

A Novel Metric of Statistical Amyloid Burden by Comparison to a Database of Health Controls

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Purpose

Statistical parametric mapping allows voxelwise comparison between florbetapir PET brain images with reference to a database of cognitively normal subjects, after having registered each brain into a stereotactic brain atlas space. Here, we propose a metric, Volumetric Statistical Amyloid Burden (VSAB) computed as the volume of gray matter that exceeds a z-score threshold when compared to a database of young healthy controls.

Materials/Methods

Consensus reads among three readers for 130 Florbetapir scans, as described in Fleisher et. al (2011)¹, were classified as either amyloid+ or amyloid-. MIMneuro 5.6 was used without intervention to deformably register each scan to a common atlas space with reference to 3 florbetapir PET templates. Z-scores were computed for every voxel in each Florbetapir scan, as compared to 74 young healthy controls. A "gray matter mask", defined as the VOI encompassing the high uptake voxels of an average of many amyloid+ patients and excluding the high uptake voxels of an average of many amyloid- patients, was used to only consider gray matter burden in computing the final VSAB metric. Z-score thresholds from 3 to 7 were considered for the computation of VSAB, defined as the percentage of voxels within the gray matter mask that exceeded the z-score threshold.

Results

The Kappa statistics for agreement with consensus reads for VSAB computed with z-score thresholds 3, 4, 5, 6, and 7 were 0.90, 0.90, 0.92, 0.94, and 0.97, respectively. The VSAB used were 30.0%, 12.8%, 4.0%, 1.4%, and 0.7%, respectively.

Figure 2
Z-score Images

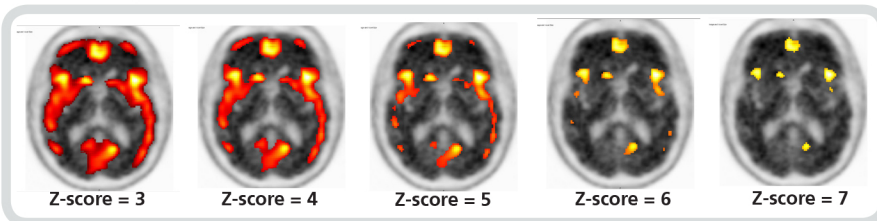


Figure 3
Results

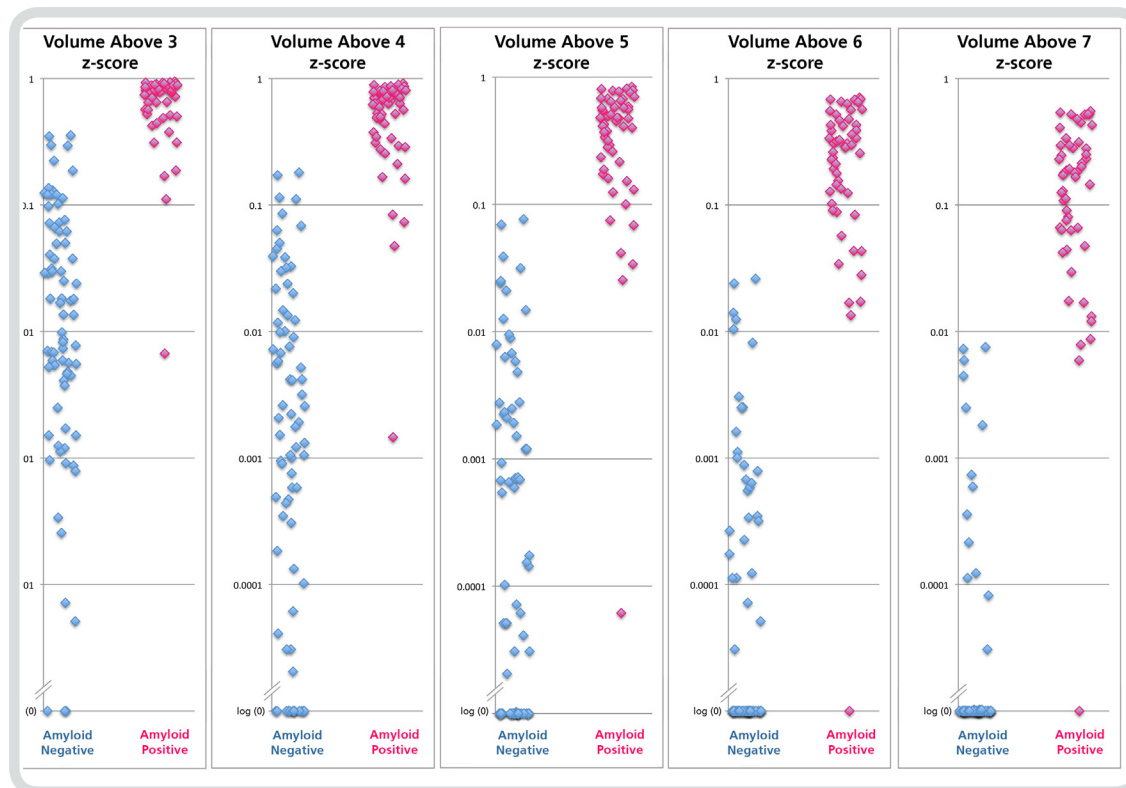
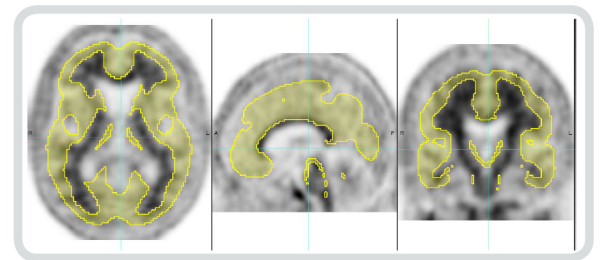


Table 1
Agreement with Consensus Reads

Z-score Thresh	VSAB (% Volume)	Kappa
3	30	0.90
4	12.8	0.90
5	4.0	0.92
6	1.4	0.94
7	0.7	0.97

Figure 1
Volumetric Statistical Amyloid Burden (VSAB)



Conclusion

Volumetric Statistical Amyloid Burden shows promise as an additional metric for distinguishing amyloid+ from amyloid-. Additionally, the agreement of this metric with visual assessment suggests that there may be value in computing voxel-level z-scores for amyloid images. Further work will investigate even more robust methods for gray matter mask definition and will compare VSAB with updated visual assessment methods.

Clinical Relevance

Incorporation of quantitative and statistical analysis of functional neuroimaging has been shown to increase the accuracy and confidence of visual interpretation of these studies.

Reference

1. Fleisher AS, Chen K, Liu X, et al. Using Positron Emission Tomography and Florbetapir F 18 to Image Cortical Amyloid in Patients with Mild Cognitive Impairment or Dementia Due to Alzheimer's Disease. Arch Neurol. 2011;68(11):1404-1411.