

Human Connectome Project (HCP)

Artifact Removal in the Context of Group ICA: A Comparison of Single-Subject and Group Approaches

- Yuhui Du, ..., Vince D. Calhoun
- Human Brain Mapping, 2016
- ICA used to identify intrinsic brain networks from fMRI data
- Group ICA computes group-level components from all data and subsequently estimates individual-level components to recapture inter subject variability
- 2 approaches compared
 - first ICA on individual subject data to remove artifacts, then group ICA on cleaned data – Individual ICA based artifacts removal plus group ICA (IRPG)
 - pros: good for extreme intersubject variability in artifacts sources
 - problems: identifying artifacts-related ICs for each individual data; determining the appropriate number of ICs
 - ICA on group data, then removes group-level artifact components, subject-specific ICAs using group-level non-artifact components as spatial references – Group Information Guided ICA (GIG-ICA)
 - takes advantage of the fact that components which show similarity among subjects tend to not be corrupted by unique artifacts
 - GIG-ICA has greater performance compared with IRPG
 - Also GICA, group ICA
- two ways to apply ICA on fMRI data: spatial & temporal
- Experiment 1: Effect of data quality and quantity

- to evaluate spatial/temporal accuracy of each estimated subject-specific non-artifact IC/TC, computed absolute value of Pearson correlation coefficient b/t each IC/TC & corresponding GT source/TC
- ICs from GIG-ICA cleaner & largely non-overlapping
- Experiment 2: Effect of variable number of sources among subjects
 - absolute values of Pearson correlation coefficients b/t obtained ICs (individual ICs from IRPG or group ICs from GIG-ICA) & related artifact templates
 - GIG-ICA had better mean of overall IC/TC accuracy across
- Experiment 3: Effect of spatially unique artifacts
 - spectral information of individual TCs
- Experiments using resting-state fMRI data
 - classifier trained to automatically identify individual-subject artifacts
- Conclusion: IRPG & GIG-ICA benefits over GICA, & GIG-ICA improvements over IRPG in performance & implementation

Insula reactivity to negative stimuli is associated with daily cigarette use: A preliminary investigation using the Human Connectome Database

- Dias, Peechatka, Janes 2015
- Negative mood with smoking withdrawal
- Hypothesis: number of cigarettes an individual smokes per day related to insult reactivity to negative stimuli
 - insular cortex: interoceptive awareness, motor control, self awareness, emotions
- fMRI emotional processing task data from Human Connectome Project

- 21 daily tobacco smokers, 5~20 cigarettes per day
- fMRI task presented to subjects
 - face stimuli (angry, fearful faces)
 - shape stimuli
- spatially smoothed to 4mm full width half max & high pass temporal filter
- subjects who smoke more daily cigarettes showed greater right insult reactivity to negative stimuli
- general linear model, two regressors, one corresponding to emotional faces block, the other to shapes block
 - boxcar functions of length equal to the duration of the block, convolved with the double gamma hemodynamic response function
 - motion modeled using 6 motion regressors (x, y, z, translation, rotation)
 - insula ROIs extracted for each participant
 - 5-mm spheres at MNI coordinates (+34, 26, 2)
 - right & left mid (+8, 2, 2) & posterior insula (+38, -14, 8)
 - Pearson's correlation coefficient calculated between number of cigarettes smoked per day & right and left insult reactivity to negative faces > shapes
- positive association between cigarettes smoked & reactivity in right, not left anterior insula
 - no associations in posterior insula

Abnormal striatal resting-state functional connectivity in adolescents with obsessive-compulsive disorder

- Bernstein et al. 2015

- resting-state fMRI used to investigate functional connectivity in the cortico-striatal-thalamic-cortical (CSTC) circuitry in pediatric OCD
 - previous research implicated CSTC circuitry in OCD, abnormalities in CSTC
- seed-based, whole brain approach
 - anatomically defined seeds in bilateral caudate, putamen, and nucleus accumbens
 - R-fMRI assesses spontaneous slow-wave functions of blood-oxygen-level-dependent (BOLD) signals between brain areas at rest
 - methods to minimize ROI errors & correct for confounds due to motion
 - FSL tools used → preprocessing steps, including skull removal, distortion correction, motion correction, registration to MNI space
 - FSL MELODIC program, ICA on processed data on individuals
- adolescents with OCD exhibited significantly lower functional connectivity between the left putamen & single cluster of right-sided cortical areas
 - cortical areas including orbitofrontal cortex, inferior frontal gyrus, insula, operculum
- used FreeSurfer to create individual anatomically-based ROIs
 - ROIs aligned to individual's fMRI data using bbregister & time series extracted
 - FSL FEAT used
 - time series of each ROI used as primary regressor in general linear model
- used higher-level FEAT analysis to examine main effect of group
- results
 - adolescents with OCD compared with controls exhibited lower functional connectivity between the left putamen & single right-sided cortical region
 - size of cluster 331 voxels
 - no group differences present

- no correlation between measure of functional connectivity & severity of OCD symptoms, between connectivity & dimensional scores, & between connectivity & impairment due to OCD
- others employed ICA to analyze whole brain functional connectivity data in pediatric OCD
 - ICA data-driven approach: evaluates interactions among multiple brain regions and does not rely on selection of seed regions

Abnormal amygdala resting-state functional connectivity in adolescent depression

- Cullen et al. 2014
- doesn't use HCP data, but explains the previous RSFC methods
- RSFC analysis (resting state functional connectivity)
 - seed-based whole-brain approach
 - anatomically based ROIs, FreeSurfer-based right & left amygdala ROIs registered to the preprocessed rsfMRI data, mean time series of voxels extracted from region
 - time series used as primary regressors in general linear model analyses of all other voxel time series, resulting in whole-brain amygdala RSFC maps

Training shortest-path tractography: Automatic learning of spatial priors

- Kasenburg et al. 2016
- tractography is the standard tool for automatic delineation of white matter tracts from diffusion weighted images
 - but requires expert prior knowledge
 - study demonstrates how such prior knowledge can be automatically incorporated into a shortest-path tractography approach to produce more robust results
 - & how such prior can be automatically learned from a population

- diffusion weighted imaging (DWI) provides local estimates of water diffusion
 - voxel-wise diffusion orientation distribution functions dODFs, transformed into fiber orientation distribution functions fODFs, representing estimates of fiber directions within a voxel
 - tractography delineates underlying anatomical tracts connection brain regions by inferring inter-voxel connectivity from the fODFs
 - post-processing of tractography outputs using waypoint or exclusion regions required
 - possible priors → existence/absence of connection
- study presents algorithm that can include any type of prior information about spatial location of tract
 - for example, per-voxel white matter probabilities, which guide tractography through white matter, or anatomical knowledge in form of tract atlas
 - can also learn spatial priors from previous tractography results
 - shortest-path tractography approach SPT: finds globally optimal path connecting two voxels
 - based on graph-based shortest-path tractography
 - each DWI voxel is a node, connected to all white matter voxels in 3x3x3 neighborhood
 - weight of edge: probability of connection
 - calculated by integrating fODF of the voxel along all 26 directions
 - undirected graph, symmetrical edge weights
 - most-likely-path found by using shortest-path algorithm on modified graph that has log-transformed edge probabilities
 - also returns confidence score, quantitative measure of how well a shortest path is supported by underlying fODFs and prior info

- integrate spatial prior information into shortest-path tractography algorithm
 - assign prior probability to every node such that $p_v(v)$ reflects probability that node v lies in the sought tract
 - waypoints & exclusion masks: if waypoint exists, then prob from voxel to every other direction is set to 0
- learned spatial prior
 - tractography performed on N training subjects
 - confidence map, scalar confidence value for voxel v
 - normalized to 1 & warped into common standard space
 - then population heat map by averaging subject data
 - $p_v^{\text{learned}}(v)$ quantifies how likely a voxel is to lie on a tract between two specific ROIs

Allen Brain Atlas (ABA)

Linkage of cDNA expression profiles of mesencephalic dopaminergic neurons to a genome-wide in situ hybridization database

- Alvian, Simon 2009
- dopaminergic neurons in ventral midbrain, SNpc among others
 - Parkinson's disease PD degeneration of DA neurons in SNpc
- ABA large-scale collection of gene expression patterns
 - high throughput, semi-automated in situ hybridization (ISH) on mouse brain sections
- comprehensive expression profile of mesDA neurons
 - verified expression of identified genes from six other studies using ABA

Analysis of the network of feeding neuroregulators using the Allen Brain Atlas

- Olszewski et al. 2008
- use ABA to research central regulations of feeding
 - searched 57 feeding-related genes in ABA
 - gene systems linked to energy needs, reward or satiation display a remarkably high level of overlap
 - calls into question the classical concept of brain sites viewed as independent hunger or reward centers
 - favors theory of widespread feeding network comprising multiple neuroregulators affecting numerous aspects of consumption
- 3D images & corresponding photomicrographs analyzed visually & subjectively using the Brain Explorer by two scorers
 - mostly subjective view on ABA images, which can be inaccurate
- analysis of distribution of feeding-related genes in ABA strongly supports the hypothesis stating that the central regulation of consummatory behavior is governed by a widespread central network
 - genes classically viewed as mediators of different aspects of feeding are in multiple regions, and multiple genes in the single regions

Analyzing in situ gene expression in the mouse brain with image registration, feature extraction, and block clustering

- Jagalur et al. 2006
- Study presents an end-to-end approach for processing raw in situ expression imagery and performing subsequent analysis
 - non-linear, information theoretic based image registration technique specifically adapted for mapping expression images to anatomical annotations

- method for extracting expression information within an anatomical region
- goal to gather statistics about common expression patterns in anatomical structures across experiments

Analysis of Chaperone mRNA Expression in the Adult Mouse Brain by Meta Analysis of the Allen Brain Atlas

- Andrew Tebbenkamp, David Borchelt 2010
- chaperone are proteins that assist the covalent folding or unfolding and the assembly or disassembly of other macromolecular structures
 - includes heat shock proteins (HSPs)
- used ABA to analyze chaperon expression levels
 - study provides analysis of how variations in chaperone gene expression may modulate the vulnerability of specific neuronal populations of mammalian brain
 - mined ABA to provide baseline expression of the chaperone network to provide framework to explore basis of neural vulnerability
 - study reveals relatively little diversity in expression patterns of chaperones, chaperonins, and the HSFs
- common feature of neurodegenerative disease is accumulation of misfiled and aggregated proteins in pathologic inclusion bodies in specific populations of neurons
 - chaperone proteins help protect against misfolded proteins
- data analysis
 - search for HSPs in NCBI database, cross-referenced with ABA
 - searched for expression data in ABA
- results: expression data in the ABA database assigned numerical values for strength of signal (relative to positive control, dopamine receptor Drd1a) with values from 0 to 100

- HSPAs major chaperones that respond to cell stress
- and other genes

Identification of a set of genes showing regionally enriched expression in the mouse brain

- D'Souza et al. 2008
- goal to identify genes displaying regionally enriched expression in the mouse brain so that promoters designed from orthologous human genes can be tested to drive reporter expression in a similar pattern in the mouse brain
- identification of brain region-enriched gene expression by LongSAGE
- data mining genes showing regionally enriched expression from ABA
 - examine expression patterns of genes identified as regionally enriched by SAGE and/or the literature
 - also the anatomic search tool to identify additional genes whose expression patterns cluster within brain regions of interest

Evolution of the Aging Brain Transcriptome and Synaptic Regulation

- Lurch et al. 2008
- goal: to obtain greater insight into how brain aging has evolved
 - compared age-related gene expression changes in the cortex of humans, rhesus macaques, and mice on a genome-wide scale
- phylogenetic analysis of brain aging in humans, macaques, and mice
 - used all-against-all protein BLAST to identify orthologous genes between rhesus predictions and the other two species
 - at least 80% alignment of human or mouse protein sequence with the rhesus sequence

- ABA for identifying cell types in the brain that exhibit prominent age-related changes in gene expression
 - ABA → includes genes in which expression was significantly enriched in one of five specific cell types
 - 3D imaging & ISH of adult mouse brain
 - subset of age-related gene expression changes was localized to specific cell types
 - combined cell type analysis with mouse gene expression data
 - genes predicted to be enriched in astrocytes and neurons in the mouse brain by ABA were also enriched in the corresponding cell types derived from the human cortex
 - localize age-related gene expression changes in both human & mouse
 - genes enriched in specific cortical cell types based on ABA were analyzed in the aging mouse and human gene expression profiles
 - types: astrocyte-enriched, choroid plexus-enriched, near ubiquitous, neuron-enriched, oligodendrocyte-enriched
 - % genes up- or down-regulated with age for humans & mouse
- analysis of cultured human cortical cell types
 - human cell type enrichment score for every human-mouse cell type combination

Comparative Analysis of Selenocysteine Machinery and Selenoproteome Gene Expression in Mouse Brain Identifies Neurons as Key Functional Sites of Selenium in Mammals

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