

Greater Than Age-Related Decline in Temporal and Occipital Cortices of Methamphetamine Users

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INTRODUCTION: Prior brain morphometric studies in methamphetamine (METH) users show conflicting results of either gray matter decrease or increase compared to control subjects^{1, 2}. One issue that has been neglected is that of age-related gray matter decline. Therefore, we evaluated for possible differential effects of aging on gray matter volumes between METH users and non-users.

METHODS:

Participants: A total of 78 subjects (44 METH users and 34 non-METH using controls) were evaluated clinically and with high-resolution structural MRI. METH-users were included if they were abstinent (up to 5 years) or were current METH users. All subjects were required to be healthy, HIV seronegative, without a history of other drug-dependence according to the DSM IV criteria, and without significant mental or neurological illness.

Image acquisition and processing: MRI was performed on a 3T Siemens Trio system. For each subject, we acquired a 3D axial T₁ weighted magnetization prepared rapid gradient echo (MP-RAGE) scan (TR/TE/TI=2200/4.91/1000 ms; 1 NEX; 256x208x144, 1mm isotropic resolution). Regions of interest (ROIs) were created based on Talairach definitions of cerebral lobes and Brodmann areas. The ROIs were transformed from the Talairach to the higher resolution Montreal Neurological Institute's (MNI's) standard space, using a nonlinear transform. In order to examine atrophic changes by controlling for variations in intracranial volume (an index of premorbid brain size) between subjects, we used FSL's SIENAX program to obtain a cranial volume index. Skull removal, registration, and segmentation were carried out using the FSL software package, version 3.3 (Oxford, UK). We employed custom software to correct gyral clipping at the boundaries of the ROIs due to variations in cortical folding between subjects before volume measurements were performed.

RESULTS:

Clinical characteristics: The two groups were well matched by gender, age, and body mass index, and comprised 49 men and 29 women ages 35.0 ± 8.67 years (range: 18-55 years). However, METH users had lower educational attainment (12.4 ± 1.3 vs 14.8 ± 2.0 years, $p < 0.0001$), lower estimated verbal IQ (98.6 ± 7.5 vs 110.2 ± 10.1 , $p < 0.0001$), and higher systolic blood pressure (121.4 ± 13.2 vs 115.0 ± 9.1 , $p < 0.05$). Meth users had a mean lifetime use of $3,163 \pm 5,401$ grams, first age of use of 19.9 ± 6.3 years, duration of meth use of 126 ± 80.5 months, and 5.2 ± 2.0 days/week. Mean days since last use was 187 ± 373 days.

High-resolution MRI: Using the cranium volume-adjusted MRI volumes, the prefrontal, insular, limbic, parietal, temporal and occipital lobes showed similar volumes between the two subject groups. However, METH-subjects showed significantly steeper age-related decline than the control subjects in the temporal lobe (METH: $R = -0.59$, $p < 0.0001$; Controls: $R = -0.09$, $p = 0.6$; ANCOVA interaction- $p = 0.0068$) and in the occipital lobe (METH: $R = -0.49$, $p = 0.0007$; Controls: $R = 0.12$, $p = 0.49$, ANCOVA interaction- $p = 0.045$); see Figure. Specifically, temporal gray matter volumes declined by 0.7%/decade in controls, but by 5.9%/decade in METH subjects. Similarly, the occipital gray matter declined by 1.0%/decade in the control subjects, but 5.0% per decade in the METH users.

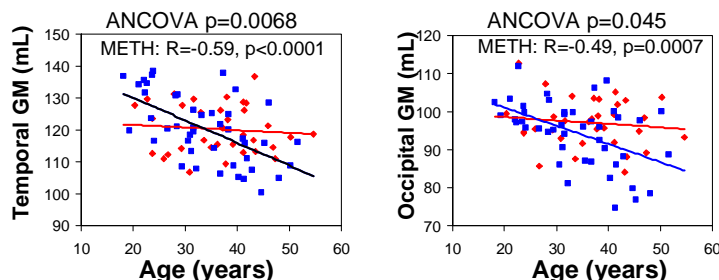


Figure: METH users (blue) show significantly steeper age-related decline than controls (red) in gray matter volume, both in the temporal lobe (left) and in the occipital lobe (right).

DISCUSSION: Gray matter is known to decline with normal aging³. Individuals who eventually developed mild cognitive impairment demonstrated greater than age-related decreases in gray matter volumes, and the earliest atrophy typically occurs in the anteromedial temporal lobes bilaterally⁴. Therefore, our finding of 8-fold greater temporal gray matter decline as a function of age suggests that METH users may be at a higher risk to develop cognitive disorders (such as dementia) at an earlier age, compared to non-drug users. Furthermore, smaller occipital gray matter volume was associated with chronic schizophrenia and possibly the manifestation of visual hallucinations⁵. Consequently, greater than normal age-related decline in the occipital lobe gray matter in our METH subjects may explain why METH users have more psychiatric symptoms such visual hallucinations. Further analyses will determine whether these age-dependent brain volume changes are related to performance on neuropsychological tests and to psychiatric symptoms in these individuals.

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