DETECTION & MAPPING OF ABNORMAL BRAIN STRUCTURE IN METHAMPHETAMINE USERS

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We detected a pattern of brain structure deficits in chronic methamphetamine users, including severe cortical and hippocampal atrophy that correlated with impaired memory performance. To sensitize the analysis for detecting cortical deficits, we developed cortical pattern matching analyses that help combine structural MRI data across subjects.

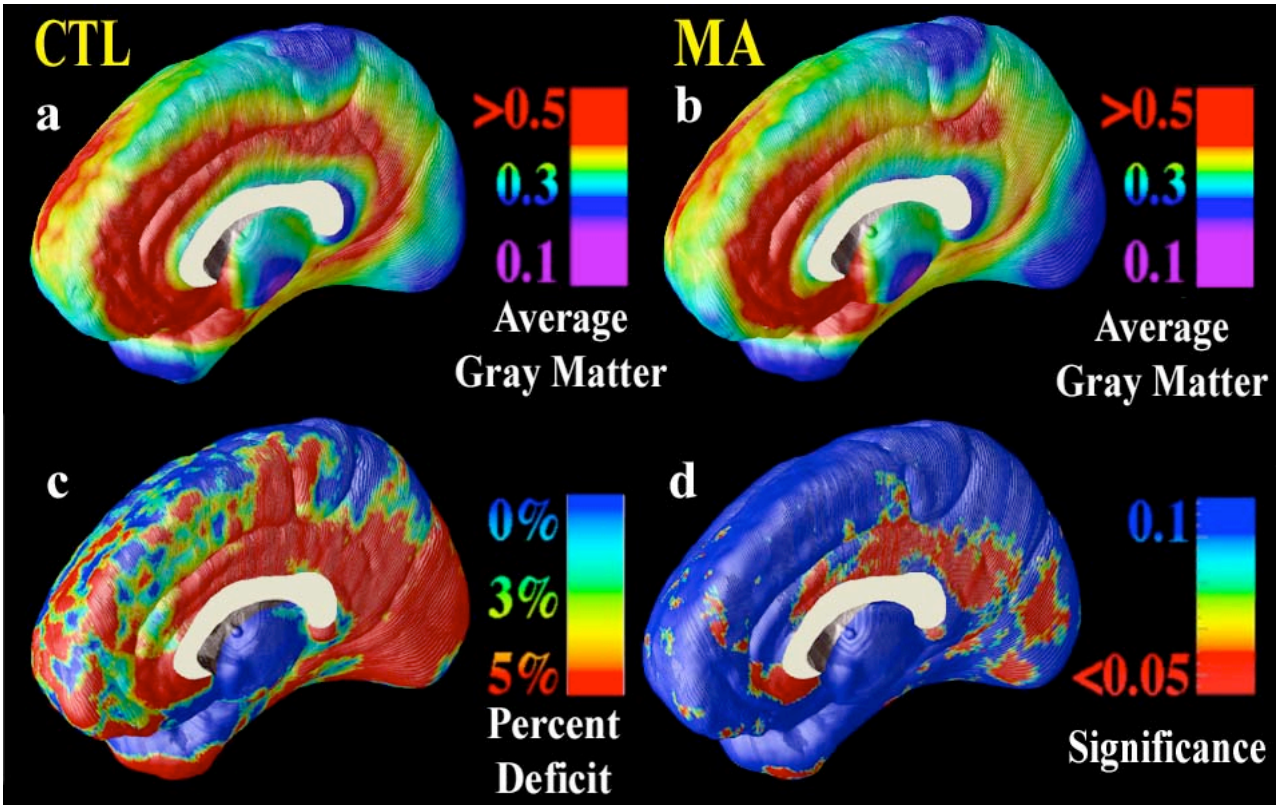
Methods. 43 T1-weighted MRI scans (256x256x124 SPGR volumes) were acquired on a 3 Tesla scanner from 22 MA users with a history of MA dependence (age: 35.3±1.7SE years, 15M/7F) and 21 comparison subjects without a history of substance abuse (31.9±1.5SE years, 10M/11F). MA abusers had used the drug (primarily by smoking), on average, for 10.5 years, beginning in their mid-twenties, consuming about 3 g/week of MA. All 43 MRI scans were aligned to ICBM space, and segmented into gray matter, white matter, and CSF using an automated Gaussian mixture classifier. 72 surface sulci per brain were traced on parametric surface models of each subject's cortex. A cortical pattern matching technique used these sulcal landmarks as anchors to drive data from all subjects into spatial correspondence, using a covariant fluid PDE model for data alignment on non-flat manifolds. At each aligned surface vertex, we fitted a general linear model to assess methamphetamine effects on gray matter density and cortical thickness, computed from the Eikonal fire equation. A smooth change of surface coordinates was induced whose local Jacobian matrix (deformation tensor) matched the smoothness of the residuals, and in the resulting coordinate system, a null distribution was developed for the area of the average cortex with group difference statistics above a fixed threshold in the significance maps. The profile of cortical atrophy was visualized.

Findings. Cortical maps revealed severe gray matter atrophy in the cingulate, limbic, and paralimbic cortices of MA abusers (averaging 11.3% below control, $p<0.03$). On average, MA abusers had 7.8% smaller hippocampal volumes than control subjects ($p<0.008$; *left:* $p<0.014$, *right:* $p<0.017$), and significant white matter excess (7.0%; $p<0.0073$). Hippocampal deficits were mapped and correlated with memory performance on a Word Recall Test ($p<0.039$).

Interpretation. Chronic methamphetamine abuse severely impacts limbic system gray matter, with profound

tissue loss in the cingulate gyrus and hippocampus. These results are consistent with animal studies that report MA-induced neuroadaption, neuropil reduction, and cell death in brain dopamine and serotonin fiber pathways. White matter increases were unexpected, and may be due to reactive gliosis or aberrant myelination. These structural brain mapping techniques may help identify how drug abuse impacts the human brain, and provide therapeutic targets for drug-induced brain injury.

Figure 1. Methamphetamine Effects on Brain Structure.



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