Normalization of Amygdala Function in Generalized Anxiety Disorder Patients Following Treatment with Venlafaxine

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Introduction

• Patients with generalized anxiety disorder (GAD) worry excessively about the future and show behavioral hypervigilance to threat (1).
• Chronic worry and GAD are also associated with emotional avoidance (2) consistent with findings of cardiovascular (3) and pupil hyporesponsivity (4).
• The amygdala is a brain area linked to emotionality and the anticipation of aversion (5), and thus has been the focus of many studies on anxiety.
• At pre-treatment, we expected the amygdala to index anticipatory hyperactivity preceding emotional pictures as well as hypoactivity in response to those pictures in GAD patients vs. healthy controls (consistent with hypervigilance and avoidance theories of GAD).
• At post-treatment, we expected venlafaxine, a commonly prescribed medication for GAD, to normalize patterns of amygdala activation.

Pre-Treatment Results

A significant Group x Period interaction at Pre-Treatment, F=32.04, p<.001 in bilateral amygdala (right - 893 voxels; left - 483 voxels). GAD patients showed significantly heightened anticipatory activation in the right amygdala during warning periods (p<.05), and decreased activation in bilateral amygdala during viewing of pictures (p<.01; left - p<.05), as compared to control subjects.

Post-Treatment Results

Extracting Post-Treatment activation values for the Pre-Treatment Group x Period amygdala clusters shown to the left, treatment effects were observed. Following 8 weeks of treatment with venlafaxine, GAD patients showed normalization of amygdala activations (Period x Group x Time interaction, F=7.50, p<.001). Anticipatory amygdala activity decreased and amygdala responses to the pictures increased (see Figure below) to the point of not differing from controls at the Post-Treatment scan (all ps>.50).

Conclusions

• Consistent with traditional symptom-report treatment outcome measures, GAD patients showed changes in neural activity in the direction of normalization following 8 wks of treatment with venlafaxine.

Methods

10 GAD patients (no other Axis I disorders); 10 Controls (no current or past Axis I disorders)
GAD patients completed an 8-week open trial of venlafaxine ER, which resulted in reduction of anxiety symptoms (Ham-A scores ranging from 18-21 Pre-Treatment and 2-13 Post-treatment). MRI scans were conducted Pre- and Post-Treatment (scans for healthy controls were also separated by 8 weeks).
Event-related design modeled after previous study in our lab (5). 0.5-s warning cue then 2.5- or 4.5-s blank screen then 1.0-s displays of negative or neutral pictures (6) then 13- or 15-s blank screen to allow hemodynamic response to return to baseline (see Figure below).

References


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