



## Cognitive and Metabolic Correlates of Single-Word and Nonword Reading in Mild Alzheimer's Disease

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## **Cognitive and metabolic correlates of single-word and nonword reading in mild Alzheimer's Disease.**

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### **Introduction**

The Dual Route Cascaded model proposes that reading is accomplished by a left dorsal pathway running from the occipital and occipito-temporal cortex, through the superior parietal lobule, to the dorsal frontal lobe, and a left ventral pathway stemming from the same regions and encompassing the posterior temporal cortex and angular gyrus (Taylor et al., 2013). The former route is specialized in reading nonwords and regular words utilizing grapheme-to-phoneme conversion rules, while the latter route processes familiar regular and irregular words by activating semantic and lexical orthographic representations. With this framework in mind, in the current study we investigated the cognitive and metabolic correlates of the ability to read single words and nonwords in mild dementia of the Alzheimer type (DAT). In fact, DAT patients tend to develop dyslexia as the disease progresses, but the cognitive and neural substrate of reading impairment in this form of dementia is still ill-defined.

### **Methods**

We assessed the ability to read words (high-frequency concrete, low-frequency concrete, low-frequency abstract and function words), nonwords and trisyllable words with unpredictable stress position (the major ambiguity in reading Italian) in 25 DAT patients in a mild disease stage, compared with 25 age-, sex- and education-matched healthy participants. Patients reading performance was correlated with scores on an extensive array of cognitive tests. Furthermore, in 21 /25 cases reading scores were correlated with brain FDG-PET using SPM8, with the aim to identify areas of reduced metabolism associated with poor reading.

### **Results**

Characteristics of the two study groups are reported in the Table. Independent Student's t-test and repeated measures ANOVA (with group as between-subject variable and type of reading stimulus as within-subject variable) did not yield any statistically significant intergroup difference or measures interaction. Linear regression analysis with total score on the reading task as dependent variable and various cognitive tests as independent variables identified only the Pyramid and Palm Trees test ( $S_b = 0.539$ ,  $p = 0.002$ ) and Letter Span ( $S_b = 0.448$ ,  $p = 0.007$ ) as predictors ( $R^2 = 0.736$ ,  $p = 0.000$ ), while there was no

significant relationship with measures of attention, episodic memory, language production or comprehension, and visuo-spatial and executive abilities.

Significant clusters of hypometabolism are shown in the Figure. A poorer total score on the reading task was associated with reduced FDG uptake in the left angular and pre-central gyri. The angular cluster emerged as unique correlate for words reading, while nonwords reading was associated with hypometabolism in left>right pre-central cortex and in left anterior cingulate cortex.

## **Conclusions**

As expected from past evidence, our mild DAT patients showed preserved ability to read words and nonwords. Results of behavioral and metabolic imaging analyses converged in highlighting that such an ability was sustained by an anatomo-functional system that involves semantic processing, mapped to the angular gyrus, phonological processing, mapped to the posterior frontal cortex, and attentional processes, mapped to anterior cingulate cortex. These brain regions have all already been reported as crucial for reading in prior neuroimaging studies and meta-analyses (Martin et al., 2015; Taylor et al., 2013; Vogel et al., 2013).

## **References**

- Martin, A., Schurz, M., Kronbichler, M., & Richlan, F. (2015). Reading in the brain of children and adults: A meta-analysis of 40 functional magnetic resonance imaging studies. *Human Brain Mapping, 36*(5), 1963–1981. <https://doi.org/10.1002/hbm.22749>
- Taylor, J. S. H., Rastle, K., & Davis, M. H. (2013). Can cognitive models explain brain activation during word and pseudoword reading? A meta-analysis of 36 neuroimaging studies. *Psychological Bulletin, 139*(4), 766–791. <https://doi.org/10.1037/a0030266>
- Vogel, A. C., Church, J. A., Power, J. D., Miezin, F. M., Petersen, S. E., & Schlaggar, B. L. (2013). Functional network architecture of reading-related regions across development. *Brain and Language, 125*(2), 231–243. <https://doi.org/10.1016/j.bandl.2012.12.016>

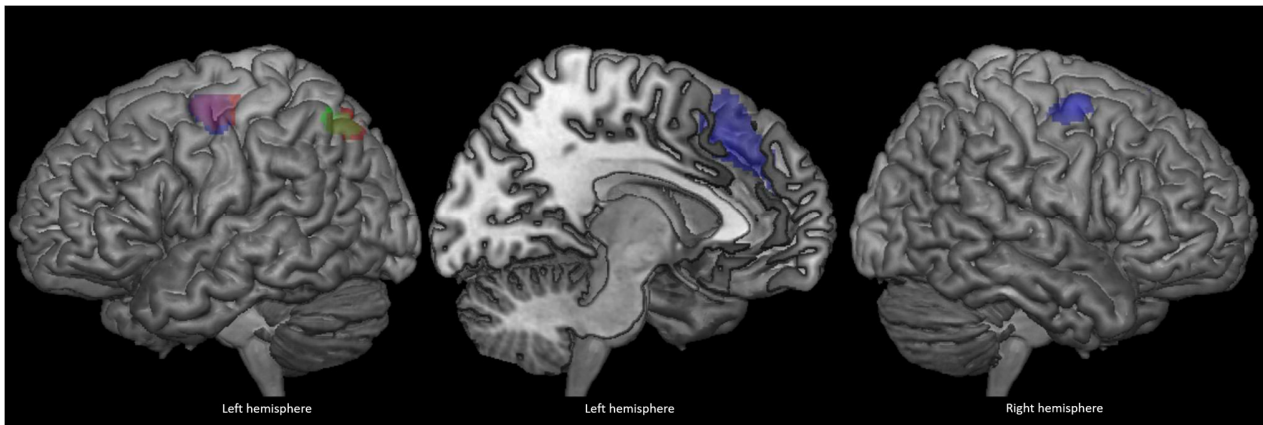
## **Acknowledgments**

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**Table 1.** General features and reading performance of patients with Alzheimer's Disease

	<b>AD patients n. 25</b>	<b>Healthy participants n. 25</b>
Age	75.9 ±4.2	72.8 ± 7.6
n. Men-Women	7 - 17	9 - 15
Education (years)	8.0 ±3.4	8.7 ± 3.4
Disease duration (years)	2.1 ±1.6	-
MMSE score	22.1 ±3.0*	27.9 ± 1.8
Reading tasks:		
Total correct W-nW (max: 100)	98.4 ±1.9	98.7 ± 1.1
Correct Words (max: 80)	79.4 ±0.9	79.6 ± 0.6
Correct Nonwords (max: 20)	18.9 ±1.4	19.1 ± 0.8
Stress errors in WUSP (max: 40)	0.7 ± 1.3	0.4 ± 0.7

\*  $p < 0.00001$ ; W = words, nW = Nonwords, WUSP = words with unpredictable stress position.



**Figure 1.** Metabolic correlates of performance on the reading task: total score is depicted in red (shown at  $p < 0.001$  uncorrected), nonwords in blue ( $p < 0.05$  FDR-corrected), words in green ( $p < 0.001$  uncorrected) (minimum cluster size for all clusters: 100 voxels).