Interference From Retrieval Cues in Parkinson’s Disease

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Objective: Existing studies on memory interference in Parkinson’s disease (PD) patients have provided mixed results and it is unknown whether PD patients have problems in overcoming interference from retrieval cues. We investigated this issue by using a part-list cuing paradigm. In this paradigm, after the study of a list of items, the presentation of some of these items as retrieval cues hinders the recall of the remaining ones. Method: We tested PD patients’ (n = 19) and control participants’ (n = 16) episodic memory in the presence and absence of part-list cues, using initial-letter probes, and following either weak or strong serial associative encoding of list items. Results: Both PD patients and control participants showed a comparable and significant part-list cuing effect after weak associative encoding (13% vs. 12% decrease in retrieval in part-list cuing vs. no part-list cuing -control- conditions in PD patients and control participants, respectively), denoting a similar effect of cue-driven interference in the two populations when a serial retrieval strategy is hard to develop. However, only PD patients showed a significant part-list cuing effect after strong associative encoding (20% vs. 5% decrease in retrieval in patients and controls, respectively). Conclusions: When encoding promotes the development of an effective serial retrieval strategy, the presentation of part-list cues has a specifically disruptive effect in PD patients. This indicates problems in strategic retrieval, probably related to PD patients’ increased tendency to rely on external cues. Findings in control conditions suggest that less effective encoding may have contributed to PD patients’ memory performance.

Keywords: part-list cuing, interference, retrieval inhibition, strategy disruption, Parkinson’s disease

Parkinson’s disease (PD) has been traditionally considered as a motor disorder characterized by manifestations reflecting pathological depletion of dopamine in neurons in regions of the ventral midbrain (Jellinger, 2001). There is, however, a growing consensus that PD, even in its earliest stages, also affects cognitive functions. In particular, a significant subset of PD patients show problems in executive functioning (e.g., Owen, 2004; Taylor, Saint-Cyr, & Lang, 1986).

A more blurred picture emerges if we consider episodic memory in PD, given that this topic has received relatively less attention and that research findings are less consistent. Some authors have proposed that PD patients may vary in the extent to which they are affected by episodic memory problems and it has been suggested that these problems may selectively involve encoding or retrieval processes (Filoteo et al., 1997; Weintraub, Moberg, Culbertson, Duda, & Stern, 2004). A specific retrieval deficit in PD patients has often been claimed, considering that the memory profile of these patients is usually characterized by poor free recall performance together with relatively spared performance on recognition and cued-recall tests (e.g., Flowers, Pearce, & Pearce, 1984; Ivory, Knight, Longmore, & Caradoc-Davies, 1999; Lees & Smith, 1983; Taylor, Saint-Cyr, & Lang, 1986). According to this view, the successful encoding of memory traces would be proved by PD patients’ better performance when retrieval cues are provided (Dujardin & Laurent, 2003; Higginson et al., 2003). However, other investigations have reported poor performance both on recognition and on recall memory tests, together with a high number of intrusion errors. As a consequence, some scholars have suggested that also encoding processes are impaired in PD (Weintraub et al., 2004), and they have pointed out a resemblance between the...
memory problems of some PD patients and the type of amnesic disorder typically observed in patients with Alzheimer’s disease (AD).

Other studies have promoted the idea that the PD patients’ memory problems may be more specific, depending on the complexity of strategic processes operating at encoding and retrieval (e.g., Knoke, Taylor, & Saint-Cyr, 1998; see also Buytenhuijs et al., 1994). Thus, the worse performance in free recall (vs. cued recall) has been explained by the greater demands associated with self-initiated retrieval strategies in the first type of test. As far as encoding processes are concerned, some studies have similarly suggested that PD patients’ memory problems may reside in the difficulty to develop efficient encoding strategies. For instance, Knoke et al. (1998) used the California Verbal Learning Test (CVLT) with three conditions of graded cuing. They suggested that the poor verbal recall performance of PD patients in the standard (uncued) condition arose from an impaired ability to subjectively organize list items at encoding. Moreover, the authors showed that cuing improved subjective organization of memory and recall especially in PD patients (see also Buytenhuijs et al., 1994; Van Spaendonck, Berger, Horstink, Borm, & Cools, 1996, for related arguments).

Working memory (WM) has also been shown to be impaired in PD patients and these difficulties have often been linked to problems in executive control, given that different aspects of supervisory attention are involved in WM tasks. WM problems in PD patients have been reported in different tasks, such as self-ordered pointing (West, Ergis, Winocur, & Saint-Cyr, 1998), spatial and nonspatial working memory (Owen, Iddon, Hodges, & Robbins, 1997), and paced auditory serial addition (Trépanier, Kumar, Lazzaro, Lang, & Saint-Cyr, 2000; see also Saint-Cyr, 2003). Recent evidence also suggests that PD patients are more impaired in the active manipulation of WM contents than in the mere maintenance of information within working memory (Lewis, Slabosz, Robbins, Barker, & Owen, 2005).

Executive functioning difficulties have been sometime singled out to explain PD patients’ memory problems (e.g., Bondi, Kaszniak, Bayles, & Vance, 1993; Dujardin & Laurent, 2003; Higginson et al., 2003; Taylor et al., 1986). Indeed, frontally based executive processes are needed to develop and apply retrieval strategies, to strategically allocate attentional resources on stimuli and retrieval cues, and to exert control over interfering memory traces (e.g., D’Esposito & Grossman, 1996; Fletcher & Henson, 2001; Smith & Jonides, 1999). In line with this view, neuropsychological studies have shown that patients with lesions to the frontal lobes can experience problems in strategic encoding and retrieval and show decreased resistance to interference (see, e.g., Gershberg & Shimamura, 1995; Incisa Della Rocchetta & Milner, 1993; Kopelman & Stanhope, 1998; Shimamura, Jurica, Mangels, Gershberg, & Knight, 1995). However, although there are theoretical reasons to hypothesize a link between PD patients’ executive functioning problems and their memory problems, it is still not clear to what extent PD patients’ memory difficulties are secondary to frontal lobe dysfunction or represent distinct problems (e.g., Beatty, Staton, Weir, Monson, & Whitaker, 1989; Bondi et al., 1993; Drag, Bielauskas, Kaszniak, Bohnen, & Glisky, 2009; Higginson et al., 2003).

A fundamental issue in the investigation of memory retrieval and executive control concerns interference management and resolution. Unfortunately, limited research has been conducted on memory interference in PD patients, and different studies obtained conflicting results. For instance, studies on proactive interference in PD have provided mixed results, with some studies showing increased sensitivity to interference in PD (e.g., Helkala, Lauluma, Soininen, & Riekkinen, 1989; Rouleau, Imbault, Laframboise, & Bédard, 2001) and others reporting normal release from proactive interference in these patients (Beatty et al., 1989; Sagar, Sullivan, Cooper, & Jordan, 1991). In a similar fashion, other studies investigating interference and inhibitory control in PD outside the domain of episodic memory found a mixed pattern of results. In particular, some of these studies suggested the presence of impaired inhibitory processes in the patients (Castner et al., 2007; Copland, 2003; Crescentini, Mondolo, Biasutti, & Stallilce, 2008; Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005; Wylie et al., 2009) while others did not find such deficits (e.g., Falkenstein, Willemsen, Hohnsbein, & Hielers, 2006; Hartikainen, Helkala, Soininen, & Riekkinen, 1993; Lee, Wild, Hollnagel, & Graffman, 1999).

The existence of contrasting findings and the limited research on memory interference in PD patients strongly motivate further studies on this topic. In particular, we are not aware of any study that examined interference generated from retrieval cues in PD patients, while the majority of existing studies have adopted proactive/retroactive interference paradigms, or have studied intrusion errors under different encoding conditions or with different kinds of preexperimentally learned materials. However, retrieval failures due to different types of interference are probably caused by different mechanisms and, consequently, results on one type of interference cannot be easily generalized to other types of interference (see Bäuml, Kessler, & Rak, 2002, for the different mechanisms underlying proactive and proactive interference vs. interference from retrieval cues).

The Part-List Cuing Effect and Paradigm

In the present study, we examined interference from retrieval cues in PD patients, employing the well-established memory paradigm of part-list cuing (e.g., Brown, 1968; Roediger & Neely, 1982; Roediger, Stellon, & Tulving, 1977; Slamecka, 1968, 1969; see also Bäuml, 2008). The part-list cuing effect occurs when, after the study of a list of items, some of these items are presented as retrieval cues and their presentation reduces, rather than enhances, the retrieval of the remaining (noncue) items (compared to a control condition in which no such cuing is provided). This effect is surprising in the light of the literature that underlines the (usually) beneficial effects of retrieval cues (e.g., Tulving & Pearlstone, 1966; Tulving & Psotka, 1971).

The part-list cuing paradigm provides a unique opportunity to study strategy-related and inhibition-related memory processes in a single experiment. In fact, as we will explain, both inhibitory control and strategic aspects of memory are thought to be involved in the part-list cuing phenomenon under different encoding conditions. Moreover, this phenomenon also has clinical relevance, considering that the provision of external cues has usually been regarded as an effective way to overcome PD patients’ memory problems (Buytenhuijs et al., 1994; Van Spaendonck et al., 1996; Weingartner, Burns, Diebel, & LeWitt, 1984).
Several explanations of part-list cuing interference have been proposed over the years (for reviews see Bäuml & Aslan, 2006; Nickerson, 1984, and Bäuml, 2008), but two of them are currently considered more supported by empirical evidence. First, an inhibitory mechanism has been proposed to underlie part-list cuing effects (e.g., Aslan & Bäuml, 2007; Aslan, Bäuml, & Grundgeiger, 2007; Bäuml & Aslan, 2004, 2006). According to this retrieval inhibition view, the presence of part-list cues leads to their early covert retrieval. The retrieval of part-list cues would have, as a side effect, the inhibition of target items, whose memory activation would be weakened. In this situation, interference from cues stems from target inhibition, and target recall requires overcoming inhibition caused by the presentation of the part-list cues.

A different account of part-list cuing effects relies on the idea of strategy disruption (Basden & Basden, 1995; Basden, Basden, & Stephens, 2002). According to this idea, retrieval is more effective when the retrieval strategy can capitalize on the way the items were encoded. In other words, retrieval would benefit from the compatibility between the encoding strategy and the retrieval strategy. Following this explanation, part-list cuing would be observed when the presentation of part-list cues disrupts the retrieval strategy that participants would have used, had the cues not been presented. When part-list cues are presented, participants may still try to apply the retrieval strategy compatible with the encoding organization (employing more cognitive resources) or they may resort to a different strategy (e.g., Basden et al., 2002). As a consequence, retrieval is usually less effective. According to this view, interference consists in the cue-induced disruption of the retrieval strategy compatible with the way stimuli were encoded, and overcoming interference means being able to apply a retrieval strategy as powerful as the compatible one.

Bäuml and Aslan (2006) have tried to reconcile retrieval inhibition and strategy disruption, providing empirical evidence for a two-mechanism account of part-list cuing in which one or the other mechanism mediates forgetting depending on the encoding condition. In particular, retrieval inhibition would apply when the degree of interferer interference is high and a serial associative retrieval strategy cannot be successfully developed at encoding (for instance because the presentation of list items is not category-blocked and the order of presentation of the items is different in consecutive study trials). In such conditions of weak associative encoding, part-list cuing inhibition would be enhanced. By contrast, strategy disruption would explain part-list cuing after strong associative encoding, namely when participants could use an efficient retrieval strategy based on a high degree of interitem serial associations. For instance, this strategy would be built at encoding by presenting category-blocked list items and keeping constant their order of presentation in consecutive study trials and in a consolidation (via retrieval) phase. Consistent with this, it has been shown that strong interitem associations promoted by repeated study-test cycles (Basden & Basden, 1995; Bäuml & Aslan, 2006-Experiment 1; Crescentini, Shallice, Del Missier, & Macaluso, 2010) or by the instruction to encode items in a serial order (Basden et al., 2002) lead participants to develop retrieval plans with preferred output orders; plans which can then be disrupted when incompatible part-list cues are presented at retrieval (Bäuml & Aslan, 2006).

Following up their previous study, Aslan and Bäuml (2007) have provided additional evidence to support their two-mechanism account of part-list cuing. In particular, they examined whether the effect is also present when randomly ordered initial-letter probes are employed (initial-letter of target words) in addition to the presentation of part-list cues. They found a part-list cuing effect after weak associative encoding but not after strong associative encoding, and they explained these findings with the inhibition of targets occurring after weak encoding and with the generally disruptive effect of initial-letter probes on retrieval strategies after strong encoding (regardless of the presence of part-list cues). Indeed, after strong encoding, initial-letter probes seem to have a disruptive effect on retrieval strategies based on item serial order, regardless of the presence of part-list cues, given that their random serial order does not agree with the serial order of the studied words.

Hypotheses

In the present study we used a version of the ‘part-list cuing + initial-letter probes’ paradigm that we employed in a previous research (Crescentini et al., 2010), in which we observed a part-list cuing effect after weak associative encoding but not after strong associative encoding in normal healthy participants. The paradigm is similar to the one used by Bäuml and Aslan (2006) and Aslan and Bäuml (2007). In the present study, PD patients and age-matched controls studied a series of categorized lists in conditions promoting or discouraging the development of a serial retrieval strategy (strong and weak associative encoding conditions, respectively). Target recall was tested either in the presence or in the absence of part-list cues, but always in the presence of the initial letter of target items (initial-letter probes).

Based on previous studies carried out on normal young adults (Aslan & Bäuml, 2007; Crescentini et al., 2010), a part-list cuing effect was expected in healthy participants after weak encoding (H1), but not after strong encoding (H2). However, if PD patients were less able than older controls to efficiently apply encoding strategies and retrieval strategies in the presence of incompatible cues, then we should expect the PD sample to show a part-list cuing effect also after strong associative encoding (H3). In other words, PD patients’ target retrieval would also be hindered by the presence of part-list cues after strong associative encoding and not only by initial letter probes. This hypothesis stems from the observations that these patients appear to be less able than normal controls to take advance of strategic encoding (Knöke et al., 1998) and, more importantly, they can experience difficulty in applying efficient retrieval strategies in the presence of incompatible external cues. In fact, it has been shown that, due to their difficulties with internal cues and strategies, PD patients rely more than control participants on external cues to guide their retrieval (e.g., Buynenhuys et al., 1994; Van Spaendonck et al., 1996). To summarize, part-list cues may be detrimental in PD patients also after strong associative encoding, given that retrieval in PD patients may depend more on external cues and that these patients’ strategic encoding and retrieval processes are usually less effective.

Relying on the existing literature on PD, two alternative hypotheses can be put forward for the weak encoding condition, assuming that target inhibition mediates forgetting in this specific condition. The first hypothesis (H4a) assumes that the inhibitory processes triggered by covert retrieval of cues are not affected by PD. In this case PD patients should be normal with weak encoding and show...
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A significant part-list cuing effect. Various studies showed that relatively automatic processes (like positive and negative priming) are generally unaffected in PD patients (e.g., Copland, 2003; Ivory et al., 1999; Possin, Cagigas, Strayer, & Filoteo, 2006) and this might hold true also for inhibitory processes involved in part-list cuing. An alternative hypothesis can be put forward starting from some studies which suggest that some types of inhibitory processes (like those involved in stimulus inhibition) could be less effective in PD patients at least in some tasks (e.g., Cagigas, Filoteo, Stricker, Rilling, & Friedrich, 2007; Filoteo, Rilling, & Strayer, 2002). If these processes are involved in part-list cuing, then we should observe a reduced interference effect in PD patients (vs. normal participants) after weak associative encoding (H4b), due to weaker target inhibition.

Finally, we also investigated whether there is a relation between the capacity to handle interference from retrieval cues and individual differences in executive functioning in PD patients. In particular, in part-list cuing conditions we expected to observe a positive correlation between PD patients’ executive functioning effectiveness and their retrieval performance after both weak and strong associative encoding (H5a). Moreover, we expected to observe negative correlations between PD patients’ executive functioning and the size of the part-list cuing effect (H5b). In fact, individuals with more effective executive processes should be also more successful in overcoming interference from retrieval cues, being more able both to recover inhibited targets and to flexibly reinstate disrupted strategies in the presence of part-list cues.

Method

Participants

Nineteen right-handed Italian PD patients (14 males and five females) were included in the study. The diagnosis of idiopathic Parkinson’s disease was established by a neurologist in accordance to the clinical criteria of the United Kingdom Parkinson’s disease Society Brain Bank (U.K.-PDSBB; Gibb & Lees, 1988). The patients were consecutive referrals to the Department of Physical Medicine of the “Gervasutta” Rehabilitation Hospital, Udine, for a standardized neuropsychological examination. All patients were in the mild stages of the disease, with scores on the Hoehn and Yahr’s scale (Hoehn & Yahr, 1967) that ranged from 1 to 2.5. Patients’ motor disability was also evaluated using the motor part of the Unified Parkinson’s disease Rating Scale (UPDRS; Fahn et al., 1987). Based on the UPDRS scores, 14 out of 19 patients were categorized as having postural instability-gait disorder predominant PD; a patient was categorized as having tremor-dominant PD while the symptoms of the remaining four patients suggested the presence of both types of deficit. Patients were screened for dementia using the Mini Mental State Examination (MMSE; Folstein, Folstein, & McHugh, 1975) and those with a score below 24 were excluded. Dementia could also be excluded for our patients based on the feedback of a clinical interview carried out by a neurologist and considering the intact performance they showed on some neuropsychological tests (see next section). PD patients were also screened for depression, and those with scores > 10 on the Beck Depression Inventory were also excluded (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961). All patients were tested in the “on” medication state. Patients with atypical parkinsonism, vascular parkinsonism, drug-induced parkinsonism, and those with parkinsonism following dementia were excluded from the study. All patients were on antiparkinsonian medication, 18 were receiving l-dopa and 15 were taking dopamine agonists. Some of the patients were also taking monoamine-oxidase-B-inhibitors (four patients), catechol-O-methyltransferase inhibitors (three), amantadine (two), antidepressants (three), and benzodiazepine (one).

A control group of 16 right-handed Italian older participants closely matched to the PD patients for age, sex, education, and MMSE scores took also part in the study. All participants provided informed consent prior to participating in the study. The study was performed in accordance with the ethical standards specified in the 1964 Declaration of Helsinki. Demographic and clinical data of PD patients and older controls are summarized in Table 1.

Table 1
Demographic and Clinical Data of PD Patients and Healthy Controls (Mean ± SD)

<table>
<thead>
<tr>
<th></th>
<th>PD patients (N = 19)</th>
<th>Control group (N = 16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>66.7 ± 8.0</td>
<td>65.6 ± 5.6</td>
</tr>
<tr>
<td>Education (years)</td>
<td>8.1 ± 2.9</td>
<td>9.9 ± 3.3</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>14/5</td>
<td>12/4</td>
</tr>
<tr>
<td>Age at Onset (years)</td>
<td>60.3 ± 9.3</td>
<td>—</td>
</tr>
<tr>
<td>Duration of illness (years)</td>
<td>6.4 ± 4.5</td>
<td>—</td>
</tr>
<tr>
<td>Hoehn and Yahr score:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage 1</td>
<td>n = 3</td>
<td>—</td>
</tr>
<tr>
<td>Stage 2</td>
<td>n = 8</td>
<td>—</td>
</tr>
<tr>
<td>Stage 2.5</td>
<td>n = 8</td>
<td>—</td>
</tr>
<tr>
<td>UPDRS motor score</td>
<td>26.2 ± 11.7</td>
<td>—</td>
</tr>
<tr>
<td>MMSE</td>
<td>29.0 ± 1.1</td>
<td>29.2 ± 0.7</td>
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<tr>
<td>BDI</td>
<td>5.9 ± 2.1</td>
<td>—</td>
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<tr>
<td>Dopamine agonists mg/day (range):</td>
<td></td>
<td></td>
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<tr>
<td>Pramipexole</td>
<td>3.1 ± 0.3 (n = 9; 3.00–4.00)</td>
<td>—</td>
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<tr>
<td>Ropinirole</td>
<td>10.4 ± 5.4 (n = 5; 4–16)</td>
<td>—</td>
</tr>
<tr>
<td>Levodopa mg/day (range)</td>
<td>540.3 ± 294.5 (n = 18; 125–1250)</td>
<td>—</td>
</tr>
</tbody>
</table>

Note. UPDRS = Unified Parkinson’s disease Rating Scale (Fahn, Elton, & Members of the UPDRS Development Committee, 1987); MMSE = Mini Mental Status Examination (Folstein, Folstein, & McHugh, 1975); BDI = Beck’s Depression Inventory (Beck, Ward, Mendelson, Mock, & Erbaugh, 1961).
Neuropsychological Measures

Neuropsychological assessment was carried out for both PD patients and older controls (two older controls did not undergo the neuropsychological assessment but were only administered the experimental task). The neuropsychological battery was as follows. Fluid intelligence was assessed using the Raven Colored Progressive Matrices (Lezak, 1995), verbal short term memory using the Forward and Backward Digit Spans (Lezak, 1995), and verbal long term memory with the Rey Auditory Verbal Learning Test (RAVLT) (Lezak, 1995). Frontal lobe functions were assessed using the Wisconsin Card Sorting Test (WCST, Heaton, Chelune, Talley, Kay, & Curtiss, 1993), a Letter Fluency Test (Lezak, 1995), the Trail Making Test A and Trail Making Test B (Lezak, 1995), the Stroop Color Word Test (Lezak, 1995), and the Brixton test (Burgess & Shallice, 1997). An examination of attentional functions was also carried out using two subtests of the Test for Attentional Performance (TAP; Zimmermann & Fimm, 2002). The TAP battery is a computer-controlled battery that allows the evaluation of several attentional components. The divided attention and go/no-go subtests were used (see Table 2). In the divided attention subtest participants have to alternate between two simultaneous tasks, one visual and one acoustic; for selective attention and inhibition the 5-stimuli version of the go/no-go subtest of TAP was used.  

Italian normative data for all tests used were as follows: for the Raven Colored Progressive Matrices we used those provided by Basso, Captuini, and Laiacona (1987); for the Forward and Backward Digit Span we used those provided in the WAIS–R by Orsini and Laicardi (2001); for the Auditory Verbal Learning Test those provided by Carlesimo et al. (1996); for the Letter Fluency Test we used those provided by Caltagirone et al. (1995); for the Trail Making Test A and B those provided by Mondini, Mapelli, Vestri and Bisiacchi (2003); for the Stroop Color Word Test those provided by Barbarotto et al. (1998); for the Brixton test those provided by Burgess and Shallice (1997); and for the WCST those provided by Hardoy, Carta, Hardoy, and Cabras (2000). Finally, for the two TAP subtests, we used the Italian normative data provided by Zoccolotti, Pizzamiglio, Pittau, and Galati (1994). For both participant groups, a test score was classified as impaired if it was below the age-appropriate cut-off (when these were available) or the fifth percentile of the normative sample. The percentage of patients and controls which obtained impaired test score was computed for each measure (see Table 2).

As shown in Table 2, PD patients performed poorly in the executive functioning tests, in particular in the WCST (42% of the patients had problems in identifying categories while 32% of them produced a high number of nonperseverative errors) and in the Brixton test (58% of the patients had an abnormal performance). They also experienced problems on the divided attention subtest of the TAP battery (53% of them made an abnormal number of omissions). However, PD patients did not show problems in fluid intelligence (none was impaired in the Raven Colored Progressive Matrices test), short-term memory tests, and verbal long term memory. These results indicate that PD patients have specific problems in executive functioning and in divided attention tests. Moreover, most of our patients (14/19) had no impairment in the verbal fluency test, which is a sensitive task for assessing cognitive dysfunction in PD. In fact, there is evidence that, unlike demented patients, nondemented PD patients can have intact verbal fluency abilities (e.g., Piatt, Fields, Paolo, Koller, & Troster, 1999; Signorini & Volpato, 2006).

Finally, group comparisons, carried out with t tests, confirmed PD patients’ poor performance in executive functioning, showing that PD patients obtained a poorer performance than control participants in the WCST (WCST categories, PD: M = 3.3, control: M = 5.3, p < .01; WCST errors, PD: M = 48.2, control: M = 30, p < .05), in the Brixton test (PD: M = 26.2, control: M = 18.8, p < .01), and marginally in the Trail test (PD: M = 19.1, control: M = 24.3, p < .10), in the Trail Making A (PD: M = 60.7, control: M = 41.2, p < .10), and in the Trail Making B (PD: M = 185.7, control: M = 139.5, p < .10).

Research Design, Procedure, and Stimuli

The research followed a 2 × 2 × 2 mixed design, with a grouping variable (PD patients vs. healthy control participants) and two repeated-measures variables: type of encoding (weak/strong associative encoding) and part-list cuing (part-list/no part-list). Figure 1 gives a diagrammatic representation of the research design and of the procedure. The procedure, similar to the ones used by Bäuml and Aslan (2006) and Aslan and Bäuml (2007) and identical to the one used by Crescentini et al. (2010), comprised alternating sequences of encoding and retrieval phases. Each sequence involved a different list of word-pair items. More specifically, in each sequence there was an initial central fixation block (rest period), an encoding phase (with two study blocks), a first distracter task, a consolidation phase (or rest phase depending on encoding condition, see below), a second distracter task and central fixation block, and finally the Critical Test phase (with two retrieval blocks).

In the encoding phase of each sequence participants were presented twice (one for each study block) with the same list of 16 category-associate word pairs (e.g., Fruit-Apple) belonging to two different semantic categories (eight items for each category). Each word pair was presented for 3,000 ms and was followed by a blank screen for 500 ms. Half of the sequences consisted of strong encoding conditions; here the presentation order in the first and the second study block was identical and blocked by category. Moreover, in order to facilitate further associative encoding in these conditions, a consolidation phase followed the two study blocks (and a first distracter task, see below and Figure 1). In the consolidation phase participants were tested on all the 16 items they had

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1 On the visual task, a series of 10 × 10 cm matrices are displayed on the screen, each for 2 seconds. A matrix consists of a regular array of 16 dots (4 × 4) with seven little “X”s superimposed randomly over them. The subject has to press a key whenever four “X”s form a square. On the acoustic task, the subject listens to a continuous series of high (2000 Hz) and low (1000 Hz) sounds (Di-Da-Di-Da, etc.) and has to detect a variation in the sequence (e.g., Di-Di or Da-Da). Fifteen visual and 15 acoustic targets are given together with 85 visual and 185 acoustic nontargets. RT and number of omissions are taken as measures of subject’s performance.

2 A 3 × 3 cm square appears alone in the middle of the screen. Two patterned squares serve as target stimuli and three as nontarget stimuli. The subject has to press the button on occurrence of a target and not press it on presentation of nontargets. A total of 60 trials (24 targets and 36 nontargets) are given. The main dependent variables are RT for correct responses and number of false responses.
learned. In this test, the category name and the first letter of the to-be-recalled item were presented on the screen (e.g., “Fruit-A”). The stimulus presentation rate and presentation order were the same as those used during the encoding phase. The participants were asked to overtly recall the category exemplars (e.g., Apple in the example).

The other half of the sequences involved the weak encoding conditions; here a passive fixation block (rest period) of 56 s replaced the consolidation phase. Moreover, in these conditions, the word pairs were presented in random order (i.e., not category-blocked) and the order of presentation was different in the first and second study block. As mentioned in the Introduction, according to

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**Table 2**

Descriptive Statistics for Neuropsychological Variables and Percentage of PD Patients (N = 19) and Healthy Older Controls (N = 14) Impaired on Each of Them

<table>
<thead>
<tr>
<th>Variable</th>
<th>PD patients (N = 19)</th>
<th>Control group (N = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Range</td>
</tr>
<tr>
<td>Raven Coloured Progressive Matrices</td>
<td>28.3 (3.8)</td>
<td>22–35</td>
</tr>
<tr>
<td>Forward digit span</td>
<td>5.4 (0.6)</td>
<td>4–6</td>
</tr>
<tr>
<td>Backward digit span</td>
<td>4.3 (0.6)</td>
<td>3–5</td>
</tr>
<tr>
<td>RAVLT immediate recall</td>
<td>40.2 (8.5)</td>
<td>28–56</td>
</tr>
<tr>
<td>RAVLT delay recall</td>
<td>9.2 (2.9)</td>
<td>5–15</td>
</tr>
<tr>
<td>Letter Fluency (FAS)</td>
<td>34.2 (15.8)</td>
<td>17–78</td>
</tr>
<tr>
<td>Stroop CW</td>
<td>19.1 (8.8)</td>
<td>7–36</td>
</tr>
<tr>
<td>TMT-A</td>
<td>60.7 (39.6)</td>
<td>25–196</td>
</tr>
<tr>
<td>TMT-B</td>
<td>185.7 (89.6)</td>
<td>52–340</td>
</tr>
<tr>
<td>WCST-n categories</td>
<td>3.3 (1.9)</td>
<td>0–6</td>
</tr>
<tr>
<td>WCST-n errors</td>
<td>48.2 (23.9)</td>
<td>7–74</td>
</tr>
<tr>
<td>WCST-n perseverative errors</td>
<td>30.4 (17.2)</td>
<td>3–54</td>
</tr>
<tr>
<td>WCST-n non perseverative errors</td>
<td>17.8 (10.1)</td>
<td>2–34</td>
</tr>
<tr>
<td>Brixton</td>
<td>26.2 (7.3)</td>
<td>17–42</td>
</tr>
<tr>
<td>Go/No-Go RT</td>
<td>580 (80)</td>
<td>456–772</td>
</tr>
<tr>
<td>Go/No-Go False reactions</td>
<td>1.5 (2.1)</td>
<td>0–9</td>
</tr>
<tr>
<td>Divided Attention RT</td>
<td>761 (170)</td>
<td>578–1289</td>
</tr>
<tr>
<td>Divided Attention Omissions</td>
<td>6.7 (6.5)</td>
<td>0–21</td>
</tr>
</tbody>
</table>

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**Figure 1.** Research design. The timing of the succession of events is reported. The first study block, the second study block, and consolidation/rest denote the conditions as weak or strong encoding. The Critical Test denotes the conditions as Part-list or No Part-list. In the study blocks stimulus presentation consists of category-associate word pairs (e.g., Fruit-Apple). In each of the two Critical Test blocks of a condition, Category refers to the category name included in the learned list of words (e.g., Fruit), Part-list cues (four are presented in each Critical Test of the Part-list conditions) refer to studied cued words (e.g., Apple); while the initial-letter probes arranged vertically below the Part-list cues (or the filler Xs in No Part-list conditions) prompt the recall of targets. Time is expressed in msec.
previous research, strong encoding (but not weak encoding) should allow the development of strong interitem chainlike associations, in which one item would serve as retrieval cue for the next item in the list (see Bäuml & Aslan, 2006; Crescentini et al., 2010). After the encoding and consolidation/rest phases, subjects engaged in a 15 s block of distractor task, followed by 15 s of passive central fixation (rest period). As for the first block of distractor task, during this second block participants had to count backward in step of three from a 3-digit number.

Finally, participants performed a retrieval phase. This involved two Critical Test blocks (see Figure 1), in which participants were asked to carry out a category-plus-initial-letter-cued-recall test. In each of the two blocks the recall of some associates (target items) belonging to one of the two learned categories was tested. In half of the sequences, the recall of target items occurred in the presence of part-list cue items (part-list cuing conditions; see Figure 1). In these conditions the name of the category was presented at the top of the screen (e.g., Fruit) and half of the studied items from this category were presented in a row below the category name (e.g., raspberry, melon, strawberry, orange). These were the part-list cues. In addition, the first letters of the remaining four target items of the relevant category (initial-letter probes) were presented vertically below the part-list cues and in random order relative to their initial presentation (see Figure 1). Both PD patients and older controls were instructed to read the part-list cues first, and then to overtly produce the four target items in whichever order they wanted.

In the other half of sequences, target recall was tested in the absence of part-list cue items. In the no part-list conditions the name of the category was still presented at the top of the screen (e.g., Insects), but the part-list cue items were replaced with a series of filler Xs (i.e., “xxx-xxx-xxx-xxx”). Irrespective of retrieval condition (part-list or no part-list), the maximum duration allowed for each Critical Test block was 17 s.

Overall, the experiment involved four types of sequences. These were: (a) part-list/strong encoding, (b) no part-list/strong encoding, (c) part-list/weak encoding, and (d) no part-list/weak encoding. Each sequence-type was repeated twice over the entire experiment. The order of the different sequence-types was fixed: no part-list/strong encoding; part-list/weak encoding; part-list/strong encoding; no part-list/weak encoding; part-list/weak encoding; no part-list/weak encoding; part-list/strong encoding.

Before the eight experimental sequences participants practiced the tasks for approximately five minutes. Subjects were presented with two lists of eight category-associate word-pairs using a procedure similar to that described above. The semantic categories employed during practice (i.e., Condimenti—substances for flavoring foods- and Nazioni -countries-) were different from those used in the experimental sequences. Examples of strong/weak encoding phases and part-list/no part-list Critical Test retrieval conditions were included in the practice session.

The stimulus set consisted of 128 words belonging to 16 different semantic categories (eight words per category). All words were selected on the basis of the category norms provided by Van Overschelde, Rawson, and Dunlosky (2004). Half the items (i.e., four) of each category served as cue items (i.e., they could be presented as part-list cues in the Critical Test; see Figure 1) while items in the second half were used as target items only (the retrieval of which was tested in the Critical Test). Thus, in total the experiment consisted of 64 part-list cue items and 64 target items. The division of stimuli into part-list cues and targets was unknown to the volunteers. Appendix 1 reports the semantic categories used.

Participants were tested individually in a silent room. They received written instructions explaining the tasks they were required to perform. The duration of the experimental session was about of 40 minutes. All participants were tested using a notebook ACER 1100 and stimulus presentation was controlled using the E-prime software (Psychology Software Tools, Inc.). Participants’ responses in the Critical Test blocks were recorded as .wav files. The responses were transcribed and checked for accuracy by the first author.

Data Analysis

Following previous studies, the main analyses concerned the proportion of correct responses in the retrieval phase of the experiment, namely the accuracy of target recall observed in the Critical Test blocks. Accuracy data was analyzed via mixed analysis of variance (ANOVA) and pairwise comparisons, according to the experimental design. The within-subject variables were the type of encoding (i.e., retrieval following weak/strong associative encoding) and part-list cuing (part-list/no part-list), while the between-subjects (grouping) variable was the group membership (PD patients vs. older controls). The standard alpha level of .05 was used. Parametric analyses were performed, given that the accuracy data did not violate assumptions of normality (all Shapiro-Wilks tests led to p > .1). Further analyses were also carried out on error type profiles across groups and to assess the relationship between cognitive measures and memory performance (including the size of the part-list cuing effect) in the different experimental conditions.

Results

Target Recall

We will initially focus on the accuracy of target recall (proportion of correct responses) observed during the Critical Test blocks of the retrieval phase of the experiment (see Figure 2). A 2 × 2 × 2 mixed ANOVA was carried out involving type of encoding (weak/strong), part-list cuing (part-list/no part-list), and group membership (PD patients/older controls).

The ANOVA showed the significant main effects of encoding \( F(1, 33) = 7.56, MSE = .01, p < .01, \eta^2 = .18 \) and part-list cuing \( F(1, 33) = 45.31, MSE = .01, p < .001, \eta^2 = .58 \), and a marginally significant main effect of group membership \( F(1, 33) = 3.66, MSE = .05, p < .10, \eta^2 = .10 \). The main effects indicated respectively that target recall was better after strong encoding; no part-list/weak encoding; part-list/weak encoding; no part-list/weak encoding; no part-list/weak encoding; part-list/strong encoding.

\footnote{In the present study, the participants could retrieve the target items in a free order after the presentation of all the initial-letter (itemspecific) cues. Aslan and Bauml (2007) forced instead participants to follow a fixed (but random) retrieval order, presenting each initial-letter probe for a maximum of 6 seconds. Due to this procedural difference, applying a retrieval strategy based on the encoding serial order is comparatively easier with our procedure, although it appears to be a rather demanding task in absolute terms.}
associative encoding than weak encoding (strong encoding \(M = 64\%\); weak encoding \(M = 59\%\)), that it was better in the control conditions than in the part-list cuing conditions (no part-list \(M = 68\%\); part-list \(M = 55\%\)), and that it was marginally better in healthy controls than in PD patients (healthy controls \(M = 65\%\); PD patients \(M = 58\%\)).

The ANOVA also showed two significant two-way interactions between type of encoding and group membership \((F(1,33) = 8.36, MSE = .01, p < .01, \eta^2 = .20)\) and between part-list cuing condition and group membership \((F(1,33) = 4.50, MSE = .01, p < .05, \eta^2 = .12)\), while the interaction between type of encoding and part-list cuing was not significant \((F(1,33) = 0.01, MSE = .01, p = .95)\). Moreover, there was also a marginally significant three-way interaction \((F(1,33) = 3.49, MSE = .01; p < .10; \eta^2 = .10)\). Of major importance, pairwise comparisons for the three-way interaction showed that PD patients and older controls differed only in the strong encoding/part-list cuing condition \((F(1,33) = 13.24, MSE = .01, p < .01)\), but not in the other conditions (in all cases \(p > .10\)).

Pairwise comparisons also showed significant part-list cuing effects in PD patients both after weak and after strong associative encoding \((F(1,33) = 9.60, MSE = .02, p < .01)\) and \((F(1,33) = 38.25, MSE = .01, p < .001\), respectively), with target recall in part-list cuing conditions being worse than target recall in the corresponding no part-list cuing conditions. Older controls showed instead a significant part-list cuing effect only after weak associative encoding \((F(1,33) = 7.68, MSE = .02, p < .01)\) but not after strong encoding \((F(1,33) = 1.73, MSE = .20, p = .19)\).

The significant two ways interactions agree with the observation that part-list cuing effects were found in PD patients in any encoding condition, while a part-list cuing effect was observed only after weak associative encoding in older healthy controls. In fact, pairwise comparisons for the interaction between part-list cuing condition and group membership showed that PD patients were worse than older controls in recalling targets in the presence of part-list cues \((F(1,33) = 5.37, MSE = .04, p < .05)\) but not in their absence \((F(1,33) = 0.81, MSE = .02, p = .37)\). Moreover, pairwise comparisons for the interaction between type of encoding and group membership, showed that the patients recalled significantly fewer target items than older controls after strong associative encoding \((F(1,33) = 9.43, MSE = .03, p < .01)\) but not after weak associative encoding \((F(1,33) = 0.11, MSE = .03, p = .74)\).

**Error Type Profiles**

Most of the errors made by both PD patients and older controls in the Critical Test blocks of the retrieval phase were missed responses (omissions). The other type of error (intrusion) was made when participants produced a word that, although being an exemplar of the currently tested category, was not part of the learned list (extralist item). The two groups significantly differed in the absolute number of omissions errors, \(t(1,33) = 2.33, p < .05\); PD patients: \(M = 22.58\); healthy controls: \(M = 16.68\), but not in the absolute number of intrusion errors, \(t(1,33) = -1.53, p = .13\); PD patients: \(M = 4.16\); healthy controls: \(M = 5.56\). However, the two groups did not differ significantly in the proportion of omission (or intrusion) errors \((z = .64, p = .51); PD patients’ omissions: 84%; healthy controls’ omissions: 75\%\).

**Correlations With Clinical Variables, Cognitive Variables, and Executive Functioning**

We initially tested for possible correlations between clinical status of PD patients and memory performance in each experimental condition. We found no significant correlation between target recall and scores obtained in the BDI, UPDRS, and Hoehn and Yahr’s scale. Age and years of illness were also not significantly correlated with memory performance. PD patients’ scores on the MMSE test were positively correlated with target recall only in the part-list cuing condition after weak encoding \((r = .55, p < .05)\). These results were replicated using as dependent variables the size of the part-list cuing effect (i.e., the difference between retrieval performance in the no part-list cuing and part-list cuing conditions). Thus, the only significant correlation between part-list cuing effects and clinical variables was a negative correlation between MMSE scores and part-list cuing after weak encoding \((r = -.53, p < .05)\), indicating a stronger part-list cuing effect in participants with lower MMSE scores. Moreover, there was a marginally significant negative correlation between the dosage of \(\alpha\)-dopa taken by each patient and target recall after weak encoding \((r = -.43, p < .10)\), indicating worse target recall in patients with a higher dosage of \(\alpha\)-dopa.

The Digit Span Forward did not correlate significantly with retrieval performance or the size of the part-list cuing effect in any condition both in PD patients and in healthy controls. Similar results were obtained for the divided attention measures. In PD patients, the Digit Span Backward showed a positive correlation with target recall after weak encoding \((r = .55, p < .05)\), while positive correlations in healthy controls were found between Digit Span Backward and target recall after strong encoding (no part-list cuing: \(r = .62, p < .05\); part-list cuing: \(r = .56, p < .05\)). However, Digit Span Backward did not correlate significantly with the size of the part-list cuing effect in any encoding condition, both in PD patients and in healthy controls.

In order to appraise the relationship between episodic retrieval and measures of executive control, we computed a compound measure of executive functioning by principal component analysis (PCA) applied on the entire sample of participants. This compound
measure was derived by those indicators of executive functioning that showed stronger bivariate correlations (Letter Fluency, Brixton, Stroop, Trail Making B, WCST categories). PCA showed that a solution with a single underlying dimension was the most appropriate, capturing over 62% of the variance (this dimension had an eigenvalue of 3.1 and factor loadings for executive tests were always > .60, while the eigenvalues of additional dimensions were lower than 1). An independent sample t test showed that PD patients’ factor scores (higher scores indicating better executive functioning) were significantly lower than healthy participants’ factor scores (p < .05).

We correlated the compound executive functioning scores with episodic retrieval performance both in PD patients and in healthy controls. In PD patients, the correlations between the executive functioning measure and target recall were positive and significant in both part-list cuing conditions (weak encoding: r = .66, p < .01; strong encoding: r = .71, p < .01), and in the no-part-list cuing condition after strong encoding (r = .57, p < .05). The size of the part-list cuing effect was also negatively and significantly correlated with the executive functioning measure after weak encoding (r = -.46, p < .05). Turning to specific executive functioning tests, Letter Fluency and Trail Making B were significantly correlated with the size of the part-list cuing effect after weak encoding (r = -.50, p < .05 and r = .47, p < .05, respectively). In healthy controls, target recall was positively correlated with the executive functioning measure only after strong encoding (part-list cuing: r = .57, p < .05; no-part-list cuing: r = .59, p < .05). However, in both encoding conditions, the size of the part-list cuing effect was not significantly correlated with the compound measure or with specific tests of executive functioning.

Finally, considering the problems in executive functioning shown by PD patients, we carried out an Analysis of Covariance (ANCOVA) to understand whether the part-list cuing effects observed in PD patients were still significant after individual differences in the effectiveness of executive functioning had been taken into account. Two ANCOVAs, carried out separately for the two encoding conditions, confirmed the main effect of part-list cuing after weak encoding (F(1, 17) = 7.96, MSE = 0.01, p < .05, \( \eta^2 = .32 \)) and after strong encoding (F(1, 17) = 31.75, MSE = 0.01, p < .0001, \( \eta^2 = .65 \)), despite the significant effect of the covariate both after weak encoding (F(1, 17) = 11.72, MSE = 0.03, p < .01, \( \eta^2 = .41 \)) and after strong encoding (F(1, 17) = 19.11, MSE = 0.02, p < .001, \( \eta^2 = .53 \)).

**Discussion**

The main goal of the study described in this paper was to investigate interference from retrieval cues in PD patients. With this aim, we used a part-list cuing paradigm, because it allows one to examine cue-related interference stemming from different sources (e.g., retrieval inhibition and strategy disruption). Accordingly, we tested memory for target items in the presence or absence of part-list cues following either weak or strong associative encoding and always using initial-letter probes. A second goal of the study was to understand whether there is a relation between the capacity to handle interference from retrieval cues and individual differences in executive functioning in PD patients, following the hypothesis that the capacity to overcome interference from part-list cues depends, at least in part, by the effectiveness of executive control processes.

The main finding of the study was that PD patients were impaired in only one of the four conditions, namely part-list cuing after strong encoding. In this condition, there was a large impairment (over 20%), while in the other three conditions the difference between PD patients and controls was less than 5%. The poor performance of the PD patients in this specific condition meant that they showed a significant part-list cuing effect after strong encoding. This was different from what observed in the older controls, who performed at similar levels in the two conditions with strong encoding (part-list cuing and no-part-list cuing). As far as target recall after weak encoding is concerned, we found that both groups of participants showed a significant and similar part-list cuing effect. Furthermore, in both groups of participants, missed responses were more frequent than intrusion errors and PD patients did not make a greater proportion of intrusion errors than healthy participants.

The present study also showed a positive relation between target recall and executive functioning. PD patients with better executive control generally achieved better results in retrieving target words. More critically, PD patients with better executive control had a smaller part-list cuing effect after weak encoding. However, the significant part-list cuing effects in PD patients were also found when individual differences in executive functioning were taken into account. Thus, our findings show the robustness of the part-list cuing effect in PD patients, but also indicate that effective executive control processes can moderate the size of the part-list cuing effect, at least in some conditions (weak encoding conditions).

In the next section we will focus on the results observed in PD patients. First, we will provide an account for the part-list cuing effect found after strong associative encoding. Next, we will discuss the part-list cuing effect observed after weak associative encoding. Then, we will consider the correlations between executive functioning, retrieval performance, and the part-list cuing effect. In the following section, we will focus on the implications that the findings on healthy older participants have in relation to part-list cuing. We will conclude by discussing some general theoretical implications of the present study, also providing some suggestions for further investigations on episodic memory in PD.

As explained in the hypothesis section, we predicted that PD patients would be specifically hindered by the part-list cues after strong associative encoding (H3). This was based on the argument derived from previous research (Buytenhuijs et al., 1994; Van Spaendonck et al., 1996) that these patients would find it particularly difficult to apply retrieval strategies flexibly when part-list cues are presented, due to their tendency to rely on external retrieval cues. As a consequence, we expected that these participants would have experienced more difficulty after strong encoding when part-list cues were presented. Our findings confirm this prediction, showing a specific negative influence of part-list cues in PD patients (but not in older controls) after strong associative encoding. In other words, these results show that the presentation of part-list cues has a specifically disruptive effect in PD patients when the encoding condition promotes the development of an effective serial retrieval strategy.

The disturbing effect of part-list cues after strong associative encoding can be explained by assuming that PD patients may find
it hard to flexibly apply the developed retrieval strategy when cues provided at retrieval are not compatible with it. A less effective strategic encoding could have exacerbated PD patients’ retrieval problems, as suggested by the observation that these participants were less able to benefit from strong associative encoding than healthy older participants. Indeed, in no part-list cuing conditions no significant difference was found in the accuracy of recall between weak and strong encoding in PD patients, \( r(18) = -0.97, p = .17, \) one-tailed test; \( M = .68 \) after strong encoding and \( M = .65 \) after weak encoding. By contrast, a significant decrement was found after weak encoding compared with strong encoding in the no part-list cuing conditions in healthy participants, \( t(15) = -1.86, p < .05, \) one-tailed test; \( M = .73 \) after strong encoding and \( M = .66 \) after weak encoding. However, it is important to point out that part-list cuing after strong associative encoding in PD patients cannot be explained only by referring to less effective strategic encoding processes, given that the presentation of cues at retrieval had a strong negative effect that was not observed when the cues were not presented.

The specific interference from part-list cues shown by PD patients after strong encoding is compatible with the findings of two lines of research: studies relating PD patients’ difficulties in episodic memory with problems in strategic encoding and retrieval, and research that explained part-list cuing effects in terms of strategy disruption. In an fMRI study, Crescentini et al. (2010) were able to identify the neural correlates of the development of a retrieval strategy during strong associative encoding (and of its application at retrieval). The left precentral gyrus was active during encoding, together with additional areas in the left prefrontal cortex, which are generally associated with semantic encoding (see Fletcher, Shallice, & Dolan, 1998). The left precentral gyrus was also more active when subjects attempt to recall targets after strong (vs. weak) encoding, and the activation of this brain region correlated with accuracy of target recall. These findings were interpreted as evidence for the development and application of an effective retrieval strategy based both on semantic organization and phonological rehearsal (see also Kapur et al., 1996). Thus, in the present study, it is likely that PD patients have encountered more difficulties in flexibly applying such a strategy in the presence of incompatible part-list cues and initial-letter probes, and it is also possible that this difficulty has been exacerbated by less effective strategic encoding processes.

Relying on the existing literature on inhibitory processes in PD, we made explicit two alternative hypotheses for the weak associative encoding condition, starting from the assumption that part-list cuing interference in this condition is due to target inhibition (Aslan & Bäuml, 2007; Bäuml & Aslan, 2004, 2006). According to the first hypothesis (H4a), which assumed normal target inhibition in PD patients, a part-list cuing effect after weak encoding was predicted. However, the effect was not predicted in the patients according to the alternative hypothesis (H4b), which assumed that the inhibitory processes underlying part-list cuing are less effective in PD patients. Our results are clearly in agreement with the first hypothesis, given that a part-list cuing effect of similar magnitude was observed in both PD patients and in older controls after weak encoding (13% vs. 12%, respectively). These findings suggest that PD patients and healthy participants are similarly hindered by cue-driven retrieval interference when encoding does not promote the development of an effective serial retrieval strategy. More generally, these results may indicate that the inhibitory processes that underlie the part-list cuing effect in this encoding condition are not significantly altered by the disease.

If one assumes that patients with more effective executive processes are more able to overcome interference from part-list cues, then one would expect a positive correlation between the executive functioning of PD patients and retrieval performance in part-list cuing conditions (H5a), and also a negative correlation between PD patients’ executive functioning effectiveness and the size of the part-list cuing effect (H5b). We observed that a compound measure of executive functioning was positively related to target recall in the two part-list cuing conditions, but also in the strong encoding/no part-list cuing condition. More critically, the size of the part-list cuing effect was negatively correlated with the executive functioning measure after weak encoding. Additionally, ANCOVAs produced a significant effect of individual differences in executive functioning on target recall in any encoding condition. However, part-list cuing effects were still significant after individual differences in executive functioning were controlled. These findings are compatible with our predictions, but they also suggest that part-list cuing in PD is not completely mediated by individual differences in executive functioning. In this respect, it is interesting to note that Bäuml et al. (2002) found that frontal lobe impairments observed in their amnesic patients did not affect the pattern of part-list cuing results and this would point to a more important contribution of the frontal lobes in free than cued recall.

The association between executive functioning effectiveness, target recall, and part-list cuing effect, observed after weak encoding specifically in PD patients, can be explained by assuming that these patients need more cognitive resources than healthy participants to retrieve weakly encoded target items in the presence of interfering cues. This result can be related again to the difficulty of PD patients who present executive control problems in handling interference from external cues during memory retrieval. Interestingly, in the domain of semantic memory, we have recently found, using different executive functioning tests, that the performance of a group of nondemented PD patients was positively correlated with their ability to correctly retrieve target words (i.e., verbs) in the presence of interfering words (i.e., nouns). This effect was especially strong when the target words were weakly related with the noun stimuli (Crescentini et al., 2008).

However, after strong encoding, an association between executive functioning effectiveness and target recall was observed both in PD patients and in healthy controls. This can be explained by assuming that the presence of initial-letter probes always makes the application of a retrieval strategy after strong associative encoding a cognitively demanding task. This is because initial-letter probes, as well as part-list cues, are thought to disrupt retrieval strategies after strong encoding (Aslan & Bäuml, 2007). However, given the executive control problems of our PD patients,

\[ \text{Future studies could examine the part-list cuing effect in PD patients in the absence of item-specific probes, in order to better disentangle the effects of probes and cues. After strong encoding, our findings suggest a small relative influence of item-specific probes in PD versus healthy participants (Figure 2, no part-list cuing conditions, comparison between PD and healthy participants) and a much stronger relative influence of part-list cues (Figure 2, part-list cuing conditions, comparison between PD and healthy participants).} \]
these participants may have found it generally more difficult to flexibly reinstate the retrieval strategies disrupted by initial-letter probes when part-list cues are also present. This would explain the fact that they were less able than healthy participants to overcome the negative influence of part-list cues.

We now turn to the general implications that the findings on healthy older participants have with respects to part-list cuing. Based on previous studies with initial-letter probes (Aslan & Bäuml, 2007; Crescentini et al., 2010), we predicted that in healthy older participants a part-list cuing effect would occur after weak associative encoding (H1) but not after strong encoding (H2). Our findings clearly support H1 and H2, replicating the results of previous studies that employed similar paradigms in younger adults. Moreover, our findings add to the limited number of studies that investigated part-set cuing in older adults, which have usually obtained a detrimental effect of cuing (Del Missier & Terpini, 2009; Marsh, Dolan, Balota, & Roediger, 2004). The significant effect of part-list cuing after weak associative encoding and with initial-letter probes is compatible with the retrieval inhibition explanation of part-list cuing in this condition (see Aslan & Bäuml, 2007). On the other hand, the absence of a part-list cuing effect after strong associative encoding in older adults can be explained, as in previous studies, by the generally disruptive effects of randomly ordered initial-letter probes on retrieval strategies regardless of the presentation of part-list cues (Aslan & Bäuml, 2007).

Thus, our findings on healthy participants agree with previous studies and they are compatible with a dual-mechanism explanation of part-list cuing effects (Aslan & Bäuml, 2007; Bäuml & Aslan, 2006).

We conclude by discussing some more general implications of the present research. First, the study highlighted a specific difficulty of PD patients in overcoming interference from part-list cues, which is likely to be related to PD patients’ difficulties in strategic retrieval and encoding. Besides adding a novel piece of information on interference in PD, the study suggests that interference from part-list cues can be more harmful for PD patients than for healthy adults when it disrupts an effective serial retrieval strategy. This conclusion indicates the need to further investigate the potentially critical link between interference and strategic processes in PD patients’ episodic memory.

The second theoretical implication of the study stems from the observation that PD patients are not impaired when part-list cuing interference is induced after weak associative encoding. Assuming that the part-list cuing effect observed in this condition can be explained by retrieval inhibition, a possible inference is that these inhibitory processes are not significantly affected by the disease. This conclusion contributes to the debate on inhibitory processes in PD, which is characterized by a mixed pattern of results (see Introduction). Considering that various types of inhibitory processes can be differentiated (Bäuml, 2008; see also Friedman & Miyake, 2004 and Nigg, 2000), future work in this area should be devoted to a more systematic assessment of these processes in PD patients, possibly by using multiple variations of basic experimental paradigms and by including inhibition-related individual differences measures.

Another implication of the study relates to applied aspects. We observed that presenting a partial list of retrieval cues harms retrieval in PD patients, regardless the encoding condition. This should to be taken into account by programs and individuals that are working to help PD patients to improve their memory performance. Providing retrieval cues to these patients can indeed have negative effects, and practitioners should pay great attention to the specific cues they are using and to the specific interactions between retrieval cues and the encoding/retrieval strategies that the patients are using. In general, retrieval cues may help memory performance when they are compatible with the encoding and retrieval strategies, when they are distinctive, and when they do not focus attention on a limited subset of items.

A fourth issue concerns patients’ medication. In our study, PD patients were under medication with L-dopa and this may have affected their memory performance. However, only a marginally significant correlation was observed between target recall after weak encoding and dosage of L-dopa. This negative correlation appears to be in line with recent studies showing that dopaminergic medication may sometimes impair cognitive performance, depending on the level of dopamine in underlying cortico-striatal circuits (i.e., performance declines when the level of dopamine is very high; e.g., Cools, Barker, Sahakian, & Robbins, 2003; Moustafa, Sherman, & Frank, 2008). Nonetheless, our patients were mainly at the stage 2 (or 2.5) of severity according to the Hoehn & Yahr scale and, at this stage, severe striatal dopamine dysfunction occurs together with fronto-parietal cortical abnormalities in noradrenergic neurotransmitter systems (for a short review on the progression of PD symptoms see Kehagia, Cools, Barker, & Robbins, 2009). Thus, it is likely that both dopaminergic and nondopaminergic pathologies have contributed to PD patients’ pattern of performance in our episodic memory task. Further investigation of memory functions in PD patients both in the “on” and “off” medication state with L-dopa could help to understand to what extent PD patients’ memory problems have a dopaminergic basis.

The final implication of the present research concerns the inconsistencies often found in the literature with respect to episodic memory in PD patients (see Introduction). In particular, our findings suggest that it is vital to consider the complex interplay between encoding strategies, retrieval strategies, and retrieval cues to gain a better understanding of episodic retrieval in PD patients. In our study, PD patients showed a specific impairment only in the condition in which effortful retrieval strategies, developed at encoding, were disrupted by part-list cues at retrieval. Although our findings are not inconsistent with the idea that PD patients may have specific problems in retrieving information in some conditions (e.g., Dujardin & Laurent, 2003), they also suggest the presence of encoding problems in the patients (e.g., Knoke et al., 1998) and, more importantly, they underline the critical interplay between encoding, retrieval, and the cues made available at retrieval, in line with theoretical models of episodic memory (Baddeley, Eysenck, & Anderson, 2009; Roediger & Guynn, 1996) and dual-mechanism accounts of part-list cuing (Bäuml & Aslan, 2006; Aslan & Bäuml, 2007).

In conclusion, the present study provides a contribution on interference in episodic memory investigating, for the first time, interference from retrieval cues in PD patients, an issue that is interesting both theoretically and practically. The results suggest that PD patients and healthy participants are similarly hindered by cue-driven interference when encoding does not promote the development of an effective serial retrieval strategy. However, when such a strategy can be developed, the presentation of part-list cues has a specifically disruptive effect in PD patients. We explained
these results by making reference to PD patients’ less effective strategic retrieval and strategic encoding processes and to their increased reliance on external cues. Moreover, our findings confirmed the role of executive functioning in episodic retrieval, showing that PD patients with better executive control are more able to overcome part-list cuing interference when an effective serial retrieval strategy is not available and that individuals with better executive control are generally more able to retrieve target items when such a strategy is available.

References


**Appendix 1**

List of Semantic Categories Used in the Study; see also Van Overschelde, Rawson, and Dunlosky (2004)

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1. **Attrezzi** (carpenter’s tools)
2. **Liquidi** (liquids)
3. **Bevande** (alcoholic beverages)
4. **Pietre** (precious stones)
5. **Professioni** (occupations or professions)
6. **Metalli** (metals)
7. **Veicoli** (transportation vehicles)
8. **Lettura** (type of reading materials)
9. **Specie** (herbs)
10. **Elementi** (chemical elements)
11. **Tessuti** (types of fabric)
12. **Uccelli** (birds)
13. **Mobilia** (articles of furniture)
14. **Insetti** (insects)
15. **Frutta** (fruits)
16. **Armi** (weapons)

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Received November 5, 2010
Revision received March 29, 2011
Accepted June 6, 2011