Variability in fMRI Signal in ADHD and Control Groups: Implications for Statistical Power

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INTRODUCTION:

• Statistical power is the probability of rejecting the null hypothesis, given that it is indeed false. In essence, power describes our ability to capture expected effects.

• In functional magnetic resonance imaging (fMRI) experiments, power is affected by a number of factors (Desmond & Glover, 2002), including:
- • effect magnitude (percent signal change)
- • intra-subject variability (error variability within the time series)
- • inter-subject variability (variability in activation across participants)

• Increased variability reduces statistical power
- • Intra-subject variability: increase number of observations per condition
- • Inter-subject variability: increase number of participants in the study

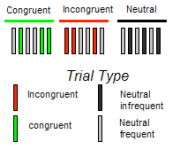
• Effects of variability on statistical power may be especially important within clinical populations, since they may exhibit increased inter- and/or intra-subject variability
- • It is common to observe both increased intra- and inter-subject variability in behavioral performance of clinical groups
- • However, question of whether clinical groups show more variability in the fMRI BOLD signal is addressed much less frequently.

• As in behavioral measures, we may expect individuals with ADHD to show both greater variability between-subjects and within-subjects.

• Indexed intra-subject and inter-subject variability in the acquired BOLD signal for
- • group of adults with ADHD-combined subtype
- • control group (sampled from same university population)

• Utilized measures of effect magnitude, within-subject variability, and between-subject variability to estimate statistical power for varying numbers of observations per condition and numbers of subjects in the ADHD group and control group.

TASK DESIGN:



16 subjects: 8 ADHD subjects; 8 control subjects

Color-word Stroop = Hybrid event-related / blocked design

- 3 blocks: congruent, **incongruent**, & **neutral**
- Each block consisted of 50% neutral frequent trials (e.g. **sum**) that appeared in all blocks and 50% trials of the specific block type (e.g. incongruent **blue**, neutral lot, congruent **red**).
- Each block consisted of 36 trials, with 12 null trials (length-matched fixations) before and after each block.
- There were 3 blocks per run, and 3 runs per subject.

fMRI AND STATISTICAL METHODS:

• **acquisition:** whole brain acquisition, 3T (GE whole-body scanner)
• gradient echo T2*-weighted EPI sequence; flip angle 90°
• 64 X 64 in-plane matrix; sampled along the AC-PC line
• 29 contiguous slices; 4-mm slice thickness; resampled into 2mm cubic voxels
• **pre-processing:** Standard image pre-processing and data analysis were performed using the FMRIB software library package FSL (http://www.fmrib.ox.ac.uk/fsl/): MCFLIRT, BET and spatial normalization to (MNI) high-resolution 152-T1 template

• **ROI identification:** ROIs were composed of voxels showing significant activation for event-related contrast of **incongruent > neutral** trials ($p < 0.001$, uncorrected, 30 or more contiguous voxels)
- • 18 ROIs were identified for the ADHD group, 27 ROIs were identified for controls
- • Only 18 ROIs from the control group were used (to avoid reliability differences)

• **effect magnitude:** cubic ROI (27 voxels) around peak voxel; percent signal change using *featquery*
• **intra-subject variability:** calculated mean variance in MR signal during blocks of resting fixation
• **inter-subject variability:** calculated mean variance in percent signal change across subjects; corrected that measure for the influence of intra-subject variability

• **power estimation:** estimated power for one-sample t-test; using equations from Cohen (1988)

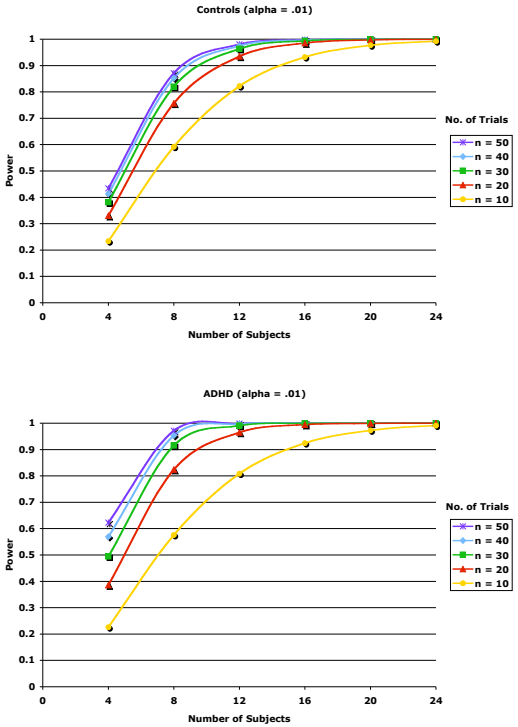
RESULTS:

Parameter Calculation:

Effect magnitude (μ_D): no group difference (ADHD = 0.322%; Controls = 0.324%)
Intra-subject variability (σ_W): ADHD > controls (ADHD = 0.657; Controls = 0.540)
Inter-subject variability (σ_B)
standard deviation in μ_D across subjects: ADHD = 0.164; Controls = 0.221
correcting for influence of σ_W: ADHD = 0.144; Controls = 0.212

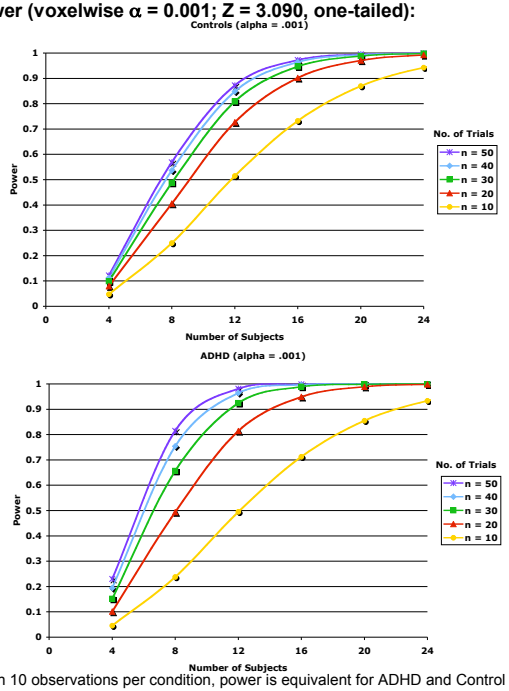
- while ADHD subjects do not differ from controls in effect magnitude, they show ***more*** intra-subject variability but ***less*** inter-subject variability

Power (voxelwise $\alpha = 0.01$; $Z = 2.326$, one-tailed):



- With 10 observations per condition, power is equivalent for ADHD and Control groups (power surpasses .80 at 12 subjects)
- Power for ADHD group at 20 observations per condition equals power for control group at 30 observations (surpasses .80 at 8 subjects)
- Increasing number of observations helps ADHD more than controls

Power (voxelwise $\alpha = 0.001$; $Z = 3.090$, one-tailed):



- With 10 observations per condition, power is equivalent for ADHD and Control groups (power surpasses .80 at 18 subjects)
- Power for ADHD group at 20 observations per condition equals power for control group at 30 observations (surpasses .80 at 12 subjects)

CONCLUSIONS:

- Effect magnitude (percent signal change / μ_D) was nearly identical for ADHD and control groups; subsequent analyses (not shown here) show that across ROI variability in percent signal change is also equivalent for control and ADHD groups
- Intra-subject variability was greater for ADHD, but inter-subject variability was smaller
- Consequently, at lower numbers of observations per condition, power was equivalent for the ADHD group than the control group; at higher numbers of observations, power was greater for ADHD group than for the control group
- With small numbers of trials (n = 20 per condition) for adults with ADHD, it may be possible to achieve power of .80 with 8 subjects ($\alpha = .01$) or 12 subjects ($\alpha = .001$)

IMPLICATIONS:

- If groups differ in intrasubject variability, equal power can be obtained by manipulating the number of trials per condition per group
-If the groups differ in intersubject variability, equal power can be obtained by utilizing different numbers of participants per group.
-To the degree that intersubject variability differs between groups, the ability to find correlations of brain activity with performance and/or symptomatology for each groups may not be equal.

REFERENCES:

- Desmond, J.E. & Glover, G.H. (2002). Estimating sample size in functional MRI (fMRI) neuroimaging studies: Statistical power analyses. Journal of Neuroscience Methods, 118, 115 - 128.
- Cohen, J. (1988). Statistical Power Analysis for the Behavioral Sciences. 2nd ed. Mahwah, NJ: Lawrence Erlbaum Assoc.
-See Poster A77 for differences in attentional control between ADHD adults and matched participants