Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Issue: *The Neurosciences and Music V*

Can rhythmic auditory cuing remediate language-related deficits in Parkinson's disease?

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Neurodegenerative changes of the basal ganglia in idiopathic Parkinson's disease (IPD) lead to motor deficits as well as general cognitive decline. Given these impairments, the question arises as to whether motor and nonmotor deficits can be ameliorated similarly. We reason that a domain-general sensorimotor circuit involved in temporal processing may support the remediation of such deficits. Following findings that auditory cuing benefits gait kinematics, we explored whether reported language-processing deficits in IPD can also be remediated via auditory cuing. During continuous EEG measurement, an individual diagnosed with IPD heard two types of temporally predictable but metrically different auditory beat-based cues: a march, which metrically aligned with the speech accent structure, a waltz that did not metrically align, or no cue before listening to naturally spoken sentences that were either grammatically well formed or were semantically or syntactically incorrect. Results confirmed that only the cuing with a march led to improved computation of syntactic and semantic information. We infer that a marching rhythm may lead to a stronger engagement of the cerebello–thalamo–cortical circuit that compensates dysfunctional striato–cortical timing. Reinforcing temporal realignment, in turn, may lead to the timely processing of linguistic information embedded in the temporally variable speech signal.

Keywords: auditory cuing; rhythm; speech and language; remediation; Parkinson's disease; ERP

Introduction

Dopamine depletion in the substantia nigra leads to basal ganglia dysfunction, the primary cause of idiopathic Parkinson's disease (IPD). During the disease progression, individuals with IPD develop a plethora of symptoms indicating primary gait dysfunction[1] as well as cognitive impairments[2] that include deficits of attentional[3] and temporal control,[4] perception of music and speech rhythm,[5,6] and language processes.[7]

Regarding language in IPD, a number of studies have indicated that either structural or neurodegenerative changes of the basal ganglia affect the computation of syntactic[8–14] as well as semantic information.[15–18] Grossman *et al.* reasoned that syntax-related computational deficits in IPD may result from impaired executive function (e.g., attention)[9,19] or altered processing speed,[20] a notion that has also been considered to explain semantic deficits[18] in IPD. It therefore appears that (1) the computation of both syntactic and semantic information in tasks demanding attention may be most affected, and/or (2) the computation of syntactic and semantic information, embedded in natural, temporally variable speech, may be impacted by a generalized temporal processing deficit reported in IPD.[4,21–23] Alternatively, it is conceivable that a generalized temporal processing deficit in IPD mostly affects the computation of language processes that are under attentional demand. This, in turn, could lead to epiphenomenal language deficits. Should this be the case, the remediation of a temporal processing deficit should lead to an improved computation of syntactic and semantic information embedded in natural speech.

doi: 10.1111/nyas.12657

We recently proposed that a generalized temporal processing deficit in IPD may affect not only the initiation and smoothness of movements but also the efficient processing of a number of nonmotor functions, including speech and language.[24–26] It is established that by providing individuals with IPD with temporally predictable (e.g., metronomic or isochronous) external auditory cues, gait dysfunction can be remediated[25,27] via the sensorimotor coupling (e.g., synchronization) of a movement and a sensory cue that reinitiates as well as recalibrates temporally precise and coordinated movement.[28,29] In addition, temporally predictable external sensory cues may not only temporally realign motor behavior but also offset dysfunctional timing in the basal ganglia system.[30,31] The question arises as to how and where such realignment occurs and whether it can impact a generalized temporal processing deficit that affects higher cognitive functions such as speech and language.

In line with the idea that temporally predictable external auditory cues generate expectations about *when* a next event occurs,[32–34] it has been suggested that the synchronization of temporally predictable external auditory cues and internal action plans (e.g., when to take a next step while walking) may stabilize movement.[26,27] It has been proposed that this process is likely supported by a cerebello–thalamo–cortical circuit[24,25,27] that interfaces with a malfunctioning striato–cortical circuit.[35] The cerebello–thalamo–cortical circuit, which is argued to support temporally predictable external auditory cuing, constitutes a domain-general network engaged in motor and perceptual timing.[31,36,37] Thus, providing IPD patients with temporally predictable external auditory cues may benefit not only gait kinematics but also temporally encoded nonmotor behavior such as the perception of speech and music.[4]

In light of the observation that the computation of linguistic information, specifically under attentional demands[9,11–13,20] and dependent on processing speed,[19] is affected in patients with structural and neurodegenerative changes of the basal ganglia, the following scenario is plausible: if we provide IPD patients with temporally predictable external auditory cues before they listen to speech, the perception of temporally misaligned linguistic information embedded in natural, temporally variable speech[24,38] may be realigned, and this may affect how successfully linguistic information is processed in time. Consequently, temporally predictable external auditory cues should reinforce the realignment of dysfunctional temporal processing in the striato–cortical network, which, in turn, should lead to improved syntactic and semantic information processing in speech.

Current case study

In this exploratory case study, we set out to test the following hypothesis: subjecting a patient with IPD to temporally predictable external auditory stimulation before he or she listens to naturally spoken sentences should lead to improved temporal processing of these sentences. More specifically, we predicted that a march meter (e.g., alternating a strong and weak beat pattern) that is more congruent with the predominant meter of the language at test (e.g., the alternation of a strong and weak syllable pattern in German) should lead to better realignment of temporal processing than a waltz meter. Should this be the case, we would also expect specific remediation of the computation of syntactic and semantic information embedded in natural, temporally variable speech. For example, both patients with IPD[39] or with focal lesions in the mid- to posterior portion of the putamen of the basal ganglia[12,13] have shown strongly altered P600 event-related potential (ERP) responses to syntactically incorrect information and temporally delayed N400 responses to semantically incorrect information in previous research. These results have indicated that responses to syntactically incorrect information at expected points in time may be more strongly affected than those to semantically incorrect information. If, as we assume, these altered language-related ERP responses result from a generalized temporal processing deficit, exposure to a temporally predictable external cue that best maps onto the metric structure of the speech signal should lead to the improved processing of unexpected (e.g., incorrect) linguistic events at expected points in time in the ongoing speech signal. In addition, and to ensure that the expected alteration of ERP responses in natural speech are not due to a generalized deficit of attention in IPD, we added an auditory oddball paradigm (e.g., altering the presentation of standard tones and deviant tones) that makes it possible to monitor selective attention.

We expected that KA, an individual diagnosed with IPD, would show an altered P600 response to incorrect syntactic information as well as a modulation of the N400 response to incorrect semantic information during natural auditory language processing. We also predicted that KA would benefit most from being exposed to a temporally predictable march rhythm that maps the predominant meter of the language (e.g., improved or normal P600 and N400 responses to ill-formed sentences) but less from a temporally predictable waltz rhythm that does not map the metrical structure of language (e.g., no or little improvement) before listening to naturally spoken grammatically well-formed as well as syntactically and semantically ill-formed sentences.

Materials and methods

Participant

A 58-year-old right-handed (Edinburgh handedness questionnaire)[40] man (KA) diagnosed with IPD with predominant right-sided motor symptoms was invited to participate in this study protocol. He gave informed consent to participate in the study according to the Declaration of Helsinki and was reimbursed for his participation. The ethics committee of the University of Leipzig agreed to the study protocol. According to clinical reports, KA had no other diagnosed neurological or psychiatric disorder, normal hearing, and was, at the time of testing, in an advanced stage of IPD (Hoehn & Yahr scale 3–4; UPDRS-III 47; 14 years post–IPD diagnosis)[41] and medicated (Nacom, ReQuip, Comtess, and Parkotil).

Experimental setup

The complete experiment consisted of four different experimental runs, each containing an auditory oddball section followed by a language section, which consisted of four miniblocks of 24 sentences each. To explore the impact of temporally predictable auditory cues conveyed by music on language processing, we manipulated the language sections of the experimental runs in the following way: the first and fourth runs served as a baseline condition in which no musical stimulation preceded the language sections. In the second experimental run, each language miniblock preceded a 3-min-long piece of march music (4/4). In the third experimental run, 3 min of waltz music (3/4; "Schneewalzer"composed by Thomas Koschat) was presented before each miniblock of language.

Auditory oddball section

To control potential attention deficits that may affect performance in the language sections of the experimental protocol, in each run an auditory oddball section was presented before the language sections. Deviant tones in the oddball paradigm were expected to elicit a P300, which indicates selective attention to deviant acoustic stimulus properties.[42] Sinusoidal tones of two frequencies were presented as standard (600 Hz) and deviant (660 Hz) in a randomized order at a rate of 4:1 (320 standards, 80 deviants). KA was asked to count the deviant tones while fixating on a white cross on the computer screen. The duration of the auditory oddball section was approximately 7 minutes.

Language section

The language stimuli were similar to those used in an earlier patient study with IPD patients.[39] Sentences were spoken by a trained female speaker of standard German in a soundproof chamber and were then digitized at a 20 kHz/12 bit sampling rate. There were 96 correct sentences (short and long) such as *Das Eis wurde (im Eissalon) gegessen/The ice cream was eaten (in the ice cream parlor)*, 48 semantically incorrect sentences resulting from a selectional restriction violation such as *Das Hemd wurde gegessen/The shirt was eaten*, and 48 syntactically incorrect sentences such as *Das Eis wurde im__ gegessen/The ice cream was in__ eaten.* KA passively listened to the sentences (no behavioral response). Stimuli were presented in four miniblocks of 24 sentences each, divided equally across the four sentence types. According to previous results, we expected that syntactically incorrect sentences, which normally elicit a larger late positive ERP response (P600) than correct sentences, would be reduced or absent in KA but that the response to semantically incorrect sentences (compared to correct sentences) would be larger but delayed.[25] Both ERP responses would indicate KA's capacity to respond to linguistically well-formed and ill-formed information during auditory language processing. The duration of the total language section was approximately 40 minutes.

EEG recording and data analyses

Continuous EEG signals were recorded from 26 Ag/AgCl electrodes mounted in an elastic cap (Electro-Cap International, Eaton, OH). The locations of the electrodes were F7/8, F3/4, Fz, FT7/FT8,

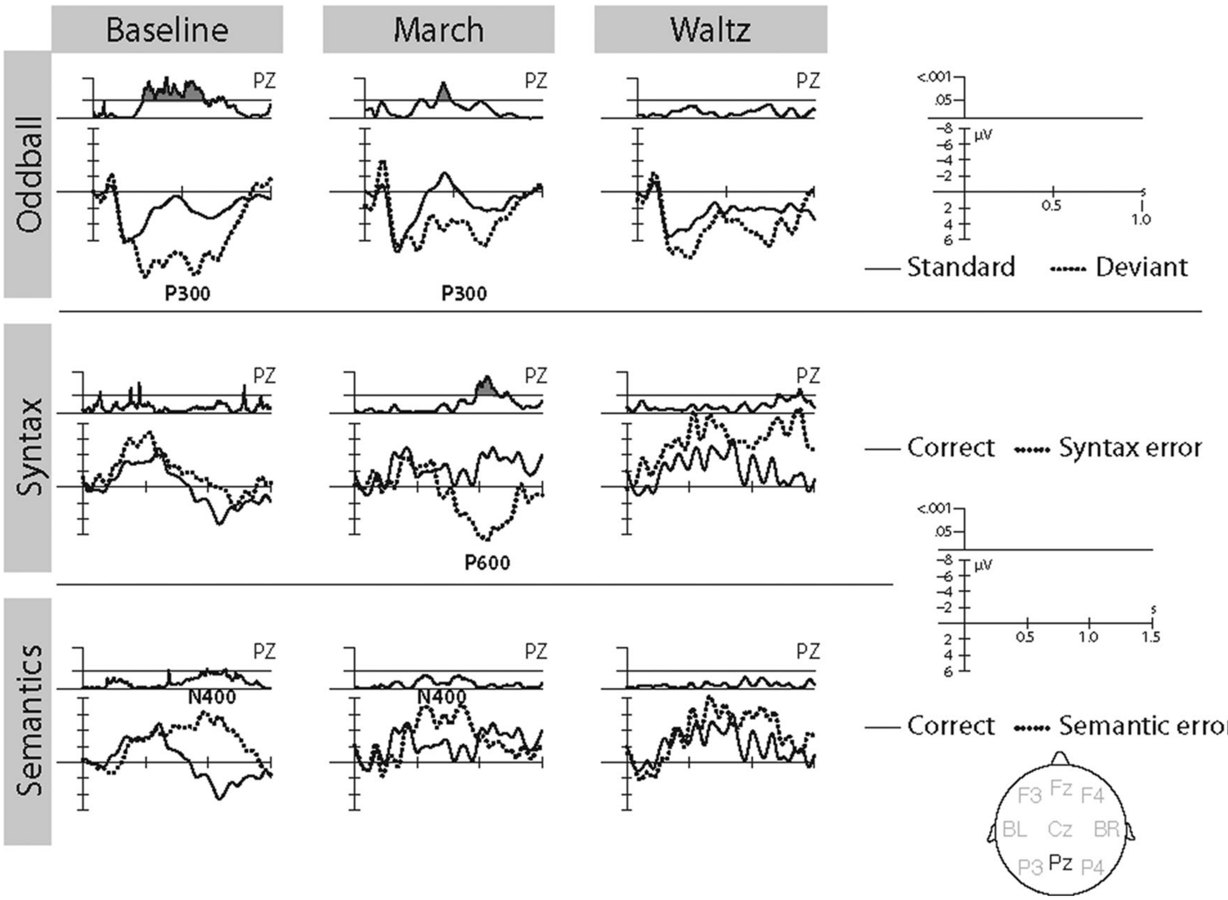

Figure 1. Displayed from left to right at a sample electrode (Pz) are the P300 effect (top row) for the baseline, march, and waltz conditions, the P600 effect (middle row), and the N400 effect (bottom row). ERP responses to unexpected tones or linguistic events are plotted in dashed lines, and expected events are plotted in bold lines. The scales for the oddball and linguistic events respectively list the voltage change and statistical significance (y-axis)[48] as well as the time course (x-axis). A schematic head display shows the position of the sample electrode amid all electrodes recorded from.

FC3/FC4, Cz, CP5/6, Pz, P7/8, P3/4, Oz, and O1/2, according to the nomenclature proposed by the American Electroencephalographic Society.[43] Additional electrodes were placed at both mastoids (A1 and A2). The ground electrode was located at FPz. To control for artifacts caused by eye movements, bipolar electrooculograms (EOGs) were recorded from the outer canthus of each eye for the horizontal EOG and from above and below the right eye for the vertical EOG. All electrodes were connected to an amplifier (TMS International, Glassport, PA), and A1 served as online reference. Signals were sampled online at 250 Hz (DC to 40 Hz). Electrode impedances were kept below 5 kΩ. EEG data were filtered offline using a high-pass filter of 0.4 Hz. During data processing, all electrodes were re-referenced to linked mastoids. Eye artifact control measures were applied to the raw data to increase the number of critical trials in each condition.[44] After this procedure, individual EEG recordings were scanned for additional artifacts by applying automatic artifact rejection using a 200-ms sliding window on the EOG (±30 mV) and EEG channels (±30 mV). On the basis of these criteria, approximately 4% of all data were excluded from further analysis. ERPs were calculated from the onset of the critical event (sound or word) until 1500 ms after stimulus onset. The first 100 ms of the critical event were used as a baseline. A 7-Hz low-pass filter was used for presentation purposes only. Because we present a single case result, we chose running t-tests to test the reliability of the differences between the correct and the incorrect conditions for each of the nine conditions (baseline/march/waltz for oddball/syntax/semantics). These t-tests were calculated at each sampling point (i.e., every 4 ms) at each electrode site. As can be seen in Figure 1, areas in which the conditions differ significantly are plotted above the electrode in a line graph. The shaded areas indicate a significance level of $P < 0.05$.

Results

Figure 1 shows the baseline condition (left column top to bottom) in which no temporally predictable external auditory rhythmic cue was given to KA. We see a clear P300 effect (deviants > standards) in the oddball condition, no significant P600 effect (syntactically incorrect > syntactically correct), and a marginally significant N400 effect (semantically incorrect > semantically correct) in a very late time window peaking around 1000 ms after stimulus onset. Note that a typical N400 peaks between 300 and 500 ms post-stimulus onset. These data thus fit the predicted pattern for IPD patients. In the march condition (middle column top to bottom), the oddball results confirm a significant P300 effect comparable to the one in the baseline condition, a very clear P600 effect, and a marginally significant N400 effect. The N400 response seems to be elicited earlier and is temporally more constrained than in the baseline condition, although it is still slower than what is found in the literature on semantic processing in middle-aged participants.[45,46] This indicates that being exposed to the temporally predictable metrical structure of the march before listening to speech leads to significantly improved computation of syntactic and semantic information. In the waltz condition (right column top to bottom), we see no significant effects for either the oddball (trend to be significant), syntactic, or semantic processing, suggesting that the temporally predictable metric structure of the waltz, which does not map onto the metric structure of the speech signal, has no effect on the computation of syntactic and semantic information, rendering the results comparable to the baseline condition.

Discussion

In this case study, we explored whether exposure to temporally predictable external auditory cues, which are known to improve synchronous motor and temporal processing in IPD,[26] can also affect the subsequent processing of higher level linguistic information embedded in the temporally variable speech signal.[4–25] The results confirmed that exposure to a highly predictable and metrically simple auditory cue, such as a march, has an impact on the subsequent computation of syntactic and semantic information processing. We consider that, if such a temporally predictable external auditory cue maps onto the metric structure of the speech signal, there may be a benefit in the realignment of dysfunctional temporal processing in the striato–cortical network, with direct consequences for linguistic information processing in the dynamic and temporally variable speech signal.

The most interesting result in this case study is that a temporally highly predictable external auditory cue, such as a march (4/4), seemed to fully restore a P600 effect in response to a syntactic expectancy violation, for example, when the listener expects to hear a noun but hears a verb instead. Although the syntactic expectancy violation in the baseline and the waltz (3/4) conditions did not elicit any late positive response, there was a robust and significant P600 response in the march condition only. This may indicate that when KA listened to a temporally predictable but metrically simple auditory cue before listening to sentences, the temporal integration of sentence constituents was facilitated by sensitizing the syntactic parser to the temporal occurrence of expected (and syntactically marked) events and highlighted when they were unexpected (i.e., when a deviation with respect to syntactic categorization occurs). This form of remediation may be best explained by recent theories of entrainment in music[33] and in speech.[47] These theories postulate that brain oscillations synchronize with temporally regular patterns (i.e., via external stimulation) and lead to efficient information processing at expected time points. Persons with IPD may therefore profit from external temporally regular sensory cues that facilitate the synchronization of temporally variable events in the speech signal (e.g., the coding of linguistic information) and internal oscillations that are potentially out of synch. Therefore, dysfunctional striato–cortical temporal processing may be remediated by building up stable attractor states so that patients with IPD can respond to unexpected syntactic events at expected points in time in the speech signal. A cerebello–thalamo–cortical circuit encoding discrete temporal events[37] may therefore serve as a facilitator to temporally realign oscillatory activity in the dysfunctional striato–cortical system.[24,25]

Although this is less clear, it seems that semantic processing also benefited from the temporally predictable external auditory cue. The marginally significant N400 effect in the march condition seemed to be elicited earlier compared to the N400 effect found in the baseline condition. The latency shift (onset and offset) of the N400 response, although less prominent than in the syntactic condition, is in line with our interpretation of the syntax effect. However, we note that the realignment of semantically unexpected events seems to affect the ERP response in a qualitatively different manner than for syntactically unexpected events. Further studies are needed to clarify why such differential effects occur, and they are currently under way.

Conclusion

We propose that the striato–cortical circuit in the healthy brain serves the synchronization and adaptation of internal oscillations with external events. Structural or neurodegenerative changes of the basal ganglia may destabilize the dynamics of internal oscillations that, in turn, may affect the computation of linguistic information (e.g., the integration of syntactic and semantic constituents into a sentence context). We were able to show that an individual with IPD who showed evidence of dysfunctional linguistic information processing can benefit from exposure to a temporally predictable external beat-based auditory cue that maps the metrical structure of the language that was tested. However, replication of this phenomenon in a larger sample and the consideration of individual differences with regard to the efficacy of such remediation training, as well as the isolation of the metrical organization as a musical variable in this form of training of speech- and language-related deficits in IPD, is clearly required.

Acknowledgments

The authors thank Ina Koch, Juliana Hofmann, and Dorothee Geyer for support during data collection and data processing and Kerstin Falke for graphics support. Special thanks also go to Katie Overy, Jessica Grahn, Lauren Trainor, Michael Schwartze, and Simone Dalla Bella for helpful feedback on a previous version of the manuscript.

Conflicts of interest

The authors declare no conflicts of interest.

References

1. Grabli, D., C. Karachi, M.L. Welter, *et al.* 2012. Normal and pathological gait: what we learn from Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry* **83:** 979–985.
2. Owen, A.M., J. Doyan, A. Dagher, *et al.* 1998. Abnormal basal ganglia outflow in Parkinson's disease identified with PET. Implications for higher cognitive functions. *Brain* **121:** 949–465.
3. Brown, P. & C.D. Marsden. 1998. What do the basal ganglia do? *Lancet* **351:** 1801–8014.
4. Harrington, D.L., G.N. Castillo, P.A. Greenberg, *et al.* 2011. Neurobehavioral mechanisms of temporal processing deficits in Parkinson's disease. *PLoS One* **6:** e17461. doi: 10.1371/journal.pone.0017461.
5. Grahn, J.A. & M. Brett. 2009. Impairment of beat-based rhythm discrimination in Parkinson's disease. *Cortex* **45:** 54–61.
6. Pell, M.D. & C.L. Leonard. 2003. Processing emotional tone from speech in Parkinson's disease. *Cogn. Affect Behav. Neurosci.* **3:** 275–288.
7. Ullman, M., S. Corkin, M. Coppola, *et al.* 1997. A neural dissociation within language: evidence that the mental dictionary is part of declarative memory, and that grammatical rules are processed by the procedural system. *J. Cogn. Neurosci.* **9:** 266–276.
8. Grossman, M., S. Carvell, S. Gollomp, *et al.* 1991. Sentence comprehension and praxis deficits in Parkinson's disease. *Neurology* **41:** 1620–1626.
9. Grossman, M., S. Carvell, M.B. Stern, *et al.* 1992. Sentence comprehension in Parkinson's disease: the role of attention and memory. *Brain Lang.* **42:** 347–384.
10. Grossman, M., S. Carvell, S. Gollomp, *et al.* 1993. Cognitive and physiological substrates of impaired sentence processing in Parkinson's disease. *J. Cogn. Neurosci.* **5:** 480–498.
11. Friederici, A.D. & S.A. Kotz. 2003. The brain basis of syntactic processes: functional imaging and lesion studies. *NeuroImage* **20:** S8–S17.
12. Frisch, S., S.A. Kotz, D.Y. von Cramon & A.D. Friederici. 2003. Why the P600 is not just a P300: the role of the basal ganglia. *Clin. Neurophysiol.* **114:** 336–340.
13. Kotz, S.A., S. Frisch, D.Y. von Cramon & A.D. Friederici. 2003. Syntactic language processing: ERP lesion data on the role of the basal ganglia. *J. Int. Neuropsychol. Soc.* **9:** 1053–1060.
14. Longworth, C.E., S.E. Keenan, R.A. Barker, *et al.* 2005. The basal ganglia and rule-governed language use: evidence from vascular and degenerative conditions. *Brain* **128:** 584–596.
15. Copland, D. 2003. The basal ganglia and semantic engagement: potential insights from semantic priming in individuals with subcortical vascular lesions, Parkinson's disease, and cortical lesions. *J. Int. Neuropsychol. Soc.* **9:** 1041–1052.
16. Copland, D.A., H.J. Chenery & B.E. Murdoch. 2000. Processing lexical ambiguities in word triplets: evidence of lexical-semantic deficits following dominant nonthalamic subcortical lesions. *Neuropsychology* **14:** 379–390.
17. Copland, D.A., H.J. Chenery & B.E. Murdoch. 2000. Understanding ambiguous words in biased sentences: evidence of transient contextual effects in individuals with

nonthalamic subcortical lesions and Parkinson's disease. *Cortex* **36:** 601–622.

18. Copland, D.A., H.J. Chenery & B.E. Murdoch. 2001. Discourse priming of homophones in individuals with dominant nonthalamic subcortical lesions, cortical lesions and Parkinson's disease. *J. Clin. Exp. Neuropsychol.* **23:** 538–556.
19. Grossman, M., J. Kalmanson, N. Bernhardt, *et al.* 2000. Cognitive resource limitations during sentence comprehension in Parkinson's disease. *Brain Lang.* **73:** 1–16.
20. Grossman, M., E. Zurif, C. Lee, *et al.* 2002. Information processing speed and sentence comprehension in Parkinson's disease. *Neuropsychology* **16:** 174–181.
21. Hallett, M. 2008. The intrinsic and extrinsic aspects of freezing of gait. *Mov. Disord.* **23:** S439–S443.
22. Allman, M.J. & W.H. Meck. 2012. Pathophysiological distortions in time perception and timed performance. *Brain* **135:** 656–677.
23. Wu, T., J. Wang, C. Wang, *et al.* 2012. Basal ganglia circuits changes in Parkinson's disease patients. *Neurosci. Lett.* **524:** 55–59.
24. Kotz, S.A., M. Schwartze & M. Schmidt-Kassow. 2009. Nonmotor basal ganglia functions: a review and proposal for a model of sensory predictability in auditory language perception. *Cortex* **45:** 982–990.
25. Kotz, S.A. & M. Schwartze. 2011. Differential input of the supplementary motor area to a dedicated temporal processing network: functional and clinical implications. *Front. Integr. Neurosci.* **5:** 86.
26. Benoit, C-E., S. Dalla Bella, N. Farrugia, *et al.* 2014. Musically cued gait training improves both perceptual and motor timing in Parkinson's disease. *Front. Hum. Neurosci.* **8:** 494.
27. Nombela, C., L.E. Hughes, A.M. Owen & J.A. Grahn. 2013. Into the groove: can rhythm influence Parkinson's disease? *Neurosci. Biobehav. Rev.* **37:** 2564–2570.
28. Lim, I., E. VanWegen, C. DeGoede, *et al.* 2005. Effects of external rhythmical cueing on gait in patients with Parkinson's disease: a systematic review. *Clin. Rehabil.* **19:** 695–713.
29. Spaulding, S.J., B. Barber, M. Colby, *et al.* 2012. Cueing and gait improvement among people with Parkinson's disease: a meta-analysis. *Arch. Phys. Med. Rehabil.* **94:** 562–570.
30. Wing, A.M. 2002. Voluntary timing and brain function: an information processing approach. *Brain Cogn.* **48:** 7–30.
31. Coull, J.T., R.K. Cheng & W.H. Meck. 2011. Neuroanatomical and neurochemical substrates of timing. *Neuropsychopharmacology* **36:** 3–25.
32. Jones, M.R. 1976. Time, our lost dimension: toward a new theory of perception, attention, and memory. *Psychol. Rev.* **83:** 323–355.
33. Large, E.W. & M.R. Jones. 1999. The dynamics of attending: how we track time. *Psychol. Rev.* **106:** 119–159.
34. Large, E.W. 2008. "Resonating to musical rhythm: theory and experiment." In *The Psychology of Time*. S. Grondin, Ed.: 189–231. West Yorkshire, UK: Emerald.
35. Lewis, M.M., C.G. Slagle, A.B. Smith, *et al.* 2007. Task specific influences of Parkinson's disease on the striato-thalamo-cortical and cerebello-thalamo-cortical motor circuitries. *Neuroscience* **147:** 224–235.
36. Merchant, H., D.L. Harrington & W.H. Meck. 2013. Neural basis of the perception and estimation of time. *Annu. Rev. Neurosci.* **36:** 313–336.
37. Schwartze, M. & S.A. Kotz. 2013. A dual-pathway neural architecture for specific temporal prediction. *Neurosci. Biobehav. Rev.* **37:** 2587–2596.
38. Kotz, S.A. & M. Schwartze. 2010. Cortical speech processing unplugged: a timely subcortico-cortical framework. *Trends Cogn. Sci.* **14:** 392–399.
39. Friederici, A.D., S.A. Kotz, K. Werheid, *et al.* 2003. Syntactic comprehension in Parkinson's disease: investigating early automatic and late integrational processes using event-related brain potentials. *Neuropsychology* **17:** 133–342.
40. Oldfield, R.C. 1971. The assessment and analysis of handedness: the Edinburgh inventory. *Neuropsychologia* **9:** 97–113.
41. Hoehn, M.M. & M.D. Yahr. 1967. Parkinsonism: onset, progression, and mortality. *Neurology* **17:** 427–442.
42. Polich, J. 2007. Updating P300: an integrative theory of P3a and P3b. *Clin. Neurophysiol.* **118:** 128–148.
43. Scarborough, F. 1991. American Electroencephalographic Society guidelines for standard electrode position nomenclature. *J. Clin. Neurophysiol.* **8:** 200–202.
44. Pfeifer, E., R. Novagk & B. Maess. 1995. "Software for EEG-ERP evaluation." In *Max Planck Institute of Cognitive Neuroscience Leipzig Annual Report*. A.D. Friederici, Ed.: 51–55. Leipzig: Max Planck Institute of Cognitive Neuroscience.
45. Gunter, T.C., J.L. Jackson & G. Mulder. 1995. Language, memory and aging: an electrophysiological exploration of the N400 during reading of memory demanding sentences. *Psychophysiology* **32:** 215–229.
46. Gunter, T.C., J.L. Jackson & G. Mulder. 1998. Priming and aging: an electrophysiological investigation of the N400. *Brain Lang.* **65:** 333–355.
47. Lakatos, P., G. Karmos, A.D. Mehta, *et al.* 2008. Entrainment of neuronal oscillations as a mechanism of attentional selection. *Science* **320:** 110–113.
48. Friederici, A.D., A. Hahne & D.Y. von Cramon. 1998. First-pass versus second-pass parsing processes in a Wernicke and a Broca's aphasic: evidence for a double dissociation. *Brain Lang.* **62:** 311–341.