

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 any modulation 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.
- Videos intended to induce a neutral versus an anxiety-related mood
 - Manipulation check: POMS ratings after completion of task
- 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 (Allegra) scanner.
- Asymmetric 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:

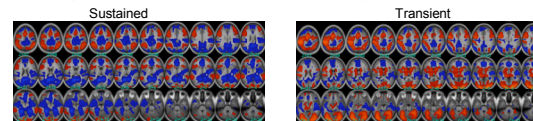
- No response time differences
- Accuracy: trend toward lower accuracy in the Low-anxious

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

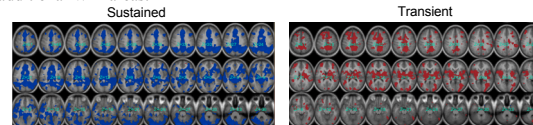
fMRI RESULTS: Neutral condition

Areas of significant activity (vs rest) for all 77 subjects.

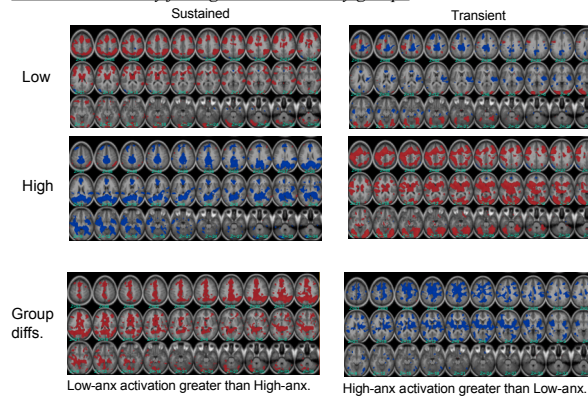


Correlation of anxiety with task-related activity

- * Negative correlation with sustained activity in WM and default-network areas.
- * Positive correlation with transient activity in many of the same areas, as well as additional WM areas.



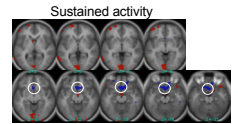
Task-related activity for high and low-anxiety groups



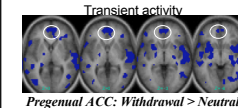
fMRI RESULTS: Withdrawal condition

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.

Differences in sustained activation: for the Withdrawal vs Neutral condition are most significant in the subgenual ACC (BA 25). Consistent with Zald et al (2002), this area increases activation in the withdrawal mood (that is, neutral-mood deactivation is attenuated). By contrast, this area showed a non-significant tendency to reduce transient activity in the withdrawal mood. Subgenual ACC is modulated by state anxiety, but is not modulated by trait anxiety.



Subgenual ACC: Withdrawal > Neutral

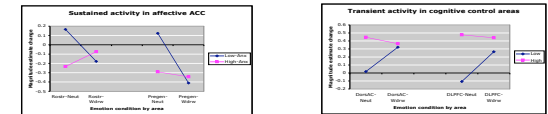


Pregenual ACC: Withdrawal > Neutral

Differences in transient activation: included pregenual ACC (BA 10/32) where activation rises in the withdrawal condition.

High and Low-anxiety group differences

For low-anxious participants, but not for high, state anxiety leads to significant deactivations of sustained activity, and significant increases in transient activity.



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-system networks. 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 videos produced little effect on medial PFC for high-anxious subjects. However, the low-anxious significantly reduced their sustained response, and increased their transient response 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.