsy
Motor disorder
Sound naming
Manipulability

ABSTRACT

Modern cognitive neuroscientific theories and empirical evidence suggest that brain structures involved in movement may be related to action-related semantic knowledge. To test this hypothesis, we examined the naming of environmental sounds in patients with corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP), two neurodegenerative diseases associated with cognitive and motor deficits. Subjects were presented with 56 environmental sounds: 28 sounds were of objects that required manipulation when producing the sound, and 28 sounds were of objects that required no manipulation. Subjects were asked to provide the name of the object that produced the sound and also complete a sound-picture matching condition. Subjects included 33 individuals from four groups: CBD/PSP, Alzheimer disease, frontotemporal dementia, and normal controls. We hypothesized that CBD/PSP patients would exhibit impaired naming performance compared with controls, but the impairment would be most apparent when naming sounds associated with actions. We also explored neural correlates of naming environmental sounds using voxel-based morphometry (VBM) of brain MRI. As expected, CBD/PSP patients scored lower on environmental sounds naming ($p < 0.007$) compared with the controls. In particular, the CBD/PSP patients scored the lowest when naming sounds of manipulable objects ($p < 0.05$), but did not show deficits in naming sounds of non-manipulable objects. VBM analysis across all groups showed that performance in naming sounds of manipulable objects correlated with atrophy in the left pre-motor region, extending from area six to the middle and superior frontal gyrus. These results indicate an association between impairment in the retrieval of action-related names and the motor system, and suggest that difficulty in naming manipulable sounds may be related to atrophy in the pre-motor cortex. Our results support the hypothesis that retrieval of action-related semantic knowledge involves motor regions in the brain.

1. Introduction

Corticobasal degeneration (CBD) and progressive supranuclear palsy (PSP) are two neurodegenerative diseases characterized by cognitive and motor symptoms. Patients with CBD often have deficits in executive function, visuospatial abilities, and language (Graham, Bak, Patterson, & Hodges, 2003). Motor symptoms of CBD can include apraxia, myoclonus, asymmetric extrapyramidal syndrome, cortical sensory loss, and alien limb phenomenon (Gorno-Tempini et al., 2006; Graham et al., 2003). Patients with PSP also exhibit motor deficits, including falls, loss of balance, axial rigidity, and bradykinesia, in addition to eye movement abnormalities (Rampello et al., 2005). Patients with PSP often exhibit cognitive impairments, including deficits in planning, monitoring and language (Krishnan, Mathuranath, Sarma, & Kishore, 2006). Damage to both cortical and subcortical structures, particularly the basal ganglia and frontal cortex, are hypothesized to contribute to motor and cognitive dysfunction in both CBD and PSP.

Recent pathological and genetic observations suggest overlap between CBD and PSP. Both disorders are adult-onset neurodegenerative disorders with tau neuropathology (Scaravilli, Tolosa, & Ferrer, 2005). However, the tau pathology occurs in slightly different brain regions in PSP and CBD: in PSP, the basal ganglia and brainstem are most affected, while neuropathology in CBD occurs in the prefrontal and pre-motor cortices with the caudate nucleus (Scaravilli et al., 2005). In addition, the extended tau 1 haplotype (H1) in the tau gene is overrepresented in CBD and PSP patients (Scaravilli et al., 2005). Despite neuropathological differences, it is hypothesized that PSP and CBD are separate phenotypes of one nosological disorder (Kertesz & Munoz, 2004; Scaravilli et al.,

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doi:10.1016/j.bandc.2009.12.003

2005). This possible overlap is still being debated, but these disorders provide an opportunity to study interactions between motor and cognitive systems.

As discussed above, changes in language function may occur in patients with CBD and PSP. However, relatively few studies of language function have been done, possibly due to the categorization of these disorders as primarily movement disorders. Patients with early-stage CBD often complain of difficulty finding words, effortful speech, and handwriting changes. Language comprehension of grammatically complex sentences is initially preserved but declines as CBD progresses. Clinically diagnosed cases of progressive non-fluent aphasia (PNFA), for example, are often associated with CBD and PSP pathology (Josephs et al., 2006). PNFA is characterized by effortful speech with relatively preserved comprehension, speech apraxia, anomia, phonemic paraphasias, and agrammatism (Neary et al., 1998). These language abnormalities in CBD are hypothesized to be due to frontal and parietal atrophy (Murray et al., 2007). In PSP, furthermore, general mental slowing and dysarthria contribute to difficulty with communication. Patients with PSP commonly have diminished fluency of speech and are impaired in confrontation naming of objects and describing pictures (Podoll, Schwarz, & Noth, 1991). More specifically, action naming and verb production are often impaired in patients with PSP and CBD (Bak et al., 2006; Cotelli et al., 2006; Daniele, Giustolisi, Silveri, Colosimo, & Gainotti, 1994). These studies suggest that the ability to name an object and the ability to physically manipulate an object are related (Cotelli et al., 2006). Thus, difficulty in naming action-related objects may reflect cortical and subcortical damage in CBD and PSP.

While the majority of these studies assess naming by asking patients to name pictures (Glaser, 1992), the ability to name sounds has not yet been examined in patients with CBD and PSP. The auditory system is another modality by which memory and language can be accessed. It is possible that visuospatial difficulties may influence performance on tests of visual object or picture naming. The perception of sound, in general, involves the ascending auditory system, including nuclei in the brainstem, midbrain, and thalamus (Recanzone & Sutter, 2008). Naming sounds also involves brain areas such as the left ventral infra-temporal region and the left frontal operculum (Tranel et al., 2003). Interestingly, one study of naming animal sounds found activation in the mesial occipital cortex, suggesting that the retrieval of conceptual knowledge depends on the production of 'internal' visual images (Tranel et al., 2003).

Different types of sounds may activate different brain areas. For example, sounds that evoke actions may activate different brain regions than sounds that do not evoke actions. They may evoke the image of action by activating visual areas such as the mesial occipital cortex (Tranel et al., 2003). The sound of a hammer pounding a nail, for example, may evoke the image of a person pounding a nail into a piece of wood with a hammer. Moreover, different parts of the auditory cortex respond to different categories of sounds. Human voices selectively activate the bilateral upper banks of the superior temporal sulcus using functional MRI methods (Belin, Zatorre, Lafaille, Ahad, & Pike, 2000). Tettamanti and colleagues (2005) found that when subjects listen to sentences describing actions involving the mouth, hand, or leg, areas of the pre-motor and motor cortex, including the inferior parietal lobule, intraparietal sulcus, and posterior middle temporal gyrus were activated in a functional MRI paradigm. This result suggests that semantic representation may be accessible by both visual and auditory pathways, and damage to different brain regions may differentially affect sound naming and identification.

Therefore, the purpose of this study was to examine naming of environmental sounds in patients with CBD and PSP. Specifically, we evaluated the effect of manipulability on sound naming. We hypothesized that patients with CBD/PSP would have deficits in naming sounds of objects but, in particular, naming sounds of manipulable objects because of the motor deficits. Finally, we explored the brain correlates of sound naming using voxel-based morphometry of brain MRI. We also included patients with Alzheimer disease (AD) and frontotemporal dementia (FTD) for comparison and also to provide anatomical variance for the MRI analysis.

2. Methods

2.1. Participants

All subjects were recruited from the University of California San Francisco's (UCSF) Memory and Aging Center and provided informed consent to participate in the procedures. Surrogates provided consent for patients with a dementia diagnosis. Clinical diagnosis was determined after a detailed clinical history, neurological examination, 1-h neuropsychological battery (Kramer et al., 2003), laboratory screening, and brain MRI (which was used to exclude patients with stroke, tumor, or other brain abnormalities). The neurologist also rated the presence or absence of oralbuccal and limb apraxia.

We included 33 subjects consisting of 10 controls and 23 patients with neurodegenerative diseases. Six of the patients were diagnosed with probable AD (McKhann et al., 1984) nine with FTD (Neary et al., 1998), and eight with CBD or PSP palsy (Litvan et al., 1996) (age range = 49–80 years; 12 males/11 females). Subjects were in the mild stage of dementia (operationally defined as a Mini-Mental State Examination score >19). Control subjects (age range = 57–73 years; 3 males/7 females) were recruited from the UCSF Alzheimer's Disease Research Center and underwent an evaluation identical to the patients. None of the controls showed evidence of impairment on neuropsychological testing or had a history of a neurological or psychiatric disorder.

Subjects were excluded if they had a current psychiatric disorder, hearing aids or significant clinical hearing impairment, head trauma with loss of consciousness greater than 10 min, substance abuse, or an additional neurological disease apart from the diagnosis of interest.

2.2. Neuropsychological battery

Subjects were administered a 1-h screening neuropsychological battery that measures multiple domains of cognition (Kramer et al., 2003). Memory was evaluated using the 10-min delayed recall trial of the California Verbal Learning Test-Mental Status (CVLT-MS) (Delis, Kramer, Kaplan, & Ober, 2000) and 10-min recall of the modified Rey-Osterrieth figure. The longest correct backward digit span was used as a measure of working memory. Executive function was assessed using modified versions of Trailmaking B, the interference trial from the Stroop task, and abstractions (i.e., providing interpretations of similar items and proverbs). Measures of verbal fluency included letter fluency (number of D words in 1 min) and animals (number in 1 min). Language was assessed using a 15-item Boston Naming Test (Kaplan, Goodglass, & Wintraub, 1983), 16 items from the Peabody Picture Vocabulary Test – Revised (Dunn & Dunn, 1981), and sentence comprehension subtest from the Curtiss-Yamade Comprehensive Language Evaluation-Receptive (CYCLE-R) (Curitss & J., 1988). The copy trial of the modified Rey-Osterrieth figure (Kramer et al., 2003) and the number location condition from the Visual Object Spatial Perception battery (VOSP) (Warrington & James, 1991) were used to assess visuospatial abilities.