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Learning of ambiguous versus hybrid sequences by patients with Parkinson's disease

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Abstract

Implicit motor learning as indexed by the serial reaction time (SRT) task has been shown to be impaired in patients with Parkinson's disease (PD). This has only been conclusively demonstrated for sequences that require learning of second-order sequential information (ambiguous sequences). This study examines implicit learning of ambiguous sequences as well as sequences which contain first-order information (hybrid sequences) in a sample of 12 early to middle stage Parkinson's disease patients and matched controls. The study used dual-task methodology in order to prevent strategic/attentional learning of second-order information. The results showed that while ambiguous sequences were not learned by either group, both patient and control groups demonstrated learning of the hybrid sequence under dual-task conditions. This suggests that first-order associations may be learned by people with Parkinson's disease, even under attentionally demanding conditions. This may be interpreted as providing evidence for a non-attentional learning mechanism which is relatively intact in Parkinson's disease.

Keywords: Implicit; Sequence; Motor; Learning; Parkinson's disease; Basal ganglia

1. Introduction

Parkinson's disease (PD) is a movement disorder resulting from the degeneration of the dopamine producing cells in the substantia nigra pars compacta. The primary symptoms of PD are tremor, rigidity and an inability to initiate and poverty of voluntary movement (akinesia). Motor deficits in individuals with PD have been examined in the laboratory using a variety of tasks tapping procedural knowledge. These patients show impaired performance on motor learning tasks such as weight biasing (Heindel, Salmon, Shults, Walicke, & Butters, 1989) and pursuit rotor (Harrington, Haaland, Yeo, & Marder, 1990). These data have contributed to the idea that the basal ganglia is an important neural component for skill learning with specific emphasis on its role in learning movement sequences. Learning of such sequences may be *implicit* or *explicit*, with the former thought to be an unconscious, automatic process which requires little or no attention and leads to *procedural* knowledge; whereas the latter is thought to use conscious, problem solving strategies that are attention demanding and leads to *declarative* knowledge. Impairment in tasks tapping procedural knowledge suggest that the implicit learning system is impaired in patients with PD. However, on the basis of empirical evidence in normals, it has been proposed that instead of one implicit learning system, there may be several dissociable sub-systems (see Curran, 1998) and that careful delineation of preserved and impaired subsystems is required.

Much of the available evidence on implicit learning in PD has been based on performance of the serial reaction time (SRT) task (Nissen & Bullemer, 1987) and a version of this task is used in the current study. The SRT task involves presenting subjects with a display of spatially arranged stimuli (e.g. an asterisk which could appear at one of the four quadrants on a computer screen). The subjects are instructed to respond as quickly as they can, using an appropriate key press to the spatial position of the stimuli that are presented on the screen. The stimuli do not appear at random but repeat in a sequence of between five and twelve elements. Learning in this task is measured via a transfer condition where, after considerable training on the original sequence, it changes without warning to either a random or to a new sequence. Typically, reaction times (RTs) increase during this transfer phase and provide an index of implicit sequence learning.

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This task is thought to tap implicit processes, since although most subjects are not aware of the sequence they nevertheless show slower RTs to the random or novel pattern.

Impairments on the SRT task have been found for patients with striatal dysfunction such as those with Huntington's disease (e.g. Knopman & Nissen, 1987; Willingham & Koroshetz, 1993) and Parkinson's disease (e.g. Ferraro, Balotta, & Connor, 1993; Jackson, Jackson, Harrison, Henderson, & Kennard, 1995) though some have reported intact learning (e.g. Corkin, Growdon, & Koroshetz, 1992; Pascual-Leone et al., 1993). The evidence regarding the generality/specificity of sequence learning deficits in PD is also controversial. Some studies suggested that PD patients show generalised deficits across motor and non-motor SRT tasks (Vakil, Kahan, Huberman, & Osimani, 2000), and others (Helmuth, Mayr, & Daum, 2000) reported that while PD patients are impaired in implicit learning of a stimulus-to-motor-response sequence they are not impaired in learning a sequence of spatial locations.

Ferraro et al. (1993) were the first to demonstrate a deficit on the SRT task in PD patients. However, they did not report any measures of explicit knowledge of the sequence. Therefore, differences in performance between the patient and control group may be due to differential levels of explicit knowledge about the sequence rather than an impairment in implicit learning in the patient group. Jackson et al. (1995) demonstrated impaired learning on the SRT task by PD patients who were unaware of the sequence, as measured by subsequent direct tests of awareness. They concluded that PD patients are impaired at either learning about complex serial-order information or expressing such knowledge.

Learning of sequential information has been shown to vary depending on the type of association between elements in a sequence. The distinction between ambiguous and unique transitions in a sequence was made by Cohen, Ivry, and Keele (1990). A unique sequence has each element consistently followed by another element (e.g. where the letters A, B, C and D denote spatial positions which form a sequenced presentation, A C D B A C would constitute a unique sequence as C is always predicted by A, D is always predicted by C and so on). Ambiguous sequences do not have any of the elements consistently followed by another element (e.g. in the sequence C A D A B C D B A, A predicts D but also B and C; D predicts A but also B, etc.). In an ambiguous sequence it is impossible to predict which element will next appear without knowing second-order information about the sequence whereas accurate prediction of the next element can be made in a unique sequence knowing only the preceding item. Cohen et al. (1990) also used hybrid sequences, which are made up of a mixture of unique and ambiguous elements. Under single task conditions, all three types of sequence could be learned. Under dual-task conditions however, learning was impaired for the ambiguous sequence. Cohen et al. proposed two separate learning mechanisms to account for these findings. An attentional mechanism which could learn hierarchical associations between elements in a sequence and a non-attentional mechanism which could only learn associations between sequentially presented stimuli. They suggested that the attentional system could not operate during dual-task performance, leaving only the pairwise association mechanism, hence explaining why the ambiguous sequence could not be learned under dual-task conditions.

It is possible that PD patients cannot learn any sequential information, complex or otherwise. Alternatively, it is possible that unlike healthy control subjects, PD patients have difficulty in utilising an attentional learning system. Without exposing them to a sequence which has unique transitions, it is impossible to determine from previous work whether PD patients have an intact non-attentional system for sequential learning. The aim of this study is to examine SRT performance under dual-task conditions for both ambiguous and hybrid sequences in a group of PD volunteers and a group of healthy matched controls. A sequence with completely unique transitions has necessarily a simple repetitive structure and may afford greater involvement of an explicit learning system therefore a unique sequence was not used. The dual-task methodology should have the effect of preventing the operation of the attentional learning system, and hence we predict that either group should not learn the ambiguous sequence. The non-attentional system should continue to function even with dual-task demands and learning should be observed for the control group. Whether the PD group learn the hybrid sequence or not will determine whether they have a profound deficit in learning sequential information or whether the underlying dysfunction seems confined to an attention-based learning system.

2. Method

2.1. Subjects

The study had the approval of our local ethics committee. Informed consent was obtained from all subjects. Twelve volunteers (eight male, four female) with medically diagnosed Parkinson's disease were recruited from a subject panel at the Institute of Neurology. All patients were diagnosed according to the criteria of the UK Parkinson's disease Society Brain Bank (Hughes, Daniel, Kilford, & Lees, 1992) and with presence of at least two of the symptoms of tremor, akinesia and rigidity. All were being treated with dopaminergic medication which was effective in controlling the symptoms. All patients were tested in the morning and had refrained from taking anti-Parkinsonian medication since the previous evening. Despite overnight withdrawal of medication, long-acting agonists could still be having an effect. Lack of pharmacological compensation can be inferred from symptom severity on standardised measures. At the time of assessment the patients had a mean rating of 10.50 (S.D. = 3.55, range 5–16) on the Webster (1968) scale. Assessment on the Hoehn and Yahr scale (1967) showed that five patients were classified as stage I, four as stage II and