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ANTIDEPRESSANT RESPONSE TO PARTIAL SLEEP DEPRIVATION IN UNIPOLAR DEPRESSION IS NOT RELATED TO STATE ANXIETY

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Abstract

One night of total or partial sleep deprivation (SD) produces a temporary remission in up to 60% of patients with major depression, yet mechanisms remain unclear. We investigated whether the antidepressant effects of SD are caused, even partially, by an improvement in anxiety. As part of a functional magnetic resonance imaging study, 19 unmedicated major depression patients and eight controls completed the Spielberger State/Trait Anxiety Inventory (STAI) (state version) at baseline and sleep-deprived scanning sessions. We found (1) greater anxiety in patients than controls; (2) no baseline or SD STAI difference between responders and nonresponders; (3) no STAI change with SD in any subject group; and (4) no significant correlation between any STAI and Hamilton Depression Rating Scale measures. Our findings did not provide support for an anxiolytic process associated with the antidepressant effects of SD.

Keywords

depressive disorder; major; psychiatric somatic therapies; Spielberger State/Trait Anxiety Inventory; psychiatric status rating scales; anxiety disorders

INTRODUCTION

One night of total or partial sleep deprivation (SD) produces a rapid temporary remission in up to 60% of subjects with a current major depressive episode [Wirz-Justice et al., 2004]. Despite many studies since this effect was first reported [Pflug and Tölle, 1971], mechanisms of the antidepressant effects of SD remain unclear.

Several lines of evidence led us to speculate that SD's antidepressant effects may be caused, at least in part, by improvement in anxiety: the high prevalence of comorbid anxiety disorders and subsyndromal anxiety symptoms in depression; common efficacy of treatments (e.g., selective serotonin reuptake inhibitors) in depression and anxiety [Ninan and Berger, 2001; disturbed, poorly restorative sleep in anxiety and depression; and evidence of overlapping pathophysiology for both disorders [Deakin, 1998]. An extensive review of the literature on the antidepressant effects of SD [Clark and Braun, manuscript in preparation] showed no analyses of anxiety rating scales and very few proxy measures for anxiety.

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In our functional magnetic resonance imaging (fMRI) study of partial *SD* (PSD) in major depression, we hypothesized the following: (1) anxiety measures will be greater in depressed patients than healthy controls; (2) anxiety measures will significantly decrease in *SD* responders but not in nonresponders; and (3) the degree of antidepressant response in depressed subjects will correlate with the amount of decrease in anxiety measures.

MATERIALS AND METHODS

Subjects, general procedures, statistics, basic demographics, and fMRI results have been published previously [Clark et al., 2006a,b]. To assess the possible effects of anxiety on fMRI and vice versa, the state version of the Spielberger State/Trait Anxiety Inventory (STAI) was obtained before and after each scanning session. Responders and nonresponders were distinguished by a decrease of $\geq 40\%$ in the modified 17-item Hamilton Depression Rating Scale (HDRS17) (omitting sleep and weight loss items) [Wu et al., 1999].

RESULTS

The 19 patients and eight controls were demographically similar, as were the five responders and 14 nonresponders (t tests, χ^2 not significant). Baseline HDRS17 (19.2 ± 2.4 responders versus 17.7 ± 5.4 nonresponders) and baseline modified HDRS17 (HDRS17Mod) (16.6 ± 1.5 responders versus 15.3 ± 4.8 nonresponders) did not differ between responders and nonresponders. HDRS17Mod diverged with PSD (SD HDRS17Mod 8.0 ± 2.5 responders versus 12.9 ± 3.7 nonresponders; between groups t tests, not significant). A group by time analysis of variance (ANOVA) showed a significant interaction effect for HDRS17Mod ($F=11.0$, $df=1,15$, $P=0.005$, $\eta^2=.42$).

Baseline STAI values were missing for three patients and one control. STAI scores before and after each scan were compared within each group at each time point. As there was no significant difference between these scores, an average STAI score for each time point (baseline and PSD) was calculated (referred to below as baseline and PSD STAI scores; see Table 1).

For STAI scores, we used a two-way ANOVA with condition (baseline versus PSD) as the within group factor and response (responder versus nonresponder versus control) as the between groups factor. Group by condition ($F=0.07$, $df=2,18$) and condition ($F=1.02$, $df=1$) effects were not significant ($P>0.33$). Rather, we found a significant group effect overall ($F=12.07$, $df=2,18$, $P=0.000$).

We then conducted separate one-way ANOVAs each for baseline and PSD STAI scores, using three groups (responders, nonresponders, and controls) with Bonferroni correction. The one-way ANOVA for baseline STAI showed a significant group effect ($F=9.7$, $df=2,18$, $P=0.001$). Controls' baseline STAI was significantly less than responders ($P=0.014$) or nonresponders ($P=0.002$), with no significant difference between responders and nonresponders ($P=1.000$; Bonferroni). Similar results were found for PSD STAI ($F=10.5$, $df=2,22$, $P=0.001$), with controls significantly less than responders ($P=0.011$) or nonresponders ($P=0.001$) and no significant difference between responders and nonresponders ($P=1.000$; Bonferroni).

We also calculated correlation coefficients (Pearson's r) for the combined patient group for all HDRS17Mod and STAI variables, i.e., baseline, PSD, decrease, and percent decrease. Correlation coefficients between change in H17Mod and change in STAI, and between percent change in H17Mod and percent change in STAI, were not statistically significant (two-tailed $P \geq 0.218$). In fact, no correlation coefficients between any STAI measure and any H17mod measure reached significance. Similar results were found with Spearman correlations.

DISCUSSION

Our most important findings were as follows: (1) greater baseline (and PSD) STAI in patients than controls; (2) no significant change in STAI between baseline and PSD in controls, responders, or nonresponders; (3) no significant difference in STAI between responders and nonresponders; and (4) no correlation between STAI and H17Mod variables. We found no evidence consistent with an anxiolytic effect of PSD in depression.

Given the frequency of anxiety symptoms in major depression disorder, greater baseline anxiety in patients than controls is not surprising. Using measured anxiety as a covariate may be useful in fMRI studies of depressed patients versus controls.

Our lack of significant STAI change in controls with PSD is at variance with Sagaspe et al. [2006], whose normal subjects increased STAI with total *SD*. Reasons for the difference are not clear but may be related to much higher baseline STAI in Sagaspe et al's group (39.41) than in our controls (26.1±6.8).

The lack of significant decrease in STAI from baseline to PSD for responders may be related to our small subject numbers ($t=-1.889$, $\eta^2=.47$). However, 40% of panic disorder subjects had panic attacks the day after *SD* [Roy-Byrne et al., 1986]. *SD* produced no improvement in obsessive compulsive disorder, [Joffe and Swinson, 1988] social phobia, or generalized anxiety disorder [Labbate et al., 1998].

CONCLUSIONS

We found no evidence consistent with an anxiolytic process associated with the antidepressant effects of *SD*. Small subject numbers and the anxiety measure used may have contributed to negative findings. Given the overlap between depression and anxiety, further studies are warranted to clarify whether the antidepressant effects of *SD* are related to state anxiety.

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TABLE 1

Spielberger State Trait Anxiety Inventory, state scores

	Controls (7)	Responders (4)	Nonresponders (10)	Patients (14)
Baseline ^a	26.1±6.8	45.1±6.4	45.3±11.5	45.2±10.0
PSD ^a	27.6±4.2	43.1±7.6	45.5±11.3	44.7±10.0
Decrease	-0.8±3.6	-2.1±2.3	-1.3±7.7	-1.5±6.5
% decrease	-5.6±13.8	-5.1±6.0	-4.2±15.3	-4.5±13.1

^aControls less than responders or nonresponders ($P<0.05$); responders versus responders not significantly different. SD, sleep deprivation; PSD, partial SD.