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Retention of Implicit Sequence Learning in Persons who Stutter and Persons with Parkinson's Disease

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Abstract

This study investigated the retention of implicit sequence learning in 14 persons with Parkinson's disease (PPD), 14 persons who stutter (PWS) and 14 control participants. Participants completed a nonsense syllable serial reaction time task in a 120-minute session. Participants named aloud four syllables in response to four visual stimuli. The syllables formed a repeating 8-item sequence not made known to participants. After one week, participants completed a 60-minute retention session that included an explicit learning questionnaire and a sequence generation task. PPD showed retention of general learning equivalent to controls but PWS's reaction times were significantly slower on early trials of the retention test relative to other groups. Controls showed implicit learning during the initial session that was retained on the retention test. In contrast, PPD and PWS did not demonstrate significant implicit learning until the retention test suggesting intact, but delayed, learning and retention of implicit sequencing skills. All groups demonstrated similar limited explicit sequence knowledge.

Performance differences between PWS and PPD relative to controls during the initial session and on early retention trials indicated possible dysfunction of the cortico-striato-thalamo-cortical loop. The etiological implications for stuttering, and clinical implications for both populations, of this dysfunction are discussed.

Keywords

Stuttering; Parkinson's disease; Speech; Retention; Learning; Implicit Sequence Learning

Introduction

Implicit Learning and Implicit Sequence Learning

Procedural memory is a primarily unconscious type of long-term memory for how to do things, guiding the processes we perform. Procedural learning, also known as implicit learning, involves repeating a complex activity over and over again until relevant neural systems collaboratively and automatically execute the skill (Saint-Cyr, 2003). In implicit sequence learning, participants are unaware of, and unable to verbally define, the sequence they are performing. Nevertheless, they learn to anticipate and combine known movement components into a rapid, accurate sequence. Implicit sequence learning is associated with specific neurological structures and connections (particularly cortico-striato-thalamo-cortical connections) and acknowledged as a relatively independent functional brain system (Doyon & Benali, 2005; Saint-Cyr, Taylor & Lang, 1988).

The main objective of this research study was to infer, from performance on the serial reaction time task, the functional integrity of cortico-striato-thalamo-cortical connections in people who stutter (PWS) and people with Parkinson's disease (PPD) by examining implicit sequence learning and specifically retention of implicit sequence learning.

The Serial Reaction Time Task (SRTT)

Extensive previous research has established high internal validity for the SRTT as a methodology for examining implicit sequence learning (Nissen & Bullemer, 1987). SRTT paradigms typically involve presenting stimuli in one of four locations on visual display, such as a computer monitor (Eimer, Goschke, Schlaghecken & Sturmer, 1996). Each stimulus is associated with a movement or verbal response (e.g., pushing one of four buttons, saying one of the numbers “one” through “four” aloud). The stimuli are presented in a repeated sequence (e.g. 1, 3, 4, 3, 1, 3, 4, 3) meant to be unnoticeable to the participant (Smith & McDowall, 2004). Impairment of cortico-striato-thalamo-cortical connections can be implied (as one possible etiological factor) for patient populations that demonstrate impaired performance on the SRTT. It is important to note, however, that studies have also noted other brain areas important for motor learning, such as decreased premotor (Pre-SMA) and cerebellar volume (Exner, Koschack & Irle, 2002), that correlated with decreased performance on the SRTT.

General Learning on the SRTT—General learning involves both explicit (conscious, fact-based) knowledge and implicit (unconscious, procedural) knowledge and can be inferred from reaction time and accuracy improvements over practice blocks on the SRTT (Nissen & Bullemer, 1987). General learning includes characteristics of recalling the instructions of the task, matching motor responses to stimuli (stimulus-response learning), and habituation to the task environment and to the timing of the stimuli (Nissen & Bullemer, 1987). General learning is typically assessed by comparing groups' reaction time improvements over blocks of practice of the sequenced trials.

Implicit Sequence Learning on the SRTT—In contrast, experimenters insert trials of random stimuli that violate the sequence to assess implicit sequence learning. Implicit

sequence learning is inferred by comparing reaction time for sequence items (which are practiced and frequently occurring) to random items (which are relatively unpracticed and occur rarely; Wilkinson & Jahanshahi, 2007). Implicit sequence learning is typically assessed by comparing the difference between a) groups' reaction time after practice on sequence trials and b) groups' reaction time for random stimuli introduced after several blocks of practice. Previous researchers have found that faster reaction times for the sequence stimuli vs. random stimuli on the SRTT effectively captured the anticipation associated with implicit learning.

Performance of Patients with Parkinson's Disease (PPD) on the SRTT

Impairment in implicit sequence learning in PPD, as measured by the SRTT, has been reported in several studies (Ferraro, Balota & Connor, 1993; Jackson, Jackson, Harrison, Henderson & Kennard, 1995; Smith & McDowall, 2004; Westwater, McDowall, Siegert, Mossman & Abernethy, 1998). In contrast, Exner et al. (2002) examined MRI brain volumes of patients with focal basal ganglia lesions (e.g., lacunar strokes) and controls. Patients in Exner et al.'s study did not show impairments on the SRTT relative to controls. Similarly, no sequence-specific learning impairments were reported for PPD by Smith, Siegert, McDowall and Abernethy, 2001. However, Smith et al.'s results were contradicted by a recent study with a larger sample size which found significantly impaired implicit sequence learning by PPD relative to controls (Smith & McDowall, 2004).

Several studies have reported impaired implicit sequence learning for PPD (or patients with basal ganglia stroke) specific to some experimental conditions but not others (Helmuth, Mayr & Daum, 2000; Sommer, Grafman, Clark & Hallett, 1999; Vakil, Kahan, Huberman & Osimani, 2000; Werheid, Zysset, Muller, Reuter & von Cramon, 2003). Both Helmuth et al. (2000) and Vakil et al. (2000) reported that PPD showed a deficit in learning a motor sequence but were unimpaired at learning a sequence of spatial locations. Sommer et al. (1999) concluded that nigrostriatal impairment selectively affected performance of complex learning tasks that were competitive and required alertness, such as the SRTT, but did not affect simple learning procedures such as eye blink conditioning. Werheid et al. (2003) reported that sequence specific learning was impaired in PPD only when stimuli and responses were spatially compatible.

A relatively recent and comprehensive meta-analysis, in summary of these multiple reports, indicated that the SRTT, whether manual or verbal, has reliably found poor motor execution of implicit sequence learning in patients with impaired striatal systems such as Huntington's Disease (Saint-Cyr et al., 1988), and Parkinson's disease (see Siegert, Taylor, Weatherall & Abernethy, 2006, for a meta-analysis).

Performance of Persons who Stutter (PWS) on the SRTT

Recently, Smits-Bandstra and Gracco (2013) compared implicit sequence learning in PWS and PPD using a nonsense syllable SRTT. PWS and PPD showed similar significant difficulty when initially acquiring general stimulus-response learning but demonstrated performance equivalent to the control group after practice. Both PWS and PPD showed similar significant difficulty in implicit sequence learning relative to controls. The authors

suggested that impairment of cortico-striatothalamo-cortical connections could be inferred as a possible etiological factor of stuttering because PWS and PPD demonstrated similarly impaired performance on the SRTT. The current study reports the results of a retention test one week following the Smits-Bandstra and Gracco (2013) study, examining retention of implicit sequence learning.

Retention of Implicit Learning in Patients with Parkinson's Disease

Implicit learning is not well established, nor invulnerable to interference, until after extensive practice and a consolidation period (Brashers-Krug, Shadmehr & Bizzi, 1996; Hauptmann & Karni, 2002; Shadmehr & Brashers-Krug, 1997). A number of studies have investigated the importance of the striatal system for retention of implicit skills. Studies which examined procedural skills over one session or over a few days found good retention by PPD (Harrington, Haaland, Yeo & Marder, 1990; Rostami & Ashayeri, 2009), while those which looked over months of practice found increasing differences in skill retention between PPD and control participants (Agostino et al., 2004; Doyon et al. 1998; Kawai, Kawamura & Kawachi, 1999; Mochizuki-Kawai, Kawamura, Hasegawa, Mochizuki, Oeda, Yamanaka & Tagaya, 2004; Vakil & Herishanu-Naaman, 1998).

However there is little research to date investigating PPDs' retention of implicit sequence learning relative to control participants. The characterization of impairments in sequence learning and retention is particularly relevant to rehabilitation professionals involved in optimization of self-care and communication skills of PPD (e.g., buttoning, writing, gesturing and speaking).

Retention of Implicit Learning in Persons who Stutter

As with PPD, the ability of PWS to establish, retain and implement implicit memories has been brought into question in previous research (Max, 2004; Smits-Bandstra & Gracco, 2013) and relapse after treatment is an acknowledged problem in this population (Blomgren et al., 2005). Smits-Bandstra, De Nil and Saint-Cyr (2006) found that PWS demonstrated significantly slower reaction times for an explicitly known ten-item nonsense syllable sequence relative to control participants on a retention test given approximately one hour after practice. Slower more variable performance was also reported for PWS relative to control participants when retention of a nonsense syllable sequence was examined one to three days following initial practice (Namasivayam & van Lieshout, 2008). Max and Baldwin (2010) assessed PWS' fluency for passages, read repeatedly, after 2 hours and 24 hours. They reported retention (increased fluency) was observed for the repeated sentences. However, PWS' retention of implicit sequence learning has never been investigated.

Purpose of the Current Study

The initial study by Smits-Bandstra and Gracco (2013) pointed to implicit sequence learning deficits for PWS and PPD. The focus of the current study was to expand on the initial results to examine retention of implicit learning in these two populations using a seven-day retention test. The primary objective of the current study was to compare retention of an implicit nonsense syllable sequence in PWS, PPD, and control participants using the SRTT. The current study will be an important addition to the existing body of stuttering research

because functional deficits of the implicit memory system on the SRTT, which involves the cortico-striato-thalamo-cortical loop, will provide information regarding possible etiological factors of stuttering. Nonsense syllable stimuli were specifically chosen for the SRTT because characterization of implicit learning and retention abilities in patient populations will be critical in designing more effective rehabilitative protocols for speech in the future.

Methods

Participants

All of the participants participated in the initial 120 minute experimental session reported in a previous publication (Smits-Bandstra & Gracco, 2013). Participants in the initial study agreed to return one week after the initial session to complete the second part of the study, a retention test. Participant information (identical to that presented in a previous publication; Smits-Bandstra & Gracco, 2013) is presented in Tables 1 and 2.

Participants included 14 English-speaking PPD (7 females; 64.5 years, SD 6.9). PPD were outpatients with idiopathic Parkinson's disease. Diagnosis by a licensed neurologist was based on the presence of a rigidity-akinesia syndrome, and responsiveness to Levodopa, without signs of pyramidal, cerebellar, or oculomotor deficits.

PPDs' conversational speech was rated on overall intelligibility and dysarthria characteristics by the primary investigator, a certified speech-language pathologist (see Appendix A). The speech and reading samples of all PPD scored below (2.8, SD 2.7) the very mild range (10-17) on the Stuttering Severity Instrument 4 (SSI-4; Riley, 2009). All PPD demonstrated less than 3% of syllables stuttered for their speech and reading samples. Table 2 also includes a rating of speech affectedness from the Activities of Daily Living subsection of the Unified Parkinson's Disease Rating Scale (Fahn, Elton & Members of the UPDRS Development Committee, 1987), and overall stage of disease (modified Hoehn & Yahr, 1967; see Appendix B). Twelve PPD had intelligibility between 95-100%, and two PPD had intelligibility between 85-95%.

A second rater, a certified speech language pathologist and Ph.D. student with three years of stuttering research experience, blind to the conditions of the study, also rated 20% of PPDs' speech samples. Inter-rater reliability calculated using the kappa coefficient was 100% for intelligibility ratings, 84% for dysarthria characteristics, 94.7% for stuttering frequency of speech samples and 97.3% for stuttering frequency of reading samples.

All PPD were tested during the ON-cycle of their medication within 60-90 minutes of their last dose. Medicated patients were selected to minimize bradykinesia at baseline because dopaminergic treatment speeds up the execution of motor sequences (Benecke, Rothwell, Dick, Day, & Marsden, 1986).

Participants included 14 English-speaking PWS (6 females; 65.1 years, SD 5.7). PWS' conversational speech was evaluated on the SSI-4 (Riley, 2009) by the primary investigator, a certified speech-language pathologist. The speech and reading samples of PWS (10.3, SD 7.2), scored in the very mild (9 PWS), mild (3 PWS) and moderate (2 PWS) range on the

SSI-4 (Riley, 2009). All participants reported onset of stuttering in early childhood on the screening questionnaire. It is noteworthy that the large majority of PWS scored in the very mild to mild range on the SSI-4. On average, PWS demonstrated an average of 3% of syllables stuttered during speaking (ranging from 1% - 15%). A second rater, a certified speech language pathologist and Ph.D. student with three years of stuttering research experience, blind to the conditions of the study, also rated 20% of PWS' speech samples. Inter-rater reliability using the kappa coefficient was 94.8% for stuttering frequency of speech samples and 93.7% for stuttering frequency of the reading samples. Fourteen English-speaking participants (6 females; 65.5 years, SD 5.6) served as matched control participants.

Participant Exclusion Criteria and Recruitment Methods—As described in Table 1, all PWS and PPD were screened for depression (Beck, Ward, Mendelson, Mock & Erbaugh, (1961), mental state (Folstein, Folstein & McHugh, 1975) and handedness (Oldfield, 1971). All participants were screened for forward and backward digit span (Wechsler, 1997), hearing, vision, medication use (other than PPD medication), neurological and motor control difficulties (other than PD), and speech and language difficulties (other than those associated with PD or stuttering). PWS and PPD who had received speech therapy within the last 6 months were excluded as these treatments typically teach slowed rate of speech which may have interfered with the task.

Written informed consent was obtained and all participants were treated according to ethical treatment of human participant guidelines established by McGill University, the University of Toronto and the Baycrest Centre in Toronto. Participants self-selected to participate in the study by responding to support group web page advertisements as well as poster advertisements placed on campuses, in nursing homes, in outpatient centers and in hospitals of Quebec and Ontario. Neurologists and speech language pathologists at the Montreal Neurological Hospital and the Baycrest Centre in Toronto served as initial contacts to PPD who met eligibility requirements. PWS were also identified using an existing database of stuttering participants who participated in past studies at McGill and the University of Toronto and gave written informed consent to participate in other studies.

Procedures

The current SRTT paradigm was based on the SRTT paradigm presented by Nissen and Bullemer (1987) in their foundational study. The methodology also closely mirrored recent verbal response paradigms used by Westwater et al. (1998) and Smith and McDowall (2004). All of these studies required participants to produce four different motor responses to four different horizontally presented stimuli within a hidden sequence.

The retention session took place approximately seven days after an initial 120-minute session (Smits-Bandstra & Gracco, 2013) for controls, ($M = 6.7$, $SD = 3.1$), PWS ($M = 6.1$, $SD = 1.2$), and PPD ($M = 5.9$, $SD = 1.8$), respectively. A one-way ANOVA found no significant differences between the groups in days between the initial session and the retention test. Stimuli were presented on a 15-inch lap top screen with a viewing distance of 18-20 inches. Participants were instructed to say aloud one of four syllables when an "X"

appeared over one of four horizontal lines on a computer screen. For example, participants said “PA” when an ‘X’ appeared above the top left line on the screen, “PE” for top right, “PI” for bottom left, and “PO” for bottom right (see Figure 1). The spatial locations of the stimuli were explained to the participants as “alphabetical” from left to right and top to bottom (e.g., A, E, I, O). Unknown to the participants, the stimulus locations appeared in a predictable sequence of eight locations/syllables (i.e. PO PI PO PE PI PA PE PA). Stimulus items with initial /p/ were chosen (instead of 1-4 or A-D, used in previous studies) to more easily identify voice onset (and lip EMG onset – results not reported in this paper) from acoustic waveform analysis.

Stimuli were presented using the Presentation 0.8 (Neurobehavioral Systems, 2004) software program. Participants practiced each sequence (8 trials) nine times per block for a total of two blocks (144 trials). Trials in Block 3 were pseudorandom, with the constraint that no syllable was repeated (e.g., PA PA). The overall order of the initial session and the retention session is presented in Appendices C and D.

No feedback was provided during the retention test with the exception that, after every 16 to 24 trials, a “reminder” was presented on the computer monitor. The “reminder” briefly showed the correct syllable under each X location. If the “reminder” was not attended to, the investigator came into the session during a scheduled break and provided direct instruction (e.g., “If the X appears here you need to say PI”).

Immediately after the initial session, participants completed the “Initial” questionnaire to evaluate the extent of explicit learning (see Appendix E). Immediately after the retention session participants completed the “Retention” questionnaire and a generate task to evaluate the extent of explicit learning (see Appendix F). Similar to questionnaires used in previous research (Eimer et al., 1996; Ghilardi, Feigin, Battaglia, Silvestri, Mattis, Eidelberg & Di Rocco, 2007; Russeler & Rosler, 2000), the questionnaire presented two-, three-, and four-syllable portions of the sequence so as not to underestimate explicit knowledge of parts of the sequence. The generate task was a computer task presented, without pause, following the ‘random’ block (Block 3). The generate task was identical to the experimental task described above with one exception. After a portion of each sequence had been completed (e.g., three trials), participants were presented visually with a “?” on the computer screen instead of the usual ‘X’ on one of four horizontal lines. When they saw the “?”, participants were instructed to “say the syllable corresponding to where they thought the ‘X’ would next appear.”

Dependent Variables

Inaccuracy was defined as incorrect syllable substitutions resulting from an incorrect vowel (e.g. “PA” for “PE”). PPD were in early stages of the disease with well-preserved speech skills (see Table 2). Dysarthria, voicing errors or distorted articulation of the initial consonant did not noticeably affect single syllable productions for these patients. There were no instances of an incorrect initial consonant. After outliers (very short or very long reaction times) were removed, excluded trials were removed (yawns, sneezes, equipment glitches, etc.), and disfluencies were excluded, productions were categorized as correct productions or incorrect substitutions.

An entire block was removed if there were three consecutive presentations, or 4 out of 5 presentations, when the *same* incorrect syllable was substituted in place of the correct syllable (e.g., PE for PI), indicating the participant had forgotten the instructions during training. In these cases, participants typically made the same substitution consistently throughout the block and the investigator had to intervene for corrective feedback during scheduled breaks. The Kappa coefficient for agreement with an independent rater on the occurrence of inaccuracies was 99.4%, based on 10% of the sequences.

Disfluencies were defined as silent blocks or any repeated, prolonged, or effortful sounds or syllables observed on-line, through videotape recordings or through waveform acoustic analyses. Disfluencies were omitted from accuracy and reaction time analysis. Inordinately long or short reaction times were categorized as outliers ($2\pm$ SD from each individual mean) and were removed from analysis. Although, anecdotally, many PWS report difficulty with bilabial stops such as /p/, very few disfluencies were recorded for PWS during the experiment. This was likely because the response was limited to one syllable in length and the four different syllables were repeated hundreds of times. The Kappa coefficient for agreement with an independent rater on the occurrence of disfluencies was 97.2%, based on 10% of the sequences.

Participant's speech was recorded using a dual channel digital audio tape recorder (Tascam DA-01, Mississauga, Ontario, Canada) with 16 bit resolution and 48 kHz sampling rate. Reaction time (voice onset time) was measured as the time from the onset of the stimulus presentation to the voice onset of the syllable after the stop gap and acoustic burst of the initial /p/. Reaction times were calculated off-line using the waveform acoustic analysis software program Speech Analyzer 3.0.1 (SIL, 2007). The primary investigator determined voice onset time manually by placing the cursor on the onset of the vowel for each trial. An independent trained rater, blind to the conditions of the study, re-analyzed 10% of the participants' acoustic waveforms to determine reaction time. Occurrence agreement inter-rater reliability for cursor placement to determine reaction time within 10ms was 98%. There was a strong positive correlation between the voice onset time recorded by the primary investigator and the independent rater ($r = .99$, $r^2 = .98$).

Questionnaires

Explicit questionnaire score reflected the extent to which sequencing performance could be accounted for by explicit rather than implicit knowledge. Participants were awarded single points for portions of the sequence they correctly identified as occurring “always” or “often”. Additional single points were awarded for sequence violations correctly identified as occurring “rarely” or “never”.

Data Analysis

Reaction Time for Retention of General Learning—Analysis of the current retention study was designed to closely mirror the analysis done in the initial study by Smits-Bandstra and Gracco (2013). As in the initial study, a traditional block contrast was completed as well as a more detailed learning curve contrast.

Reaction Time for Retention of General Learning: Block Contrast—For the more traditional block contrast, the mean of the first two sequences (16 trials) from Block 4 of the initial session was subtracted from the mean of the first two sequences from Block 1 of the retention session. A large difference between the means suggested poor retention.

Reaction time for Retention of General Learning: Learning Curve Contrast—In the learning curve contrast for the initial study, reaction time means were taken from the *beginning* of each practice block to observe the process of general learning, particularly as it progressed from early trials in Block 1. This method of analysis was successful in detecting group differences in several previous studies with PWS (Smits-Bandstra & De Nil, 2009; Smits-Bandstra, De Nil & Saint Cyr, 2006; Smits-Bandstra & Gracco, 2013). Furthermore, in a methodological paper Smits-Bandstra (2010) reported that averaging trials across entire blocks masked important early changes noted for PWS.

In the initial study (Smits-Bandstra & Gracco, 2013), general learning was inferred from *quadratic* (Portney & Watkins, 1993) learning curves in reaction time over practice across the initial session. In the current study retention of general learning was assessed by comparing the quadratic learning curves in reaction time over practice across both the initial session *and the retention session*. Polynomial contrasts were used to assess the shape of the learning curves, where large increases in reaction time upon introduction of the retention test indicated poor retention. For the learning curve contrast, the first two sequences from the first and final practice block of the initial session (Block 1 and 4) and the retention session (Block 1 and 2) were analyzed.

Reaction time for Retention: Implicit Sequence Learning—Similar to the initial study, probability-based analysis was conducted in order to separate general learning from implicit (sequence-specific) learning. Based on Wilkinson and Jahanshahi's (2007) probability-based analyses, random block (Block 3) trials were divided into syllable pairs that occurred frequently and conformed to the sequence (SEQ), or pairs that occurred rarely and violated the sequence (RAN; see Appendix D). The mean of the first 16 SEQ trials was subtracted from the mean of the first 16 RAN trials of Block 3. A large difference between SEQ and RAN means indicated implicit learning had taken place.

Reaction time for Retention: Change in Implicit Sequence Learning—A second analysis was done to compare implicit sequence learning across sessions. This was done to assess if groups differed in their ability to demonstrate implicit learning on the initial session vs. after a retention period. The difference between SEQ and RAN trials for the initial session was subtracted from the difference between SEQ and RAN trials for the retention session. In this comparison the difference between the first 16 SEQ and 16 RAN trials from the pseudorandom block of session one (Block 5) was compared to the difference between the first 16 SEQ and 16 RAN trials from the pseudorandom block (Block 3) from the retention test.

Retention Accuracy—Accuracy of the three groups was compared over Block 4 of the initial session and Block 1 of the retention session. In addition, the three groups' accuracy

for the random block (Block 3) was compared to the three groups' accuracy for a sequence block (Block 2).

Results

Group Reaction Time Differences Before the Retention Session

A one-way ANOVA compared the reaction times of the groups in the fourth and final block of the initial session. There were 13 controls, 14 PWS and 12 PPD with complete data sets for the comparison and all ANOVA assumptions were met. The comparison was not significant indicating there was no significant group difference at the end of the initial session which may confound group differences found for the retention session.

Reaction Time for Retention of General (Non-Specific) Learning

Reaction Time for Retention: Block Contrast—There were 14 controls, 14 PWS and 13 PPD with complete data sets for the retention block contrast. Controls had 19 (4.3%) excluded trials, PWS had 19 (4.3%) excluded trials and PPD had 19 (4.6%) excluded trials. Data transformations were not successful in equalizing error variances between groups or normalizing the distributions for post hoc comparisons therefore nonparametric tests were used. Three independent samples Mann-Whitney U tests compared the difference scores (reaction time of Block 4 of the initial session subtracted from Block 1 of the retention session) of controls versus PPD, controls versus PWS, and PPD versus PWS. PWS had larger difference scores (slower reaction times on the retention test) relative to controls ($z = -1.7$, $p = .08$, $r = .32$). Although non-significant, a medium effect size was found (Portney & Watkins, 1993). Controls, PWS, and PPD had average ranks of 11.9, 17.1, and 12.5, respectively. The difference scores of controls relative to PPD and PWS relative to PPD were not statistically significant.

Reaction Time for Retention: Learning Curve Contrast—Analyses were also completed to compare the learning curve across the initial and retention session between groups. There were 13 controls, 13 PWS and 13 PPD with complete data sets. Controls had 36 (4.3%) excluded trials, PWS had 35 (4.2%) excluded trials and PPD had 40 (4.8%) excluded trials. A log transformation was successful in satisfying Box's test of co-variance and Levene's test of group variance. The Greenhouse Geisser correction was used for violations of the assumption of sphericity.

Three Group (2) x Block (8) ANOVAs compared reaction times across sessions for PWS vs. control participants, PPD vs. PWS and PPD vs. control participants. All three contrasts showed a significant Block main effect with linear and/or quadratic contrasts, $F(1.7, 24.3) = 8.1$, $p = .01$, $\eta^2 = .24$, $F(1.7, 24.3) = 14.1$, $p = .00$, $\eta^2 = .36$, and $F(1.7, 24.3) = 7.0$, $p = .01$, $\eta^2 = .23$, respectively.

Reaction times became shorter across practice blocks for all groups

Two significant polynomial contrasts indicated that PWS showed a significant increase in reaction time upon introduction of the retention test relative to control participants, $F(1.7,$

24.3) = 4.7, $p = .04$, $\eta^2 = .16$ and PPD, $F(1.7, 24.3) = 4.6$, $p = .04$, $\eta^2 = .16$ (see Figure 2). No other significant differences were found.

Reaction time for Retention: Implicit Sequence Learning—Analysis for implicit learning was completed using 384 (7.7% excluded) trials for controls, 411 trials (8.2% excluded) for PWS and 395 trials (5% excluded) for PPD. There were 13 controls, 14 PWS and 13 PPD with complete data sets. A Group (3) x Condition (2) ANOVA revealed that a Condition main effect, $F(1, 36) = 25.0$, $p = .00$, $\eta^2 = .46$, was the only significant finding. RAN reaction times were slower than SEQ reaction times. Groups' reaction times did not significantly differ on the retention test.

Reaction time for Retention: Change in Implicit Sequence Learning—Data transformations were not successful in equalizing error variances between groups or normalizing the distributions for comparisons therefore nonparametric tests were used. Three independent samples Mann-Whitney U tests compared the difference scores (RAN vs. SEQ of the initial session subtracted from RAN vs. SEQ of the retention session) of controls vs. PPD, controls vs. PWS, and PPD vs. PWS. Controls had the largest difference scores relative to PWS ($z = -2.5$, $p = .01$, $r = 4.8$) and PPD ($z = -2.2$, $p = .03$, $r = 4.2$). The effect sizes were moderate to large (Portney & Watkins, 1993). In other words, Controls' SEQ vs. RAN difference was approximately 200ms on session one and approximately 0ms on the retention test. In contrast, both PWS and PPD showed smaller SEQ vs. RAN differences on session one (0 – 100ms) but greater improvements (approximately 100 - 200ms) on the retention test. Controls, PWS, and PPD had average ranks of 18.3, 10.6, and 9.9, respectively. The difference scores of PWS relative to PPD were not significantly different.

Accuracy

Accuracy for General (Non-Specific) Learning—After excluded trials (yawns, sneezes, equipment glitches, etc.), excluded disfluencies and excluded blocks (see dependent variables section), analysis was completed using 33 blocks for controls, 39 blocks for PWS and 36 blocks for PPD. Complete accuracy data sets for this contrast were available for 11 controls, 13 PWS and 12 PPD. A Group (3) x Block (Block 4 of initial session vs. Block 1 of retention session) ANOVA revealed no significant differences.

Accuracy for Implicit Sequence-Specific Learning—After excluded trials, analysis was completed using 22 blocks for controls, 26 blocks for PWS and 22 blocks for PPD. Complete accuracy data sets for this contrast were available for 11 controls, 13 PWS and 11 PPD. A Group (3) x Condition (SEQ trials in Block 3 vs. RAN trials in Block 3) ANOVA revealed no significant differences.

Explicit Questionnaires

Control participants, PWS, and PPD scored 4.3 (2.1), 5.1 (1.4), and 5.2 (1.3) out of 10, respectively on the "Retention" questionnaire. Groups' scores did not significantly differ, and all groups performed near chance levels. Control participants, PWS, and PPD scored 3.7 (1.5), 3.6 (1.4), and 3.4 (1.7) out of 9 respectively for the generate task. Groups' scores were not statistically different and all groups performed near chance levels.

Discussion

General Learning

All groups achieved a mean reaction time of approximately 900ms by Block 2 in the retention session suggesting that the reaction times of PPD and PWS were not slower, in general, than those of control participants. Utilization of verbal responses, and participation by early stage, medicated PPD appeared to successfully minimize the confounding effects of akinesia/bradykinesia on sequence execution. Participants in the current study demonstrated significant differences in general and implicit sequence learning indicating our experimental manipulation of verbal stimuli and responses was successful. Nonsense syllable stimuli were specifically chosen so that the study results would have implications for future research investigating the efficiency of speech therapy.

The control participants showed a trend (see Figure 2) toward improvement in retention from initial testing to follow-up, which is consistent with enhancement of retention due to sleep and intact memory systems (Shadmehr & Brashers-Krug, 1997). This is likely why the learning curve differences reached statistical significance, because controls showed improvement from Block 4 of the initial session to Block 1 of the retention session while PWS showed the opposite pattern. These results suggested that PWS appeared unable to elicit general learning of the acquired skill (practiced approximately 216 times over an initial session of 120 minutes) on initial attempts after a rest period (e.g., after one week/on a retention test).

A significant interaction effect found for the initial session of the Smits-Bandstra and Gracco (2013) study revealed PWS were significantly slower, relative to controls to recall and execute syllables in response to stimuli during the first block. However, this difference diminished and even reversed by the final block. Smits-Bandstra, De Nil and Rochon (2006) and Smits-Bandstra and De Nil (2009) also reported that PWS were significantly slower than controls to extract and concatenate known components of 10-item finger-tapping and nonsense syllable sequences from memory, particularly in early trials.

This finding also concurs with a previous study finding PWS differed from controls in the immediate and spontaneous tendency to organize a 10-syllable sequence into pauses, for motor planning, and chunks of fluent motor performance during the first few trials of a sequence (Smits-Bandstra & De Nil, 2013). Finally, in a review of PWS' performance on reaction time studies in general, this "slow start" was also noted (Smits-Bandstra, 2010).

This result has potential clinical relevance because it intimates that some PWS will struggle in typical speech situations, where they are required to recall and implement learned fluency skills the first time they make a statement. This struggle may persist despite the fact that they have practiced and successfully committed the skills to procedural memory. This result may also partially explain why PWS continue to stutter on words and phrases they have practiced exhaustively, but specifically on the initial attempt to produce them. Furthermore, these results could be interpreted to suggest that several surreptitious practice trials immediately before "performing" will ensure more success in speaking fluently in target situations. Clearly further research is needed in this area, as an important limitation of the

current study is the lack of generalization from our visual, nonsense syllable task to conversational speech or typical speech skills taught in speech therapy.

These results suggest that PWS do seemed to show general learning across the learning blocks, and the initial higher reaction times likely resulted from a motor execution difficulty rather than learning per se. One speculative explanation for PWS' difficulty with speech movement elicitation is that learned sensory context and/or movement patterns for the syllables were not easily accessible/identifiable for selection and facilitation. Facilitation of sequential movement patterns is thought to be regulated by the cortico-striato-thalamo-cortical circuit (Graybiel et al., 1998). The functional effectiveness of this circuit may be disrupted due to aberrant white matter physiology within the motor cortex of PWS found in previous studies (Chang, Erikson, Ambrose, Hasegawa-Johnson & Ludlow, 2008; Chang, Horwitz, Ostuni, Reynolds & Ludlow, 2011; Sommer, Koch, Paulus, Weiller, Buchel, 2002; Watkins, 2008). Watkins et al. (2008) hypothesized that "stuttering is a disorder related primarily to disruption in the cortical and subcortical neural systems supporting the selection, initiation and execution of motor sequences necessary for fluent speech production (pg. 50).

During early trials it has been hypothesized that participants use compiled sensory information to guide recognition and facilitation of appropriate preexisting learned movement patterns (synergies) while inhibiting irrelevant ones (Saint-Cyr, 2003). The critical role of the cortico-striato-thalamo-cortical circuit for this process is well established within the neuroscience literature (Grafton, Hazeltine, & Ivry, 2002; Carbon & Eidelberg, 2006), as is PPDs' difficulty establishing skill in early trials, sometimes called "acquisition of set" (Saint-Cyr, 2003). Several researchers have suggested that the striatum "plays a significant role in the selection of the most appropriate responses in the context created by both the current and previous stimuli" (p. 179; Peigneux et al., 2000). It is important to qualify that other areas of the brain are critical contributors to implicit learning, and some would argue, perhaps the primary contributors, to this type of learning.

Exner et al. (2002) examined MRI brain volumes of patients with focal basal ganglia lesions (e.g., lacunar strokes) and controls. Interestingly, the authors reported larger brain volumes in general for patients, as well as a significant positive correlation indicating patients with greater left pre-SMA and cerebellum volumes had better implicit learning. The authors postulated that these results might indicate the importance of the cerebellum and pre-SMA, instead of the basal ganglia, for implicit sequence learning.

The involvement of the cerebellum and premotor-frontal regions for sequence learning has been reliably demonstrated (Carbon & Eidelberg, 2006; Chang et al., 2008; Chang et al., 2011; Doyon et al., 1997; Grafton et al., 2002; and Mentis, Dhawan, Figin, Delalot, Zgaljardic, Edwards & Eidelberg, 2003). However, Exner et al.'s results could also be interpreted to suggest that increased functional cortical and cerebellar compensation in patients led to the increased brain volumes that were found. Furthermore, it could be postulated that those patients who demonstrated increased cortical and cerebellar compensation demonstrated better implicit sequence learning. This postulation is supported by the research of Mentis et al. (2003). Mentis et al. (2003) reported that patients'

impairments in learning specific associations, due to Parkinson's disease, were effectively compensated for by premotor frontal areas and the cerebellum in early stages of the disease for relative short sequences.

Implicit Sequence Learning

For both the initial session (Smits-Bandstra & Gracco, 2013) and the retention session, SEQ reaction times were significantly (statistically) faster than RAN reaction times indicating that our experimental manipulation was successful in eliciting implicit learning (Nissen & Bullemer, 1987).

As expected in the initial session (reported by Smits-Bandstra & Gracco, 2013), control participants demonstrated faster reaction times for SEQ vs. RAN syllable pairs relative to PWS and PPD. This finding suggested impaired implicit learning by PWS and PPD and concurred with results of previous studies with PPD (Smith & McDowall, 2004; Westwater et al., 1998). Unexpectedly, the current analyses of RAN vs. SEQ differences across the initial session and the retention session revealed additional differences between the groups. While controls made more significant improvements in the initial session, PWS and PPD made more significant improvements during the retention session.

This finding could be interpreted to suggest that controls demonstrated early implicit learning during the initial session and minimal further implicit learning during the retention session. This is not surprising because the retention session contained relatively few practice trials and was meant to be a sample of retention of learned skills rather than an additional practice session. In contrast, PPDs' and PWS' performance on the implicit learning task across the initial 120 minute session of learning was significantly impaired relative to controls. However, both PPDs' and PWS' performance reflected significant implicit learning, equivalent to controls, after a rest period (e.g., after one week/on the retention test). These preliminary retention test results suggest that PPDs' and PWS' performance across the initial learning session was impaired and not implicit learning per se.

Perhaps some aspect of sequence learning did occur, but improved motor *responses* as a result of implicit learning were not demonstrated until the time of the retention test. One interpretation of the present analyses is that PPD and PWS acquired some aspects of the implicit sequence during session one, but were unable to demonstrate this learning until after it had consolidated (Hauptmann & Karni, 2002).

Especially noteworthy is the lack of differentiation between SEQ and RAN trials during session one and the poor retention for RAN trials during the retention session for PWS relative to other groups. The advantage PWS demonstrated for random trial reaction time in the initial session is apparent in Figure 3. One possible explanation is that PWS were better than the other groups at general learning, which was externally cued, after a practice period. Perhaps they focused on, and excelled at explicit aspects of the task such as externally cued stimulus-response associations. Well-developed general learning strategies may have developed to compensate for initial delays in implicit skill acquisition. This finding is not unprecedented. For example, in studies employing externally versus self-cued reaction times

(Siegert, Harper, Cameron & Abernethy, 2002) PPD performed similarly to, or even outperformed healthy subjects when attentional focus was guided by external stimuli.

By the end of the retention session the performance of PPD, PWS and controls was roughly equivalent indicating good implicit sequence learning and retention, if somewhat delayed for PWS and PPD. The findings of relatively good retention of implicit sequence learning for PPD were in agreement with comparable studies with PPD that examined retention over several days and found minimal or no impairment reported in the introduction (Harrington et al., 1990). This finding is a positive one, suggesting that learned skills for rehabilitation for both PWS and PPD are likely to be maintained, at least in the short-term. However replication of this research examining retention of typical skills taught in speech and occupational therapy is required for this conjecture to be confirmed.

Conclusion

In the initial 120-minute practice session (previously reported by Smits-Bandstra & Gracco, 2013) both PWS and PPD showed general learning difficulties on initial trials of a nonsense syllable task relative to controls. This effect was confirmed by a significant interaction effect with slower reaction times for PWS, relative to controls, on initial trials and equivalent or better reaction times for PWS for later trials. During the initial session both PWS and PPD showed implicit sequence learning difficulties for a nonsense syllable task relative to controls. Notably, neither PWS nor PPD differed from controls on general learning or implicit sequence learning of the nonsense syllable task on the retention test.

Taken in conjunction, one possible interpretation of these findings is that PWS and PPD had typical retention of general and implicitly learned skills, but did not, or were not able, to demonstrate or perform skills to their full potential during early trials. However, given the small group effects in the current study, replication is required for support of this contention. It must be considered that, for both PPD and PWS, the stability of the system on any given day may determine how well learned sequences can be expressed as long sequences planned in advance of the movement (Smiley-Oyen, Lowry & Kerr, 2007). General and implicit learning may, in fact, be intact, but are only incompletely or sporadically expressed due to instability of the motor planning/execution systems. This tentative proposal requires further investigation.

It must also be mentioned that sequential learning by PWS or PPD might have been affected by differences in the focus of attention, especially in the beginning of the test. If attention and cognitive processing resources required for implicit sequence learning were diverted for speech motor execution, reduced implicit sequence learning would likely result. Both PPD and PWS have demonstrated difficulties in the face of dual task demands (see Smits-Bandstra & De Nil, 2007 for a review) indicating a need for further study of the effects of attention in this area.

As a next step, it will be necessary to investigate how the manipulation of variables such as explicit instruction, practice, and feedback will influence learning and retention in

disordered populations. Future research must also have greater generalizability to functional speech tasks and speech treatment techniques than the current study.

Acknowledgments

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Appendix

Appendix A

Dysarthria Rating Scale

	(participant code)		(rater)
Pitch	Low	Normal	High
Variation of Pitch	Normal	Lack of variation	
Steadiness of Pitch	Normal	Tremor	
Loudness	Soft	Normal	Loud
Rate of Speech	Slow	Normal	Fast
Stress/Emphasis Pattern	Normal	Excess stress	
Nasality	Hyponasal	Normal	Hypernasal
Laryngeal	Harsh	Normal	Breathy
Articulatory Precision	Normal	Reduced clarity	

Intelligibility

Percentage of clear words:

95-100%	85-95%	50-85%	< 50%
All clear	Most clear	More than ½ clear	Less than ½ clear

Appendix B

Unified Parkinson's Disease Rating Scale

(Fahn, Elton, & Members of the UPDRS Development Committee, 1987)

II. Activities of Daily Living***5. Speech***

0 = Normal.

1 = Mildly affected. No difficulty being understood.

2 = Moderately affected. Sometimes asked to repeat statements.

3 = Severely affected. Frequently asked to repeat statements.

4 = Unintelligible most of the time.

Modified Hoehn and Yahr Staging

(Hoehn & Yahr, 1967)

STAGE 0 = No signs of disease.

STAGE 1 = Unilateral disease.

STAGE 1.5 = Unilateral disease plus axial involvement.

STAGE 2 = Bilateral disease, without impairment of balance.

STAGE 3 = Mild bilateral disease, with recovery on pull test.

STAGE 4 = Severe disability; still able to walk or stand unassisted.

STAGE 5 = Wheelchair bound or bedridden unless aided.

Appendix C

Initial Experimental Session

Block 1 = Total 72 trials

<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
1	2	3	4	5	6	7	8
<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i> * - Break
9	10	11	12	13	14	15	16
PO	PE	PI	PA	PE	PA	PO	PI
17	18	19	20	21	22	23	24
PO	PE	PI	PA	PE	PA	PO	PI - Break
25	26	27	28	29	30	31	32
PA	PE	PA	PO	PI	PO	PE	PI
33	34	35	36	37	38	39	40
PA	PE	PA	PO	PI	PO	PE	PI
41	42	43	44	45	46	47	48
PA	PE	PA	PO	PI	PO	PE	PI - Break
49	50	51	52	53	54	55	56
PI	PA	PE	PA	PO	PI	PO	PE
57	58	59	60	61	62	63	64
PI	PA	PE	PA	PO	PI	PO	PE
65	66	67	68	69	70	71	72

Block 2 = Total 72 trials

<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
1	2	3	4	5	6	7	8
<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i> - Break
9	10	11	12	13	14	15	16
PO	PE*	PI	PA	PE	PA	PO	PI
17	18	19	20	21	22	23	24
PO	PE	PI	PA	PE	PA	PO	PI - Break
25	26	27	28	29	30	31	32
PA	PE	PA	PO	PI	PO	PE	PI
33	34	35	36	37	38	39	40
PA	PE	PA	PO	PI	PO	PE	PI
41	42	43	44	45	46	47	48
PA	PE	PA	PO	PI	PO	PE	PI - Break
49	50	51	52	53	54	55	56
PI	PA	PE	PA	PO	PI	PO	PE
57	58	59	60	61	62	63	64
PI	PA	PE	PA	PO	PI	PO	PE
65	66	67	68	69	70	71	72

Block 3 = Total 72 trials

<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
1	2	3	4	5	6	7	8
<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i> - Break
9	10	11	12	13	14	15	16
PO	PE*	PI	PA	PE	PA	PO	PI
17	18	19	20	21	22	23	24
PO	PE	PI	PA	PE	PA	PO	PI - Break
25	26	27	28	29	30	31	32
PA	PE	PA	PO	PI	PO	PE	PI
33	34	35	36	37	38	39	40
PA	PE	PA	PO	PI	PO	PE	PI
41	42	43	44	45	46	47	48
PA	PE	PA	PO	PI	PO	PE	PI - Break
49	50	51	52	53	54	55	56
PI	PA	PE	PA	PO	PI	PO	PE
57	58	59	60	61	62	63	64
PI	PA	PE	PA	PO	PI	PO	PE
65	66	67	68	69	70	71	72

Block 4 = Total 72 Trials

PO PI PO PE PI PA PE PA
 1 2 3 4 5 6 7 8
 PO PI PO PE PI PA PE PA - Break
 9 10 11 12 13 14 15 16
 PO PE* PI PA PE PA PO PI
 17 18 19 20 21 22 23 24
 PO PE PI PA PE PA PO PI - Break
 25 26 27 28 29 30 31 32
 PA PE PA PO PI PO PE PI
 33 34 35 36 37 38 39 40
 PA PE PA PO PI PO PE PI
 41 42 43 44 45 46 47 48
 PA PE PA PO PI PO PE PI - Break
 49 50 51 52 53 54 55 56
 PI PA PE PA PO PI PO PE
 57 58 59 60 61 62 63 64
 PI PA PE PA PO PI PO PE
 65 66 67 68 69 70 71 72

Pseudorandom Block (Block 5) – Total 72 trials

PIPE** PI PA **PI** PO PI **PE***
 RAN 1 RAN 2 SEQ 1 SEQ 2 RAN 3 SEQ 3 SEQ 4 RAN 4
 PI PO PE PA PO PI PA PE - Break
 SEQ 5 SEQ 6 SEQ 7 SEQ 8 SEQ 9 SEQ 10 SEQ 11 SEQ 12
PI PA PO PI **PE** PI **PE** PI
 RAN 5 SEQ 13 SEQ 14 SEQ 15 RAN 6 SEQ 16 RAN 7 SEQ 17
 PO PE PI PO PE PI PA PE - Break
 SEQ 18 SEQ 19 SEQ 20 SEQ 21 SEQ 22 SEQ 23 SEQ 24 SEQ 25
PI PO PE PA PO PE **PO** PE
 RAN 8 SEQ 26 SEQ 27 SEQ 28 SEQ 29 SEQ 30 RAN 9 SEQ 31
 PA **PI** **PE** PA PE **PO** **PA** PO
 SEQ 32 RAN 10 RAN 11 SEQ 33 SEQ 34 RAN 12 RAN 13 SEQ 35
PA **PI** PO **PA** PO **PA** PO PE - Break
 RAN 14 RAN 15 SEQ 36 RAN 16 SEQ 37 RAN 17 SEQ 38 SEQ 39
PI **PE** PI PA **PI** PO PI **PE**
 RAN 18 RAN 19 SEQ 40 SEQ 41 RAN 20 SEQ 42 SEQ 43 RAN 21
PO PE PI PA PE PA PO PI
 RAN 22 SEQ 44 SEQ 45 SEQ 46 SEQ 47 SEQ 48 SEQ 49 SEQ 50

Day One Questionnaire

Note. *Statistical analysis included means of **BOLDED** trials of each block (see data analysis section in Smits-Bandstra & Gracco, 2013, for more detail).

PI** – Shaded syllables indicate random trials (RAN) which violate the sequence order.

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Appendix D

Retention Session

Block 1 = Total 72 trials

<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
1	2	3	4	5	6	7	8
<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
9	10	11	12	13	14	15	16
<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>
17	18	19	20	21	22	23	24
<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i> - Break
25	26	27	28	29	30	31	32
<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>
33	34	35	36	37	38	39	40
<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>
41	42	43	44	45	46	47	48
<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i> - Break
49	50	51	52	53	54	55	56
<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>
57	58	59	60	61	62	63	64
<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>
65	66	67	68	69	70	71	72

Block 2 = Total 72 trials

<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
1	2	3	4	5	6	7	8
<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>
9	10	11	12	13	14	15	16
<i>PO</i>	<i>PE</i> *	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>
17	18	19	20	21	22	23	24
<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i> - Break
25	26	27	28	29	30	31	32
<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>
33	34	35	36	37	38	39	40
<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>
41	42	43	44	45	46	47	48
<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i> - Break
49	50	51	52	53	54	55	56
<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>
57	58	59	60	61	62	63	64
<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>
65	66	67	68	69	70	71	72

Pseudorandom Block (Block 3) = Total 72 trials

<i>PI</i> **	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PI</i>	<i>PO</i>	<i>PI</i>	<i>PE</i> *
RAN 1	RAN 2	SEQ 1	SEQ 2	RAN 3	SEQ 3	SEQ 4	RAN 4
<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PA</i>	<i>PE</i> - Break
SEQ 5	SEQ 6	SEQ 7	SEQ 8	SEQ 9	SEQ 10	SEQ 11	SEQ 12
<i>PI</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>	<i>PE</i>	<i>PI</i>	<i>PE</i>	<i>PI</i>
RAN 5	SEQ 13	SEQ 14	SEQ 15	RAN 6	SEQ 16	RAN 7	SEQ 17
<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i> - Break
SEQ 18	SEQ 19	SEQ 20	SEQ 21	SEQ 22	SEQ 23	SEQ 24	SEQ 25
<i>PI</i>	<i>PO</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PE</i>	<i>PO</i>	<i>PE</i>
RAN 8	SEQ 26	SEQ 27	SEQ 28	SEQ 29	SEQ 30	RAN 9	SEQ 31
<i>PA</i>	<i>PI</i>	<i>PE</i>	<i>PA</i>	<i>PE</i>	<i>PO</i>	<i>PA</i>	<i>PO</i>
SEQ 32	RAN 10	RAN 11	SEQ 33	SEQ 34	RAN 12	RAN 13	SEQ 35
<i>PA</i>	<i>PI</i>	<i>PO</i>	<i>PA</i>	<i>PO</i>	<i>PA</i>	<i>PO</i>	<i>PE</i> - Break
RAN 14	RAN 15	SEQ 36	RAN 16	SEQ 37	RAN 17	SEQ 38	SEQ 39
<i>PI</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PI</i>	<i>PO</i>	<i>PI</i>	<i>PE</i>
RAN 18	RAN 19	SEQ 40	SEQ 41	RAN 20	SEQ 42	SEQ 43	RAN 21
<i>PO</i>	<i>PE</i>	<i>PI</i>	<i>PA</i>	<i>PE</i>	<i>PA</i>	<i>PO</i>	<i>PI</i>
RAN 22	SEQ 44	SEQ 45	SEQ 46	SEQ 47	SEQ 48	SEQ 49	SEQ 50

Day Two Questionnaire and Generate Task

Note. *Statistical analysis included means of **BOLDED** trials of each block (see data analysis section in Smits-Bandstra & Gracco, 2013, for more detail).
 ** - Shaded syllables indicate random trials (RAN) which violate the sequence order.

Appendix E

Initial Session Questionnaire

- 1) Did you notice anything about the syllables? YES NO. If yes, what did you notice?
 2) Circle the number that fits best with what you remember about the syllables.

The syllables Always appeared In this order 1	The syllables Often appeared In this order 2	The syllables Sometimes appeared in This order 3	The syllables Rarely appeared In this order 4	The syllables Never appeared In this order 5
--	--	--	--	--

- 1) PO PI 1 2 3 4 5
 2) PE PA 1 2 3 4 5
 3) PI PA 1 2 3 4 5
 4) PE PO PE 1 2 3 4 5
 5) PA PO PE 1 2 3 4 5
 6) PI PA PE 1 2 3 4 5
 7) PE PO PA 1 2 3 4 5
 8) PE PA PO PE 1 2 3 4 5
 9) PA PO PI PA 1 2 3 4 5
 10) PI PO PE PI 1 2 3 4 5

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Appendix F

Retention Questionnaire – Page 1

Subject Code _____

- 1) Did you notice anything about the order of the syllables? YES NO. If yes, what did you notice?

- 2) What number describes your belief about the syllables during the experiment?

Very sure the syllables sometimes appeared in a predictable order 1	Somewhat sure the syllables sometimes appeared in a predictable order 2	Guess the syllables sometimes appeared in a predictable order 3	Guess the syllables appeared in a random order 4	Somewhat sure the syllables appeared in random order 5	Very sure the syllables appeared in random order 6
--	--	--	--	--	--

- 3) Sometimes the syllables were part of a repeating sequence and they occurred in a predictable order.
 Put the syllables in the correct order as well as you can.

(PA, PA, PE, PE, PI, PI, PO, PO)

Appendix F

Retention Questionnaire – Page 2

Subject Code _____

- Circle the number that fits best with what you remember about the syllables.

Very sure this is part of the sequence 1	Somewhat sure this is part of the sequence 2	Guess this is part of the sequence 3	Guess this is not part of the sequence 4	Somewhat sure this is not part of the sequence 5	Very sure this is not part of the sequence 6
---	---	---	---	--	---

- A) PO PA 1 2 3 4 5 6
 B) PE PO 1 2 3 4 5 6
 C) PA PE 1 2 3 4 5 6
 D) PI PE 1 2 3 4 5 6
 E) PO PI PO 1 2 3 4 5 6
 F) PE PI PA 1 2 3 4 5 6
 G) PA PE PA 1 2 3 4 5 6
 H) PI PO PA 1 2 3 4 5 6
 I) PO PI PO PE 1 2 3 4 5 6
 J) PE PI PA PE 1 2 3 4 5 6
 K) PA PE PA PO 1 2 3 4 5 6
 L) PI PO PA PE 1 2 3 4 5 6

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Figure 1.

A diagram depicting a training trial and the visual and auditory stimuli presented during a single trial

Figure 2.

Reaction time means in seconds for control participants, persons who stutter and persons with Parkinson's disease for the initial 16 trials of Blocks 1 through 4 of the initial session and Blocks 1 and 2 of the retention session. The vertical lines capped with horizontal markers are error bars. Error bars represent 1 SD of intersubject variability unique to each group.

Sequence-Specific Reaction Time for Control Subjects, PWS and PPD on The Initial Session and the Retention Session

Figure 3.

The reaction time means (in seconds) for syllables in random pairs and syllables in sequenced pairs are contrasted for control participants, persons who stutter and persons with Parkinson's disease. The difference between random and sequence pairs is presented for the three groups for the first session and for the retention session. The vertical lines capped with horizontal markers, are error bars. Error bars represent 1 SD of intersubject variability unique to each group.

Table 1

Participant Information and Screening Test Scores

Group	Control	PWS	PPD
Sample Size	14 (6♀)	14 (6♀)	14 (7♀)
Age (<i>M, SD</i>)	65.5 (5.6)	65.1 (5.7)	64.5 (6.9)
Yrs From Diag.	N/A	childhood onset	8 (1-5 yrs), 6 (6-12yrs)
Medication	no	no	Anti-Parkinson's Med.
Handedness	14 R	14 R	13 R, 1 Ambidex.
Fwd Digit Span	12.1 (2.3)	12.1 (1.9)	11.4 (2.1)
Bwrld Digit Span	8.9 (2.4)	8.5 (2.1)	8.1 (2.2)
SSI-IV (10-17 = very mild)	N/A	10.3 (7.2)	2.8 (2.7)
MMSE (out of 30)	N/A	N/A	29.6 (0.5)
BDI (normal = less than 6)	N/A	1.3 (1.8)	0.2 (0.6)

Note. Screening measures included the; Edinburgh Handedness Inventory (Oldfield, 1971), Verbal Digit Span Subtest of the Wechsler Adult Intelligence Scale, 3rd Ed. (WAIS-III; Wechsler, 1997), Stuttering Severity Index 3 (Riley, 1994), Mini-Mental State Exam (Folstein et al., 1975) and Beck Depression Inventory (Beck et al., 1961). Diagnosis of idiopathic Parkinson's disease by a licensed neurologist was based on the presence of a rigidity-akinesia syndrome, and responsiveness to Levodopa, without signs of pyramidal, cerebellar, or oculomotor deficits. All participants were screened for hearing, vision, medication use, neurological and motor control difficulties, and speech and language difficulties.

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Table 2

Screening Information for Persons with Parkinson's Disease

Subject #	Dysarthria Characteristics	Stage H&Y ⁴²	Speech UPDRS ⁴³	Anti-Parkinson's Medication *
1	–Loud, +Harsh	2	2	Levodopa, Carbidopa
2	+Tremor, + Harsh	1	0	Levodopa, Comtan
3	+Tremor, –Loud	1	1	Recrit, Sinemet, Comtan
4	–Loud, –Variation	1	0	Sinemet
5	–Loud, – Rate	3	2	Levodopa, Amantadine, Comtan
6	+Pitch, +Harsh	3	2	Not disclosed
7	+Rate, + Harsh	2.5	1	Sinemet, Mirapex
8	+Rate, + Harsh	1	0	Levodopa, Carbidopa, Amantadine, Sinemet, Comtan, Mirapex
9	+Harsh, –Precision	1	1	Levodopa, Carbidopa
10	+Rate, +Nasal	1	0	Levodopa, Carbidopa, Amantadine, Parsitan
11	–Loud, +Rate	1	0	Levodopa, Carbidopa
12	–Rate, –Loud	1	0	Levocarb, Mirapex Selegiline
13	+Rate, –Precision	3	2	Levodopa, Sinemet, Comtan
14	+Rate, –Loud	1	0	Levodopa, Sinemet, Requip

Note. Patients medication is self-reported. PPD were tested within 60-90 minutes of their last dose of medication. Specific dosage information was not collected. H & R = Modified Hoehn & Yahr scale (Hoehn & Yahr, 1967). UPDRS = Unified Parkinson's Disease Rating Scale Section II (Activities of Daily Living), subsection 5 (Speech; Fahn et al., 1987).

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