Introduction

- The majority (95%) of Down syndrome (DS) cases result from a triplication of chromosome 21.
- It is hypothesized that the overexpression of gene products, like amyloid precursor protein, predisposes young adults with DS to developing Alzheimer disease (AD)-like neuropathology.
- Neurofibrillary tangles and amyloid-β plaques have been observed in virtually all adults with DS by age 40.
- The goal of this UW/UPMC collaborative project was to use [11C]PiB PET to image the pattern of amyloid-β deposition in nondemented adults with DS and determine the relationship of deposition with normal aging.

Methods

- 68 nondemented adults with DS (age 30-53) underwent [11C]PiB PET scans. Trisomy 21 was confirmed with genetic testing.
- Standard uptake value ratio (SUVR) images were created using the cerebellum as the reference region.
- Regions of interest (ROIs) included the commonly affected regions in AD: anterior cingulate, frontal cortex, parietal cortex, precuneus, striatum, and temporal cortex.
- Multiple linear regression models tested for significant correlations between SUVR and age in six ROIs, correcting for gender and APOE4 allele status.
- Sparse k-means clustering determined PiB positivity.

Results

- All regions showed a slight, but highly significant, positive correlation (corrected p<0.05) of SUVR with age.
- The striatum showed the strongest correlation, followed by the precuneus, parietal cortex, anterior cingulate, frontal cortex, and temporal cortex.
- 17 out of 68 subjects were classified as PiB positive. 94% of the PiB positive subjects were above the threshold in the striatum.
- Elevated cortical [11C]PiB retention was observed in subjects above age 35.

Discussion

- As a pattern of elevated cortical retention becomes apparent, the correlation loses significance. This suggests that factors unrelated to aging may drive a rapid increase in amyloid-β deposition in the early stages of AD pathogenesis.
- While there are shared aspects of pathogenesis between DS and AD, these data reveal that early involvement of the striatum is a defining pattern among the DS population.

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