

## **Combining Neuroimaging and Human Genetics (introductory remarks for a panel discussion)**

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In the first part of the Second Annual Imaging Genetics symposium, the conference's content focused on technological issues and analytic strategies, mainly driven by the necessity of controlling for multivariate data comparisons and simultaneously avoiding false discoveries without losing effect size. However, the center of attention of subsequent presentations shifted to the issues of application, particularly on the usefulness of genotypes to partition or capturing the variability present in functional or neurochemical imaging data. In his introductory talk, Dr. Frey wanted to show a particular model in the opposite direction, that is, the use of imaging as a way to "discover" gene effects on disease. With this idea in mind, investigators have been working on an initiative called the Tourette Syndrome Association Neuroimaging Consortium (TSANIC), on which a cohort of siblings of TS probands that have been recruited all over USA, Canada and UK, underwent MRI scans of their brains. TS is a complex genetic disorder with half to 2/3 of the cases being familial and most probably due to an autosomal dominant gene alteration. What these investigators have found is that significant reductions in gray matter density and volume of nucleus accumbens are present in TS subjects compared to controls, replicating previous findings from manual segmentation imaging studies, and furthermore, identifying a familial distribution of these changes, suggesting a possible endophenotype for the study of this highly genetic disorder. Once he presented this evidence, Dr. Frey promoted an open discussion between the audience and two of the speakers of the symposium, Dr. Lukas Pezawas and Dr. David Brooks. The topics discussed were mainly oriented to the following issues: in terms of phenotype searching, which approach is better? The focused approach (gene and/or region or interest) or the genome & brain wide approach? The second topic was on whether establishing heritability is really necessary for identifying imaging endophenotypes and how to determine it. The next topic was on the feasibility of using imaging to discover genes, which may be the case of syndromes like Tourette's but most probably not the case of mayor psychiatric disorders or neurodegenerative disorders such as Parkinson's Disease. The last topic discussed in the panel session covered imaging as a useful tool to improve diagnostic accuracy and to help select the right candidates for specific therapeutic modalities.