Specialty area: Single Subject Neuroimaging http://ismrm.org/13/WK05.htm

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Title: ***"What's Normal? Accounting for Population Variability"***

Highlights:

- Subject-specific analysis of neuroimaging data by comparison to normative data.
- Longitudinal, age-indexed modeling of average/variability of image-derived measures.
- Driving applications in autism, Down's syndrome, Huntington's disease and TBI.

Target Audience: This talk will discuss the building of normative data for rich sets of quantitative measures derived from brain imaging. Measures include volumetric measurements, image appearance in multi-modal imaging, white matter diffusivities associated to fiber tracts and circuits, and shapes of anatomical structures and complexes thereof. We will address the topic of extending statistical concepts and the generation of normative data, methods which are well known for scalar data, to statistics of complex data as measured in structural and functional neuroimaging. This topic may therefore benefit all users and/and or researchers using clinical neuroimaging for diagnosis, monitoring of disease progression or efficacy of therapeutic intervention. In addition, this lecture discusses serial, longitudinal imaging to assess brain change trajectories, which might be of interest to users involved in studies of neurodevelopment, neurodegeneration and drug trials.

Purpose: Subject-specific patient evaluation via imaging requires a quantitative comparison of image-derived measures to normative data in order to derive conclusions in regard to deviation from normal. Whereas such comparison data exists for measures like height, weight, head circumference, and standardized cognitive assessments, often as a function of age, there are to our knowledge currently no normative standard data available for morphometric and functional measurements extracted from neuroimage data. Moreover, the problem is greatly exacerbated in view of changes over time, as a comparison may not only have to include cross-sectional analysis at a specific age but the comparison of change trajectories. This is in particularly relevant for pediatric studies with rapid changes of brain anatomy and appearance, but also for the development of robust, sensitive measures of brain changes over specific observation periods. Clinical neuroimaging studies address this problem by comparing patient groups to matched controls groups. In a personalized health care situation, however, one needs to compare subject-specific information to existing standards in the form of normative data.

Methods and Results: Current research by the image analysis community focuses on building comprehensive "atlas" data and on making such data available to the community. The term "atlas" is not limited to simple average brain MRI data, but is represented as a database of images, segmented structures, derived quantitative measures, and statistics on these measures which includes average, variability and distributions. Such data is indexed by subject variables like gender, age and other clinically relevant categorization. Making use of existing longitudinal MRI/DTI data, one can construct age-indexed normative data, which includes expected average values and population variability. This lecture will report work in progress from several ongoing neuroimaging projects:

- Construction of longitudinal MRI and DTI atlases for pediatric neuroimaging studies where quantitative measures of brain tissue volumes and fiber tract diffusivities are available across the age range from birth to 2 years.
- Use of normative morphometric, shape and diffusion data in study of infants at risk for autism.

- Compare normative brain data to MRI and DTI imaging in Down's Syndrome (DS).
- Use of normative trajectories to explore brain changes in the PREDICT Huntington's Disease (HD) study.
- Evaluate brain tissue and lesion changes between acute and chronic phases in subjects with severe traumatic brain injury (TBI).

Outcome & Educational Objectives:

Learners will be informed about ongoing research efforts to generate normative data derived from multimodal brain imaging, to use such data in a personalized individual subject scenario, and about recent efforts in longitudinal image analysis which aims at modeling brain changes over time (for example in neurodevelopment, neurodegeneration, aging). In particular, participants will learn about:

- The need for standardization of imaging and image analysis in order to be compatible to normative data to be used for comparison of individuals to the norm.
- Challenges and obstacles to make control neuroimaging data, which exists at most neuroimaging centers, available to scientific community.
- Ongoing efforts to provide normative data as a function of age, gender and other clinically relevant variables, and to develop and apply metrics of "differences from normal".
- The use of control data in a broad variety of neuroimaging studies ranging from infant autism studies over DS, HD to TBI.
- Work in progress of the image analysis community to extend biostatistical concepts, currently limited to small sets of image-derived measures, to complex data such as anatomical shapes and white matter tracts, with extensions to four-dimensional (4D) spatiotemporal analysis.

Selected References:

1. Sadeghi N, Prastawa M, Fletcher PT, Wolff J, Gilmore JH, Gerig G., "Regional characterization of longitudinal DT-MRI to study white matter maturation of the early developing brain," Neuroimage. 2013 Mar;68:236-47. doi: 10.1016/j.neuroimage.2012.11.040
2. Irimia A, Chambers MC, Alger JR, Filippou M, Prastawa MW, Wang B, Hovda DA, Gerig G, Toga AW, Kikinis R, Vespa PM, Van Horn JD, "Comparison of acute and chronic traumatic brain injury using semi-automatic multimodal segmentation of MR volumes", J Neurotrauma. 2011 Nov;28(11):2287-306. doi: 10.1089/neu.2011.1920
3. Fishbaugh J, Prastawa M, Durrleman S, Piven J, Gerig G; IBIS Network, "Analysis of longitudinal shape variability via subject specific growth modeling", Med Image Comput Comput Assist Interv. 2012;15(Pt 1):731-8. PMID: 23285617