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Spatial distortion related to time compression during spatiotemporal production in Parkinson's disease

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ABSTRACT

To produce coordinated manual actions within specific space and time, their relationship must be properly dealt with in a sensorimotor system. This study examined how such a coordination system might be impaired in normal aging and in Parkinson's disease (PD). Using a tablet device, young participants, elderly participants, and patients with PD were tested for concurrent production of distance and duration as well as single production of distance or duration alone. Results were analyzed in relation to deficiency of presynaptic dopamine transporter (DaT) in the striatum. We observed different patterns of impairment between normal aging and PD. Elderly participants exhibited duration overproduction when they had to produce distance and duration concurrently, but were normal in single production of either distance or duration. In contrast, PD patients exhibited normal distance production and marked underproduction of duration when either distance or duration was produced alone, but both duration and distance were underproduced when they were concurrently produced. These findings suggest that aging yields impaired performances in both elderly people and PD patients, but that temporal underproduction in PD patients entrains spatial production as if the distance to be produced were made consistent with their duration underproduction. We also observed that striatal DaT deficit was correlated with the extent of duration underproduction in PD patients. The deficit may be associated with the severe time compression and the entrainment during spatiotemporal production in PD patients.

1. Introduction

Comprehension and production of distance and duration are essential for coordinated action control; without them, it would be virtually impossible to move an object to a certain location at certain timing without any sensory cue to location or time. Manually produced distance and duration are also important tools for information sharing and nonverbal communications with others in social activities. What mechanisms underlie such spatiotemporal production? Space and time are known as closely coupled psychological dimensions, as demonstrated by psychophysical (Morrone et al., 2005; Frassinetti et al., 2009; Cai and Connell, 2015), neuropsychological (Cappelletti et al., 2009), and neuroimaging studies (Bonato et al., 2012). Classical studies have also documented that spatial and temporal dimensions are interrelated in various contexts, such as time influencing space perception (the tau effect; Helson, 1930) and space influencing time perception (the kappa effect; Cohen et al., 1953). Studies on the neural basis of space perception have put emphasis on the connections from the visual to parietal cortex (PC) and then to prefrontal cortex (PFC) (Quintana and Fuster, 1993; Chafee and Goldman-Rakic, 1998), whereas time perception may involve striatal networks interconnected with the hippocampus, PC, and PFC (Buhusi and Meck, 2005); the PC, PFC, and their combination may play an important role in spatiotemporal integration (Oliveri et al., 2009). Some researchers have also proposed "a theory of magnitude" which states that space, time, and number are represented in equivalent formats and processed in a common analog magnitude system implemented in the PC (Walsh, 2003; Bueti and Walsh, 2009). What remains to be elucidated is the way these internally represented spatial and temporal values are expressed by human motor control such as hand movement.

To examine this, we measured performance of concurrent production of space and time in a single action by asking participants to make horizontal movement of a hand for a certain travelling size and for a certain time interval, hereafter called "distance" and "duration"

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respectively, and compared the performance of this task with that of single production of distance or duration. If each dimension is processed separately, the motor outputs for all tasks should be similar. Conversely, they should differ if the computations for the two dimensions compete for common cognitive resources during the concurrent productions, as seen in behavioral performances in dual tasks in general (Hartley, 2001; Pashler, 1994). In such cases, spatial and temporal productions can interact in various ways; for example, the production of one dimension may exhibit a greater dispersion whereas the production of the other dimension is relatively unaffected. However, the motor outputs would be effectively similar between the concurrent and single tasks for healthy young people, given that the tasks are simple enough for them to execute concurrently with a negligible effect of resource competition. In contrast, age-related decline may make the effect of resource competition more explicit and thereby impair the concurrent productions of distance and duration. Therefore, comparison of results between young and elderly may elicit identifiable features of spatiotemporal production.

To examine whether conditions affecting time production also affects space production in such a cognitively challenging situation of concurrent productions, we attempted to test concurrent production in patients with conditions that are known to affect time production. Some neurological diseases accompany disordered temporal processing, and this is particularly true for Parkinson's disease (PD), which is marked by difficulties in both comprehension and production of time (Allman and Meck, 2012; Piras et al., 2014). Patients with PD have decreased levels of dopamine (DA) (Haber, 2014) and may further develop disorders related to striatal proteins such as presynaptic dopamine transporter (DaT), which is responsible for the incorporation and transmission of DA components (Vaughan and Foster, 2013). Patients with PD tend to underestimate time intervals (Lange et al., 1995; Smith et al., 2007), and administration of a DA agonist leads to a shift toward normal in produced duration (Pastor et al., 1992), indicating that DA levels are associated with time perception. Furthermore, these characteristics suggest that the basal ganglia are involved in temporal processing (Koch et al., 2008; Torta et al., 2010). On the other hand, distance production has not been tested in patients with PD. We predicted that PD patients would accurately produce distance but would underproduce duration in the single production task, as has been reported previously (Allman and Meck, 2012). What prediction could be made for the concurrent production task? If the computations for productions of space and time are independent of each other with a negligible effect of resource competition, patients would correctly produce distance but underproduce duration. Conversely, if spatial and temporal processes do interact with each other under the condition of resource competition, both distance and duration would differ between single and concurrent production tasks. The concurrent production in patients exhibiting disordered mental time may thus shed light on the underlying mechanism of spatiotemporal processing.

Productions of distance and duration in concurrent production task could be generally less accurate than those in single tasks for both the elderly participants and PD patients, since aging per se would potentially impair performances requiring sensorimotor coordination (Salthouse, 1996; Hartley, 2001). Studies of spatiotemporal comprehension have revealed that temporal representation more heavily depend on spatial representation, than vice versa (Boroditsky, 2000; Casasanto et al., 2010). If this were also true for spatiotemporal production in normal aging, the spatial aspects of internal information would play a more dominant role than the temporal aspects. For the same reason, in patients with PD, the concurrent production of distance and duration may also be impaired. However, it is possible that disordered temporal processing associated with PD still yields severe time compression even with accurate spatial production.

We conducted behavioral experiments to identify the effects of PD and aging on spatial and temporal productions by contrasting their performances with those for normal controls, and used brain imaging to identify the effects of striatal DaT deficit on manual productions in patients with PD. We also confirmed that, when a spatial and/or temporal cue was visually available during task, all the participants had an ability to understand the task, to follow object movement, and to attend to the cue. Furthermore, since elderly people and PD patients may present cognitive deficits, such as inefficient learning in visual discrimination (Price and Shin, 2009) and motor skills (Vandenbossche et al., 2013; Gobel et al., 2013), we examined whether the participants improved distance and/or duration production after feedback.

2. Material and methods

2.1. Participants

This study was approved by the ethics committees of Showa University Hospital and of the University of Tokyo and was conducted according to the principles of the Declaration of Helsinki. All participants provided written informed consent. Clinical neurologists recruited 39 patients with PD who met the diagnostic criteria of the Parkinson's Disease Society Brain Bank (Daniel and Lees, 1993), and 19 (mean age = 72.63) of them were selected as the participants of this study as having no signs of dementia as determined by two cognitive assessment batteries, the Mini-Mental Status Examination (MMSE; score > 25) testing individual memory, attention, and language abilities (Folstein et al., 1975), and the Montreal Cognitive Assessment (MoCA; score > 25) testing short-term memory, visuospatial abilities, executive functions, attention, concentration, working memory, and language abilities (Nasreddine et al., 2005). We also recruited 18 elderly controls (EC: mean age = 67.72) and 20 young controls (YC: mean age = 18.45) with no neurological disease history and no signs of dementia (Table 1). The difference in age between EC and PD groups was not significant (unpaired *t*-test: $t_{35} = 1.973$, $P > 0.05$). Handedness was assessed by verbal report from the participants and all of them were very confident that they exclusively used the right hand for writing in daily life. The PDs and ECs showed no brain abnormalities on magnetic resonance imaging with fluid attenuated inversion recovery and diffusion-weighted imaging. PD severity was measured using the Unified Parkinson's Disease Rating Scale (UPDRS) (Martinez-Martin et al., 1994), the Hoehn–Yahr scale, and disease duration. All patients were taking a DA agonist (carbidopa/levodopa equivalent daily dose), which had no influence on DaT imaging (Kägi et al., 2010), and participated in behavioral experiments under the *On* condition under which medicine was being administered.

Table 1
Participant details.

		YC (n = 20)	EC (n = 18)	PD (n = 19)
Age (years)		18.45 (0.60)	67.72 (6.59)	72.63 (6.91)
Sex				
	Female	10	9	11
	Male	10	9	8
Hand dominance				
	Right	20	18	19
	Left	0	0	0
MMSE		29.75 (0.44)	27.67 (0.84)	27.68 (1.29)
MoCA		28.65 (0.99)	27.33 (1.41)	27.67 (1.23)
UPDRS		–	–	39.7 (27.59)
Hoehn-Yahr stage		–	–	2.7 (0.91)
PD duration (years)		–	–	7.2 (4.65)

YC: Young controls. EC: Elderly controls. PD: Patients with Parkinson's disease. MMSE: Mini-Mental State Examination. MoCA: Montreal Cognitive Assessment. UPDRS: Unified Parkinson's Disease Rating Scale. The standard deviations are shown in parentheses.