The Influence of Dopamine on Semantic Activation in Parkinson’s Disease:
Evidence From a Multipriming Task

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Research has suggested that semantic processing deficits in Parkinson’s disease (PD) are related to striatal dopamine deficiency. As an investigation of the influence of dopamine on semantic activation in PD, 7 participants with PD performed a lexical-decision task when on and off levodopa medication. Seven healthy controls matched to the participants with PD in terms of sex, age, and education also participated in the study. By use of a multipriming paradigm, whereby 2 prime words were presented prior to the target word, semantic priming effects were measured across stimulus onset asynchronies (SOAs) of 250 ms and 1,200 ms. The results revealed a similar pattern of priming across SOAs for the control group and the PD participants on medication. In contrast, within-group comparisons revealed that automatic semantic activation was compromised in PD participants when off medication. The implications of these results for the neuromodulatory influence of dopamine on semantic processing in PD are discussed.

Keywords: dopamine, levodopa, Parkinson’s disease, semantic priming, signal-to-noise ratio

Parkinson’s disease (PD) is a neurodegenerative condition characterized by degeneration of the nigrostriatal dopaminergic system (Mink, 1996). Although the most recognized clinical manifestations of the disease are motor symptoms such as tremor, rigidity, and bradykinesia, various cognitive deficits are also frequently identified. For instance, adults with PD typically perform more poorly than healthy adults on tests of planning, working memory, attention set shifting, visuospatial function, and verbal fluency (e.g., Azuma, Cruz, Bayles, Tomoeda, & Montgomery, 2003; Green et al., 2002; Mohr et al., 1990; Owen et al., 1992). Such cognitive deficits are not unexpected, as dopaminergic neurons may play a key role in regulating cognitive function (Nieuflon, 2002). Hence, in addition to its role as a neurotransmitter, dopamine’s neuromodulatory influence is also well recognized.

Servan-Schreiber, Printz, and Cohen (1990) proposed that the function of dopaminergic modulating systems is to amplify stronger signals while dampening weaker signals in neural areas. Furthermore, Cepeda and Levine (1998) suggested that dopamine is capable of increasing the signal-to-noise ratio (SNR) in the neostriatum by integrating relevant information and screening out less relevant information. We find it interesting that measures of semantic priming have illustrated that dopamine may also exert a neuromodulatory influence on the SNR of language processing.

Semantic priming refers to the faster recognition of a target word when it is preceded by a semantically related word (i.e., the prime) compared with an unrelated word, and it is typically attributed to either an automatic spreading of activation within semantic networks or controlled processes such as expectancy generation or postlexical semantic checking (Neely, 1991). By varying the amount of time between presentation of the prime and the target (i.e., the stimulus onset asynchrony or SOA), it is possible for one to examine the process of semantic activation over time. Using measures of both direct (e.g., tiger stripes) and indirect (e.g., lion stripes) semantic priming, Kischka et al. (1996) examined the influence of dopamine on semantic activation by administering either a levodopa or placebo capsule to healthy young adults. The results revealed reduced indirect semantic priming in the participants who ingested levodopa, which was attributed to an increased SNR in semantic networks for these participants. In contrast, similar research by Angwin, Chenery, Copland, Arnott, et al. (2004) indicated an earlier onset and decay of semantic activation in participants who had ingested levodopa, suggesting that the time course of semantic processing may also be influenced by dopamine. Accordingly, it may be expected that striatal dopamine deficiency in PD will lead to a reduced SNR in semantic networks and/or delays in semantic activation.

Certainly, a number of studies have illustrated a delayed time course of semantic activation in some participants with PD (e.g., Angwin, Chenery, Copland, Murdoch, & Silburn, 2004; Arnott, Chenery, Murdoch, & Silburn, 2001; Grossman et al., 2002). In contrast, the potential influence of a reduced SNR on semantic processing in PD has been less well defined, possibly because the methodologies typically used to assess semantic activation in PD to date (as in the priming studies identified above) have been...
primarily insensitive to such changes in information processing. Hence, a divergence from traditional priming paradigms may be necessary for the nature and extent of change to semantic processing in PD to be more precisely defined.

The use of a multipriming paradigm, such as that implemented by Balota and Paul (1996), may prove to be a useful measure of such changes in PD. This paradigm differs from standard semantic priming tasks by presenting two prime words before the target. Consequently, although standard priming effects can be measured from one related prime that directly precedes the target (e.g., soup stripe TIGER), semantic priming effects can also be measured in conditions that are not available in traditional single-prime lexical-decision tasks. Specifically, priming effects can also be measured when only the first prime word is related to the target (e.g., lion chair TIGER), allowing researchers to assess whether semantic priming effects persist across an intervening unrelated word. Researchers may also assess whether a summation of activation occurs, such that the use of two related prime words (e.g., lion stripe TIGER) yields larger priming effects than the single related prime conditions.

Recently, we used the multipriming paradigm to investigate semantic activation in PD (Angwin, Chenery, Copland, Murdoch, & Silburn, 2003). The results revealed that the time course of automatic semantic activation appeared to be intact in PD, as evidenced by significant priming effects at a short SOA when both prime words or the second prime word were related to the target. In contrast, however, no priming effects were evident when only the first prime word was related to the target. Consistent with the potential neuromodulatory influence of dopamine deficiency on information processing, we suggested that the SNR of semantic processing was reduced in PD. More specifically, we suggested that because of a reduction in the salience of a related prime word (i.e., the signal), or an increase in the salience of an unrelated prime word (i.e., the noise), semantic priming effects may be disrupted when an unrelated word is presented between the related prime and the target.

Research also suggests, however, that PD participants experience difficulties attending to relevant information and ignoring irrelevant information (Levin, Llabre, & Weiner, 1989). Moreover, using a semantic priming task and a long SOA, Copland (2003) demonstrated that although priming was evident only for the dominant meaning of ambiguous words in healthy adults, priming effects were significant for both subordinate and dominant meanings of ambiguous words in PD participants. These results suggest that controlled semantic inhibitory processes may be impaired in PD. Similarly, such difficulties may also extend to automatic semantic processing in PD, such that spreading activation cannot be constrained to the related prime word in a multipriming task when an unrelated word directly precedes the target. More precisely, whereas healthy adults may inhibit any disruptive influence of an intervening unrelated word on semantic activation, reduced inhibition of this unrelated prime in PD might lead to a disruption in semantic activation. Hence, a reduced SNR and/or reduced semantic inhibition may have contributed to the semantic priming deficits we observed in PD (Angwin et al., 2003).

Nonetheless, it is difficult to attribute these deficits directly to dopamine depletion, as participants were tested only while optimally medicated with levodopa. As illustrated by Grossman et al. (2001), a more effective strategy for establishing the role of dopamine on language processing may be to test the same PD participants when on and off levodopa medication. Unfortunately, few studies have used such within-group comparisons to investigate the neurochemical basis for language processing deficits in PD, with fewer still analyzing semantic priming effects. Arnott, Chenery, Murdoch, and Silburn (2000) and Murdoch, Arnott, Chenery, and Silburn (2000) compared semantic priming in PD participants when on and off levodopa and revealed a significant negative priming effect for PD participants off medication. Murdoch et al. (2000) also observed a significant reduction in facilitation effects (i.e., faster lexical decisions to a target word when preceded by a related, as opposed to a neutral, prime word) for PD participants off medication. The results of both studies were attributed to a reduction in dopamine during medication withdrawal in PD. Although these results supported the tenet that dopamine has a neuromodulatory influence on semantic activation, additional research may clarify the precise mechanisms underlying dopaminergic alterations to semantic processing.

The aims of the present study were based on proposals that dopamine depletion may compromise semantic activation in PD. Specifically, this research aimed to examine semantic activation across time in PD participants (both on and off levodopa medication) and healthy controls using a multipriming paradigm and two SOAs (250 ms and 1,200 ms). We predicted that a disruption to semantic activation would be observed for participants with PD, as evidenced by a delayed time course of semantic activation when both prime words or the second prime word were related to the target, and an absence of semantic priming when only the first word was related to the target. Further, we also predicted that disruptions to semantic priming would be more evident for PD participants when off, compared with on, medication.

Method

Participants

We have previously reported the results of a multipriming task whereby semantic priming effects were measured across three SOAs in 20 participants with PD (Angwin, Chenery, Copland, Murdoch, & Silburn, 2005). In that study, all participants received the three lexical-decision experiments in the same order (i.e., SOA 1–3), with each experiment completed during a different testing session held at least 2 weeks apart. For the purposes of the present study, a subset of these PD participants agreed to perform the same multipriming task at two SOAs while off their dopaminergic medication. This PD group was composed of 7 participants diagnosed with idiopathic PD (4 men, 3 women; mean age = 64.14 years, SD = 6.77; mean education = 13.14 years, SD = 2.54), and data obtained from these participants while off medication were compared with the data collected previously from these participants while on medication. The data obtained from 7 matched nonneurologically impaired, healthy participants (4 men, 3 women; mean age = 63.86 years, SD = 2.54; mean education = 12.43 years, SD = 2.99) who also participated in the previous research (Angwin et al., 2005) were selected to provide control data in the present study. The mean age and education of the two groups was not significantly different (p = .607 and p = .605, respectively). All participants were right-handed, native speakers of English with no history of neurological surgery, drug or alcohol abuse, or dementia and were not taking any antidepressive or anticholinergic medications. Prior to the commencement of testing, the cognitive status of the participants was assessed with the Dementia Rating Scale-2 (DRS-2; Jurica, Leitzen, & Mattis, 2001), with a mean score of 139.71 (SD = 2.36) for the PD group and 143.00 (SD = 1.41) for the control group. Although the mean DRS-2 score for the PD group was
significantly lower than that for the control group, *t*(12) = −3.16, *p* = .008, all scores were above the recommended lower boundary for normal performance.

The PD group had a mean disease duration of 3.71 years (SD = 1.89) and a mean age at onset of 60.57 years (SD = 7.28). We used Hoehn and Yahr (1967) scores to classify the disease severity of the PD participants, with a mean score of 2.07 (SD = 0.45). Predominant symptoms were tremor for 6 participants and bradykinesia/rigidity for 1 participant. In addition, symptoms were predominantly left sided for 2, right sided for 3, and bilateral for 2 participants. All participants were taking levodopa in the form of either Madopar or Sinemet, and 4 participants were also taking cabergoline (Cabaser). The average daily dosage for levodopa was 339.29 mg (SD = 107.87), and the average daily dosage for cabergoline was 2.5 mg (SD = 1.75). Five of the PD participants also experienced a predictable “wearing off” effect associated with their levodopa medication, such that motor symptoms typically increased approximately 3–4 hr after dosage. With respect to our previous study of multipriming in 20 participants with PD (Angwin et al., 2005), it should be noted that the average age of onset, disease duration, Hoehn and Yahr score, and DRSS–2 score of this 20-participant sample did not differ significantly from the data of the 7 participants who were tested off medication for the purposes of the present study (*p* = .703, *p* = .386, *p* = .988, and *p* = .630, respectively). In contrast, the average daily dosage of medication for participants taking levodopa in the original sample of 20 participants (*M* = 606.94, SD = 360.33) was larger compared with the 7 participants who were tested off medication for the present study (*p* = .009, equal variances not assumed).

The experimental tasks in the present study were administered to participants as a subcomponent of a larger battery of tests. PD participants were tested at their homes in both an on and an off medication state. The participants as a subcomponent of a larger battery of tests. PD participants with a mean score of 2.07 (SD = 0.45). Predominant symptoms were tremor for 6 participants and bradykinesia/rigidity for 1 participant. In addition, symptoms were predominantly left sided for 2, right sided for 3, and bilateral for 2 participants. All participants were taking levodopa in the form of either Madopar or Sinemet, and 4 participants were also taking cabergoline (Cabaser). The average daily dosage for levodopa was 339.29 mg (SD = 107.87), and the average daily dosage for cabergoline was 2.5 mg (SD = 1.75). Five of the PD participants also experienced a predictable “wearing off” effect associated with their levodopa medication, such that motor symptoms typically increased approximately 3–4 hr after dosage. With respect to our previous study of multipriming in 20 participants with PD (Angwin et al., 2005), it should be noted that the average age of onset, disease duration, Hoehn and Yahr score, and DRSS–2 score of this 20-participant sample did not differ significantly from the data of the 7 participants who were tested off medication for the purposes of the present study (*p* = .703, *p* = .386, *p* = .988, and *p* = .630, respectively). In contrast, the average daily dosage of medication for participants taking levodopa in the original sample of 20 participants (*M* = 606.94, SD = 360.33) was larger compared with the 7 participants who were tested off medication for the present study (*p* = .009, equal variances not assumed).

The experimental tasks in the present study were administered to participants as a subcomponent of a larger battery of tests. PD participants were tested at their homes in both an on and an off medication state. The on medication sessions were conducted approximately 45 min after dosage, such that maximum clinical benefit from the medication was achieved at the time of testing. The off medication sessions were conducted after participants had been without dopaminergic medication for 12 hr.

**Stimuli**

Experimental stimuli consisted of 12 critical word triplets, the first two words being the primes (P1 and P2, respectively), and the third, the target. For each critical word triplet, primes were either related or unrelated to the target, resulting in the following prime conditions: related–related (RR), related–unrelated (RU), unrelated–related (UR) and unrelated–unrelated (UU). We used the UU condition to calculate priming effects in each of the three related conditions. Thus, with four prime conditions per critical word triplet, a total of 48 critical trials were created. An example of these prime conditions was as follows:

- (RR) summer–snow–winter
- (RU) summer–hill–winter
- (UR) island–snow–winter
- (UU) island–hill–winter

The critical target words and their related primes were derived from the Edinburgh Associative Thesaurus (Kiss, Armstrong, Milroy, & Piper, 1973), such that the probability that a target word would be produced as an associate to the prime word was high. Furthermore, all related prime words shared an obvious semantic relationship with the target word (e.g., judge–jury). Unrelated prime words were matched in length and frequency (Kucera & Francis, 1967) to the related prime words already serving as stimuli in the experiment. Both related and unrelated prime words in each condition were always unrelated to each other according to the Edinburgh Associative Thesaurus (Kiss et al., 1973).

We also created an additional 48 filler triplets to lower the relatedness proportion of the experiment. Consistent with the construction of the critical trials, we constructed the filler trials by selecting 12 target words and 4 different prime words for each target. Thus, each filler target was repeated 4 times, but with a different prime combination on each trial. The repeated nature of the filler target words was intended to reduce the salience of the repeated critical trial presentations. All prime and target words were matched in length and frequency to the critical stimuli. Further, all prime words used in the filler trials were both unrelated to each other and unrelated to the target. The resulting relatedness proportion of the experiment following the addition of these filler trials was .38.

In addition to the 96 word target trials, a further 12 pronounceable nonword targets were created. We derived all nonwords by changing one to three phonemes in existing English words (not already serving as stimulus items in the experiment), which were matched in length and frequency to the critical word targets used in the experiment. For each nonword target, four prime words were selected by use of the same criteria as that used for the selection of the filler trials. The nonword ratio (defined as the number of word prime/nonword targets divided by the number of word prime/unrelated word targets plus word prime/nonword targets) was 0.44, and the probability of a nonword was 0.38.

Two separate stimulus lists were constructed for each SOA (i.e., 250 ms and 1,200 ms). Each list consisted of the same 144 trials (48 critical targets, 48 filler targets, and 48 nonword targets), but the order of these trials was pseudorandomized for each list and then held constant for each participant. To avoid presenting the four prime conditions for each critical word triplet (i.e., RR, RU, UR, UU) in the same order, we counterbalanced the order of presentation within each list. Consistent with Hagoort (1989), we achieved counterbalancing by taking a different random sample of 12 from the 24 possible orders of presentation for each of the three experiments. These 12 orders were then assigned randomly to the 12 critical word triplets for each experimental list. Furthermore, to reduce the influence of repeated exposure to the same target stimuli, a minimum of 20 trials separated the repetition of any critical target word. Nonetheless, we recognized that response times (RTs) may still be influenced by the repeated nature of the critical targets. For the purposes of statistical analyses, therefore, the position of each target in the list (i.e., first, second, third, or fourth presentation) was recorded. We then used this position as a covariate during analyses, to account for any influence repetition may have had on RTs.

All participants received the two lexical-decision experiments in the same order (i.e., the 250 ms SOA before the 1,200 ms SOA), but each experiment was completed during a different testing session held at least 2 weeks apart to reduce the influence of repeated exposure to the same stimuli. Further, although all PD participants were tested while on medication first, the off medication sessions did not commence until 6 months after the on medication sessions were completed. All stimuli were presented on a portable laptop computer using Superlab experimental software (Version 2.0; Cedrus Corporation, 1996), which measured participants’ RTs with a Cedrus response pad (model RB-420, Cedrus Corporation, Phoenix, AZ; accurate to within 1 ms) and collected all error and RT data automatically.

**Procedure**

Participants were informed that three consecutive words would appear in the center of the computer screen. They were asked to make a lexical decision to the third word as quickly and as accurately as possible by pressing the *yes* button if it was a real word or the *no* button if it was a nonword. A set of 12 practice trials (six word targets and six nonword targets) was given to each participant prior to testing, which they were free to repeat until they felt comfortable with the procedure.

All stimuli were presented in the center of the computer screen in 70-point Arial font, with prime words in lowercase letters and target words in uppercase letters. The sequence of events for all trials was as follows: A fixation point appeared in the center of the screen for 500 ms, followed by a blank screen interval of 200 ms. The first prime word was displayed for 100 ms. A blank screen was then presented, followed immediately by the second prime for 100 ms. A blank screen was then displayed again,
followed immediately by the target word, which was displayed for 3,000 ms or until the participant had made a response. The next trial was then activated automatically after 1,200 ms. The blank screen intervals between P1 and P2, and P2 and the target, were either 25 ms or 500 ms, resulting in SOAs of 250 ms or 1,200 ms. Figure 1 illustrates the procedure used for a typical trial (from P1 to target). Experimental stimuli were presented to participants in three blocks of 48 trials, with short rest breaks provided to participants between each block. Five buffer trials were included at the beginning of each block, but the RTs to these trials were not recorded.

Results

Only RTs for the critical trials were analyzed. Further, although participants in the control group and the PD group on medication were originally tested at three SOAs (Angwin et al., 2005), only data for the 250 ms and 1,200 ms SOAs were analyzed in the present study, as the PD group off medication was only tested at these SOAs. All participant errors and all RTs less than 200 ms or greater than 1,500 ms were removed from analyses, resulting in the removal of 2.23% of the PD “on” group’s data, 3.27% of the PD “off” group’s data, and 1.49% of the control group’s data. Because of the low percentage of errors, no analyses were conducted on the error data. We treated both individual and group outliers by discarding any RTs more than two standard deviations above or below the mean. These outliers accounted for less than 10% of the data for each group. Table 1 displays the mean RTs (covaried for position of target presentation) for the control group and for the PD group both on and off medication. We conducted separate analyses to compare the control group with the PD group on medication and to compare the PD group on and off medication.

Controls Versus PD on Medication

Individual participant RTs were entered into a mixed linear model analysis with participant as a random factor, group (control, PD) as a between-participants factor, SOA (250 ms, 1,200 ms) and prime (RR, RU, UR, UU) as within-participant factors, and position as a covariate. The results revealed a significant main effect of prime, \( F(3, 1177) = 12.18, p < .001 \); interaction effects of Group \(
\times SOA, F(1, 1177) = 22.69, p < .001 \), and SOA \(
\times Prime, F(3, 1177) = 5.55, p = .001 \); and a main covariate effect of position, \( F(1, 1177) = 76.33, p < .001 \).

Although the significant SOA \(
\times Prime interaction indicates that priming effects differed across SOA, the absence of Group \(
\times Prime and Group \(
\times SOA \times Prime interactions also indicates that semantic priming did not differ between the two groups. Accordingly, the data was collapsed across groups, and the pattern of priming across time was investigated with planned pairwise comparisons between the related prime conditions (RR, RU, UR) and the UU condition at each SOA. We conducted these comparisons after adjusting for the significant effect of position, using additional mixed linear model analyses.

Analysis of the data revealed significant priming for the RR, RU, and UR prime conditions at 250 ms SOA, \( t(1184) = -5.86, p < .001 \); \( t(1184) = -3.83, p < .001 \); and \( t(1184) = -5.71, p < .001 \), respectively, but priming effects at the 1,200 ms SOA were not significant. Figure 2 illustrates the magnitude of these different priming effects (calculated by subtracting related from unrelated RTs) at 250 ms SOA. Although these analyses provide an indication of which priming effects were significant at each SOA, they fail to establish whether the magnitude of priming differed for any of the related prime conditions. More important, they also fail to establish whether a summation of priming occurred for either group at each SOA (i.e., whether the magnitude of priming for the RR condition was larger than that of both the RU condition and the UR condition). Hence, further planned pairwise comparisons were conducted among the three related prime conditions. The analyses revealed that at 250 ms SOA, RTs for the RR condition were significantly faster than RTs for the RU condition, \( t(1184) = -2.04, p = .041 \), and faster RTs for the UR condition compared with the RU condition were just outside significance (\( p = .065 \)). No other comparisons were significant. These results do not indicate summation priming, as RTs for the RR condition were not significantly faster than RTs for either the RU or UR conditions.

PD on Versus off Medication

Individual participant RTs were entered into a mixed linear model analysis with participant as a random factor; medication (on, off), SOA (250 ms, 1,200 ms), and prime (RR, RU, UR, UU) as within-participant factors; and position as a covariate. The results revealed significant main effects of SOA and prime, \( F(1, 1160) = 6.31, p = .012 \), and \( F(3, 1160) = 8.81, p < .001 \), respectively; a significant interaction effect of Group \(
\times SOA \times Prime, F(3, 1160) = 2.99, p = .030 \); and a main covariate effect of position, \( F(1, 1160) = 60.64, p < .001 \). A significant interaction effect of SOA \(
\times Prime was just outside significance, \( F(3, 1160) = 2.50, p = .058 \).

These significant interaction effects suggest that the pattern of priming effects across SOA differed between the PD group on versus off levodopa. Hence, the pattern of semantic priming was examined separately for each group by way of planned pairwise comparisons between the related prime conditions (RR, RU, UR) and the UU condition at each SOA. Analysis of the PD “on” group’s data revealed significant RR, RU, and UR priming effects at 250 ms SOA, \( t(1160) = -3.40, p = .001 \); \( t(1160) = -2.79, p = .005 \); and \( t(1160) = -3.57, p < .001 \), respectively, but no priming effects were significant at 1,200 ms SOA. In contrast, analysis of the PD “off” group’s data revealed only significant priming effects

Figure 1. An illustration of the procedure used for a typical trial (from Prime 1 to target) during the lexical-decision task.
for the RR and UR conditions at 250 ms SOA, \(t(1160) = -3.24,\) \(p = .001,\) and \(t(1160) = -2.66,\) \(p = .008,\) respectively, with no priming effects significant at the 1,200 ms SOA. The differing pattern of priming between the two groups was confirmed, with pairwise comparisons illustrating that the magnitude of priming for the RU condition was significantly larger in the PD group on medication, \(t(1160) = -2.10,\) \(p = .036,\) than the PD group off medication. No other pairwise comparisons were significant. Figure 3 illustrates the magnitude of the different priming effects (calculated by subtracting related from unrelated RTs) for the PD group on and off levodopa at 250 ms SOA.

Given the significant priming effects evident at 250 ms SOA, we also conducted further planned pairwise comparisons between the three related prime conditions for each group, to determine whether a summation of priming occurred. Analysis of the PD “on” group’s data revealed no significant difference in RT for any of the related prime conditions. Analysis of the PD “off” group’s data revealed that RTs for the RR and UR conditions were both significantly faster than the RU condition, \(t(1160) = -3.38,\) \(p = .001,\) and \(t(1160) = -2.80,\) \(p = .005,\) respectively. These results did not indicate the presence of summation priming for either group.

### Discussion

The present study assessed the influence of dopamine depletion on semantic activation across time in PD. The results revealed that PD participants on levodopa medication demonstrated a similar pattern of priming to healthy control participants across both short and long SOAs. Analysis of PD participants on compared with off medication, however, revealed a different pattern of priming at 250 ms SOA for PD participants off medication. These results are considered in terms of the potential neuromodulatory influence of dopamine depletion on semantic activation in PD.

### Controls and PD on Medication

It was predicted for the PD group on medication that semantic activation would be delayed and that no priming effects would be obtained in the RU condition. Inconsistent with these predictions, analysis of the data revealed that both the control group and the PD group on medication showed significant priming effects for each prime condition at 250 ms SOA. These results are also at odds with those we previously reported for the larger cohort of PD participants also tested while on medication (Angwin et al., 2005), which indicated an absence of RU priming in PD at 250 ms SOA. It should be noted, however, that the average levodopa dosage for PD participants in that study was significantly larger than the average levodopa dosage for PD participants in the present study. These differences in medication may have contributed to the

![Figure 2](image2.png)

**Figure 2.** Semantic priming effects at 250 ms stimulus onset asynchrony (calculated by subtracting related from unrelated response times) collapsed across the control group and the Parkinson's disease on levodopa group. Error bars represent the standard error for each priming effect. RR = related–related condition; RU = related–unrelated condition; UR = unrelated–related condition.

![Figure 3](image3.png)

**Figure 3.** Semantic priming effects at 250 ms stimulus onset asynchrony (calculated by subtracting related from unrelated response times) for the Parkinson's disease (PD) on medication group and the PD off levodopa group. Error bars represent the standard error for each priming effect. RR = related–related condition; RU = related–unrelated condition; UR = unrelated–related condition.
differing findings between the two studies, but further research is required to investigate this issue.

Although findings of intact semantic activation at 250 ms SOA in the present study are in keeping with suggestions that automatic semantic activation is intact in PD (Copland, 2003; Filoteo et al., 2003; Longworth, Keenan, Barker, Marslen-Wilson, & Tyler, 2005), it has also recently been illustrated that delays to automatic semantic activation are only evident in some participants with PD (Grossman et al., 2002). Interpreting their results, Grossman et al. suggested that the magnitude of cognitive slowing in PD might depend on the extent of endogenous dopamine depletion for each participant, such that delays in lexical retrieval may only be evident in participants with greater magnitudes of dopamine depletion. Accordingly, a plausible explanation for the intact semantic priming in the PD group of the present study may be that the magnitude of dopamine depletion in these participants when medicated was not sufficient to disrupt the speed of automatic semantic activation.

It is interesting that abnormally large levels of semantic priming have also been observed in PD at a short SOA when the number of word trials exceeded the number of nonword trials (Brown et al., 2002). Brown et al. (2002) suggested that these findings in PD might be due to processes operating during the decision-making component of the lexical-decision task. Despite the larger number of word trials in the present study, the magnitude of priming in PD was similar to that of the control group. In contrast to the present study, however, Brown et al. encouraged participants to expect target words from a specific category (e.g., an animal) if a certain prime word was presented (e.g., metal). Hence, hyper-priming in PD may be dependent on the nature of the lexical-decision task used. Additional research that manipulates the semantic relationship between word pairs may further elucidate the mechanisms underlying hyper-priming in PD.

Another important result was that although priming effects were significant for both the control and PD groups at 250 ms SOA, RTs in the RR condition were significantly faster than RTs in the RU condition, and the faster RTs in the UR relative to the RU condition also approached significance (see Figure 2). These results are consistent with Balota and Paul (1996), who obtained similar results using associatively related word pairs. As suggested by these researchers, a smaller magnitude of RU priming could be related to various factors, including a disruption to priming across an intervening unrelated word and/or a temporal decay in the magnitude of semantic priming.

It should also be noted that although priming was significant for the RR condition at 250 ms SOA, no summation of priming was evident in this condition. To date, results on summation of priming in healthy adults have been equivocal, with some researchers demonstrating significant summative priming effects (e.g., Balota & Paul, 1996; Milberg, Blumstein, Giovanello, & Misirksi, 2003) and others demonstrating none (Angwin et al., 2003; Chenery, Copland, McGrath, & Savage, 2004). Hence, the influence of multiple related primes on semantic activation is unclear, and further research is necessary to determine the mechanisms by which a summation of priming can occur.

Finally, despite the significant priming effects for all prime conditions at the 250 ms SOA, no priming effects were evident for the two groups at the 1,200 ms SOA. This result is surprising, given that the emergence of controlled processes or expectancies may typically be expected to facilitate semantic priming effects at longer SOAs (Neely, 1977). Previous research has illustrated, however, that older adults may experience difficulties maintaining expectancies across longer SOAs under conditions of a short prime duration (Balota, Black, & Cheney, 1992). Hence, the short prime duration of 100 ms used in the present study may have contributed to the absence of priming at 1,200 ms SOA for the participants in the control and PD groups.

**PD on and PD off Medication**

As hypothesized, within-group comparisons illustrated a different pattern of priming when the PD participants were off relative to on medication. In particular, at 250 ms SOA, only the PD group off medication demonstrated an absence of priming for the RU condition (see Figure 3), which may be consistent with the influence of reduced SNRs on semantic processing. Specifically, because of reduced salience of the related prime word (i.e., the signal) or an increased salience of the unrelated word (i.e., the noise), automatic semantic activation may be susceptible to disruption in the RU condition. The fact that the disruption to priming was only evident in PD participants off medication lends additional credence to the specific neuromodulatory role of dopamine in this process.

It is important to note that deficits to inhibitory processes in PD may also account for the absence of RU priming in the PD group off medication. Filoteo et al. (2003) have previously illustrated an increase in identity priming (i.e., priming that results from an identical prime–target pair such as chair–chair) in PD relative to healthy controls, which the researchers suggested might be a result of reduced inhibition of the prime and target in PD. Such reduced inhibition may also explain the results of the present study. Specifically, reduced inhibition of prime and target words in PD may exacerbate any disruptive influence of an intervening unrelated prime word on semantic activation, thereby eliminating RU priming. Supporting this notion are suggestions that reduced inhibitory mechanisms may contribute to an extended period of facilitation for the subordinate meanings of ambiguous words in PD (Copland, 2003) as well as to PD participants’ difficulties selecting an appropriate word in the presence of semantic competitors on a word search task (Gurd & Oliveira, 1996).

Filoteo et al. (2003) suggested that the reduced inhibitory processes they observed in PD might result directly from impaired frontal-basal ganglia functioning. This notion is consistent with the functional role of the basal ganglia in motor control, whereby the basal ganglia act to select appropriate motor programs and suppress competing mechanisms (Mink, 1996). Thus, the present results appear consistent with increased basal ganglia dysfunction in PD during medication withdrawal, which causes a reduction in inhibitory processes.

Researchers have also suggested that increased dopamine depletion in PD may cause delays in semantic activation (Grossman et al., 2002). In keeping with this theory, it may be expected that PD participants off medication will also show a delayed time course of semantic activation. It is interesting that the disruption of priming in the RU condition has occurred for the PD participants off medication, despite intact automatic semantic activation, as evidenced by priming effects in the UR and RR conditions (see Figure 3). This particular pattern of results replicates those we
obtained in our earlier research on semantic activation in PD using
the multiprime paradigm (Angwin et al., 2003). There appears to
be converging evidence, therefore, to suggest that changes to
SNRs or inhibitory processes may occur independent of any delay
in the time course of semantic activation. One plausible explana-
tion for these results may be that the speed of semantic activation
is less sensitive to the magnitude of dopamine depletion. More
specifically, it is possible that although mild levels of dopamine
depletion may be sufficient to reduce SNRs or inhibitory mecha-
nisms, a greater magnitude of depletion is necessary to signifi-
cantly delay the time course of semantic activation. With respect to
the present study, this theory suggests that even while participants
were off medication, the magnitude of dopamine depletion in the
PD group was not sufficient to delay semantic activation. Indeed,
all PD participants in the present study were classified as mildly
impaired and experienced few motor symptoms while off levo-
dopa, which may be consistent with mild levels of dopamine
depletion in these participants.

Although the present study provides critical insights into the
potential neuromodulatory role of dopamine on semantic activa-
tion, Sealfon and Olanon (2000) suggested that both dopamine
depletion and dopamine supplementation may lead to altered sig-
aling patterns in the brain. Further, Obeso et al. (2000) have
suggested that intermittent dopamine administration may act as a
destabilizing stimulus by alternately exposing the basal ganglia to
large concentrations of extrasynaptic dopamine, followed by se-
vere dopamine depletion. Accordingly, additional research to de-
fine the differential effects of dopamine depletion and exogenous
dopamine supplementation on language function in PD is
warranted.

Furthermore, although PD is characterized primarily by striatal
dopamine deficiency, presynaptic dopaminergic function in PD is
also reduced in the mesocortical system (Ouchi et al., 1999).
Research suggests that the mesocortical system may influence
various cognitive functions (e.g., Delis, Direnfeld, Alexander, &
Kaplan, 1982), including the processing of semantic information
(Kischka et al., 1996). As illustrated by Carbon and Marie (2003),
however, little is currently known about the differential influence
of the striatum and mesocortical systems on cognitive function in
PD. Hence, further research to delineate the roles of these different
systems will be beneficial, as will research examining the influence
of nondopaminergic pathology on language function.

Finally, the results of the present study may also have significant
implications for deficient semantic processing in other neurologi-
cal populations. Chenery et al. (2004) revealed an absence of
priming for the RU condition in schizophrenia, despite priming for
the UR and RR conditions. Accordingly, this result may be con-
sistent with the alterations to dopaminergic activity reported in
this population (see Salome, Boyer, & Fayol, 2000, for a review).
Similarly, changes to dopaminergic activity in schizophrenia may
also account for findings of an increased spreading of activation
during semantic priming tasks (e.g., Moritz et al., 2001; Spitzer,
Braun, Maier, Hermle, & Maher, 1993).

Conclusions

The current study investigated semantic activation in PD par-
ticipants on and off levodopa medication and healthy adults. We
proposed that dopamine depletion and frontal-striatal dysfunction
in PD may lead to reduced inhibition and/or a reduced SNR of
semantic activation. Such changes may increase the influence of an
unrelated word on semantic processing, such that automatic se-
manetic activation becomes disrupted in conditions in which an
unrelated word is presented between the related prime and the
target. One caveat of the present study that must be considered is
that only a small number of PD participants were able to partici-
pate in the research while off their medication. The results of this
research need to be validated, therefore, using a larger cohort of
PD participants tested both on and off dopaminergic supplemen-
ation.

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