Trait and state anxiety differentially modulate sustained and transient neural activity

C.L. Fales¹, G.C. Burgess¹, A. Schaefer², T. S. Braver¹, D.M. Barch¹, and J.R. Gray²
Departments of Psychology, ¹Washington University, St. Louis, Missouri. and ²Yale University, New Haven, Conn.

INTRODUCTION
Theories of trait anxiety posit that anxious individuals may be subject to greater autonomic arousal, and that the degree of arousal may modulate activity in medial prefrontal cortex (mPFC) (Simpson, Drevets et al., 2001). Demanding cognitive activity has also been shown to modulate mPFC areas (Simpson, Snyder, et al., 2001), as well as other “default network” areas that are deactivated during cognitive processing (Shulman et al., 1997). However, evidence on the direction of this modulation is so far equivocal, with some studies showing reduced activation in these areas with anxiety, and others showing increases.

In this study, we examined sustained and transient activity while subjects performed a demanding cognitive task, to observe effects of both trait and state anxiety on neural response. We asked whether anxiety would be reflected in the level of sustained activation in medial PFC (as expected of a constant trait), or in the transient response, as predicted by studies finding reduced cognitive control with increased anxiety (e.g. Bishop et al., 2004).

METHODS
Participants: (n=77) Healthy younger adults (ages 18-36, 33 male) from Washington University and the surrounding community. Sample size for high and low-anxious sub-groups was high-anxious (n=15,1 male) and low-anxious (n=14, 8 male).

DAY 1: Anxiety assessment: combined scores for anxious arousal
- Taylor Manifest Anxiety Scale and Penn State Worry questionnaire
Neuropsychological assessment:
- Working memory span (rotation, symbol, operation, word)
- Fluid intelligence: Raven’s Matrices, Cattell culture-fair test

DAY 2: Mood manipulation: exposure to a 10-minute video before each run.
Working memory task:
- Verbal 3-back task, using words as stimuli
- One trial every 2 seconds, 36 seconds inter-trial interval

FMRI METHODS
We used a mixed blocked/event-related fMRI design to isolate sustained and transient neural activity in two runs, each with two blocks of trials (16 trials each) and two rest blocks. (Four other runs were conducted for a separate study.)

Scanning methods: Siemens 3T (Alligea) scanner
- Axial T2: spin-echo echo-planar sequence. TR=2.36
- Whole brain images, 32 transverse slices (3.75mm thick), 3.75 x 3.75-mm in-plane
Data analysis methods: Functional imaging data were movement-corrected, co-registered, smoothed and pooled across subjects. Regions of interest were identified by a conjunction analysis that held all voxels to a p<.0025 significance level (for sustained data) or a p<.0001 level (for transient data).

BEHAVIORAL RESULTS
Task performance (3-back) for High-anxiety and Low-anxiety groups:
• No response time differences
• Accuracy: trend toward lower accuracy in the Low-anxious

Neuropsychological tests: High-anxious participants showed a trend toward impairments in tests of:
- Fluid intelligence (Raven’s Matrices, Cattell test)
- Working memory span: Rotation, Symbol, Operation & Reading

fMRI RESULTS: Neutral condition
Areas of significant activity (vs rest) for all 77 subjects.

Correlation of anxiety with task-related activity:
• Positive correlation with transient activity in many of the same areas, as well as additional WM areas.

Sustained activity, and significant increases in transient activation.

fMRI RESULTS: Withdrawal condition
Differences in correlations between activity and trait anxiety: SUSTAINED response: Negative correlations with sustained activity in default-network areas (that were found in neutral condition) disappear in virtually all areas in withdrawal condition. TRANSIENT response: Areas of positive correlation with anxiety are sharply reduced in withdrawal compared to neutral condition.

CONCLUSIONS
Even in absence of performance differences, state and trait anxiety modulate both transient and sustained activity during cognitive task performance.

Neutral condition: Effects of trait anxiety
Low anxious participants show significantly greater activation than high anxious in both working memory and default network systems. High anxious show greater transient activation than low anxious in both networks.

For the total sample, transient and sustained activation maps include both working memory and default network areas. However, low-anxious subjects can activate working memory areas on a sustained basis, which the high-anxious do not. Instead, the high-anxious activate working memory areas transiently. These results support the notion, proposed by Braver, Gray & Burgess (2005), that high anxious subjects may show a preference for reactive rather than proactive forms of cognitive control.

The extensive sustained deactivation of default-network areas, shown by the high anxious but not the low, may reflect two possible processes: (1) inhibition of systems mediating regulation and awareness of physiological arousal or (2) compensatory default system deactivation that may facilitate cognitive performance.

Withdrawal condition: Effects of state anxiety
The anxiety produced by the ‘risky’ condition elicited a PFC effect in high-anxious subjects. However, the low-anxious showed a significant reduction in their sustained response, and increased their transient responses in the same areas. These changes abolished the strong correlations found between anxiety scores and medial PFC in the neutral condition and suggest that state anxiety moves the activity patterns of low-anxious people in the direction of high-trait-anxiety patterns.

Supported by the National Institute of Mental Health (5R01 MH06886)
Email: cfales@artsci.wustl.edu