Digital Dynamic Brain Atlases

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Mapping the human brain, and the brains of other species, has long been hampered by the fact that there is substantial variance in both the structure and function of this organ among individuals within a species. Previous brain atlases have relied on information from, at best, a few samples to draw conclusions. These limitations and the lack of quantification for the variance in brain structure and function have limited the pace and accuracy of research in the field of neuroscience. This talk describes the development and application of theoretical framework and computational tools for the construction of probabilistic atlases of large numbers of individuals in a population. Results have demonstrated that both structural and functional variance can be quantified and made useful at both a microscopic and macroscopic level.

Genetic influences on brain morphology clearly contribute to the degree of variance. A variety of sophisticated brain-mapping approaches relating genetic influences on brain structure establishes a regional distribution for this relationship that is consistent with behavioral studies. Other factors, such as the environment, obviously play a role, and can influence morphology, especially during development.

Data has been collected from thousands of normal human subjects using MRI technology as well as substantial numbers of *post mortem* specimens to obtain microscopic anatomy and chemical architecture of the brain. This work was done in parallel with the development of mathematical and computational approaches to detect brain structure, variability and change with unprecedented sensitivity both spatially and temporally. The resulting four-dimensional maps of brain anatomy are warehoused in population-based brain atlases. Here, statistical tools compare brain changes across subjects and populations, adjusting for complex differences in both structure and function. Brain changes in an individual can be compared with a normative database comprised of subjects matched for age, gender and other demographic factors. Strategies to measure, map and visualize these brain changes are of immense value in basic and clinical neuroscience. Such tools can reveal subtle changes in adolescence and aging and link these changes with measurable differences in brain function. Such maps can also be correlated with genotypes thereby providing the first large-scale comparison of genotype-phenotype and behavior in the human species.

Dynamic brain maps offer key biological markers for understanding development and a wide range of nervous system disorders including neurodegenerative diseases, mental illness, multiple sclerosis, vascular disease and neoplasms. When fully implemented at a clinical level, such tools can serve an important diagnostic role by quantifying the range and confidence limits of normality from brain structure and function. When applied to individual patients and patient populations, they can also quantify disease burden and provide objective, quantifiable tools for use in experimental therapies and therapeutic trials.