Parkinson’s disease alters multisensory perception: Insights from the Rubber Hand Illusion

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Background: Manipulation of multisensory integration induces illusory perceptions of body ownership. Patients with Parkinson’s disease (PD), a neurodegenerative disorder characterised by striatal dopamine deficiency, are prone to illusions and hallucinations and have sensory deficits. Dopaminergic treatment also aggravates hallucinations in PD. Whether multisensory integration in body ownership is altered by PD is unexplored.

Objective: To study the effect of dopamine neurotransmission on illusory perceptions of body ownership.

Methods: We studied the Rubber Hand Illusion (RHI) in 21 PD patients (on- and off-medication) and 21 controls. In this experimental paradigm, synchronous stroking of a rubber hand and the subject’s hidden real hand results in the illusory experience of ‘feeling’ the rubber hand, and proprioceptive mislocalisation of the real hand towards the rubber hand (‘proprioceptive drift’). Asynchronous stroking typically attenuates the RHI. Results: The effect of PD on illusory experience depended on the stroking condition (b = −2.15, 95% CI [−3.06, −1.25], p < .001): patients scored questionnaire items eliciting the RHI experience higher than controls in the illusion-attenuating (asynchronous) condition, but not in the illusion-promoting (synchronous) condition. PD, independent of stroking condition, predicted greater proprioceptive drift (b = 15.05, 95% CI [6.05, 24.05], p = .0022); the longer the disease duration, the greater the proprioceptive drift. However, the RHI did not affect subsequent reaching actions. On-medication patients scored both illusion (critical) and mock (control) questionnaire items higher than when off-medication, an effect that increased with disease severity (log (OR) = .014, 95% CI [.01, .02], p < .0001).

Conclusion: PD affects illusory perceptions of body ownership in situations that do not typically induce them, implicating dopamine deficit and consequent alterations in cortico-basal ganglia-thalamic circuitry in multisensory integration. Dopaminergic treatment appears to increase suggestibility generally rather than having a specific effect on own-body illusions, a novel finding with clinical and research implications.

1. Introduction

Multisensory integration—the interactive processing of somatic and special senses—is integral to a coherent perceptual awareness of ourselves and the world around us, including discriminating our own bodies from our environment (Ehrsson, 2012). Although the neural mechanisms underlying multisensory integration in general are gradually being revealed (Trommershauser et al., 2011), gaps remain in our understanding of multisensory integration in relation to bodily self-awareness, including how perceptual inference is influenced by modulation of sensory cue gains due to alteration of neurotransmitter systems in the brain such as dopamine (Conte et al., 2013).

Certain psychometric manipulations of sensory cues, particularly their synchronicity, may result in own body illusions. Much of our understanding of multisensory integration in bodily self-awareness comes from the Rubber Hand Illusion (RHI), where subjects’ ‘feel’ touch applied to a replica rubber hand as if it were their own hand (measured by questionnaires), when it is stroked synchronously with
their hidden real hand (Botvinick and Cohen, 1998). They also perceive their unseen real hand to be closer to the rubber hand after synchronous stroking (measured as ‘proprioceptive drift’). Asynchronous stroking does not typically induce this illusion (Botvinick and Cohen, 1998; Shimada et al., 2009). The importance of temporal synchronicity was further highlighted in Blank et al.’s (2014) ‘feeling of presence’ experiment, where asynchronously disrupting expected spatial-temporal patterns of self-touch (administered via a master-slave robotic device) caused subjects to attribute self-touch to an unseen and non-existent ‘presence’—akin to ‘feeling of presence’—the vague and illusory feeling of someone nearby when nobody is there.

In idiopathic Parkinson’s disease (PD), a neurodegenerative disorder in which cortico-basal ganglia-thalamic circuitry is altered primarily due to loss of dopaminergic midbrain neurons (Wichmann and Delong, 2002), there is a well-characterised spectrum of illusions and hallucinations, including ‘feeling of presence’ (Ravina et al., 2007). Illusions—false perceptions of real stimuli—are typically visual, such as mistaking an object for an animal (Fénelon et al., 2000; Ravina et al., 2007). Hallucinations—false perceptions that are not based on physical stimuli—can involve any sensory modality and commonly include ‘feeling of presence’ or ‘passage’ (‘a feeling of movement past you [the patient] when there was nothing to account for this feeling’), and seeing people and animals that are not there (Fénelon et al., 2000; Wood et al., 2015). These false perceptions are common but prevalence estimates vary due to methodological differences: a prospective cohort study of 216 PD patients found illusions and ‘feeling of presence’ or ‘passage’ in 25.5%, visual hallucinations in 22.2%, and auditory hallucinations in 9.7% of patients in the preceding 3 months (Fénelon et al., 2000). In comparison, in a recent cross-sectional study of 414 PD patients, 50% reported ‘feeling of presence’ or ‘passage’, and 15.5% reported visual hallucinations (Wood et al., 2015). The pathophysiology of visual hallucinations in PD is thought to involve neurotransmitter imbalances including dopamine, anti-Parkinson medication (typically levodopa or dopamine agonists) and impaired visual-spatial processing (Büttner et al., 1994; Ravina et al., 2007). However this does not fully account for non-visual hallucinations like ‘feeling of presence’ or ‘passage’, which occur even in drug-naive patients (Pagonabarraga et al., 2016) and where abnormalities in multisensory integration may be at play.

Patients with PD also have deficits in the detection and discrimination of sensory cues. Deficits potentially relevant to bodily self-awareness include: impaired visual discrimination of colour and contrast (Bulens et al., 1987; Büttner et al., 1994; Price et al., 1992); and proprioceptive deficits, such as decreased sensitivity to passive joint movement (Schneider et al., 1987), and joint position (Maschke et al., 2003). Moreover, temporal processing of sensory data is abnormal (Pastor et al., 1992) with impaired detection of paired visual, tactile and auditory stimuli (Artieda et al., 1992). Interestingly, dopaminergic drugs improve visual and temporal deficits (Artieda et al., 1992; Bulens et al., 1987; Büttner et al., 1994), which can be understood in terms of a dopamine-related deficit in sensory gain modulation (Conte et al., 2013). Theoretically, improving sensory cues with dopaminergic drugs could ‘normalise’ multisensory integration and reduce false perceptions (Büttner et al., 1996). On the other hand, dopaminergic treatment has been reported to worsen proprioceptive deficits (O’Sullivanbain et al., 2001) and to induce or aggravate hallucinations including ‘feeling of presence’ (Moskovitz et al., 1978; Rascol et al., 2000; Wood et al., 2015).

For these reasons, PD offers a valuable window upon multisensory integration in bodily self-awareness. Because PD patient (1) are prone to illusions and hallucinations in situations that would not typically induce them and (2) have visual, proprioceptive, tactile and temporal deficits that may impair optimal sensory cue integration, our first hypothesis was that PD patients would be more susceptible to the RHI compared with controls of a similar age. Specifically, we predicted that PD would increase both the RHI experience (questionnaire) and proprioceptive drift, in both the illusion-promoting synchronous and illusion-attenuating asynchronous conditions—as reported in other populations prone to hallucinations, such as people given ketamine (Morgan et al., 2011) and people with schizophrenia (Graham et al., 2014; Kaplan et al., 2014; Thakkar et al., 2011).

Then, we examined the effect of dopaminergic treatment on illusory perception relating to bodily self-awareness. Because these drugs induce or aggravate illusions and hallucinations in PD patients (Moskovitz et al., 1978; Rascol et al., 2000; Wood et al., 2015), our second hypothesis was that dopaminergic treatment also has an amplifying effect on the RHI. Specifically, we predicted that the RHI experience (questionnaire) and proprioceptive drift would be greater in the relatively dopamine-replete (‘on-medication’) state than after medication has been withdrawn (‘off-medication’ state).

Finally, we included a reach task at the end of the RHI experiment to assess whether illusory own-body perception affects subsequent action in PD. This is controversial in healthy subjects, with discordant reports on whether the RHI affects the accuracy of pointing (Kammers et al., 2009a,b; Zopf et al., 2011) and the trajectory of reach-to-grasp actions (Heed et al., 2011; Kammers et al., 2010; Palmer et al., 2013). The situation is even more complex in PD, where patients have motor deficits that impair speed and scale of movement (Kalina and Lang, 2015; Wichmann and Delong, 2002). Our third hypothesis was that the RHI would affect the already compromised proprioception of PD patients, with increased perceptual mismatch causing further slowing and changing the initial trajectory of reach movements in the illusion-promoting synchronous condition compared with the illusion-attenuating asynchronous condition.

Confirming these hypotheses will shed light on the role dopamine and associated cortico-basal ganglia-thalamic circuitry play in multisensory integration and body self-awareness. A practical consequence of our study is that it could also explain mechanisms underlying the illusory perceptions in PD.

2. Materials and methods

2.1. Participants

We recruited 21 PD patients from our Movement Disorders Clinic. Patients with deep brain stimulators, delirium, dementia, other neurological diagnoses or clinically significant sensory deficits were excluded. All patients met United Kingdom Brain-Bank criteria for ‘definite’ PD (Hughes et al., 1992), and were receiving dopaminergic drugs (Supplementary material Table A). The mean age was 65 years (SD 8.29) and the median disease duration from diagnosis was 9 years (IQR 4–12). Motor severity in defined on- and off-medication states was assessed by a neurologist using the Movement Disorders Society Unified PD Rating Scale (MDS-UPDRS) Part III. Non-motor symptoms were assessed using MDS-UPDRS Part I; four patients had experienced hallucinations in the past but none had active hallucinations in the week leading up to the experiment.

For the control group, we recruited 21 people from the community, aged between 50 and 80. The demographic and clinical characteristics of all subjects are listed in Table 1. There were more men in the PD group, but the groups were similar in age, hand dominance, and scores for cognition, mood and apathy. This study was approved by the Monash Health Research Ethics Committee (HREC 12350B) and all subjects gave written informed consent.

2.2. Experimental design

All subjects were tested twice (on separate days). In counterbalanced order, patients completed one session whilst taking their regular anti-Parkinson drugs (on-medication state) and the other session after all anti-Parkinson drugs had been withdrawn for at least 12 h (off-medication state) (Fig. 1C). Each session comprised two trials
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