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Exploring the recognition memory deficit in Parkinson's disease: estimates of recollection versus familiarity

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Current theories postulate that recognition memory can be supported by two independent processes: recollection (i.e. vivid memory for an item and the contextual details surrounding it) versus familiarity (i.e. the mere sense that an item is old). There is conflicting evidence on whether recognition memory is impaired in Parkinson's disease, perhaps because few studies have separated recollection from familiarity. We aimed to explore whether recollection or familiarity is more likely to be affected by Parkinson's disease, using three methods: (i) the word-frequency mirror effect to make inferences about recollection and familiarity based on recognition of high- versus low-frequency words, (ii) subjective estimates of recollection (remembering) versus familiarity (knowing), and (iii) a process-dissociation procedure where participants are required to endorse only some of the previously studied items on a recognition memory test, but not others. We tested Parkinson's disease patients (n = 19 and n = 16, age range = 58–77 years and age range = 50–75 in Experiments 1 and 2, respectively) and age- and education-matched controls (n = 23 and n = 16 in Experiments 1 and 2, respectively). Overall, the Parkinson's disease group showed a reduction in recognition memory, but this appeared to be primarily due to impairment of familiarity, with a lesser decline in recollection. We discuss how this pattern may be related to dysfunction of striatal, prefrontal and/or medial temporal regions in Parkinson's disease.

Keywords: recognition memory; recollection; familiarity; Parkinson's disease

Abbreviations: MTL = medial temporal lobe; PDP = process-dissociation procedure

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Introduction

Parkinson's disease is a progressive neurodegenerative disorder with its epicentre in the substantia nigra, causing reduced dopaminergic flow to the basal ganglia and cerebral cortex. The cardinal signs of the disease are motoric, including resting tremor, rigidity and akinesia (for review, *see* Lang and Lozano, 1998*a*, *b*). Parkinson's disease can also impair cognition, however. As one of the Lewy body spectrum that includes dementia with Lewy bodies, Parkinson's disease can often lead to dementia. Yet, even patients who do not meet criteria for dementia can show deficits in language, visuospatial processing, executive function, and memory (for reviews, *see* McPherson and Cummings, 1996; Bondi and Troster, 1997; Saint-Cyr, 2003; Zgaljardic *et al.*, 2003; Owen, 2004).

The status of recognition memory in Parkinson's disease is controversial. Initial studies suggested that recognition is preserved in Parkinson's disease (e.g. Flowers *et al.*, 1984; Taylor *et al.*, 1986; Breen, 1993; Gabrieli *et al.*, 1996), but subsequent reports have shown that recognition can be significantly impaired (e.g. Sahakian *et al.*, 1988; Massman *et al.*, 1990; Bondi *et al.*, 1993; Cooper *et al.*, 1993; Owen *et al.*, 1993; Ergis *et al.*, 1998; Stebbins *et al.*, 1999), and a

recent meta-analysis concurred with the latter findings (Whittington *et al.*, 2000). Many factors may influence whether one observes recognition memory impairment in Parkinson's disease, including disease stage, whether patients are tested on or off medication, screening for dementia and depression, and ceiling and floor effects.

One other possibility, however, is that variation in recognition memory may depend on the distinction between impairment of recollection versus familiarity. Several researchers have developed dual-process models of recognition memory, because single-process models are not sufficient to explain the myriad behavioural and neurological dissociations in the literature (Atkinson and Juola, 1974; Mandler, 1980; Jacoby and Dallas, 1981; Tulving, 1983; Gardiner, 1988; Jacoby, 1991). These dual-process models posit that recognition can be based on one of two processes: *recollection* is a vivid, clear memory of an item and the contextual details surrounding it, whereas *familiarity* is based on a more intuitive feeling that the stimulus has been encountered recently without awareness of the context in which it appeared. People can usually employ either process to support a recognition memory decision, so the researcher must tease the two apart, to estimate the relative contributions of each. Although there is a growing consensus that dual-process models provide a good description of memory, different researchers use different operational definitions of recollection and familiarity, and thus use different paradigms to estimate their relative contributions. For this reason, we sought convergence among three different methods, which are outlined below.

The word-frequency mirror effect

The first way we examined recollection and familiarity was using the word-frequency mirror effect. A mirror effect occurs on a single-probe 'yes–no' recognition memory task when a factor that increases one's hit rate decreases one's false alarm rate, or vice versa. Studies of recognition memory in healthy young adults have usually found that hit rates are higher for low- than high-frequency words, whereas false alarm rates are lower for the former than the latter (Glanzer *et al.*, 1993, 1998). Several researchers (e.g. Hirshman and Arndt, 1997; Joordens and Hockley, 2000; Reder *et al.*, 2000) have suggested that hit and false alarm rates are differentially dependent on recollection and familiarity, and thus can be used to estimate the relative contributions of these two processes to memory. For example, Reder *et al.* proposed that for each item encountered at study, two kinds of information are coded: first, there is an increase in the global strength/baseline familiarity of the item; and second, there is the encoding of situation-specific information from the study episode. High-frequency words have been seen on many occasions and in many different contexts in the past, leading to a high level of global strength/baseline familiarity for them, but also a decrease in the relative distinctiveness of the most recent context in which they were encountered (i.e. the study episode). Thus, high-frequency words give rise to a sense of familiarity more often than recollection. Low-frequency words, on the other hand, have been encountered rarely in the past, so they will tend to have a lower level of global strength/baseline familiarity, and the situation-specific information from their most recent presentation (i.e. the study episode) will stand out. Thus, low-frequency words tend to be recollected. Reder *et al.* argue that using these rules one can make inferences about the relative contributions of recollection and familiarity to performance. As one's ability to use recollection increases, one will show a greater hit rate advantage for low- as compared with high-frequency words. In contrast, if one is relying heavily on global strength/baseline familiarity, one will show an elevated false alarm rate, especially for high- as compared with low-frequency words.

Studies of the brain locus of the word-frequency mirror effect, although rare, have suggested that medial temporal lobe (MTL) regions support the recollection process that yields the low-frequency recognition advantage (Huppert and Piercy, 1976; Wilson *et al.*, 1983; Balota *et al.*, 2002). Functional neuroimaging studies, however, have yet to consistently show MTL involvement in the effect (Chee *et al.*, 2004; de Zubicaray *et al.*, 2005).

Judgements of Remembering versus Knowing

The second way of estimating recollection and familiarity is to have participants report on their subjective experience. Initially outlined by Tulving (1983), the Remember/Know distinction has been adapted by Gardiner (1988; for a review, *see* Gardiner and Richardson-Klavehn, 2000) and others to assess states of awareness in episodic recognition. For each test item that participants endorse, they are asked to introspect on whether they have a sense of *remembering* (a vivid sense of re-experiencing the item, along with remembering aspects of its study context) or instead merely have a sense of *knowing* that they have encountered the item recently (without being able to attribute this sense to a specific source).

Human lesion and neuroimaging studies have suggested that Remembering is supported by both frontal (Levine *et al.*, 1998; Henson *et al.*, 1999*b*; Wheeler and Stuss, 2003; for a review, *see* Wheeler *et al.*, 1995) and MTL regions, particularly the hippocampus (Knowlton and Squire, 1995; Schacter *et al.*, 1996*a*, 1997; Blaxton and Theodore, 1997; Yonelinas *et al.*, 1998, 2002, 2005; Henson *et al.*, 1999*b*; Eldridge *et al.*, 2000; Baddeley *et al.*, 2001; Moscovitch and McAndrews, 2002; Addis *et al.*, 2004; Gilboa *et al.*, 2004; Ranganath *et al.*, 2004; Wheeler and Buckner, 2004). Knowing appears to be less dependent on frontal areas (but *see* Ranganath *et al.*, 2004; Wheeler and Buckner, 2004; Duarte *et al.*, 2005) and more dependent on the MTL,

although it may implicate extra-hippocampal structures more than hippocampus proper (Knowlton and Squire, 1995; Schacter *et al.*, 1996, 1997; Blaxton and Theodore, 1997; Yonelinas *et al.*, 1998; Henson *et al.*, 1999*b*; Eldridge *et al.*, 2000; Moscovitch and McAndrews, 2002; Yonelinas *et al.*, 2002, 2005; Ranganath *et al.*, 2004).

Process-dissociation procedure (PDP)

The third method that we used to estimate recollection and familiarity was Jacoby's (1991) process-dissociation procedure (PDP; *see* also Mandler, 1980). It involves a participant studying two different lists of stimuli, and later performing two different memory tests. On the *inclusion* test, he or she endorses all of the previously studied items, and rejects the new ones. Endorsement of any one target in this phase could be due to either recollection or familiarity. On the *exclusion* test, he or she must only endorse items from one of the two study lists. An *exclusion error*, in which he or she mistakenly endorses an item from the wrong list, reflects that the subject found the item familiar but failed to recollect its list. If one assumes that recollection and familiarity are independent and work in concert during the inclusion test, but work in opposition during the exclusion test, then one can estimate the relative influence of these two processes on memory.

In a pattern very similar to the subjective Remember/Know data, both frontal (Henson *et al.*, 1999*a*; Davidson and Glisky, 2002; Hay *et al.*, 2002) and MTL regions (Verfaellie and Treadwell, 1993; Verfaellie, 1994; Mayes *et al.*, 1995; Christensen *et al.*, 1998; Yonelinas *et al.*, 1998; Henson *et al.*, 1999*a*; Davidson and Glisky, 2002; Hay *et al.*, 2002) have been implicated in recollection. The MTL has been associated with familiarity in many of these same studies. Some researchers have gone so far as to suggest that the MTL can be divided along functional lines, with hippocampus proper supporting recollection, and parahippocampal/perirhinal cortex supporting familiarity (Gabrieli *et al.*, 1997; Yonelinas *et al.*, 1998, 2002; Aggleton and Brown, 1999), but this is a contentious assertion (e.g. Manns *et al.*, 2003).

We sought converging evidence on the effects of Parkinson's disease on recollection and familiarity by estimating these processes using all three methods outlined above (unlike most studies, which just use one method), which may shed light on why previous reports on recognition memory in Parkinson's disease have varied so much. As far as we are aware, however, this approach has rarely been taken. First, the word-frequency mirror effect appears never to have been examined in the disease. Second, we can find only one previous study of Remembering versus Knowing in Parkinson's disease: Barnes *et al.* (2003) reported no recognition impairment, and normal levels of Remembering and Knowing, in Parkinson's disease patients as long as they were free of hallucinations. Finally, although the PDP has not been used to examine recognition memory *per se*, it has been employed in a word-stem completion paradigm that used the same underlying logic. In that study, Hay *et al.* (2002) reported that moderate Parkinson's disease reliably impaired both recollection and familiarity. Using the same method, they also found that focal damage to the basal ganglia (the structures most prominently affected by Parkinson's disease) produced a selective deficit in familiarity.

Two other regions decline in Parkinson's disease, however. Most qualitative reviews of Parkinson's disease have focused on dysfunction of prefrontal cortex as the predominant characteristic of the disease, and parallels between non-demented Parkinson's patients and focal frontal lesion patients have been discussed at length (e.g. Taylor *et al.*, 1986, 1990; Sagar *et al.*, 1988; Vriezen and Moscovitch, 1990; Cooper *et al.*, 1993; Pillon *et al.*, 1993; Knoke *et al.*, 1998; for reviews, *see* Taylor *et al.*, 1990; Troster and Fields, 1995; McPherson and Cummings, 1996; Bondi and Troster, 1997; Prull *et al.*, 2000; Zgaljardic *et al.*, 2003; Owen, 2004). Such results are consonant with the well-established reductions in dopaminergic innervation of the basal ganglia and the prefrontal cortex (via the mesocortical pathway), leading to dysfunction of each, and of their interconnections (for review, *see* Lang and Lozano, 1998*a*, *b*). In addition, Parkinson's disease may involve dysfunction of the connections between the basal ganglia and temporal lobes (Saint-Cyr *et al.*, 1990; Middleton and Strick, 1996), and the MTLs are reduced in volume in Parkinson's disease, even in patients free of dementia (Double *et al.*, 1996; Laakso *et al.*, 1996; Reikkinen *et al.*, 1998; Braak *et al.*, 2003; Camicioli *et al.*, 2003; Bruck *et al.*, 2004; Nagano-Saito *et al.*, 2005; Tam *et al.*, 2005, cf. Burton *et al.*, 2004). Taken together, these findings lead to the hypothesis that Parkinson's patients should be impaired in recollection (owing to frontal and/or MTL dysfunction), but possibly also in familiarity (owing to MTL and/or basal ganglia decline).

Experiment 1

Introduction

In Experiment 1, we estimated recollection and familiarity by examining memory for low- and high-frequency words (using the model from Reder *et al.*, 2000, reviewed above), and also collected subjective estimates of Remembering and Knowing. For the mirror effect, recollection is thought to make a relatively greater contribution to the hit rate than to the false alarm rate, and also a relatively greater contribution to the hit rate for low-frequency than high-frequency words. If patients are impaired in recollection, then they should show a decrease in hit rate overall and an attenuation of the hit rate advantage for low- versus high-frequency words. In contrast, familiarity is thought to make a relatively greater contribution to false alarms than hits, and so the more participants are relying on a sense of baseline familiarity, the more false alarms they should make, especially to high-frequency foils.

Method

Participants

We recruited 19 Parkinson's disease patients (*M* age = 67.05 years, range = 58–77 years; *M* education = 15.00 years) and 23 age- and education-matched healthy control participants (*M* age = 67.43 years, range = 58–77 years; *M* education = 14.95 years). All but one of the patients were recruited from a Parkinson's disease education programme at Baycrest Centre for Geriatric Care (the other was recruited from the Movement Disorders Clinic at Toronto Western Hospital). Patients were taking their routine medication regimens when tested: 17 of the patients were taking a dopamine precursor (which was levodopa/carbidopa for all but one) and/or a dopamine agonist (pramipexole or pergolide; one patient was enrolled in a double-blinded clinical drug trial, and drug data were unavailable for another patient). Six of the patients were also taking amantadine, and one was taking an anti-cholinergic drug (ethopropazine). All participants were community dwelling, had normal or corrected-to-normal vision and hearing and were screened for depression (Beck Depression Inventory Short Form; Beck *et al.*, 1961; Furlanetto *et al.*, 2005), cognitive impairment [Mini-Mental State Examination (MMSE); Folstein *et al.*, 1975] and drug or alcohol abuse. Demographic characteristics are shown in Table 1. All were native English speakers, or had learned English in early childhood.

Materials

We chose 96 words from the MRC Psycholinguistic database (http://www.psy.uwa.edu.au/mrcdatabase/uwa_mrc.htm). Half of the words were low-frequency (*M* = 1.23 occurrences per million in the Francis and Kučera, 1967 norms), and half were high-frequency (*M* = 204.38 per million). The frequency categories were matched for concreteness and word length (number of letters). We divided the words into two lists, each containing 24 words from each frequency category (matched again for concreteness and word length). Half of the participants studied the first list, with the second list serving as the distractor during the test, whereas the assignment of lists was reversed for the other participants.

Table 1 Demographic and neuropsychological information for participants in Experiment 1

	Healthy controls (n = 23)		Parkinson's disease (n = 19)	
	M	SD	M	SD
Age (years)	67.43	5.93	67.05	7.54
Education (years)	14.95	2.85	15.00	3.40
MMSE (/30)	29.33	0.90	29.32	1.00
Mill Hill vocabulary (/33)	20.07	4.40	22.05	3.99
Duration of illness (years)	–	–	5.79	2.46

MMSE = Mini-Mental State Examination (Folstein *et al.*, 1975).

We also administered tests of executive function—letter fluency (to the cues F, A, and S; Spreen and Strauss, 1998) and the Wisconsin Card Sorting Test (Kongs *et al.*, 2000) to the patients and 11 of the healthy controls.

Procedure

Participants were tested individually, and gave informed consent (for both experiments herein, consent was obtained according to the Declaration of Helsinki, and the project was approved by the research ethics board of Baycrest Centre for Geriatric Care). In the study phase, they were asked to say each word out loud and memorize it for a future memory test. Words were presented for 2500 ms at the centre of the screen using E-prime software (2000), with a 2000 ms inter-stimulus interval. Following a ~10 min filled delay, we conducted the test phase.

The test phase consisted of 96 words, half old ('target') and half new ('distractor'), with an equal proportion of low- and high-frequency items. For each word, participants were to make a key press to indicate one of three judgements: *Remember*, *Know*, or *New*. They were to give a Remember response when they recognized that the word had been studied, and were consciously aware of specific details associated with the study episode. They gave a Know response if they could not recollect the word but nevertheless believed that it had been studied. They gave a New response if they did not think they had studied the word. The instructions and examples given to participants were similar to those used previously (e.g. Gardiner and Java, 1990; Reder *et al.*, 2000). Each word appeared in the centre of the screen until the participants' response. The inter-trial interval was 1000 ms.

Results

The word-frequency mirror effect

We performed a mixed 2 × 2 × 2 ANOVA (analysis of variance) comparing hit and false alarm rates for each group (Parkinson's disease versus healthy control) by frequency category (high versus low), irrespective of subjective judgement of Remember versus Know. As shown in Table 2 (word frequency), the two groups were comparable in their hit rate for both low- and high-frequency words but differed in their false alarms. This observation was supported by a significant three-way interaction, $F(1, 40) = 4.16$, mean squared error (MSE) = 0.01, $P < 0.05$.

Follow-up analyses were performed separately for hits and false alarms. A mixed 2 × 2 ANOVA comparing hit rates for each group (Parkinson's disease versus control) by frequency category (high versus low) revealed that both groups had similar hit rates to one another ($F < 1$), and both groups made more hits to low-frequency than high-frequency words, $F(1, 40) = 27.20$, MSE = 0.01, $P < 0.001$. The interaction term was not reliable ($F < 1$).

A similar two-way ANOVA conducted on false alarm rates revealed that the Parkinson's disease group made slightly more false alarms than the controls [$F(1, 40) = 2.87$,

Table 2 Hit and false alarm rates for Experiment 1, shown for word frequency and subjective Remember/Know judgements

	Healthy Controls		Parkinson's disease	
	M	SD	M	SD
Word frequency				
Hit rate				
Low frequency	0.84	0.13	0.86	0.14
High frequency	0.72	0.22	0.73	0.17
False alarm rate				
Low frequency	0.12	0.12	0.15	0.15
High frequency	0.20	0.19	0.33	0.21*
d'				
Low frequency	2.56	1.00	2.54	0.93
High frequency	1.81	0.51	1.30	0.69*
Subjective Remember/Know judgements				
Hit rate				
Remember	0.42	0.28	0.52	0.29
Know	0.36	0.27	0.28	0.23
False alarm rate				
Remember	0.05	0.07	0.07	0.08
Know	0.12	0.12	0.17	0.14
d'				
Remember	1.62	0.79	1.64	0.86
Know	0.93	0.67	0.39	0.68*

*$P < 0.05$ between groups.

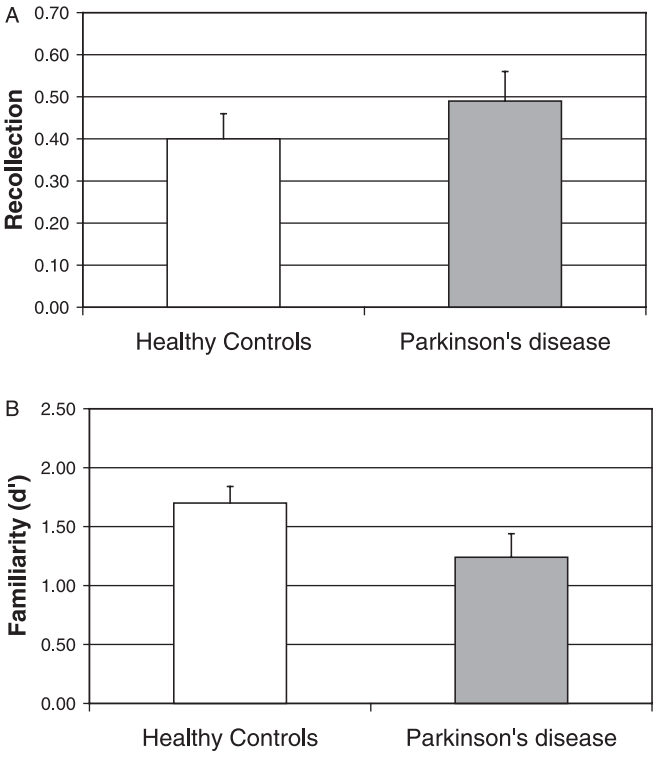

Fig. 1 Estimates of recollection (**A**) and familiarity (**B**) from the Remember/Know ratings in Experiment 1 (following Yonelinas *et al.*, 1998).

MSE = 0.04, $P = 0.10$], and both groups made fewer false alarms to low-frequency than to high-frequency foils [$F(1, 40) = 25.40$, MSE = 0.02, $P < 0.001$]. More importantly, a marginally significant interaction was obtained [$F(1, 40) = 3.78$, MSE = 0.02, $P = 0.06$], indicating that the Parkinson's disease patients had near-normal false alarm rates to low-frequency foils ($t < 1$), but significantly elevated false alarm rates to high-frequency foils $t = 2.07$, $P < 0.05$), as shown in Table 2 (word frequency).

We calculated discrimination (d') for both groups, shown in Table 2 (word frequency). A 2 × 2 ANOVA on group (Parkinson's disease versus control) by frequency category (high versus low) showed no main effect of group ($F = 1.43$, n.s.), and better discrimination in both groups to low-frequency than high-frequency words, $F(1, 40) = 75.63$, MSE = 0.27, $P < 0.001$. The interaction term was also reliable, however [$F(1, 40) = 4.58$, MSE = 0.27, $P = 0.04$), indicating that the two groups showed equivalent memory for low-frequency words ($t < 1$), but the Parkinson's disease patients were reliably impaired in memory for the high-frequency words, t (40) = 2.76, $P = 0.009$.

Judgements of Remembering versus Knowing

We also examined participants' subjective judgements of Remembering and Knowing (irrespective of frequency category), shown in Table 2 (subjective Remember/Know judgements). Several analyses were conducted to assess the rates of recollection and familiarity: first, a measure of sensitivity (d') was computed for Remember and Know responses. Although the two groups did not differ in Remembering ($t < 1$), the Parkinson's disease patients were significantly impaired in Knowing ($t = 2.57$, $P = 0.01$).

We also derived the estimates of recollection and familiarity from the data using the formulae provided by Yonelinas *et al.* (1998). Although there is controversy surrounding exactly how to estimate recollection and familiarity, we employed the Yonelinas *et al.* model because it (i) leads to consistency among studies using the Remember–Know method (Yonelinas *et al.*, 1998), (ii) allows for comparison between Remember–Know and process-dissociation methods because it uses the same underlying assumptions for each, and (iii) allows us to compare our results with most of the recent neuropsychological and neuroimaging studies, which have used this method. These estimates are shown in Fig. 1A and B. For recollection, an independent t-test showed no significant difference between groups ($t = 1.00$). For familiarity, however, the Parkinson's disease group was marginally impaired, $t = 1.78$, $P = 0.08$.

Executive measures. The patients and controls were not significantly different on letter fluency ($M = 43.32$ and 44.93 for patients and controls, respectively, $t < 1$) or the Wisconsin Card Sorting Test for categories ($M = 2.63$ and 3.55 for patients and controls, respectively, $t = 1.45$, $P = 0.16$) or perseverative errors ($M = 10.00$ and 9.00 for patients and controls, respectively, $t < 1$).

Discussion

In the word-frequency mirror effect, recollection is thought to be reflected in the hit rate advantage for low-frequency words (Reder *et al.*, 2000; Balota *et al.*, 2002; Joordens and Hockley, 2002). The Parkinson's disease patients showed hit rates that were the same as controls, for both low- and high-frequency words, indicating intact recollection. In their false alarm rates, as expected, both groups showed a greater tendency to make false alarms to high-frequency foils. This tendency, however, was exaggerated in the Parkinson's disease patients. According to the models proposed by Reder *et al.* and Joordens and Hockley, this pattern in false alarm rates reflects a greater tendency on the part of the patients to rely on 'baseline familiarity,' which is greater for high-frequency words because they have been seen repeatedly over the lifespan. One way to explain this pattern is to posit that there are at least two sources of familiarity that can be confused by participants in this paradigm: one long term, reflecting the frequency of exposures to a word over the lifespan ('baseline familiarity') and another, more transient one, reflecting recency of occurrence. The Parkinson's disease patients may have been relying on a faulty strategy of using 'baseline familiarity' as a guide to their response. That is, if on the memory test the Parkinson's disease patients had more trouble than normal at determining whether a given target had appeared at study (because of a weaker familiarity signal based on recency), they might have been more susceptible to another source of familiarity (the 'baseline familiarity' built up over the lifespan), causing them to make false alarms to high-frequency foils. Ergis *et al.* (1998) reported a similar pattern to this: Parkinson's disease patients made a greater proportion of false alarms than normal to foils that were synonyms of targets (e.g. 'disease' versus 'illness') than to unrelated foils. If there actually is more than one kind of familiarity that can contribute to recognition memory (as we have hypothesized with our distinction between 'baseline' versus 'transient' familiarity, see also Jacoby et al., 1989), one possible way to dissociate them might be to use novel stimuli and manipulate the frequency with which participants are exposed to them during an initial familiarization phase, as well as the interval between study and test. Then one could begin to examine how 'baseline' and 'transient' familiarity processes interact. Another possibility would be to use a computational model, in which one could create different weightings for different kinds of familiarity, and use this to predict how recognition performance would be affected.

The impaired ability to differentiate ambiguous items along the familiarity dimension seen in the Parkinson's disease patients may be due to dopaminergic reduction, which has been posited to lead to a de-focusing of activity patterns in the basal ganglia, resulting in ambiguity of stimulus encoding (Filion *et al.*, 1988; Bar-Gad and Bergman, 2001). Alternatively, one might interpret these findings as showing that although recollection in the Parkinson's disease group was good enough to support memory for low-frequency words, it was not good enough to distinguish the difficult high-frequency targets from foils, and so Parkinson's disease patients relied more heavily on familiarity. This alternative interpretation, however, is not supported by the results of the Remember/Know ratings.

The Remember/Know ratings indicated preserved recollection in the Parkinson's disease group—in fact, the estimate of recollection was numerically greater in the Parkinson's disease patients than in controls. In contrast, the Parkinson's disease group showed a reliable impairment in memory based on familiarity. This pattern suggests that Parkinson's disease patients are less likely to recognize individual items than normal, but in cases where they do, they are just as capable of remembering the surrounding context as normal controls.

Experiment 2

Introduction

Both the mirror effect and Remember–Know estimates suggested that Parkinson's disease patients showed a greater reduction in familiarity than in recollection. In both methods, however, 'recollection' is assumed to reflect memory for contextual information, but neither of the methods provides objective evidence that this is actually the case. For example, in the Remember/Know procedure, even if one's subjective sense of recollection is strong, it can be inaccurate: sometimes brain-injured patients can commit 'false recollection' errors in recognition memory (e.g. Schacter *et al.*, 1996*b*), and even neurologically intact people can have clear, vivid recollections of events that never occurred, both in the laboratory (Deese, 1959; Roediger and McDermott, 1995) and in the real world (Loftus, 2005). Thus, in Experiment 2 we used an objective measure of memory for context when estimating recollection and familiarity, employing a PDP that had been used recently with older adults (Davidson and Glisky, 2002). In that study, Davidson and Glisky used a process-dissociation list discrimination task, and found that older adults who were below average on either frontal or MTL function (based on neuropsychological testing) had impaired recollection, whereas only those who were below average on MTL function showed impaired familiarity.

Method

Participants

We recruited 16 Parkinson's disease patients (*M* age = 66.56 years, range = 50–75 years; *M* education = 15.94 years, range = 11–22 years) and 16 age- and education-matched healthy control participants (free of neurological or psychiatric illness; *M* age = 67.44 years, range = 51–82 years; *M* education = 14.69 years, range = 12–19 years) from the same pools, and using the same criteria, as in Experiment 1. For demographic and neuropsychological information on the two groups, see Table 3. Patients were taking drugs on their normal regimens when tested: 14 of the patients

Table 3 Demographic and neuropsychological information for participants in Experiment 2

	Healthy controls (n = 16)		Parkinson's disease (n = 16)	
	M	SD	M	SD
Age (years)	67.44	9.36	66.56	7.20
Education (years)	14.69	2.36	15.94	3.30
MMSE (/30)	28.50	1.37	29.13	1.09
Mill Hill vocabulary (/33)	21.94	5.07	22.13	4.02
Duration of illness (years)	–	–	6.13	2.67

MMSE = Mini-Mental State Examination (Folstein *et al.*, 1975).

were taking a dopamine precursor (which was levodopa/carbidopa for all but one) and/or a dopamine agonist (pramipexole or pergolide; one patient was enrolled in a double-blinded clinical drug trial, and drug data were unavailable for another). Six of the patients were also taking amantadine, and one was taking an anti-cholinergic drug (ethopropazine).

Materials

We created 4 lists of 24 concrete words each (from Francis and Kucera, 1982), matched for frequency and word length. We designated two as target lists, and the other two as distractor lists. Both target lists were shown at study, and all the words from them were shown at test (divided so that both the inclusion and exclusion tests contained 24 target words, 12 from each study list). Each test also included 24 distractors.

As in Experiment 1, we administered letter fluency (Spreen and Strauss, 1998) and the Wisconsin Card Sorting Test (Kongs *et al.*, 2000) to the patients and controls.

Procedure

Participants were tested individually, and gave informed consent. In the study phase, they were told that they would see two lists of words separated by a short break, and should say each one out loud and try to remember it and in which list it occurred for a later memory test. The words appeared for 2000 ms each with a 500 ms inter-stimulus interval at the centre of a personal computer screen (using Superlab Pro, 1997). Following the first study list, there was a ~10 s break, during which participants were reminded that they had just seen the first list and were moving on to the second list. They then viewed the second list in the same way as the first. We added two words to the beginning and the end of each study list, to reduce primacy and recency effects.

As soon as the study phase was finished, participants received the inclusion and exclusion tests. On the inclusion test, they were to press the *Y* key if they had seen the word on either of the study lists, and the *N* key if not. On the exclusion test, they were to press the *Y* key only if they had seen the word on the first study list, and the *N* key if not (i.e. for words from the second study list and new words). Words that were endorsed from the wrong study list were classified as 'exclusion errors.' We counterbalanced the order of the study lists, the pairings of target and distractor lists, and the order of the inclusion and exclusion tests.

Table 4 Hit, exclusion error, and false alarm rates for Experiment 2

	Healthy controls		Parkinson's disease	
	M	SD	M	SD
Inclusion				
Hit rate	0.87	0.15	0.80	0.10*
False alarm rate	0.15	0.15	0.28	0.17
Exclusion				
Hit rate	0.69	0.19	0.56	0.21*
Exclusion error rate	0.54	0.27	0.49	0.22
False alarm rate	0.13	0.18	0.18	0.16

*P < 0.05 between groups.

Results

Hit, exclusion error and new false alarm rates

We performed a mixed 2 × 2 ANOVA comparing hit rates for each group (Parkinson's disease versus control) by test phase (inclusion versus exclusion). As shown in Table 4, the Parkinson's disease group was reliably impaired compared with the controls on each of the test phases, $F(1, 30) = 4.70$, MSE = 0.04, $P = 0.04$. Both groups made more hits during the inclusion than the exclusion phase, $F(1, 30) = 35.83$, MSE = 0.02, $P < 0.001$. The interaction term was not significant ($F < 1$).

We conducted a similar ANOVA for false alarm rates, also shown in Table 4. The Parkinson's disease group made marginally more false alarms than the controls, $F(1, 30) = 3.72$, MSE = 0.04, $P = 0.06$. The difference between test phases was not significant ($F = 2.57$, $P = 0.12$), and neither was the interaction term ($F = 1.52$, $P = 0.23$). An independent t-test showed that the exclusion error rate did not differ between groups (*see* Table 4).

Overall, when we calculated a traditional d' measure of discrimination based on hit and false alarm rates from the inclusion condition (which is essentially a standard yes–no recognition memory test), we found that the Parkinson's disease group ($M = 1.53$) were impaired relatively to the healthy controls ($M = 2.71$), $t(30) = 5.43$, $P < 0.001$.

Recollection and familiarity

More telling than the raw scores for hits and false alarms, or the traditional measure of discrimination, are the estimates of recollection and familiarity. These were derived using the model provided by Yonelinas *et al.* (1995, 1998) [Although there is still controversy over exactly how to estimate these two processes, and alternative models exist

for both Remember/Know (Rotello *et al.*, 2004) and process-dissociation methods (e.g. Joordens and Merikle, 1993; Mayes *et al.*, 1995; Ratcliff *et al.*, 1995), we chose the Yonelinas *et al.* (1995, 1998) method because it provides convergence between the Remember/Know and PDP methods and uniformity across multiple studies using the same method (*see* Yonelinas *et al.*, 1998), and has been used most often in neuropsychological and neuroimaging studies of recollection and familiarity. Briefly, the model assumes that recollection is a threshold process, whereas familiarity is signal-detection process. The model uses a spreadsheet-based algorithm that computes recollection, familiarity (represented as a measure of discriminability, d') and criteria (Cin and Cex) for both test phases. The model uses the traditional PDP equations, but replaces the familiarity term (F) with Φ ($d'/2 - c$), where Φ represents the probability of an item's familiarity exceeding the criterion. To correct for floor or ceiling effects in either hit or false alarm rates, we substituted values of $1/(2N)$ and $1 - 1/(2N)$ for scores of 0.00 and 1.00, respectively (Macmillan and Creelman, 1991)], and these are shown in Fig. 2A and B. For recollection, an independent t-test indicated that the two groups were not significantly different ($t = 1.36$, $P > 0.10$). In contrast, the Parkinson's disease group was reliably impaired on the estimate of familiarity, t (30) = 4.09, $P < 0.001$.

Executive measures. We found no differences between groups on verbal fluency ($M = 45.56$ and 48.06 for patients and controls respectively, $t < 1$) or the Wisconsin Card Sorting Test for categories ($M = 3.06$ and 2.67 for patients and controls, respectively, $t < 1$) or perseverative errors ($M = 8.69$ and 10.67 for patients and controls, respectively, $t = 1.08$).

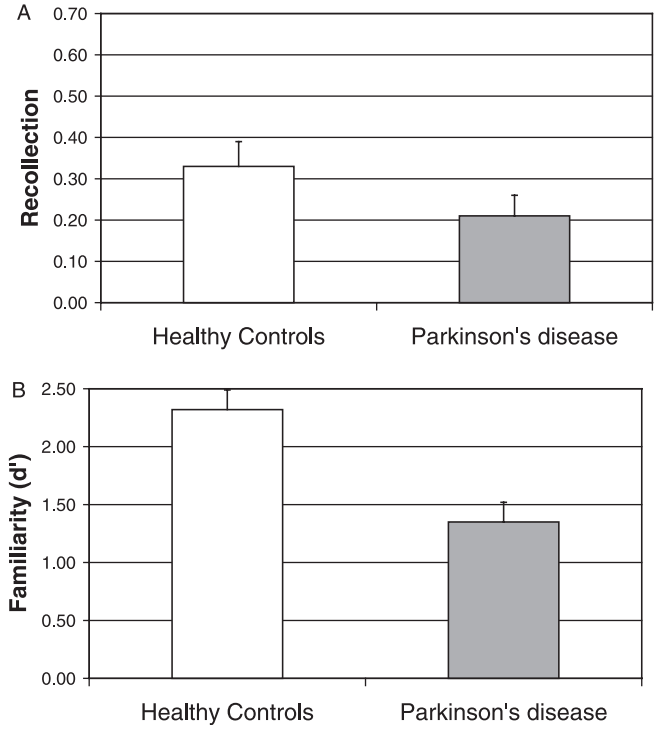

Fig. 2 Estimates of recollection (**A**) and familiarity (**B**) from the process-dissociation data in Experiment 2 (following Yonelinas *et al.*, 1995).

Discussion

Although the Parkinson's disease patients showed a small, non-significant decrement in the raw exclusion error rate and thus in the recollection estimate, this was overshadowed by their poor item recognition and significantly impaired familiarity estimate. We had expected to find a clearer temporal order deficit in the patients, following previous studies (e.g. Taylor *et al.*, 1986, 1990; Sagar *et al.*, 1988; Vriezen and Moscovitch, 1990; Ergis *et al.*, 1998). However, a recent report showed the same pattern as us: Vingerhoets *et al.* (2005) found that Parkinson's disease patients were significantly impaired in memory for previously shown items, but, for those items that they could remember, they had no problem remembering where or when they had seen them. A strong relation between frontal lobe impairment and poor temporal order memory has been noted by other researchers (e.g. Milner *et al.*, 1991), and if Parkinson's patients are impaired on the former they may consequently have trouble with the latter. Note, however, that the Parkinson's disease patients in our study did not show prominent executive function impairments, and thus may have had relatively intact frontal function. If so, this might explain why their temporal order memory was relatively good.

Conclusions

We used three methods (the word-frequency mirror effect, subjective Remember–Know judgements and the PDP) to estimate the relative contributions of recollection and familiarity to recognition memory in Parkinson's disease. To our knowledge, few previous studies have used any of these measures to estimate recollection and familiarity in Parkinson's disease, and none have used all three. Across all three methods, we found evidence that recollection was not significantly impaired in Parkinson's disease, whereas familiarity was. This apparent decrement in familiarity in the face of preserved recollection was especially apparent in the Remember/Know data from Experiment 1, and is the opposite dissociation from the one normally reported in populations with brain diseases or damage (see also Blaxton and Theodore, 1997; Hay *et al.*, 2002). This finding may help bolster the case for independence between these two putative memory processes.

Although the process-dissociation estimates of recollection and familiarity from Experiment 2 yielded the same statistical pattern as in Experiment 1, Fig. 2 suggests that recollection was somewhat depressed in the Parkinson's disease group, albeit not reaching statistical significance. The reasons for this minor discrepancy between studies may be related to individual differences. That is, Experiment 2

was performed several months after Experiment 1; we could not test exactly the same subjects in the two experiments, and even if we had, Parkinson's patients can be quite variable in their performance from day to day. Alternatively, it may be due to differences between the methods used to estimate recollection and familiarity. For example, the Remember/Know method is subjective and probably relies on metamemory to a greater extent than the PDP (for a discussion, *see* Gardiner and Richardson-Klavehn, 2000). In addition, in the process-dissociation method differences between groups in false alarm rates and/or criterion-setting can complicate estimates of recollection and familiarity, and although the patient and control groups had similar false alarm rates in Experiment 1, they differed in Experiment 2. Finally, in our interpretation of the results of Experiment 1, we postulate that there are different kinds of 'familiarity,' and there may well be multiple kinds of 'recollection' as well. Nonetheless, taken together, the two experiments herein suggest that in the context of dual-process models of recognition memory, the decline in familiarity is more robust, or begins at an earlier stage of Parkinson's disease, than a decline in recollection, although as the disease progresses recollection will probably become impaired, too (*see* Hay *et al.*, 2002).

To what should we attribute this pattern of performance? One possibility is that the Parkinson's disease patients' trouble was due to lapses of attention at encoding, which many complained about in everyday life during debriefing (*see* also Brown *et al.*, 1984; Sharpe, 1990; for reviews, *see* McPherson and Cummings, 1996; Bondi and Troster, 1997; Serrano and Garcia-Borreguero, 2004). Such deficits may be linked to decline in cholinergic (Whitehouse, 1989; Dubois *et al.*, 1990; Bedard *et al.*, 1999) or noradrenergic systems (Agid, 1991; Bedard *et al.*, 1998) in Parkinson's disease. If the patients were more easily distracted or had more trouble maintaining vigilance than normal, then they may have failed to encode items as richly or as fully as normal. This could have led to the pattern we observed, namely, trouble remembering whether they had encountered an item recently (as shown by lower hit and higher false alarm rates, and lower familiarity measures, than normal), but if they did remember having encountered it, they could remember its context at near-normal levels (as shown by unimpaired exclusion error rates in Experiment 2, and unimpaired recollection measures in both experiments). Studies of divided attention in healthy young people tend to lead to a decline in recollection more so than in familiarity. It may be, however, that the attentional impairment that such paradigms produce in young people is relatively mild and constant over time, leading to just enough capacity being left over to encode items without enough attentional resources to encode context information, whereas the attentional problems in Parkinson's disease may vary more over time, waxing and waning so that sometimes item and associated contextual information are well encoded, but other times relatively little is encoded.

There are three main brain regions that deteriorate in Parkinson's disease and might underlie the memory impairment seen here. First, the most obvious changes that take place in Parkinson's disease occur in the basal ganglia, owing to loss of dopaminergic input from the substantia nigra (for a review, *see* Saint-Cyr, 2003). Although studies of focal basal ganglia lesions are rare, Hay *et al.* (2002) studied one such patient on a word fragment completion task that used the process-dissociation logic. He showed a deficit in familiarity with no effect on recollection, suggesting that the deficit in familiarity shown by the Parkinson's disease group may be the result of caudate damage.

Second, frontal regions are also compromised in Parkinson's disease, and behavioural studies have emphasized parallels between focal frontal lesion patients and Parkinson's patients in memory (e.g. Taylor *et al.*, 1986, 1990; Sagar *et al.*, 1988; Vriezen and Moscovitch, 1990; Cooper *et al.*, 1993; Pillon *et al.*, 1993; Knoke *et al.*, 1998; for reviews, *see* Taylor *et al.*, 1990; Troster and Fields, 1995; McPherson and Cummings, 1996; Bondi and Troster, 1997; Prull *et al.*, 2000; Zgaljardic *et al.*, 2003; Owen, 2004). Note, however, that even if the patients' memory impairment was due to FL dysfunction, the patients in our study did not show executive impairment exceeding that of age-matched controls (at least, on the basis of the measures that we used). Many researchers have suggested that memory impairment in Parkinson's disease is secondary to poor executive function, reflecting a decreased ability to 'work with memory' strategically at retrieval. Some have even reported that memory impairments in Parkinson's disease can be attenuated or eliminated statistically by using executive function or working memory scores as a covariate (Bondi *et al.*, 1993; Gabrieli *et al.*, 1996; Stebbins *et al.*, 1999; Blanchet et al., 2000; but *see* Stefanova *et al.*, 2001). In both our experiments, however, we showed a dissociation between recognition memory and executive function (as measured by the Wisconsin Card Sorting Test, and verbal fluency). The patients were significantly worse than age-matched controls in memory, but not in executive function. Executive dysfunction may become more obvious as Parkinson's disease progresses, but it does not appear necessary for memory to be impaired at early stages of the disease (*see also* Stefanova *et al.*, 2001).

Third, volumetric neuroimaging studies suggest that MTL decline can occur even in non-demented Parkinson's disease patients (Double *et al.*, 1996; Laakso *et al.*, 1996; Reikkinen *et al.*, 1998; Braak *et al.*, 2003; Camicioli *et al.*, 2003; Bruck *et al.*, 2004; Nagano-Saito *et al.*, 2005; Tam *et al.*, 2005; cf. Burton *et al.*, 2004). Some researchers have speculated that within the MTL system, recollection may be more dependent on hippocampus proper, whereas familiarity may be more related to parahippocampal/perirhinal cortex (Gabrieli *et al.*, 1997; Yonelinas *et al.*, 1998, 2002; Aggleton and Brown, 1999). Given that the patients in this study were more impaired in familiarity than in recollection, it would be interesting to know whether

parahippocampal or perirhinal structures are affected earlier in the disease than hippocampus proper (e.g. Braak *et al.*, 2003; Camicioli *et al.*, 2003).

In summary, we examined the relative contributions of recollection and familiarity to recognition memory in Parkinson's disease. All three methods suggested a more robust decline in familiarity than in recollection. The present results suggest that the degree to which recognition memory depends on each of these two processes will determine whether an impairment is found in Parkinson's disease patients. A critical next step is to disentangle the relative contributions of the basal ganglia and frontal and MTL regions, along with dopaminergic and other neurotransmitter systems, to this pattern of memory performance in Parkinson's disease. Because so many changes take place in the disease, these may be difficult to tease apart. For example, although the basal ganglia and frontal lobes may play separate roles in memory (e.g. Pasupathy and Miller, 2005), their functions may be difficult to dissociate in Parkinson's disease, where both are affected. In addition, in most studies of Parkinson's disease, normal older adults serve as control subjects. However, even healthy ageing is correlated with changes in neurotransmitter systems (including dopamine; Hedden and Gabrieli, 2004) as well as structural and functional decline, especially in frontal and MTL regions (Raz, 2000). Thus, even if Parkinson's disease patients were not significantly worse in recollection than older controls, both groups would almost certainly have been impaired relative to young people. There may also be considerable heterogeneity in both age-related neurological decline and Parkinson's disease (e.g. Huber *et al.*, 1991; Filoteo *et al.*, 1997; Lewis *et al.*, 2003). Consequently, whether one sees impairment in Parkinson's patients may be influenced to some extent by individual differences. For these reasons, seeking converging evidence from lesion, pharmacological and physiological studies may be the best way to further our understanding of why recognition memory can be impaired in Parkinson's disease.

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