# Stability of the fMRI BOLD signal in reading disability: Insights we can gain from beta series analysis

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## INTRODUCTION

- Recent findings suggest a noisy and disrupted brain circuit rather than a damaged reading circuit in reading disabled (RD) individuals (Hornickel et al., 2009; 2013; Pugh et al., 2008)
- MRS spectroscopy has revealed elevated levels of glutamate in children with RD (Pugh et al., 2014)
- Elevated levels of glutamate have been associated with hyper-excitability and disrupted processing systems (Tseng et al., 2004)
- **Research Question**: How does this relate to the BOLD signal? Will RD individuals show increased trial-wise variability in response to words?

## METHODS I

*Re-analysis of Pugh et al. (2008, JoCN)*

### Participants

- 27 participants (17 male, 10 female)
- Reading skill ranging from typically developing (TD; n=14) to individuals with reading disability (RD; n=13)

### Behavioral Assessments

A battery of diagnostic assessments were administered to evaluate reading and other more general cognitive skills.

1. Wechsler Abbreviated Scale of Intelligence (WASI)
2. Woodcock-Johnson Test of Achievement, 3rd Edition (WJ-III)
3. Test of Word Reading Efficiency (TOWRE)
4. Peabody Picture Vocabulary Test (PPVT)

Individuals considered RD if they had a prior diagnosis of dyslexia or had < 90 on a Standardized Reading Composite consisting of the average between the standard scores from:

- (1) WJ-III Basic Reading
- (2) WJ-III Spelling SS
- (3) TOWRE Total Reading.

## METHODS II

### fMRI Task

#### Stimuli

- 208 mid-frequency nouns used as visual print stimuli
- 4-5 letters long; regular spelling to sound mapping
- 65% of words non-living items; 35% of words living items
- 6-8 functional runs (~6 minutes each); 56 total trials per run
- Out of 56 trials: 20 novel words; 6 words repeated 6 times (36)
- Novel words distributed evenly throughout the run
- 2 counterbalanced lists used to rotate novel & repeated words

#### Procedure

- Participants instructed to complete the task as quickly as possible
- Each word presented on screen for 2500 milliseconds
- Participants made animacy judgment on words via button press
- Data for accuracy and response latency collected via button press

#### fMRI Acquisition & Analysis

- GE Signa 1.5 Tesla and Siemens Sonata 1.5 Tesla MR scanners
- Data analysis software: AFNI analysis package, developed by NIH
- Single-subject analysis: following standard pre-processing, regression was performed to generate activation maps (beta coefficients) for each trial in each condition
- **Current analysis considers <u>only</u> trials with novel words**
- Any beta-values more extreme than ±500 were treated as outliers and removed from analysis
- Standard deviation of beta-coefficients calculated based on same number of trials for all participants (first 153 good trials)
- Colin TT_N27 atlas used to functionally define ROIs
- Across-subjects analyses: voxel-wise correlation of standard deviations with behavior; voxel-wise threshold $p < .01$; cluster-wise correction $p < .05$

## RESULTS I

| | Gender | Age | WJ-III Word Attack | TOWRE SS | WJ-III Reading SS | WJ-III Spelling SS | Reading Avg. | VIQ | PIQ | FSIQ | PPVT SS |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **TD** (SD) | M = 9 F = 4 | 12.9 (2.5) | 71.6 (21.6) | 112.6 (12.6) | 113.4 (9.6) | 119 (10.9) | 115.0 (8.9) | 112.4 (12.6) | 110.8 (13.1) | 112.9 (12.6) | 83.1 (22.3) |
| **RD** (SD) | M = 8 F = 6 | 12.9 (2.4) | 24.2 (7.4) | 79.9 (8.3) | 88.5 (4.6) | 88.2 (7.9) | 85.5 (6.4) | 100.5 (12.9) | 108.2 (16.1) | 104.4 (14.0) | 66.2 (28.9) |
| **Overall** (SD) | M = 17 F = 10 | 12.9 (2.4) | 48.8 (29.0) | 96.9 (19.7) | 101.4 (14.8) | 104.2 (18.3) | 100.8 (16.7) | 106.7 (13.9) | 109.6 (14.4) | 108.9 (13.8) | 75 (26.6) |

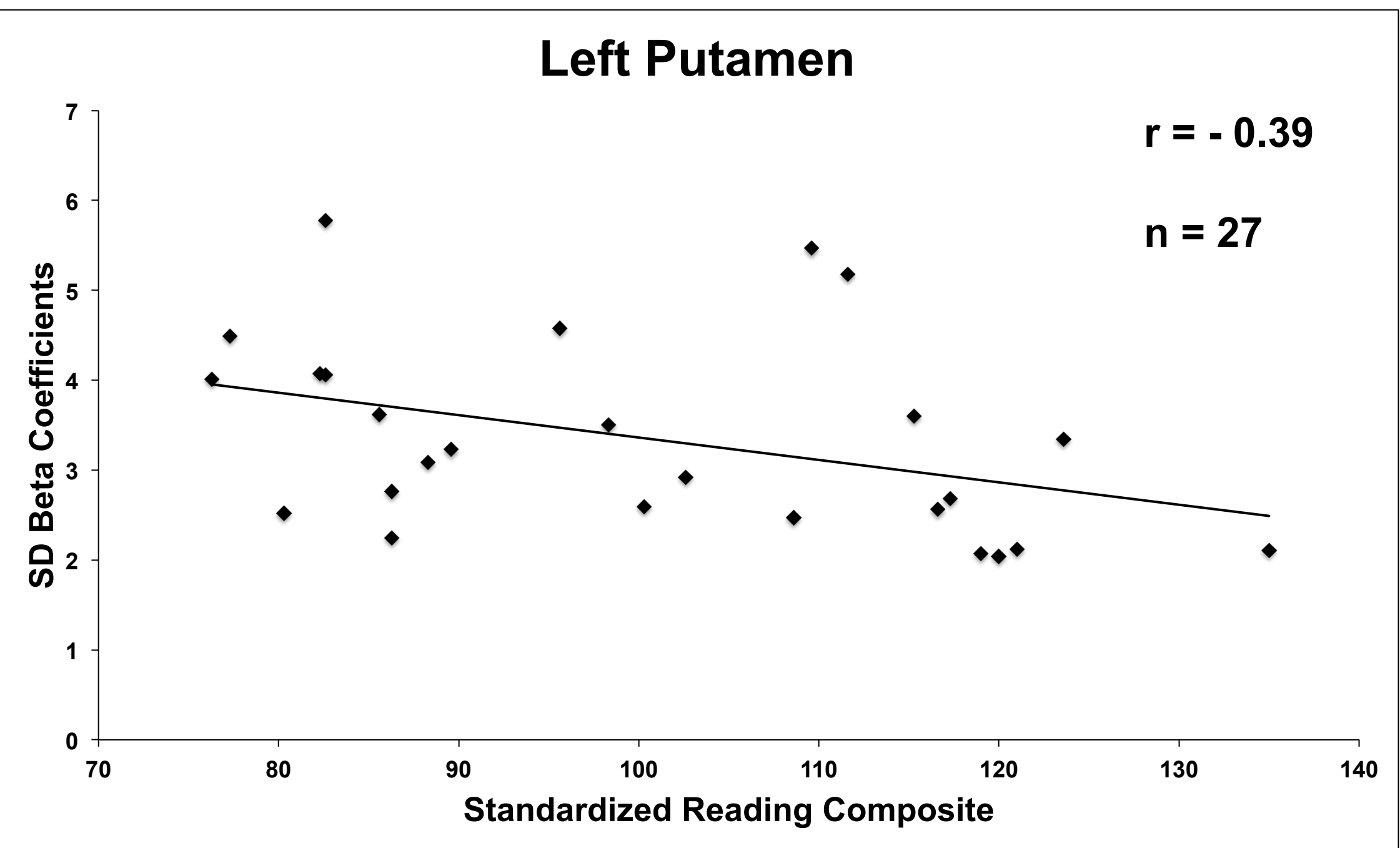**Table 1.** Summary of Behavioral Data

## RESULTS II



**Figure 1 (above) & Figure 2a (below).**
Correlation between Standard Deviation of Beta Values in Left Putamen and Standardized Reading Average
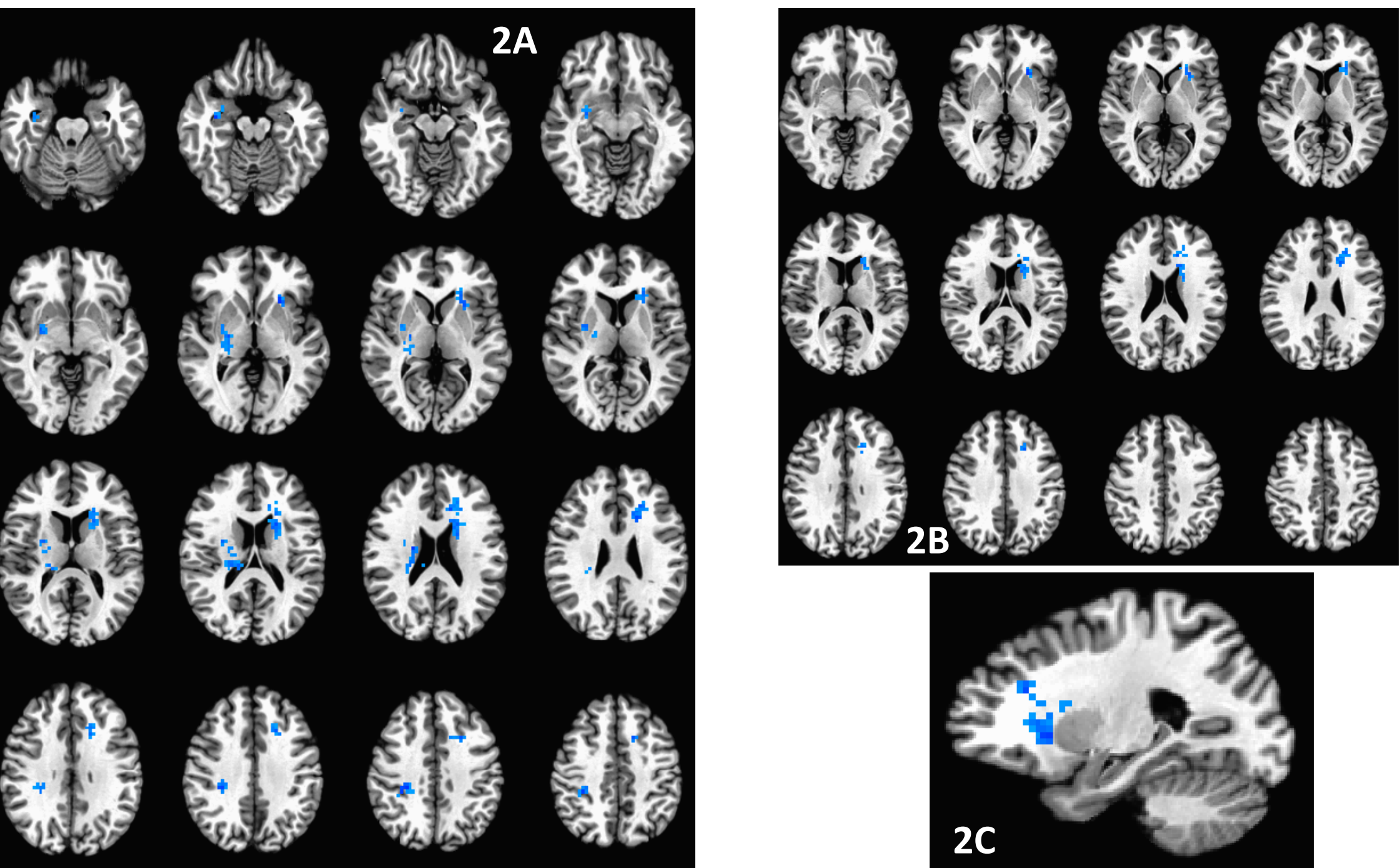


**Figure 2B, 2C (above) & Figure 3 (below)**
Correlation between SD of Beta Values in Right Thalamus and WJ-III Spelling Standard Score. Blue indicates a negative correlation between SD and reading measures.
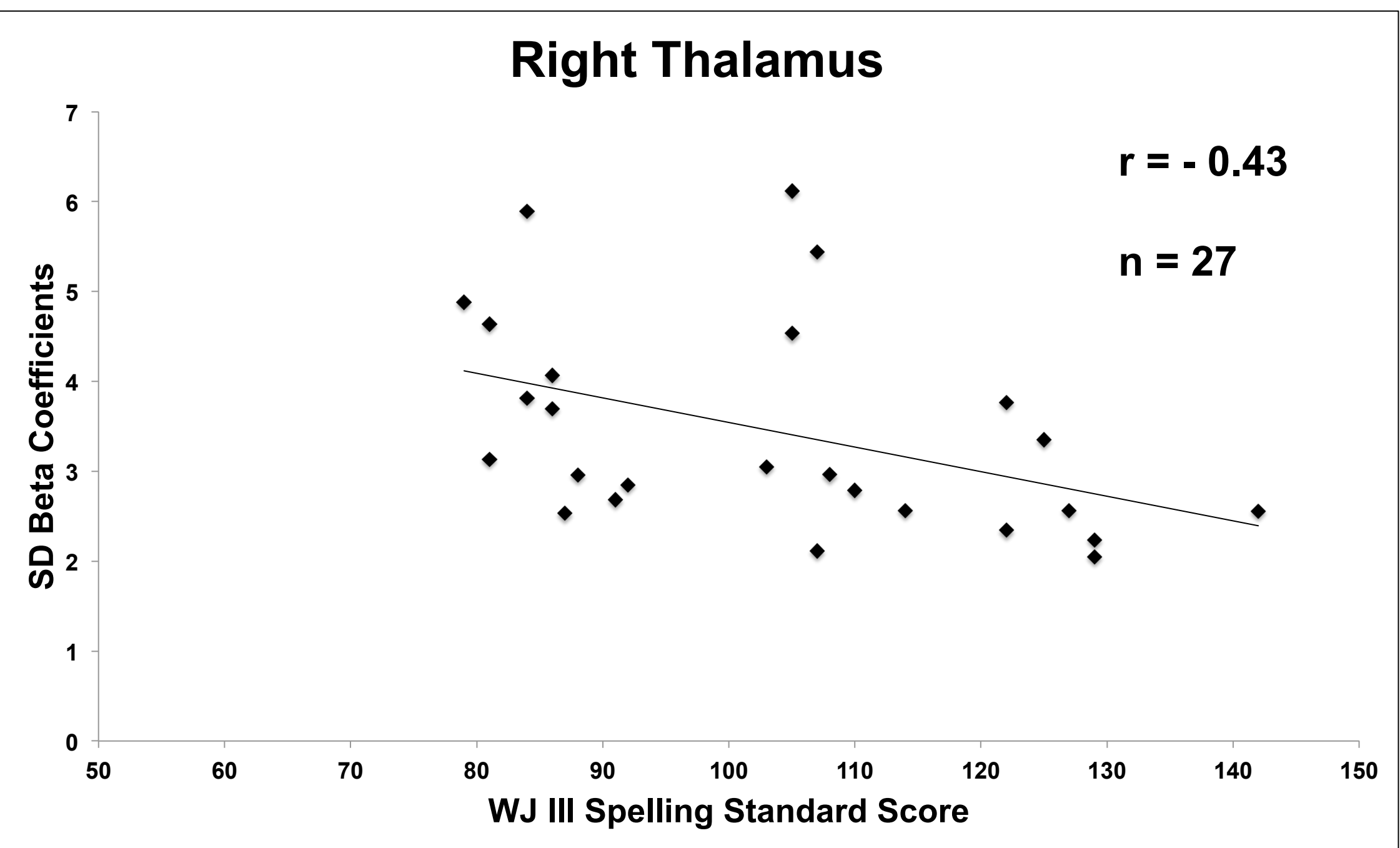


**Figure 3**

## CONCLUSIONS

- Findings suggest individual differences in the variability of BOLD activation in certain ROIs (L Putamen, R Thalamus)
- Strong negative correlations exist between reading measures and the amount of variability found in the BOLD signal for the printed word
- Regions in the posterior thalamus have been previously implicated in the learning circuit and have been shown to correlate highly with reading skill (Pugh et al, 2013), therefore increased variability based on skill is unsurprising.
- **Future Directions**: Does the variability in BOLD response grow stronger or weaker with repetition of words? Do different brain regions become implicated over subsequent repetitions?

## REFERENCES

1. Hornickel, J., & Kraus, N. (2013). Unstable Representation of Sound: A Biological Marker of Dyslexia. *Journal of Neuroscience, 33(8)*, 3500–3504. doi:10.1523/JNEUROSCI.4205-12.2013.
2. Hornickel, J., Skoe, E., Nicol, T., Zecker, S., & Kraus, N. (2009). Subcortical differentiation of stop consonants relates to reading and speech-in-noise perception. *Proceedings of the National Academy of Sciences, 106(31)*, 13022.
3. Pugh, K.R., Frost, S.J., Rothman, D.L., Hoeft, F. Del Tufo, S.N., Mason, G.F....Fulbright, R.K. (2014).Glutamate and Choline levels predict individual differences in reading ability in emergent readers. *Journal of Neuroscience, 34(11)*, 4082-4089.
4. Pugh K.R., Frost, S.J., Sandak, R, Landi, N., Rueckl, J.G., Constable, R.T.,... Mencl, W.E. (2008). Effects of stimulus difficulty and repetition on printed word identification: An fMRI comparison of nonimpaired and reading-disabled adolescent cohorts. *Journal of Cognitive Neuroscience, 20(7)*, 1146–1160.
5. Pugh, K.R., Landi, N. Preston, J.L. ,Mencl, E.W., Austin, A.C, Sibley, D., Fulbright, R.K., Seidenberg, M.S., Grigorenko, E.L., Constable, R.T., Molfese, P., Frost, S.J. (2013). The relationship between phonological and auditory processing and brain organization in beginning readers. *Brain and Language, 125, 2*, 173-183.
6. Tseng, M.H., Henderson, A., Chow, S.M., Yao, G. (2004). Relationship between motor proficiency, attention, impulse, and activity in children with ADHD. *Developmental Medicine & Child Neurology, 46(6)*, 381–388.

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