

Background

- Levodopa is the primary medication for the treatment of general limb motor symptoms in Parkinson's disease (PD), however its effects on speech intensity and rate have been inconsistent^{1,2,3}.
- Two recent studies of the effects of levodopa on dysphonia and speech disfluency found that responsiveness was significantly associated with the severity of these speech symptoms^{4,5}.
- Duration of PD diagnosis and duration of levodopa use may affect the response to levodopa and its effects on speech. It has been suggested that speech becomes levodopa resistant, particularly after 10 years of use^{6,7}.

Objectives

To examine the effects of levodopa on speech intensity and speech rate and to explore the potential association between levodopa responsiveness and the severity of these speech symptoms in PD.

Methods

- 54 individuals with PD (IWDPs) and 11 age-matched healthy controls (HC) participated in this study.
- IWDPs were evaluated OFF-medication, at least 12 hours after their last dose of levodopa. After testing, IWDPs took a controlled dose of 300 mg of levodopa. ON-medication condition testing began 1 hour after this dose.
- IWDPs had a mean age of 65.94 years (SD = 7.38, range 47-82 years). Demographic information is presented in Table 1. Controls have a mean age of 62.09 years (SD = 6.55, range 52-72).
- Speech tasks were categorized as: 1) syllable repetition (10x of puh, tuh, kuh, 5x ai slow and fast), 2) reading sentences (the Rainbow passage and the Patty sentence).
- Praat was used to obtain average speech intensity (dB SPL) and duration (ms) of each speech task (the first 5 or 10 syllables of each syllable repetition task and each of the 4 selected sentences).
- T-tests and correlations were used to evaluate differences between groups/medication conditions and associations between selected variables.

Table 1. Demographic information for IWDPs

	Mean (SD)	Range
Age	65.94 (7.38)	47-82
Duration of diagnosis	9.15 (4.18)	2-16
Duration of levodopa use	7.45 (3.86)	2-16
UPDRS OFF-medication	29.94(8.39)	14-51
UPDRS ON-medication	16.25 (7.12)	3-32
Levodopa equivalent dose	1027.2 (449.2)	300-2200

Results

Levodopa and Speech Intensity

- Administration of levodopa medication produced a significant increase in speech intensity in the IWD group, illustrated in Table 2.
- Negative correlations suggest that IWDs with more severe (lower) speech intensity may experience a larger medication-related increase than those with less severe (higher) speech intensity (Figure 1).
- IWDs were split into Severe "Low Intensity" and Mild "High Intensity" groups based on their OFF-medication speech intensity relative to the HC intensity average.
- Individuals were divided based on a cut-off score 2SD below the average HC speech intensity.
- The Severe group had significantly larger medication-related (improvement) in speech intensity (Figure 2).

Table 2. Means and standard deviations of speech intensity

Task	IWPD OFF Mean (SD)	IWPD ON Mean (SD)	Off-On p-value	HCs Mean (SD)	Off-Control P-value
ppp10	66.97 (3.72)	68.37 (4.44)	.005*	69.45 (4.31)	.028*
kkk10	66.24 (4.17)	67.53 (4.09)	.002*	68.97 (3.95)	.025*
aiFast	71.25 (4.19)	72.92 (4.36)	.000*	72.49 (3.88)	.183
Rain1	66.12 (4.12)	67.03 (4.61)	.052	68.99 (3.31)	.017*
Rain3	64.57 (3.86)	65.70 (4.45)	.006*	67.44 (2.85)	.012*

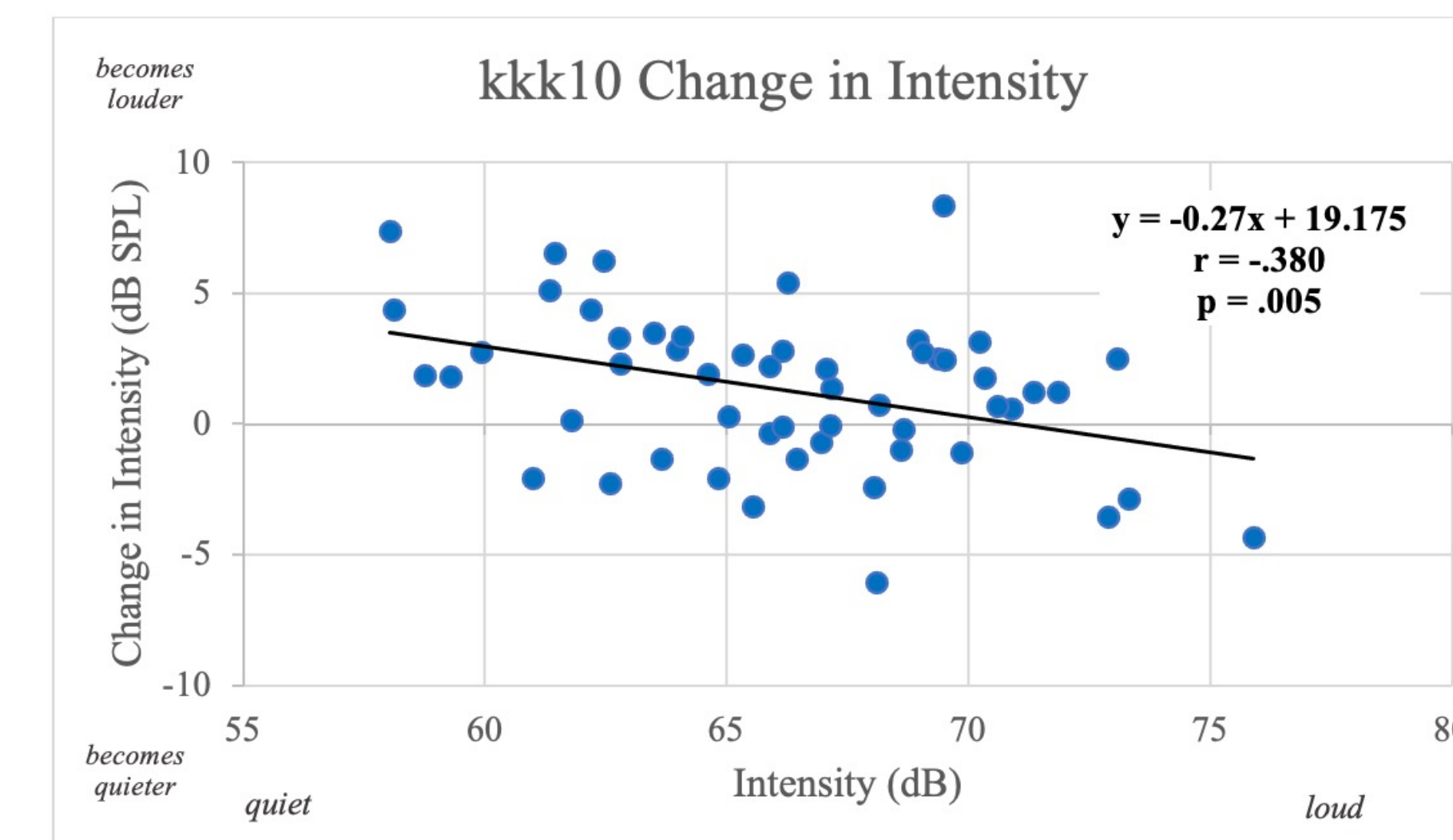


Figure 1. Scatterplot of medication-related change in intensity vs. the OFF-medication speech intensity

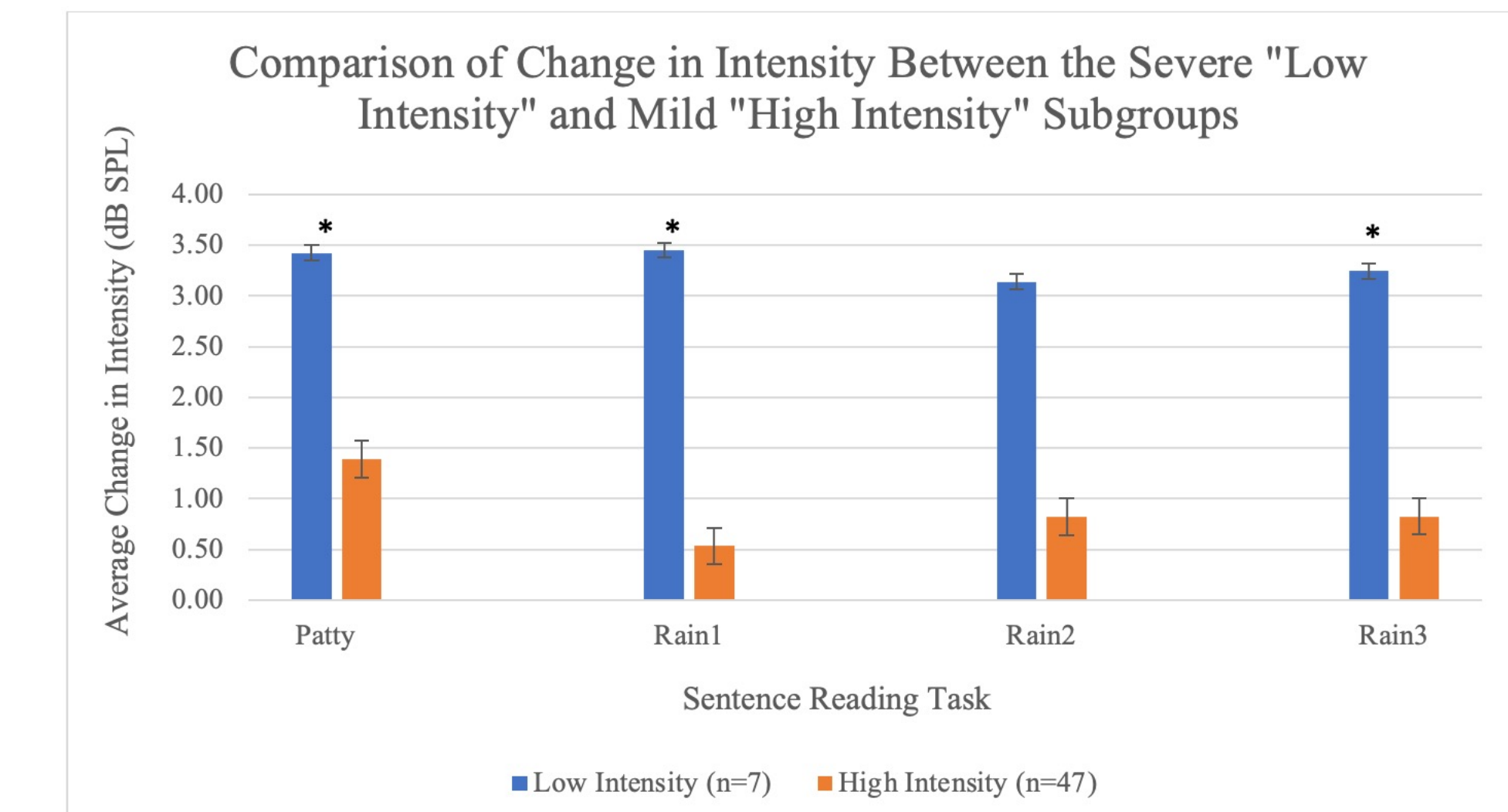


Figure 2. Average levodopa medication-related change in speech intensity for Mild and Severe subgroups

Levodopa and Speech Time/Rate

- Levodopa was not found to significantly affect speech time/rate in the PD group. IWDs were not found to be significantly different from controls (Table 3).
- The significant negative correlations suggest that IWDs with slower rate of speech experience a larger medication-related change in speech time than those who speak faster (Figure 3).
- IWDs were split into "Fast" and "Slow" subgroups based on their OFF-medication speech time relative to the HC average speech time (-1SD).
- The Slow group had significantly larger medication-related (improvement), relative to the Fast group, for several of the speech tasks (Figure 4 and 5).

Table 3. Means and standard deviations of speech time/rate

Task	IWPD OFF Mean (SD)	IWPD ON Mean (SD)	Off-On p-value	HCs Mean (SD)	Off-Control P-value
tft10	1.90 (.43)	1.83 (0.32)	.182	1.71 (.28)	.147
aiSlow	0.91 (.22)	0.86 (0.20)	.058	0.99 (.23)	.274
Patty	2.03 (0.28)	2.02 (0.31)	.548	2.04 (0.29)	.983
Rain2	3.83 (1.13)	3.91 (1.18)	.404	3.66 (0.54)	.614

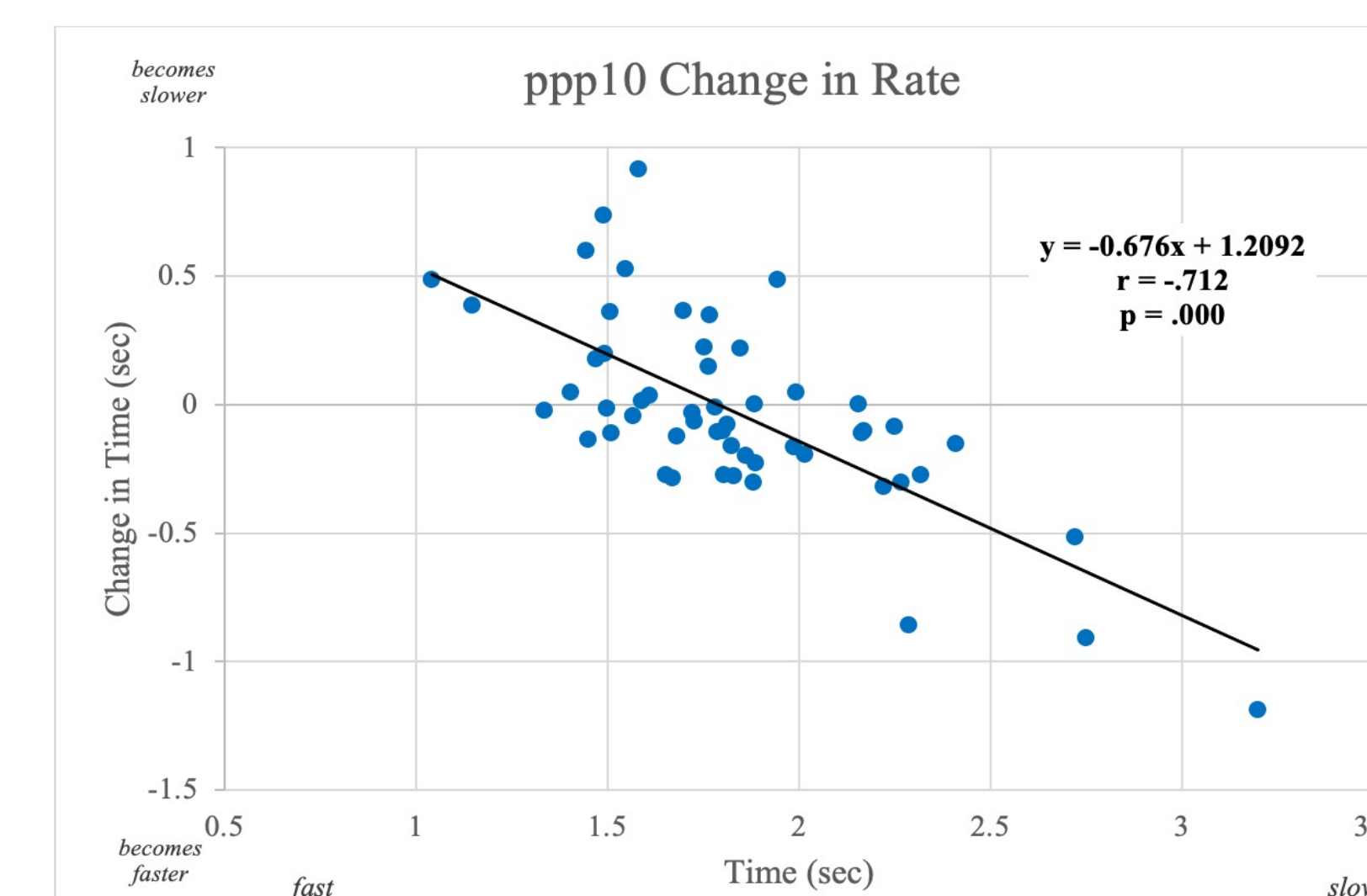


Figure 3. Scatterplot of medication-related change vs. the OFF-medication speech time/rate

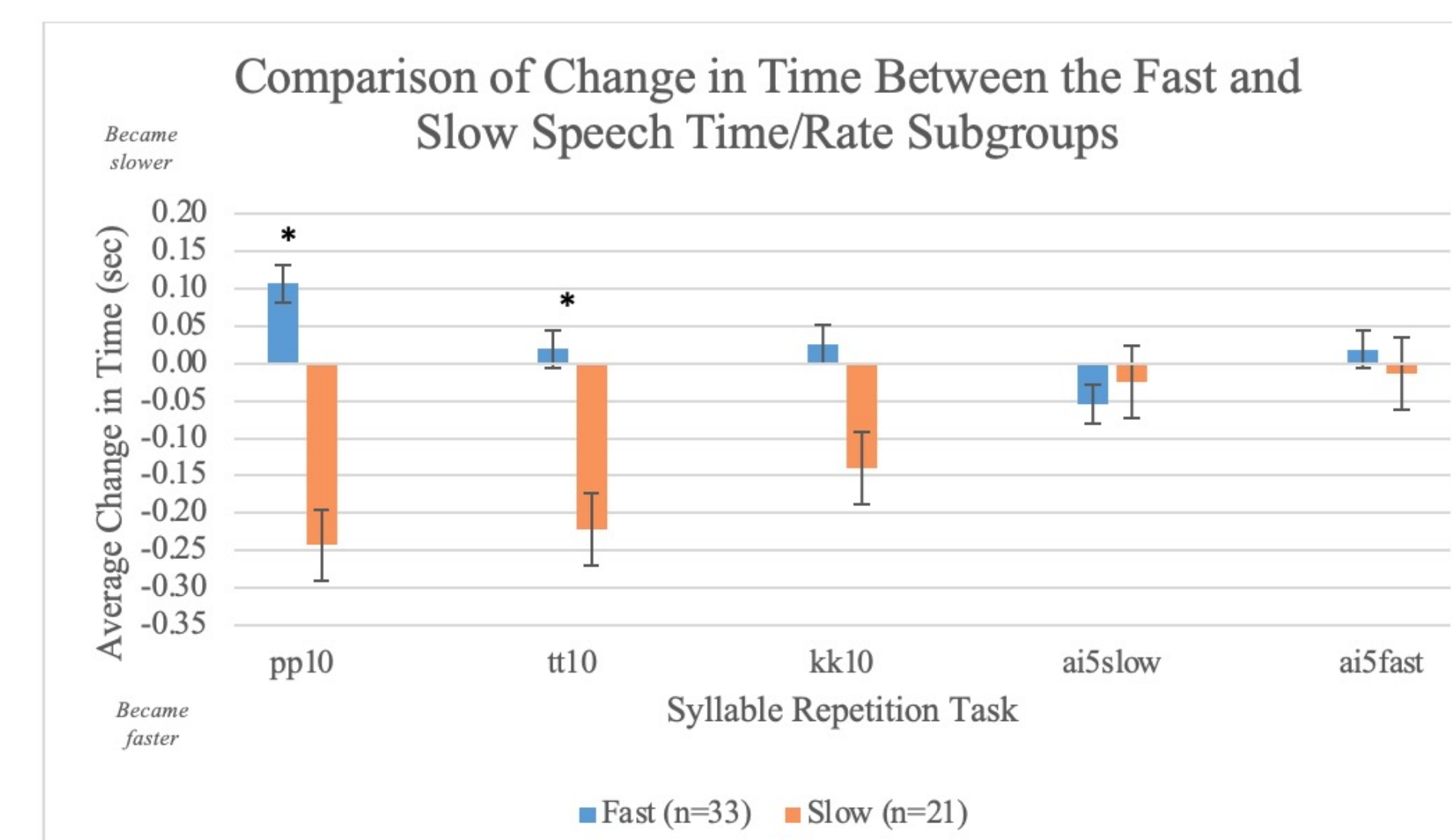


Figure 4. Average levodopa medication-related change in speech rate for Fast and Slow subgroups

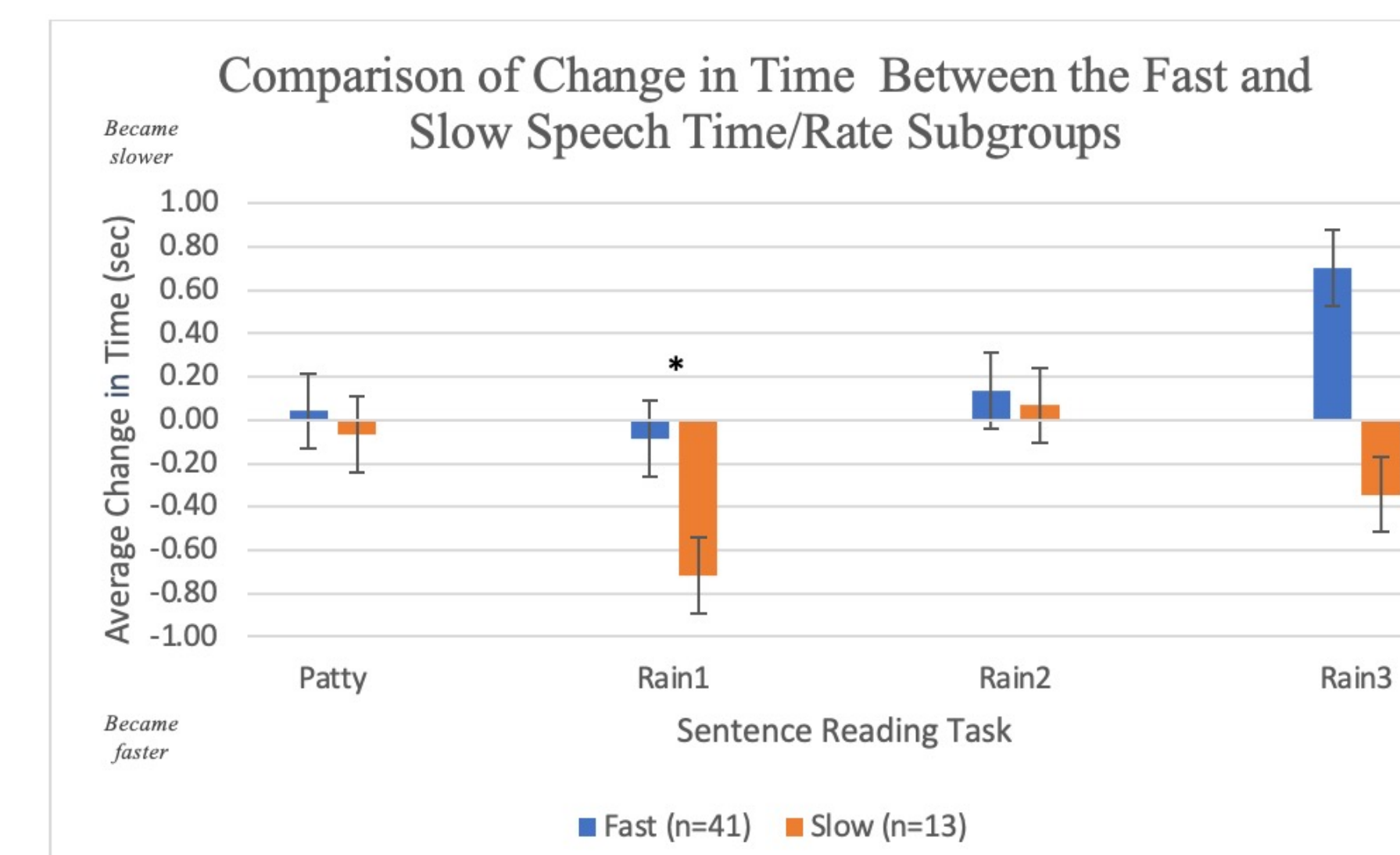


Figure 5. Average levodopa medication-related change in speech rate for Fast and Slow subgroups

Conclusions

- In this group of IWDs, levodopa had a significant effect on speech intensity but not speech time/rate. However, variation in severity appeared to influence the results.
- An important relationship was observed between the medication-related changes in speech intensity/rate and the OFF-medication severity of these symptoms.
- This study provides additional support for the "Speech Severity Responsiveness Hypothesis" which proposed that individuals with more severe speech symptoms show a greater degree of response to levodopa medication.

Acknowledgements

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- Skodda, S., Visser, W., & Schlegel, U. (2010). Short- and long-term dopaminergic effects on dysarthria in early Parkinson's disease. *Journal of Neural Transmission*, 117(2), 197-205.
- Ho, A.K., Bradshaw, J.L., and Iansek, R. (2005). For better or worse: The effect of levodopa on speech in Parkinson's disease. *Movement Disorders*, 23, 574-580.
- Spencer, K. A., Morgan, K. W., & Blond, E. (2009). Dopaminergic medication effects on the speech of individuals with Parkinson's disease. *Journal of Medical Speech Language Pathology*, 17(3), 125-144.
- Cushnie-Sparrow, D., Adams, S., Abeysekera, A., Pieterman, M., Gilmore, G., & Jog, M. (2018). Voice quality severity and responsiveness to levodopa in Parkinson's disease. *Journal of Communication Disorders*, 76, 1-10.
- Im, H., Adams, S., Abeysekera, A., Pieterman, M., Gilmore, G., and Jog, M. (2019). Effect of Levodopa on Speech Dysfluency in Parkinson's Disease. *Mov Disord Clin Pract*, 6, 150-154.
- Klawans, H. L. (1986). Individual manifestations of Parkinson's disease after ten or more years of levodopa. *Movement Disorders*, 1(3), 187-192.
- Bonnet, A.-M., Loria, Y., Saint-Hilaire, M.-H., Lhermitte, F., & Agid, Y. (1987). Does long-term aggravation of Parkinson's disease result from non-dopaminergic lesions? *Neurology*, 37, 1539-1542.