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Cognitive correlates of hallucinations and delusions in Parkinson's disease

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ABSTRACT

Background: Hallucinations and delusions that complicate Parkinson's disease (PD) could lead to nursing home placement and are linked to increased mortality. Cognitive impairments are typically associated with the presence of hallucinations but there are no data regarding whether such a relationship exists with delusions.
Objective: We hypothesized that hallucinations would be associated with executive and visuospatial disturbance. An exploratory examination of cognitive correlates of delusions was also completed to address the question of whether they differ from hallucinations.
Methods: 144 PD subjects completed a neuropsychological battery to assess cognition and the SAPS to examine psychosis. Correlational analyses assessed associations between hallucinations and delusions with cognitive domains.
Results: 48 subjects (33%) reported psychotic symptoms: 25 (17%) experienced hallucinations without delusions, 23 (16%) had symptoms dominated by delusions. Severity and/or number of hallucination subtypes were significantly correlated with lower scores in language, memory, attention, executive functioning, and visuospatial ability. Correlations with delusions were non-significant. Tests of differences in the size of the correlations between groups revealed a significant relationship between language and visuospatial performance with hallucinations.
Conclusions: Cognitive correlates of hallucinations and delusions appear to be different in PD, suggesting distinct pathogenic mechanisms and possibly anatomical substrates. Hence, delusions may not share the same associations with dementia as hallucinations. Since this is a new finding, further studies will be needed to confirm our results.

1. Introduction

Hallucinations and delusions are potentially serious, often chronic, psychiatric complications of Parkinson's disease (PD) that can impact quality of life, lead to nursing home placement and are risk factors for increased mortality [1–3]. Hallucinations are defined as sensory phenomena that are not induced by physical stimuli, whereas delusions are defined as irrational beliefs [3]. Both symptom complexes are usually considered and measured together and are generally thought to progress through a process that starts with mild hallucinations and leads to more severe hallucinations without insight and paranoid delusions [4].

Psychotic symptoms overall have been reported to occur in approximately 60% of PD patients in longitudinal cohorts [5]. Hallucinations appear to occur earlier in the course of disease with a prevalence of about 10% in patients within the first five years [6]. Stereotyped and repetitive visual hallucinations including seeing people, furry animals and insects are the most common type of psychotic symptoms in PD [7]. Auditory hallucinations are less common and may include the indistinct sounds of background voices or music [8]. The presence of hallucinations is thought to be a prodrome or co-morbidity to the development of dementia [9]. Paranoid delusions are more serious than hallucinations in that they are more likely to lead to hospitalization and self-injury and occur in an estimated 5% of PD patients, with the most common symptoms reported as jealousy [3,7]. Despite the notion that hallucinations and delusions are interconnected, delusions have been reported to occur in isolation [10].

A recent study conducted at our Center involving 500 PD subjects indicated that global cognitive dysfunction is associated with the presence of psychotic symptoms in general [11]. However, the measures included brief screening tools: psychosis was assessed by item 2 in the mental section (part 1) of the Unified Parkinson's Disease Rating Scale (UPDRS), and cognitive status was determined by the Mini-Mental State Examination (MMSE). The purpose of the current study was to examine this relationship more closely by using in depth measures of each

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symptom complex including a full neuropsychological battery for cognition and the Schedule for Assessment of Positive Symptoms (SAPS). This approach allowed us to examine the clinical profile of different hallucinations and delusions and their association with specific cognitive domains in a representative cohort of PD subjects. We hypothesized that hallucinations and delusions may be independent since they can occur separately and would differ in relation to cognitive correlates. More specifically, we hypothesized that hallucinations would be related to executive dysfunction and visuospatial disturbance as reported in prior smaller studies [12,13]. Since no published data have examined cognitive correlates specifically for delusions in PD our examination of subjects with this phenomenon was exploratory.

2. Methods

2.1. Subjects

This study was approved by the Emory University Institutional Review Board. All participating subjects signed an IRB approved consent document. Recruitment started February 9, 2009 and ended September 14, 2010. The subjects were recruited consecutively from the practices of two neurologists (SAF and AF) in the Emory University Movement Disorder Center to avoid bias and the target was 150 subjects. The study visit was separate from the routine clinic visit. All enrolled met standard clinical diagnostic criteria for PD (modified UK brain bank criteria [14]). Subjects were enrolled regardless of age at disease onset, family history of PD, or treatment status (treated or not, with any combination of antiparkinsonian medications). Exclusion criteria included late stage dementia where subjects were unable, due to their cognitive deficits, to perform instrumental activities of daily living as assessed in a clinic interview, history of cerebrovascular disease, findings suggestive of atypical parkinsonism (extraocular movement abnormalities, pyramidal tract signs, ataxia, early dementia), past neuroleptic use prior to PD onset, and past history of multiple head injuries. There were no other clinical selection criteria.

2.2. Assessments

2.2.1. Psychotic symptoms

Subjects underwent a Structured Clinical Interview for DSM-IV-TR (SCID) by a psychiatrist to assess past and present psychiatric diagnoses. The diagnosis followed previously established criteria for psychosis in PD [2]. Subjects, and wherever possible, their spouses or caregivers, were administered the SAPS by a trained psychometrist as the primary measure of psychotic symptoms [15]. SAPS was initially developed to measure symptoms of schizophrenia, but has since been utilized as a means of identifying psychotic symptoms in PD [16]. It is a recommended scale by the Movement Disorder Society, consists of a structured set of questions, does not require specialized training to administer, and has good (>0.80) interrater reliability [17]. We chose this scale because we were planning to examine non- or mildly demented subjects and it gave us the opportunity to assess hallucinations and delusions separately as well as their various subtypes and to examine their cognitive correlates. The hallucination subscale assesses six subtypes (auditory, voices commenting, voices conversing, somatic or tactile, olfactory, and visual), and the delusion subscale evaluates 12 subtypes (persecutory, jealousy, sin or guilt, grandiose, religious, somatic, ideas of reference, being controlled, mind reading, thought broadcasting, thought insertion, and thought withdrawal). Each subtype is rated on a scale ranging from 0 (absent) to 5 (severe). In addition, a Global Rating of Severity (ranging from 0 to 5) provides an overall score for the entire domain.

2.2.2. Cognitive functioning

A comprehensive battery of neuropsychological measures [18] was administered by a trained psychometrist, under the supervision of a neuropsychologist (A.B.S., J.O.L.) in the on state. The MMSE was used to assess global cognitive status [19]. Attention was evaluated by the maximum number of correct trials for digits forward and the number of seconds needed to sequence numbers using a pencil (Trailmaking A). Language was examined via the 60-item version of the Boston Naming Test and timed phonemic fluency. The evaluation of memory included verbal episodic memory (delayed story recall and delayed recall of words), visual episodic memory (delayed recall of designs), and semantic memory (timed generation of animal names in 60 s). Visuospatial skills were assessed using a motor free, untimed measure requiring judgment of the angular orientation of lines. Finally, executive functioning was measured via set shifting tasks involving mental manipulation of digits and timed alternation of numbers/letters and symbols (Trailmaking B and Digit Symbol) as well as the ability to inhibit a prepotent response [Stroop Color-Word] and to generate hypotheses [Wisconsin Card Sorting Test].

2.2.3. Motor function

Each patient underwent a UPDRS part 3 motor examination in the "on" state completed by one investigator (S.A.F.).

2.3. Statistical analyses

To reduce the likelihood of Type I errors, the individual tests comprising the domains of attention, language, memory, and executive functioning were each converted to z scores based on the performance of the entire group. The z scores were then averaged to form a composite score reflecting performance on each domain. Analyses of variance (ANOVA) and Fisher exact tests were conducted to evaluate group differences in demographic and clinical features and cognitive performance. Spearman Rank-Order correlations were performed to analyze relationships between the current total number of different subtypes of hallucinations (1–6) and their global severity (0–5) with each cognitive domain score for patients who experienced isolated hallucinations without delusions. These analyses were performed as well for the total number of different subtypes of delusions (1–12) as well as a rating of their overall global severity (0–5) with each cognitive domain score for patients with delusions. Delusions were dominant in this group, and we included those with or without co-existing hallucinations. Fisher R to Z transformation tests were run to contrast the size of the correlations between the hallucinations and delusions groups.

3. Results

3.1. Frequency and types of hallucinations and delusions

Complete data were available for 144 of 152 (95%) enrolled subjects regarding the presence and severity of hallucinations and delusions, information about the use of PD medications that could impact psychosis (included use of the drugs but dosage data were not available), motor assessment and performance on the full battery of neuropsychological measures. These subjects are the focus of this analysis.

Psychotic symptoms were present in 48 (33%) of the subjects. Of these, 25 (52%) subjects experienced hallucinations without delusions, 11 (23%) had delusions without hallucinations, and twelve (25%) experienced both. None of the subjects had a history of prior schizophrenia or other psychotic disorders. Table 1 shows demographic and clinical features of three subgroups: those with no psychotic symptoms, those with hallucinations without delusions and those where delusions dominated with and without hallucinations. There were no significant differences among the groups in age, education, and distribution of gender and past history of depression, or in disease duration, age of onset, and UPDRS motor score. A greater proportion of subjects in the hallucinations only group was taking medications that could potentially cause psychosis (levodopa, dopamine agonists, amantadine, monoamine oxidase inhibitors) compared to the no psychosis group ($p < .01$), and there was a trend as well for the delusion group relative to the no