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Diffusion tensor MRI contributes to differentiate Richardson's syndrome from PSP-parkinsonism

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Abstract

This study investigated the regional distribution of white matter (WM) damage in Richardson's syndrome (PSP-RS) and progressive supranuclear palsy-Parkinsonism (PSP-P) using diffusion tensor (DT) magnetic resonance imaging (MRI). The DT MRI classificatory ability in diagnosing progressive supranuclear palsy (PSP) syndromes, when used in combination with infratentorial volumetry, was also quantified. In 37 PSP (21 PSP-RS, 16 PSP-P) and 42 controls, the program Tract-Based Spatial Statistics (TBSS; www.fmrib.ox.ac.uk/fsl/tbss) was applied. DT MRI metrics were derived from supratentorial, thalamic, and infratentorial tracts. The magnetic resonance parkinsonism index (MRPI) was calculated. All PSP harbored diffusivity abnormalities in the corpus callosum, frontoparietal, and frontotemporo-occipital tracts. Infratentorial WM and thalamic radiations were severely affected in PSP-RS and relatively spared in PSP-P. When MRPI and DT MRI measures were combined, the discriminatory power increased for each comparison. Distinct patterns of WM alterations occur in PSP-RS and PSP-P. Adding DT MRI measures to MRPI improves the diagnostic accuracy in differentiating each PSP syndrome from healthy individuals and each other.

Keywords: Richardson's syndrome; PSP-Parkinsonism; Diffusion tensor MRI; Atrophy

1. Introduction

Progressive supranuclear palsy (PSP) is an atypical parkinsonian disease with onset in the middle sixties, characterized by tau protein deposition, neuronal loss, and gliosis affecting the brainstem, subcortical, and cortical structures (Hauw et al., 1994). Two population-based prevalence studies conducted in the UK and a general population-based survey in Olmsted County, Minnesota, estimated a prevalence of 6.0–6.4 per 100,000 for PSP (Bower et al., 1997; Nath et al., 2001; Schrag et al., 1999). Its incidence increases with age, from 1.7 cases per 100,000 per year at 50–59 years to 14.7 per 100,000 per year at 80–99 years (Bower et al., 1997, 1999).

PSP can occur with 2 main clinical presentations (Williams et al., 2005). Over 50% of cases show early onset postural instability and falls, supranuclear vertical gaze palsy, cognitive dysfunction, and are classified as Richardson's syndrome (PSP-RS) (Williams et al., 2005). Another 20%–35% of cases are classified as PSP-parkinsonism (PSP-P), which is characterized by asymmetrical onset,

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tremor, rigidity, moderate initial response to levodopa (L-dopa), a later age at onset, and a more favorable disease course compared with PSP-RS (Williams et al., 2005). In PSP-P cases, the distinction from Parkinson's disease (PD) may be impossible early in the disease (Williams and Lees, 2010; Williams et al., 2005). However, late drug-induced dyskinesias, late autonomic dysfunction, and any visual hallucinations have been found to be very uncommon in PSP-P and may help to distinguish PSP-P from PD later in the course of the disease (Williams and Lees, 2010; Williams et al., 2005). Clinicopathological studies showed that tau deposition (Jellinger, 2008; Morris et al., 2002; Williams et al., 2007a) as well as gray matter (GM) and white matter (WM) atrophy (Schofield et al., 2011) are significantly more widespread and severe in PSP-RS than in PSP-P cases.

The conventional magnetic resonance (MR) parkinsonism index (MRPI), which combines measurements of midbrain and pons areas as well as superior (SCP) and middle (MCP) cerebellar peduncle widths, has been proven to be an accurate measure to contribute to the differential diagnosis between PSP-RS and PD or the Parkinson variant of multiple system atrophy (MSA) (Quattrone et al., 2008). Volumetric magnetic resonance imaging (MRI) can also be useful in distinguishing PSP subtypes (Agosta et al., 2010; Longoni et al., 2011). PSP-RS was found to be associated with a greater brain atrophy compared with PSP-P, which was more severe in the SCP (Agosta et al., 2010; Longoni et al., 2011), cerebral peduncles, and along the corticospinal tracts (CST) (Agosta et al., 2010). WM tract degeneration is, therefore, likely to be a major contributor to the different clinical presentations of PSP.

Diffusion MRI measures the effect of tissue microstructure on the random translational motion of water molecules in biological tissues (Basser and Pierpaoli, 1996). A full characterization of diffusion can be provided by diffusion tensor (DT)-based methods. Providing image contrast that is not available with routine MR techniques and unique information on WM integrity, DT MRI has the potential to reveal injury that may not be apparent with other MR modalities (Basser and Pierpaoli, 1996). Abnormal DT MRI measures of the SCP were reported in PSP-RS patients (Seppi and Poewe, 2010). A few studies showed that PSP-RS patients had DT MRI alterations also in the corpus callosum, internal capsulae, and long-range WM tracts (Canu et al., 2011; Knake et al., 2010; Nilsson et al., 2007; Padovani et al., 2006; Wang et al., 2011; Whitwell et al., 2011). However, most of the DT MRI studies conducted until now did not include the atypical clinical presentations of PSP.

In this study, we wished to use DT MRI to investigate in vivo similarities and differences of the regional distribution of WM tract damage in PSP-RS and PSP-P, compare these results with the corresponding patterns of brain atrophy, and quantify the ability of DT MRI in differentiating PSP syndromes at an individual level, when used in combination with the MRPI. We hypothesized that there may be more severe and widespread microstructural abnormalities in PSP-RS, particularly involving the cerebellar peduncles and frontal brain regions. We also predicted that adding DT MRI variables to brainstem volumetric measures would improve the diagnostic accuracy in differentiating each PSP syndrome from healthy elderly individuals and each other.

2. Methods

2.1. Subjects

Eligible subjects were identified by searching the database at the Clinic of Neurology, University of Belgrade, Serbia, for patients seen between January 1999 and September 2010, meeting criteria for probable or possible PSP at the time of the last visit (Litvan et al., 1996). In order not to exclude PSP-P patients from the selection, the criterion "in the first year of the disease" (Litvan et al., 1996) was not applied, as previously described (Agosta et al., 2010; Longoni et al., 2011). To be included, patients had to have available clinical case files for at least 2 years from disease onset, no PD (Gibb and Lees, 1988), multiple system atrophy (Gilman et al., 1999), corticobasal syndrome (Boeve et al., 2003), or pure akinesia with gait freezing (Williams et al., 2007b) diagnoses, no other neurological, psychiatric, major medical conditions, or history of substance abuse, and no other causes of brain damage, including lacunae, and extensive cerebrovascular disorders on routine MRI scans.

At study entry, eligible patients were clinically evaluated to confirm the diagnosis. The Unified Parkinson's Disease Rating Scale (UPDRS) (Fahn and Elton, 1987), Hoehn and Yahr score (Hoehn and Yahr, 1967), Mini Mental State Examination (MMSE) (Folstein et al., 1975), Hamilton Anxiety (HARS) (Hamilton, 1959), and Depression (HDRS) (Hamilton, 1960) Rating Scales, and Apathy Evaluation Scale (AES) (Marin et al., 1991) were administered. Then, all case files of each patient were reviewed independently by 2 experienced neurologists, who were blinded to MRI results, to classify patients as PSP-RS or PSP-P based on clinical criteria (Williams et al., 2005) and recent recommendations (Williams and Lees, 2010) (Supplementary Appendix 1). The patients were included in the study only if the 2 neurologists came to the same diagnosis (concordance rate: 89.6%).

Forty PSP patients were considered eligible and performed MRI, but 3 subjects were excluded from the analysis because of motion artifacts in the MRI scans. Therefore, 37 PSP patients were included (11 women, 26 men; mean age, 66 years; range: 53–83 years). There were 21 PSP-RS (all probable PSP) and 16 PSP-P patients (14 probable, 2 possible PSP) (Table 1). Early and late clinical features of patient groups are presented in Supplementary Table 1. In the PSP-P group, initial diagnoses were idiopathic PD (4 patients), "parkinsonism" (10 patients), and "atypical parkinsonism" (2 patients). The diagnosis of "parkinsonism/