Emerging Discipline of Computational Neuropsychiatry

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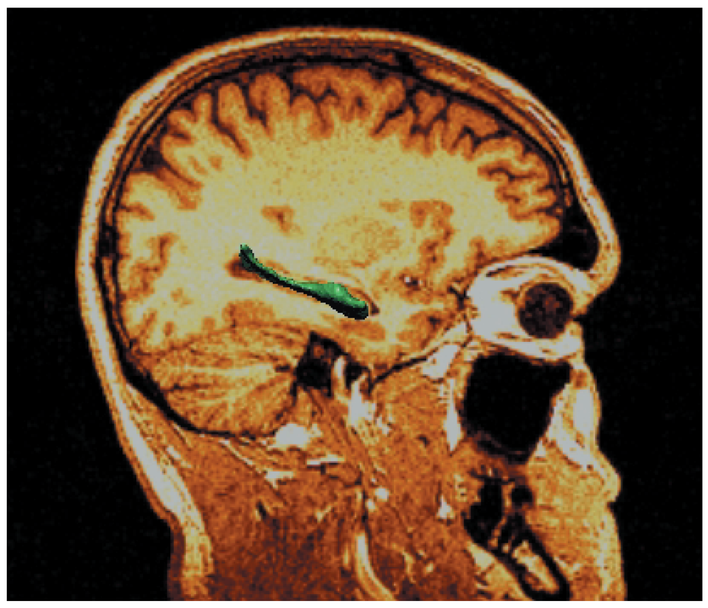
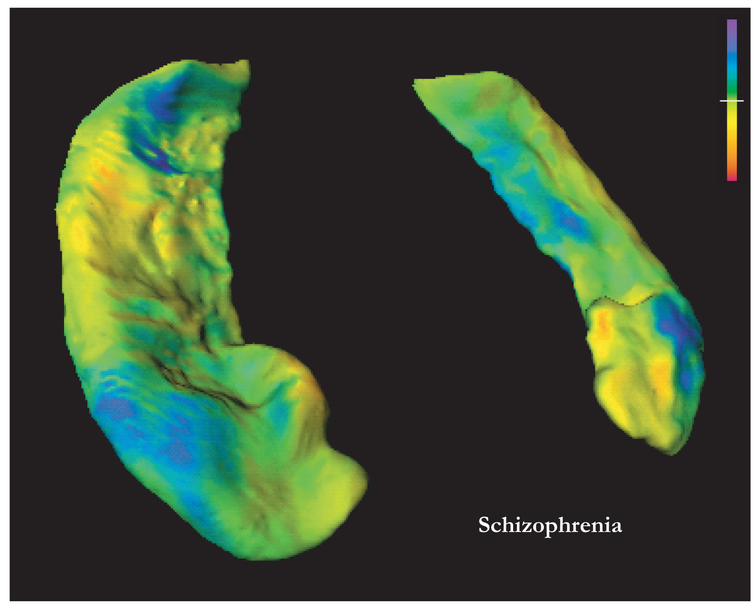
Introduction

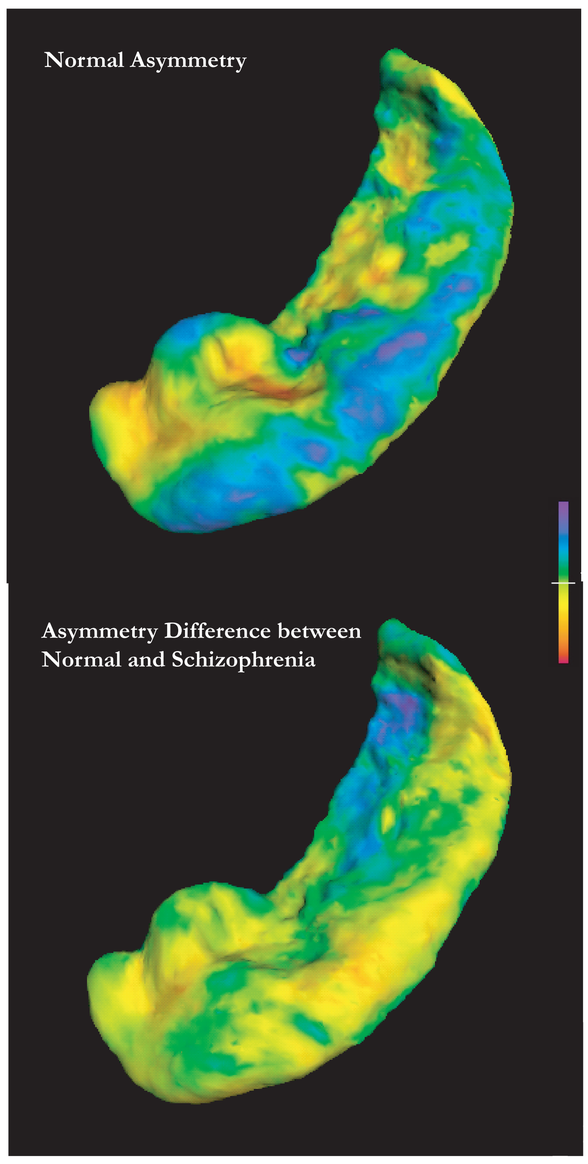
The field of Computational Neuropsychiatry has been exploding with applications of large deformation brain mapping technology providing mechanisms for discovering neuropsychiatric disorders of many types. The hippocampus is a region in the brain (depicted in green in the image on the right) that has been implicated in schizophrenia and other neurodegenerative diseases such as Alzheimer's. Using large deformation brain mapping tools in computational anatomy, researchers can define, visualize, and measure the volume and shape of the hippocampus. These methods allow for the precise assessment of changes in the hippocampal formation.



Schizophrenia

Researchers at the Center for Imaging Science (CIS) used mapping tools to compare the left and right hippocampuses (below) in 15 pairs of schizophrenic and control subjects. In the schizophrenic subjects deformations were localized to hippocampal subregions that send projections to the prefrontal cortex. The deformations strongly distinguish schizophrenic subjects from the control subjects. The pictures indicate inward deformations by cooler colors, outward deformations by warmer colors, and little deformation by a neutral green color. These results support the current hypothesis that schizophrenia involves a disturbance of hippocampal-prefrontal connections.



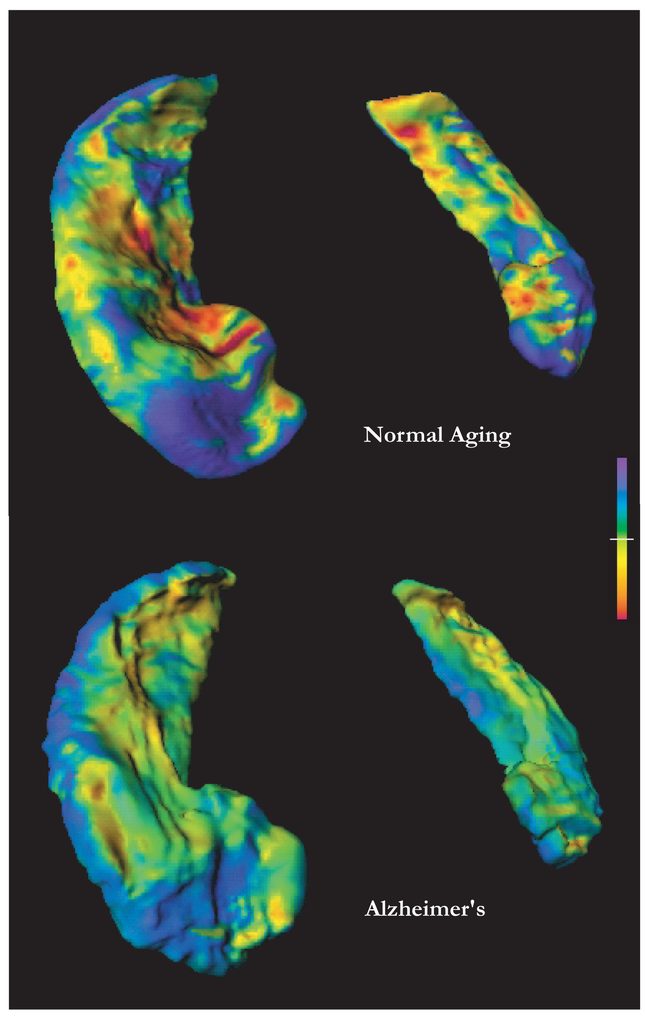


Asymmetry in Schizophrenia

In a separate study CIS researchers also compaired asymmetry between the left and right hippocampuses. The left and the right side of normal brains develop at different rates. Structures on both sides of the brain are similar, but not identical. This is normal brain asymmetry. If a different asymmetry pattern exists in schizophrenic subjects, this may indicate a disturbance of the left-right balance during early stages of brain development. Researchers found that the left hippocampus was narrower along the outside edge than the right hippocampus. This asymmetry was similar in schizophrenic and normal subjects (upper left image). However further comparison revealed a significant difference in asymmetry patterns of the hippocampal area called the subiculum (lower left image). People with Schizophrenia tend to have a more pronounced depression and a downward bend in the surface of that stucture.

Normal Aging versus Alzheimer's

As part of Washington University's Healthy Aging and Senile Dementia (HASD) program, CIS researchers applied the brain mapping tools to assess the structure of the hippocampus in older human subjects (depicted in the images to the right). They compared measurements of hippocampal volume and shape in 18 subjects with early Dementia of the Alzheimer type (DAT) with 18 healthy elderly and 15 younger control subjects. Hippocampal volume loss and shape deformities observed in subjects with DAT distinguished them from both elderly and younger control subjects. The pattern of hippocampal deformities in subjects with DAT was largely symmetric and suggested damage to the CA1 hippocampal subfield. Hippocampal shape changes were also observed in healthy elderly subjects, which distinguished them from healthy younger subjects. These shape changes occurred in a pattern distinct from the pattern seen in DAT and were not associated with substantial volume loss. These assessments indicate that hippocampal volume and shape derived from computational anatomy large deformation brain mapping tools may be useful in distinguishing early DAT from healthy aging.



References:

1. L. Wang, S. Joshi, M. I. Miller, J. G. Csernansky, "Statistical Analysis of Hippocampal Asymmetry in Schizophrenia," *NeuroImage*, 14, 531-545, 2001.
2. J. G. Csernansky, L. Wang, S. Joshi, J. P. Miller, M. Gado, D. Kido, D. McKeel, J. C. Morris, M. I. Miller, "Early DAT is Distinguished from Aging by High Dimensional Mapping of the Hippocampus" *Neurology*, 1, 1636-1643, 2000.
3. U. Grenander and M. I. Miller "Computational Anatomy: An Emerging Discipline," *Quarterly of Applied Mathematics,* Vol. LVI, #4, pp. 617-694, December 1998.

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