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Time-course of masked response priming and inhibition in Parkinson's disease

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Abstract

Parkinson's disease patients have enhanced interference effects arising from the conflict between competing responses, as probed in various 'conflict tasks'. The possibility that this is due to an inhibitory deficit received recent support from a masked response priming task [Seiss, E., & Praamstra, P. (2004). The basal ganglia and inhibitory mechanisms in response selection: Evidence from subliminal priming of motor responses in Parkinson's disease. *Brain*, *127*, 330–339]. The added information from a masked priming task is that the introduction of a delay between presentation of prime and target stimuli reveals an inhibition of the covert response activation induced by the masked prime stimulus. This inhibition results in a reversal of normal priming effects, such that performance is better with incompatible than with compatible prime-target pairs. We previously found that this reversal is attenuated in Parkinson's disease, when tested at a prime-target delay of 100 ms, thus revealing deficient inhibition of covert response activation. The present study was undertaken to investigate the time course of the underlying inhibition process, using five prime-target ISIs between 0 and 200 ms. While we reproduced the attenuation at ISI 100 ms, the time course information revealed that the rate of change of the compatibility effect over ISIs from 0 to 200 ms was identical for patients and controls. This result indicates that the inhibition underlying the reversal of masked priming effects is normal in Parkinson's disease.

Keywords: Parkinson's disease; Masked priming; Inhibition; Response conflict; Flanker task

1. Introduction

Contemporary views on the function of the basal ganglia emphasise the architectural feature of opponent processes of activation and inhibition, by means of which the basal ganglia can modulate cortical activity. Disruption of the balance between activation and inhibition through indirect and direct striato-pallidal pathways has provided a coarse model to explain excess of movement in Huntington's disease and paucity of movement in Parkinson's disease (Alexander, Crutcher, & DeLong, 1990). Applied to normal movement, the opponent action of facilitatory and inhibitory effects exerted through striato-pallidal pathways is thought of as a mechanism that enables movement by disinhibiting desired movements and inhibiting competing movements (Mink, 1996). The latter view converges with related theoretical perspectives that place the basal ganglia at the interface between in and output processes, outlining response selection as an important function of the basal ganglia (Boraud, Bezard, Bioulac, & Gross, 2002; Brown & Marsden, 1998; Robbins & Brown, 1990).

If the basal ganglia coordinate activation and inhibition to implement selective access to the motor execution apparatus, it is to be expected that diseases of the basal ganglia result in response selection impairments (Wylie, Stout, & Bashore, 2005). Wylie et al. (2005) investigated response selection in Parkinson's disease (PD) by testing patients' ability to select between competing responses in a version of the Eriksen flanker task. Their results showed greater response interference effects of distractors in PD than in age-matched controls, replicating and extending previous findings obtained with the flanker and related conflict tasks in PD (Castiello, Bonfiglioli, & Peppard, 2000; Cope, Georgiou, Bradshaw, Iansek, & Phillips, 1996; Praamstra & Plat, 2001; Praamstra, Plat, Meyer, & Horstink, 1999; Praamstra, Stegeman, Cools, & Horstink, 1998). Together, these results establish

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that PD patients are susceptible to distracting visual information leading to incorrect response activation that interferes with correct response initiation and execution.

We recently used a masked response priming task to investigate the resolution of response conflict in PD, aiming to clarify the response selection deficit of which it is considered a direct manifestation (Seiss & Praamstra, 2004). The task was set up as a masked version of the Eriksen flanker task. In the flanker task, response-irrelevant distractors flank a central target stimulus. If the flankers are identical to the target, they will speed up the response; if they are instantiations of the stimulus that instructs for the alternative response, they will slow the response to the target and increase the error rate (Eriksen & Eriksen, 1974). Presenting the flanker stimuli for a very short duration, followed by the presentation of a masking stimulus, prevents conscious perception of the flankers, but does not eliminate their effect (Schwarz & Mecklinger, 1995). Moreover, as demonstrated by EEG recordings of the lateralized readiness potential (LRP), effects of masked response priming originate at the response level (Eimer & Schlaghecken, 1998; Leuthold & Kopp, 1998; Seiss & Praamstra, 2004), just as in the standard Eriksen task (Gratton, Coles, Sirevaag, Eriksen, & Donchin, 1988).

The value of a masked response priming task as a means to investigate response selection deficits in PD is the following. As discovered by Eimer and Schlaghecken (1998), the insertion of a delay between prime and target stimuli leads to a reversal of normal priming effects, such that compatible primes result in slower and more error-prone responses to the subsequent target than incompatible primes. This reversal is often attributed to an automatically invoked inhibition of the prime-induced response activation (Eimer & Schlaghecken, 1998; Lingnau & Vorberg, 2005; Praamstra & Seiss, 2005; Schlaghecken & Eimer, 2002; Seiss & Praamstra, 2004).[1] While revealed only when a delay is introduced between masked prime and target, this inhibition process probably contributes to the control of incorrect response tendencies generally (Eimer & Schlaghecken, 2003; Seiss & Praamstra, 2004). Indeed, testing PD patients in the masked response priming version of the flanker task, we found that reversed priming effects were attenuated, thus supporting deficient inhibition as an underlying cause of the enhanced susceptibility to response interference in PD (Seiss & Praamstra, 2004).

A limitation of our masked priming study in PD is that we tested participants only at prime-target delays (ISIs) of 0 and 100 ms. As outlined by Lingnau and Vorberg (2005), whether or not one can infer that covert response activation is inhibited should not depend on a sign reversal of priming effects (a change from a positive to a negative compatibility effect) at an arbitrarily chosen prime-target interval. Response inhibition can be assessed more reliably from the time course of masked response priming effects obtained by testing at a range of different prime-target intervals. Obviously, this recommendation is especially relevant where a comparison between a normal and pathological condition is involved. In theory, the attenuated reversed priming effect that we found in PD (Seiss & Praamstra, 2004) might not reflect a reduced inhibition but an altered time course of the inhibition process. Also conceivable would be a difference in compatibility effects between groups that remains stable across different tested ISIs. Such a pattern would indicate that the inhibitory process responsible for the change of masked response priming effects over time operates in the same way in both groups.[2]

The present study sought to extend our previous investigation of masked response priming in PD, by testing participants at a range of different prime-target ISIs between 0 and 200 ms. A second aim was to investigate the relation between deficient inhibition, as established by the masked response priming task, and the severity of patients' motor symptoms. Hence, we tested strongly asymmetric patients who responded in half of the experiment with their more affected hand, and in the other half with the less affected hand. A joystick was used to implement two response alternatives on the same hand, thus allowing a comparison between response hands.

Table 1
Patient characteristics

Patient number	Age (years)	Gender (F/M)	UPDRS	Medication (per 24 h)
1	38	M	30	Ropinirol 16 mg
2	57	M	16	Ropinirol 9 mg
3	59	M	28	Ropinirol 16 mg
4	51	F	30	Pergolide 1.5 mg
5	56	M	19	Sinemet 600 mg
6	64	M	8	Sinemet 300 mg
7	47	M	18	Sinemet 450 mg
8	53	F	19	Sinemet 600 mg Entacapone 400 mg
9	62	F	23	Pergolide 4 mg
10	54	F	32	Ropinirol 9 mg
11	55	M	33	Ropinirol 9 mg

2. Methods

2.1. Participants

The investigation included two experimental groups, PD patients ($n = 11$) and age-matched controls ($n = 11$). All participants gave informed consent and the investigation was approved by the South Birmingham local research ethics committee. The PD group consisted of seven men and four women (age: 54 ± 7 years). All patients had mild to moderate disease severity and were on dopaminergic medication (see Table 1). All but one patient, who was ambidextrous (handedness quotient: -0.1), were right handed (handedness quotient: 0.94 ± 0.12), as determined by the Edinburgh Handedness Questionnaire (Oldfield, 1971). Motor symptoms were assessed using the Unified Parkinson's Disease Rating Scale (UPDRS; Lang & Fahn, 1989). The median score on the motor subsection

[1] It should be noted that this account has recently been disputed. An alternative explanation for reversed masked priming effects is the active masking account (Lleras & Enns, 2004; Verleger, Jaśkowski, Aydemir, van der Lubbe, & Groen, 2004). This account assumes that the prime-mask sequence creates a perceptual state that primes the response opposite to the response indicated by the prime.

[2] This implication was not considered in Seiss and Praamstra (2004). Their data showed positive compatibility effects of 55 and 64 ms (ISI 0 ms) and 8 and 25 ms (ISI 100 ms) for control subjects and PD patients, respectively. There was no interaction between the factors Group, Compatibility, and ISI ($F(1, 22) < 1$).