Official Title: PET and MRI Brain Imaging of Bipolar Disorder

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Proposed Statistical Plan for [11C]-DASB (5-HTT) & [11C]-CUMI-101 (5-HT1A) from Parsey Bipolar Study

Outcomes
DASB: V_T/f_p + bootstrap ROI error
CUMI: BP_F + bootstrap ROI error (BP_{ND} ??)

A priori ROIs
DASB: acn, amy, midbrain, gcirc
CUMI: acn, amy, cin, dlPFC, parahippocampal gyrus, hippocampus, raphe

Statistical methods:
Linear mixed models with subject fit as random variable
LMM also with DASB & CUMI reference regions and fp
Key outcomes: p-values for main effects/interactions; overall model R^2 & p-value; standardized & unstandardized β's, 95% CIs, p-values for post-hocs

Covariates
DASB: age
CUMI: age, sex, previous med status (dichotomous – w/n 4 years)

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Post-Treatment

Sample: HC, pre BPD, post BPD

Question 1: Do post-treatment BPD levels of DASB or CUMI differ from pre-treatment levels and HCs?

Interactions of interest:
Group (relationship btw brain & Group across all regions)
Group*ROI (ROI-specific relationship btw brain & Group)

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Treatment Effects

Sample: pre/post BPD pairs

Tx response: % change in HDRS-24 (continuous) and remitter/non-remitter (dichotomous)

Question 2: Is the % change in DASB or CUMI associated with the treatment outcome?

Interactions of interest:
ΔHDRS (relationship btw brain & Tx outcome across all regions)
ΔHDRS*ROI (ROI-specific relationship btw brain & Tx outcome)

Dichotomous

Interactions of interest:
Remission (relationship btw brain & Tx outcome across all regions)

Remission*ROI (ROI-specific relationship btw brain & Tx outcome)

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Predicting Treatment Outcome

Sample: pre BPD with pre HDRS-24 + >7-week HDRS-24

Tx response: % change in HDRS-24 (continuous) and remitter/non-remitter (dichotomous) (responder ??)

Question 3: Do pre DASB or CUMI in any of the *a prioris* predict treatment response? Are the *a prioris* independent predictors of treatment response?

Interactions of interest:

PET_roi (pre-treatment PET in ROI predicts treatment response)

Interactions of interest:

PET_roi (any significant ROIs are independent predictors of Tx response (over and above the other ROIs))

Same models fit with dichotomous remission status

Additional question: Do pre DASB & CUMI together predict more of the variance in treatment response than either method alone?

Change in overall model R^2 from models with pre DASB & CUMI alone to combined model (If R^2 increases with both methods, tracers are predicting unique properties of Tx response)

Question 4: With what accuracy does pre DASB or CUMI predict treatment response?

Penalized logistic regression models

Additional question: With what accuracy do pre DASB & CUMI together predict treatment response

Metrics of interest:

Accuracy, AUC, sensitivity, specificity, NPV, PPV, model factor importance ranking or % of variance explained with each factor

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