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ORIGINAL RESEARCH

Temporal discrimination learning for treatment of gait dysfunction in Parkinson's disease: a feasibility study using single subject design

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Abstract

Freezing of gait in Parkinson's disease may be attributed to dysfunctional neural timing that alters stride time variability. This study investigated the feasibility of a five day perceptual timing training program using an auditory interval discrimination task to reduce stride time variability in Parkinson's disease. Results showed that training produced an increase in time-discrimination acuity in a Parkinson's disease patient, followed by a decrease in stride time variability. Effects persisted six weeks after training. No learning-transfer effects were found in a patient trained in a pitch discrimination task. In conclusion, interval discrimination training may reduce temporal gait irregularities in Parkinson's disease.

Introduction

Gait disorders in Parkinson's disease (PD) can be attributed to dysfunctional neural timing that alters stride time variability.[1] People with PD who fall have higher stride-to-stride variability compared to non-fallers.[2] However gait rhythm deficits in PD are difficult to treat.[3] We propose a rehabilitative approach that is based on a common mechanism for perceptual and motor timing functions (e.g., the human internal clock).[4 5 6] Specifically, prior work in unaffected individuals showed that improvements in time discrimination (a perceptual task) may be transferable to improvements in motor coordination through circuits shared during perceptual and motor timing.[4] Thus we attempted to improve mobility in PD by using intensive training on an auditory interval discrimination task (AIDT) with the hope that perceptual training could help those with PD without constant external sensory cueing.

Methods

One hour of AIDT occurred across five days in one PD patient (PD1). Before and after AIDT stride time variability was tested on a six minute walk test (6MWT) to determine if transfer of rhythm from perceptual to motor tasks occurred. As a control, another PD subject (PD2) was exposed to pitch discrimination training (PDT) over five days that required the recognition of tones, and hence was not a timing exercise.[5] Characteristics of participants are

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shown in Table 1. Each subject was tested on medications, and provided informed consent for this University of Minnesota institutional review board-approved study.

Table 1. Subject characteristics.

	Subject 1	Subject 2
Age (years)	57	58
Gender	Female	Male
Years since Diagnosis	4	5
PD Medication	Rasagiline	Rasagiline, Levodopa/ carbidopa
Modified Hoehn & Yahr Staging	2.5	2
UPDRSm*	7	15
Mini Mental State Exam	29	29
Cognitive Training	Time Discrimination	Pitch Discrimination

*UPDRSm, Unified Parkinson's Disease Rating Scale – motor section.

For AIDT, a trial consisted of the presentation of two pairs of beeps with a time interval utilized ("reference interval") based upon the subject's preferred inter-step interval of the 6MWT. The other pair of beeps was separated by either a longer or shorter interval. The subject determined if a randomly presented interval or a reference interval was longer and pressed a key. The intertrial interval was two seconds.

For PDT, two beeps were presented for each trial in random order with a comparison beep that was either of higher or lower pitch than the reference beep.

During training (approximately one hour per day), the comparison interval or pitch was adjusted adaptively to bring the stimulus closer to the reference after every three consecutive correct responses. Conversely, the comparison interval was made larger (or reference-comparison pitch difference increases) after each incorrect response to make discrimination easier.[7] As the subject was exposed to repeated trials, thresholds would decrease as the subject had improved discrimination ability with regard to either time intervals (PD1) or pitch (PD2). Six blocks of 60 trials each were presented every day for five days with no more than two days separating a training session.

The 6MWT and reductions in stride time variability helped determine if transfer of rhythm from perceptual to motor tasks occurred. Each subject wore a wireless audio foot switch that recorded each heel strike during 6MWT. The duration between right heel strike and the subsequent right heel strike was defined as the stride time interval. Stride time durations were collected into bins of ten consecutive steps. Variability of stride times in each bin was measured using the coefficient of variation (CV = (bin standard deviation) / (bin mean) × 100). Thus, if a subject took 400 steps during the 6MWT, there would be 40 CVs representing the variability of each bin of ten consecutive steps. Total step count during the 6MWT was translated into an average inter-step interval (360 seconds / total number of steps). This value was the "preferred inter-step interval."

6MWT occurred in three sessions: a few days before the five-day discrimination training period (pretest); the day after the end of the discrimination training period (posttest); and six weeks after the discrimination training period (six-week follow-up).

Data analyses included plotting discrimination thresholds to determine the change in discrimination learning over training days 5 and 7. A negative slope across training days and a significant decrease in threshold magnitude from day 1 to day 5 indicated perceptual learning. Discrimination thresholds were evaluated with a totally within subject analysis of variance (ANOVA) across training days. Separate analyses were performed for each subject. Linear regression was used to calculate the slope of the line of best fit for mean thresholds over training days.

Stride time bin variability during the 6MWT was plotted for the three sessions and the plot for each subject was evaluated visually with the aid of a celeration line for each session. Level was defined as an abrupt vertical change in the pattern of results, whereas trend was defined as an obvious change in the slope of the celeration line.

Results and Discussion

There was a significant learning effect in both subjects (Figure 1A, PD1, $F_{(4,241)} = 23.27$, $p < 0.0001$; Figure 1B, PD2, $F_{(4,265)} = 6.90$, $p < 0.0001$), with a clear decrease in interval or pitch discrimination threshold as a function of training day.

Regarding gait performance PD1, who received the AIDT (Figure 1C), showed a decrease in stride time variability in the posttest and 6 weeks after motor sessions. In contrast PD2, who underwent PDT (Figure 1D), showed a small increase in stride time variability.

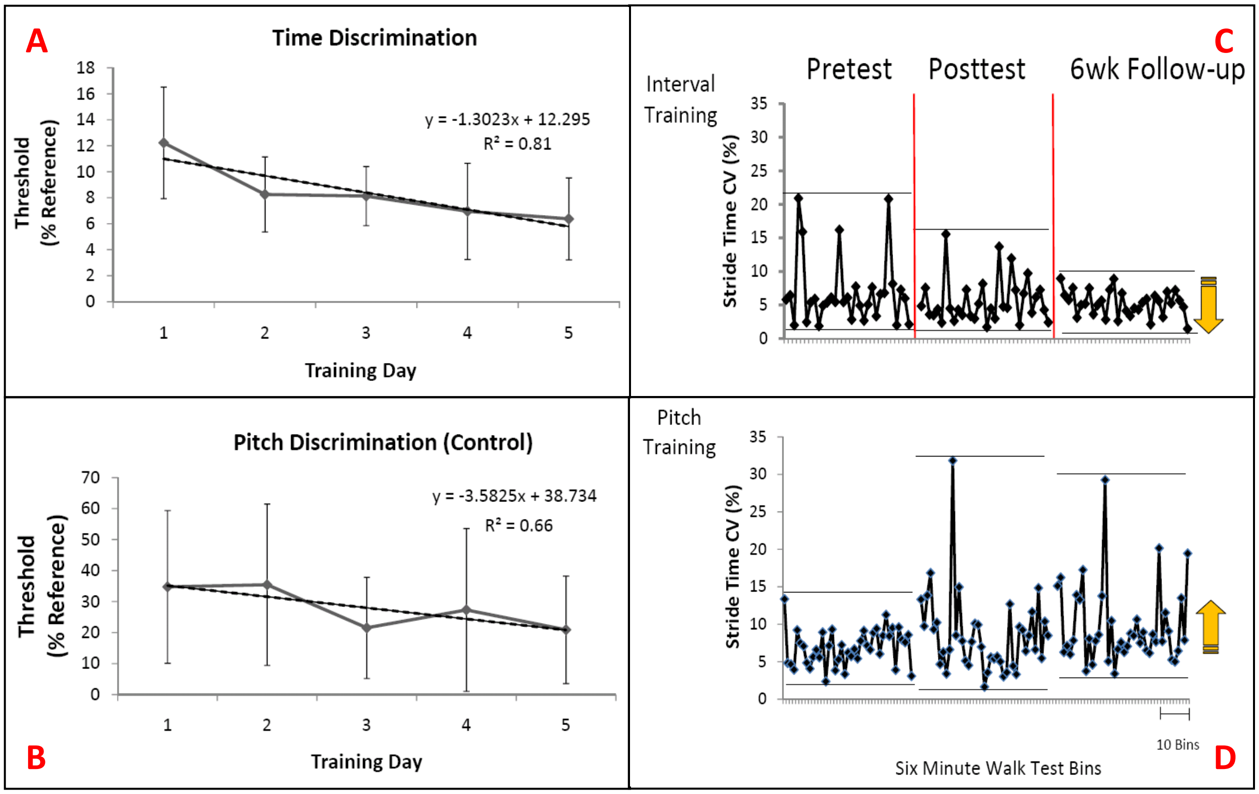

Figure 1. **A**, **B**) Discrimination thresholds across training days (note scale change in panel **B**). **C**, **D**) Stride time variability for each phase during 6 minute walk test. Each tick mark on the x axis represents a bin of 10 consecutive steps. Arrow at the end of each plot shows the direction of stride time variability over time. Abbreviations: 6MWT=six minute walk test, CV=coefficient of variation.

Rehabilitation of motor timing deficits in PD has largely focused on sensory feedback therapy and there has been little carryover of the benefits.[8 9 10] Hence there is a need for easy-to-implement therapy that would bypass the need for constant external cueing.[10] Some have used "internal cueing" to improve gait by introducing a cognitive task, while others have employed amplitude-based therapies ("think big") for improving overall gait speed.[8 11] However these approaches do not address gait rhythm or coordination since gait speed can be increased without improving step-by-step variability.[12]

This study showed gait and stepping variability improved following time discrimination training, but not following pitch discrimination training. These methods appear clinically feasible and additional study is merited to confirm these preliminary findings.

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