

# Glucose metabolism changes in cerebellar tonsils as an early predictor of cognitive decline

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## Abstract

**Background:** Mild cognitive impairment (MCI) is associated with an increased risk of dementia, but imaging biomarkers are not clearly related to the likelihood of developing cognitive decline. This preliminary study aims to investigate the brain glucose metabolic PET imaging patterns in subjects that are cognitively unimpaired older adults (CUI) and those who convert to MCI within two years.

**Method:** CUI subjects with <sup>18</sup>F-FDG PET and MR images were selected from the ADNI study. Two groups were separated in our research: (i) 36 stable CUI subjects during a minimum of 5 years; (ii) 12 subjects initially cognitively unimpaired (preCONV) that convert to MCI within two years (posCONV). Static <sup>18</sup>F-FDG PET images were co-registered with the correspondent MR image and normalized to MNI space with an 8 mm Gaussian filter. A normalized whole-brain (WB) mask was determined. Each PET was normalized by its WB mean value. Image analysis was performed using SPM 12, with proportional scaling and age-corrected. Groups have no difference in age (79.5±5)y and years of education (15.8±3)y. Brain glucose hyper- and hypometabolism were evaluated between groups (CUI versus preCONV, CUI versus posCONV) and longitudinally (preCONV versus posCONV).

**Result:** The cluster analysis ( $p(\text{unc}) \leq 0.001$ ) of CUI subjects when compared to preCONV shows brain glucose hypometabolism in the cerebellar tonsil and putamen regions, and infero-medial temporoparietal lobe, and hypermetabolism in the left parietal and right temporal and frontal lobes. CUI shows hypometabolism compared to posCONV in regions of the left and right cerebellar tonsil, culmen, frontal lobe, Brodmann Area (BA) 6 and midbrain, and hypermetabolism in the parietal lobe, including the precuneus and BA39. No differences are found between preCONV and posCONV. Just hypometabolism in cerebellar tonsil in CUI compared to preCONV and posCONV survived correction for multiple comparisons (cluster  $p(\text{FWE}) \leq 0.05$ ), showing a possible involvement in the cognitive decline beginning. Recent evidence suggests the cerebellum's involvement in the regulation of cortical areas associated with cognition as an abnormal structure in cingulo-cerebellar circuitry (Walsh K., PARKER, K.L., 2018).

**Conclusion:** Beyond brain regions of altered glucose metabolism in cognitive decline like parietotemporal regions, cerebellar tonsil shows changes that could indicate early conversion of cognitively unimpaired older adults to MCI.