Behavioural Brain Research 279 (2015) 226–233

Contents lists available at ScienceDirect

Behavioural Brain Research

journal homepage: www.elsevier.com/locate/bbr

Research report

Theory of mind and decision-making processes are impaired in Parkinson's disease

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HIGHLIGHTS

- PD patients were impaired on the affective ToM and decision making.
- The ability of affective ToM was affected by the severity of the disease.
- The affective ToM and IGT may share similar neural mechanisms.
- Memory impairment in PD could affect GDT selection strategy.

ARTICLE INFO

Article history:
Received 30 July 2014
Received in revised form
16 November 2014
Accepted 20 November 2014
Available online 28 November 2014

Keywords:
Parkinson's disease
Cognition
Theory of mind
Decision making

ABSTRACT

Prefrontal cortex plays a vital role in the theory of mind (ToM) and decision making, as shown in functional brain imaging and lesion studies. Considering the primary neuropathology of Parkinson's disease (PD) involving the frontal lobe system, patients with PD are expected to exhibit deficits in ToM and social decision making. The aim of this study was to investigate affective ToM and decision making in patients with PD and healthy controls (HC) in a task assessing affective ToM (Reading the Mind in the Eyes, RME) and two decision-making tasks (Iowa Gambling Task, IGT; Game of Dice Task, GDT). Consistent with previous findings, patients with PD were impaired in the affective ToM task, and when making decisions under ambiguity and in risk situations. The score of emotion recognition in the RME task was negatively correlated with the severity of the disease and positively correlated with the total number of advantageous cards chosen in the IGT. However, the final capital in the GDT was correlated with memory impairment. The present study implies that affective ToM and decision making under ambiguity may share similar neural mechanisms, while decision making under ambiguity and decision making under risk may involve processing within different neural networks.

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder pathologically characterized by the selective loss of dopaminergic neurons in the substantia nigra. Clinical manifestations include resting tremors, rigidity, bradykinesia, and postural instability. Besides motor impairment, dopamine depletion can also affect cognitive and social behavior [1]. Cognitive impairment is one of the most common and important non-motor aspects of PD and greatly affects functioning and quality of life [2]. Most patients with PD will eventually develop impairment not only of cognitive domains such as attention [3] or executive function [4,5] but also of memory [6] and visuospatial functions [5]. Moreover, it has been suggested that "theory of mind" (ToM) [7], a concept within social cognitive neuroscience that refers to the ability to attribute mental state to oneself and to others, and decision making [8,9] are impaired in PD patients [10,11]. In fact, it has been demonstrated that some PD patients suffer from social interaction impairments, such as being unable to detect or understand emotion and making

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http://dx.doi.org/10.1016/j.bbr.2014.11.035
0166-4328/

inappropriate responses in a social situation [12–14]. Furthermore, a large number of recent studies provide direct evidence that non-demented PD patients exhibit ToM and risk decision-making dysfunction early in the disease process [15,16].

The ability of ToM is a necessary skill for successful communication and to interact effectively in a social situation. Earlier studies of ToM originally focused on the first-order and second-order false belief task performances of children. Subsequent studies developed tasks that required more elaboration on mental abilities, and included "Faux Pas Recognition" [17] and "Reading the Mind in the Eyes" (RME) [18] to examine more advanced and higher-level ToM in adults. Neuroimaging [19] and lesion studies [20,21] suggested that the prefrontal lobes are engaged in ToM. In light of the close connections between the basal ganglia and the prefrontal cortex, PD patients are expected to have deficits in ToM, which has been shown in previous studies. PD patients have been reported to perform more poorly in the strange stories task [22], false-belief tasks [10,23], the cartoon task [11], the faux pas recognition task [24], and the RME task compared to healthy controls (HC) [25–27].

While previous studies have highlighted an overall deficit of ToM in PD patients, others have attempted to differentiate the subcomponents of ToM: cognitive ToM (inferences about others' beliefs and intentions) and affective ToM (inferences about other people's emotions and feelings) [28,29]. Through the use of different ToM tasks, studies have compared performance of PD patients and controls in cognitive and affective ToM functioning. A few authors have reported deficits in cognitive ToM in patients at early to moderate PD stages and found an impairment in this ability in various tasks [10,11,24]. However, the results from several studies that adopted the RME task to assess the affective ToM component in patients with PD were not consistent. A few studies reported lower RME performance of medicated PD patients in comparison to HC [26,27,30], while other studies reported that the performance of medicated patients in the RME task may be preserved at early stages of PD [24,31]. Recently, the results from Bodden et al. [27] and Santangelo et al. [22] indicated that participants with early to moderate stage PD scored significantly lower on both the cognitive and affective ToM subscales but not on the control (memory and facts) items. Overall, these studies showed that PD patients may be impaired in tasks of cognitive ToM. However, results from previous studies have not provided any conclusive evidence of whether early to moderate stage PD patients show impairments of affective ToM.

Another function that has been associated with the frontal lobe and has been shown to be impaired in PD patients is decision making [30,32,33]. Recent studies implied that decision making rather than other cognitive deficits in PD patients is affected by the disease [32]. Decision making includes the prediction of possible outcomes, the evaluation of alternatives, the selection of action, and the learning from behavioral feedback. According to the degree of available information, decision-making situations can be classified into decisions made under conditions of ambiguity and risk [34,35]. Previous studies [32,36] found disadvantageous, risky decision making under ambiguity in PD patients using the Iowa Gambling Task (IGT). In the study of Delazer et al. [33], both PD patients without cognitive impairment and PD patients with dementia showed significant deficits in decision making under ambiguity when learning by feedback and emotional processing is required. Some authors suggested that PD patients' bias toward disadvantageous choices may be accounted for by dysfunction of the amygdala and orbitofrontal cortex (OFC) [32,37–40]. Recently, a series of neuropsychological studies have used the Game of Dice Task (GDT) to assess decision-making abilities under risk in PD and indicated that PD patients were significantly impaired in the GDT. Moreover, the poor GDT performance in PD patients correlated with both impaired executive functions and reduced use of negative feedback [9,41–44]. Neuropsychological [45] and neuroimaging investigations [40,46] indicate that the subregions of the prefrontal cortex contribute differently to IGT and GDT—the limbic loop plays a major role in IGT performance, and the number of risky decisions in the IGT task correlate with OFC function [47–49], whereas the number of risky decision options in GDT correlate with executive functions [44,50], and decision making in the GDT is considered to depend to a high degree on the integrity of the dorsolateral prefrontal loop [35,51].

In the previous literature, decision-making abilities were found not only to be associated with executive function [44] but also with emotional processes [52,53]. A few studies [54–56] suggested that neural systems supporting decision-making overlap with the components of neural circuitry subserving emotional and affective ToM. Considering that the primary neuropathology of PD involves the frontal lobe system, patients with PD are expected to exhibit deficits in affective ToM and social decision making. Declines in executive functions correlate with GDT performance, but not with decision making in the IGT. However, it is unclear whether the ability of affective ToM shares similar neural mechanisms with social decision making in general or whether it is correlated with one particular type of decision making in PD. To address this question, we examined the performance of non-demented PD patients in three tasks introduced in the previous sections: the RME, IGT, and GDT, along with a number of neuropsychological tests assessing executive function. Previous neuroimaging and neuropsychological studies suggest that dysfunctions in PD affect the dorsolateral prefrontal loop and OFC. We hypothesized that PD patients show deficits in decision making under risk (GDT) and in decision making under ambiguity (IGT). Furthermore, we expected that declines in affective ToM correlate with decision making in the IGT, while declines in executive functions correlate with GDT performance.

2. Methods

2.1. Participants

Fifteen early to moderately affected patients with PD (7 male, 8 female; 15 right-handed) and 15 HC (6 male, 9 female; 15 right-handed) participated (see Table 1). All patients with PD were diagnosed by a movement disorders specialist and were recruited from the Department of Neurology in the Third Hospital of Anhui Medical University. All patients received typical dopaminergic medication (levodopa, dopamine-agonists). Doses of dopaminergic medication were converted to levodopa equivalent daily dose (LEDD) using the formula developed by a previously published study [57]. We excluded patients and controls with other significant neurological problems by history (e.g., head trauma, stroke), cognitive impairment as indicated by a score of less than 24 on the Mini-Mental State Examination (MMSE) [58], or depression as indexed by a score of more than 7 on the Hamilton Depression Scale (HAMD) [59], which were all administered on the day of testing. Disease severity was graded according to the Hoehn and Yahr (H–Y) rating scale [60] and the motor score on Section III of the Unified Parkinson's Disease Rating Scale (UPDRS) [61]. The study was approved by the Anhui Medical University Ethics Committee, and all participants gave written informed consent before the study.

2.2. Background and neuropsychological tests

The following neuropsychological tests were administered to all participants and compared between the PD and the HC group: (1) the MMSE measured global cognitive functions; (2) the Hamilton Depression Scale measured the presence of depressive states; (3) verbal fluency (number of animals per min) measured frontal functions; (4) the Stroop test estimated the ability of inhibitory