

The Correlation of Cognitive Changes and Imaging brain amyloid in Adults with Down syndrome using Pittsburgh compound B

Peter Bulova¹, Todd Barnhart², Bradley Christian³, Darlyne Devenny¹, Regina Hardison¹, Sigan Hartley³, Ansel Hillmer³, Sterling Johnson², William Klunk¹, Chester Mathis¹, Dhanabalan Murali³, Julie Price¹, Marsha Seltzer³, Dustin Wooten³, Ben Handen¹. (1) The University of Pittsburgh (2) The Waisman Center, University of Wisconsin-Madison, (3) University of Wisconsin-Madison

Background:

Adults with Down syndrome (DS) are at high risk for developing Alzheimer's disease (AD). The high prevalence of AD in this population is due to the presence of an extra copy of chromosome 21, which codes for the amyloid-beta precursor protein gene.

Deposition of amyloid plaque is purported to play a central role in the neuropathology of AD and can be detected using the PET tracer Pittsburgh Compound-B (PiB).

Aim of the study:

We present preliminary findings from an ongoing study aimed at documenting the course of amyloid deposition in asymptomatic adults with DS. Data on the neuropsychological profile of 19 subjects evidencing amyloid deposition (PiB+) compared to 31 subjects without amyloid deposition (PiB-) will be presented.

Methods:

Fifty healthy adults ($M = 39$ years, $SD = 7$) with DS (25 male, 25 female) completed a neuropsychological battery and MRI/PET scans. Measures were selected to assess *verbal learning and memory* (Cued Recall Test, WMS-IV Logical Memory), *visual memory* (Rivermead Face and Picture Recognition), *attention/processing speed* (e.g., Corsi Span forward, WISC-IV Digit Span Forward), *executive/working memory* (e.g., Corsi Span-Backward, Stroop Cat and Dog), *visuoconstruction* (e.g., WISC Block Design, Extended Block Design), and *language* (e.g., NEPSY Verbal Fluency, PPVT-IV). Subjects were defined as PiB+ if they exceeded the SUVR threshold defined by sparse k-means clustering in any one of six ROIs or by exceeding the SUVR threshold in the global cortical region.

Separate ANCOVAs were conducted to compare mental age-adjusted means on each neuropsychological measure for the PiB+ versus PiB- subjects. The PiB+ subjects evidenced significantly lower mean scores on several neuropsychological measures, including executive/working memory, delayed recall, and attention/processing speed. These differences are hypothesized to become more pronounced at follow-up time points.

Results:

Neuropsychological Tests indicating Significant Differences between the PiB+ and PiB- Subjects controlling for Mental Age

	PiB+ Mean (SD)	PiB- Mean (SD)	p-value
Free Recall Initial # Recalled	3.80 (0.46)	4.95 (0.35)	0.05
NEPSY Visual Attention	102.38 (8.29)	79.05 (6.49)	0.03
NEPSY Visual Attention	15.27 (1.31)	18.22 (1.03)	0.08
NEPSY Verbal Fluency	3.33 (0.62)	1.92 (0.48)	0.08
WMS-IV Logical Memory Story Recall	-0.05 (0.46)	-1.13 (0.36)	0.07
Expressive One Word	64.32 (4.29)	75.38 (3.35)	0.05
Rivermead Picture Recognition	4.05 (0.70)	6.42 (0.55)	0.01
Stroop Cat and Dog	4.35 (0.96)	2.01 (0.75)	0.06

Note. Significant at one-tailed t-test value ($p < .10$) in hypothesized direction.

Older age was highly related to PiB(+) status. With individuals of age ≥ 40 years, 74% were PiB(+) and no subjects were PiB(+) of age < 36 yrs. The resulting odds ratio for PiB(+) status of 1.36 (1.17, 1.59 95% CI) per year.

Conclusions:

This study provides a unique opportunity to study the preclinical manifestations of AD. Findings may not only provide information that could affect early detection, prevention, and treatment of AD for individuals with DS, but also may offer information that will prove extremely useful for the general population.

The overall goal of this work is to examine amyloid deposition in adults with Down syndrome to study its effect on cognitive and behavioral functioning over time. Follow-up studies (30 months) are ongoing to track the changes in amyloid binding and cognitive function to deepen our understanding of AD pathophysiology in DS.