Patterns of alpha asymmetry in those with elevated worry, trait anxiety, and obsessive-compulsive symptoms: A test of the worry and avoidance models.

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Abstract

Some authors have argued that worry cues lateralization of frontal brain activity leftward, whereas other varieties of avoidance motivation cue lateralization of frontal brain activity rightward. By comparison, more right-than-left parietal activity correlates with anxious arousal. The purpose of the present report was to test two models of brain lateralization and anxiety: one model that proposed that worry correlates with more left-frontal activity and another model that proposed that avoidance motivation (including worry) correlates with more right-frontal activity. Undergraduate students were selected for worry, obsessive-compulsive symptoms, and trait anxiety using self-report questionnaires. A subset of participants also met DSM-IV criteria for Generalized Anxiety Disorder (GAD) or Obsessive-Compulsive Disorder (OCD). Alpha asymmetry and also a global-power-adjusted metric of alpha power were calculated from each participant's resting-state EEG. It was expected that participants with elevated worry and participants meeting criteria for GAD would show more left-than-right frontal activity. In contrast, participants with elevated trait anxiety, obsessive-compulsive symptoms, and those with an OCD diagnosis were expected to exhibit more right-than-left frontal activity. Participants with elevated worry, participants with a GAD diagnosis, and participants with elevated obsessive-compulsive symptoms, had more left frontal activity than low symptom individuals. Those with high scores on trait anxiety, but low worry, had greater right frontal and parietal activity compared to controls. The present results suggest that brain lateralization is not solely related to avoidance motivation, and suggest that facets of anxiety may cut across dimensions not well-represented by DSM-based categories.

Keywords: EEG alpha asymmetry, anxiety, worry, generalized anxiety disorder, obsessive-compulsive disorder

Patterns of alpha asymmetry in those with elevated worry, trait anxiety, and obsessive-compulsive symptoms: A test of the worry and avoidance models of alpha asymmetry.

Background

Characterizing clinical phenomenology by underlying neural circuitry remains an elusive undertaking that has the possibility to improve nosology, etiology, and treatment of psychopathology (Insel et al., 2010). In this regard, anxiety and mood disorders tend to be characterized by avoidance motivation which has been associated with more right-than-left frontal brain activity (Coan & Allen, 2004; Harmon-Jones, Gable, Peterson, 2010; Thibodeau, Jorgensen, & Kim, 2006). Conversely, one anxiety construct characterized by avoidance—worry—has been hypothesized to be implemented in more left-than-right frontal brain activity (Heller, Nitschke, Etienne, & Miller, 1997), yet, no study has found a direct link between left-lateralized activity and worries. It remains to be seen whether left-lateralized frontal brain activity will be observed in participants characterized specifically by worry, and in participants meeting criteria for a DSM-IV diagnoses of GAD, a disorder whose primary feature is excessive worry.

Two theories of anxiety and brain lateralization

In the 1990s, two theories of brain lateralization and anxiety gained research interest: one theory by Davidson and colleagues (1990, 1992) suggesting that avoidance motivation was related to right-lateralized activity, and another theory by Heller and others (1993, 1997) suggesting that lateralization of brain activity varied with anxiety type. Heller and coworkers (1997) suggested that brain lateralization varies with two dimensions of anxiety as proposed by Barlow (1991): worry and anxious arousal. Barlow (1991) suggested that whereas some disorders are characterized by panic, hyperarousal, and greater emotional processing, other emotional disorders are better characterized by worry and avoidance of emotional processing (see Mineka & Oehlberg, 2008 for an update). Worry is uncontrollable and unpleasant thoughts about future events that interrupts emotional processing and attenuates physiological arousal. Worry is a primary diagnostic feature of GAD (Borkovec & Inz, 1990; Meyer, Miller, Metzger, & Borkovec, 1990), and has been identified as an important transdiagnostic process related to anxiety disorders that mitigates fear extinction and can disrupt exposure-based interventions (Sibrava & Borkovec, 2006). Worry has also been characterized by enhanced avoidance motivation: worriers avoid processing of distressing and emotional information in the here and now as a way to minimize confrontation with

unpleasant stimuli (i.e., experiential avoidance; Roemer & Orsillo, 2002; Sibrava & Borkovec, 2006). Davidson proposed that individuals with greater avoidance motivation—fear of punishments, behavioral inhibition, and/or defensive reactivity to perceived threats—would be characterized by more right-lateralized brain activity based on reports showing that anxious emotional states, as well as anxiety disorders demonstrative of avoidance motivation, are frequently related to more right-than-left activity (reviewed in Coan & Allen, 2004; meta-analysis by Thibodeau, Jorgensen, & Kim, 2006). Contrary to the expectations of Davidson's theory, Heller suggested that worry cues more left-lateralized brain activity even though worry is related to anxiety and is a putative avoidance motivation process. Heller believed that worry would result in more left frontal brain activity because worry is predominantly in the form of thoughts and verbalization (not images; Borkovec & Inz, 1990) and because brain regions located underneath left-frontal electrode sites are important for verbal fluency (Hoptman & Davidson, 1998). Heller's theory is based on neurological and neuropsychological observations that verbal-linguistic processing is disproportionately represented in the left hemisphere, thus emotional disturbances predominated by hyperactive verbal-linguistic processing were predicted to result in more left-than-right activity (Heller, 1993). Researchers have observed more left-than-right brain activity when operationalizing worry as high scores on the trait version of the Spielberger State-Trait Anxiety Inventory (Heller et al., 1997), high self-reported stress (Mathersul, Williams, Hopkinson, & Kemp, 2008), and during public speaking anticipation (Hofmann et al., 2005). Importantly, *none of these previous reports actually measured worry* in their participants, and Meyer and colleagues (1990) showed that worry is distinct from the anxiety measured by the STAI-T, self-reported stress, or public speaking anticipation (also see Borkovec, Robinson, Pruzinsky, & DePree, 1983). Whereas the STAI-T, stress, and public speaking probably tap into unpleasantness more generally, worry is specific to uncontrollable and unwanted thoughts about future events. The uncontrollability and intrusiveness of worry is what makes worry distinct from other anxiety constructs (Borkovec, et al., 1983; Meyer et al., 1990; York, Borkovec, Vasey, & Stern, 1987). When participants have been selected for worry specifically—using the Penn-State Worry Questionnaire (PSWQ; Meyer, Miller, Metzger, & Borkovec, 1990) or self-identification as a worrier—worries and resting-state frontal alpha asymmetry have been unrelated (Carter, Johnson, & Borkovec, 1986; Nitschke, Heller, Palmieri, & Miller, 1999). Thus far, the evidence for Heller's model is lacking when using measures that are designed to tap worry specifically. Taken together, these findings suggest that worry has been characterized by left

lateralization of frontal brain activity in less-than-ideal samples, whereas avoidance disorders in general have demonstrated more right-than-left frontal activity.

Three anxiety constructs in two anxiety symptom clusters

Participants high in worry or obsessive-compulsive (OC) symptomatology are both characterized by greater avoidance motivation than healthy controls, yet anxious arousal in participants with worry and OC is on par with healthy controls. Comparing groups varying (i.e., individual differences / extreme groups paradigm) on the constructs proposed by Heller and Davidson—worry, anxious arousal, and avoidance—is one way to test the predictions made by their respective models of anxiety and brain lateralization. As suggested before, worry is an avoidance motivation, and GAD is a disorder defined by excessive worry. Importantly, OCD has also been characterized by significant avoidance motivation in terms of behavior (Gillan et al., 2014), event-related potentials (Endrass, Kloft, Kaufmann, & Kathmann, 2011), and right-lateralized brain activity (Ischebeck, Endrass, Simon, & Kathmann 2014; Kuskowski, et al., 1993). Davidson predicted avoidance motivation and parietal lateralization were unrelated, whereas Heller predicted that more right-than-left parietal lateralization was related to more anxious arousal: enhanced physiological arousal at rest, enhanced physiological arousal in response to emotional stimuli, and enhanced vigilance for emotional information. Heller suggested right-lateralized brain regions implement physiological arousal putatively due to the right hemisphere's importance for self-monitoring, emotional attention, and interoceptive sensitivity (Heller, 1993). The literature has been supportive of Heller's anxious arousal formulation (see Metzger et al., 2004 and Nitschke et al., 1999). Importantly, worriers (Heller et al., 1997; Mathersul et al., 2008; Nitschke et al., 1999; Sibrava & Borkovec, 2006) as well as high-OC participants (Hoehn-Saric, McLeod, & Hipsley, 1995; Ischebeck et al., 2014; Kuskowski, et al., 1993) demonstrate similar levels of anxious arousal as healthy controls. Because worriers and participants with OC are matched in terms of arousal, Heller and Davidson's theories make similar predictions in terms of parietal lateralization for these participants: parietal lateralization should be similar across healthy participants, worriers, and participants with high OC symptoms. In other words, differences in functional laterality between worriers and OC participants should be due to differences in avoidance motivation, and not confounded with anxious arousal. Altogether, worry and OC participants vary in terms of a specific avoidance technique—worry—but should be matched in terms of anxious arousal.

Thus, participants with worries and OC symptoms are interesting groups for comparing the models of Heller and Davidson because the groups vary in terms of a key theoretical construct—worry—yet have similar levels of a potential confounding variable—anxious arousal, known to cue rightward parietal brain activity (Nitschke et al., 1999)—mitigating the influence of this variable on lateralization of brain activity.

Present Report

Avoidant disorders, including mood and anxiety disorders have been described in terms of more right-than-left brain activity by Davidson and others, yet, Heller suggested that worry—a process of experiential avoidance—would instead be related to more left-than-right brain activity. Unfortunately, no study to date has directly examined this question using participants selected specifically for worry, despite the uniqueness of worry as a construct apart from other anxiety processes.

The primary question of the present study was: are worries an exception / boundary condition to Davidson's avoidance-motivation theory of right-lateralized brain activity? The research question was addressed by selecting extreme groups of participants that varied on the construct of interest (i.e., worry), yet had similar levels of anxious arousal (previously shown to cue rightward brain activity). It was expected that more right-than-left activity would be apparent in groups of participants with high avoidance and low worry, supportive of Davidson's theory. In contrast, a unique type of avoidance strategy—worry—was hypothesized to be related to more left-than-right activity, supportive of Heller's theory (see Table 2). More specifically, it was expected that participants selected for high avoidance motivation (OC, OCD, and Anxiety groups), but, low worry would show more right-than-left frontal activity concordant with an avoidance model of brain lateralization (Coan & Allen, 2004; Davidson, et al., 1990; Harmon-Jones, Gable, & Peterson, 2010). In contrast, participants high on a specific type of avoidance—worry (Worry and GAD groups)—would show more left-than-right frontal activity concordant with a worry model of lateralization (Heller et al., 1997). Moreover, right-lateralized activity in the avoidance motivation groups (OC, OCD, and Anxiety groups) and left-lateralized activity in the worry group would be supportive of the specificity of worry as a unique type of avoidance motivation related to left-lateralized brain activity (i.e., discriminant validity). It was hypothesized that parietal asymmetry would be similar between healthy controls, participants with elevated worries (Worry, GAD), and participants with elevated obsessive-compulsive symptoms (OC and OCD

groups), because these groups were believed to have similar levels of anxious arousal at rest. Heller and colleagues (1997) found more leftward frontal activity in a sample of participants selected for trait anxiety, yet anxiety and worry covary and Heller did not directly assess worry in these participants. It may have been the case that Heller's findings resulted from coincident worry in their anxious participants. To test this hypothesis, a third group of participants were evaluated in this study: participants in the Anxiety group were selected using criteria very similar to the criteria used by Heller et al., (1997) with one difference: participants were selected to be low on worries. It was expected that participants with high trait anxiety and low worries (Anxiety group) would have more right-than-left frontal and parietal activity, consistent with previous reports linking anxiety with rightward frontal and parietal activity (e.g., Thibodeau et al., 2006).

Method

Participants

Participants reporting significant anxiety symptoms (N=128) were selected for this study from among a pool of 5,273 undergraduate students who completed symptom questionnaires during an introductory psychology class. Participant selection was based on responses to the Obsessive-Compulsive Inventory-Revised (OCI-R), Penn State Worry Questionnaire (PSWQ), and Spielberger State-Trait Anxiety Inventory – Trait Subscale (STAI-T; Spielberger, 1968). Groups of participants were selected based on these self-report responses as part of another study on anxiety and electrophysiology (Zambrano-Vazquez & Allen, 2014). Participants completed the symptom scales as part of an introductory psychology course, and completed the same symptom scales once again on average 4 weeks later to determine the stability of the scores with respect to original testing. Only participants with stable scores were invited to participate, and stability in scores was defined as meeting criteria for the same anxiety group indicated by a participant's scores from the first testing occasion. Scores used in the present study are from participants' responses to the *second set* of self-report symptom scales, (1-36 days before the experimental session, M=18.5 days, SD=12.0). Participants were excluded from the analysis if they were not strongly right-handed (Chapman & Chapman, 1987, handedness inventory score ≤ 35 out of 39; N=18), if they self-reported psychotropic drug use (N=1), if they reported a history of head trauma or neurological impairment (e.g., loss of consciousness > 10 minutes, or self-reported epilepsy; N=7), or if they had insufficient usable data (technical difficulties, missing or unusable data; N= 18). History of psychiatric or psychological

treatment was not collected and was not an inclusion/exclusion criterion. The final sample presented here included 82 participants.

Participants (see Tables 1 and 3 for a description of participants' scores on anxiety questionnaires) were selected based on criteria described in Zambrano-Vazquez and Allen, 2014 for an ERP investigation comparing obsessive-compulsive symptomatology and worry. Resting-state data were previously unanalyzed. There were three anxiety groups: a Worry group, an Obsessive-Compulsive (OC) group, and a non-specific Anxiety group. The Worry group (N=17) was selected to be high on worries specifically, and lower on other anxiety measures. The OC group (N=32) was selected to be high on OCD-symptoms specifically, and lower on other anxiety measures. The Anxiety group (N=14) was selected to be high on a non-specific measure of unpleasantness and distress and lower on other scales of anxiety—worry and OCD—that tapped specific anxiety constructs. The healthy control group (N=19) was low on all anxiety measures and did not meet DSM-IV criteria for any anxiety disorder.

From these 82 participants, two additional groups were created using DSM-IV criteria for anxiety disorders. A small set of the 82 participants met full criteria at time of assessment for a primary diagnosis of OCD (N=8, 7 females) or GAD (N=11, 10 females) based on the anxiety disorders section of the Structured Clinical Interview for the DSM-IV (SCID) administered by trained laboratory personnel. Participants were not pre-selected to be in the study based on DSM-IV criteria, DSM-IV diagnoses were made after participants were invited to participate based on their self-report questionnaires. In other words, participants were sampled based on questionnaire measures (described above), not DSM-IV diagnoses. Only the anxiety disorders module of the SCID-I was administered, thus other psychiatric disturbances could not be ruled out in this study. Participants were included regardless of presence or absence of a DSM-IV disorder (there were no DSM based inclusion or exclusion criteria). History of psychiatric or psychological treatment was not collected and was not an inclusion/exclusion criterion. History of anxiety disorders was assessed, but previous history of anxiety disorder was not considered in the analyses here. Some participants had secondary diagnoses from the anxiety section of the DSM-IV. The primary diagnosis (vs. secondary diagnosis) was based on the clinical symptoms that presented with the greatest distress, so it was identified as primary. In contrast, secondary diagnoses were often symptoms related to the primary diagnosis; for example, worries or panic attacks about not acting upon compulsions. Two participants with a primary diagnosis of OCD also had a secondary diagnosis of GAD. Two participants with a primary

diagnosis of OCD had a secondary diagnosis of Panic Disorder. Of the participants with a primary diagnosis of GAD, one participant had secondary OCD, one participant had secondary specific phobia, and one participant had secondary agoraphobia without history of panic. Diagnoses were made by graduate students trained in SCID administration working under the supervision of a licensed clinical psychologist (JJBA).

All data were collected in accordance with IRB guidelines for conducting ethical human subjects' research.

Procedure

First, subjects completed consent forms and questionnaires unrelated to the current study, and then received a brief description of the study. Second, participants' symptoms were evaluated using the anxiety disorders section of the Structured Clinical Interview for DSM-IV disorders (SCID-I). Participants were then prepared for EEG setup, and resting-state EEG was recorded. Additional EEG/ERP data were collected following resting-state EEG collection and are reported elsewhere (Zambrano-Vazquez & Allen, 2014).

Questionnaires

Self-report symptom scales included the OCI-R, the PSWQ, and the STAI-T. The OCI-R demonstrated excellent internal consistency in the present sample ($\alpha=.92$), and has demonstrated good convergent and discriminant validity, and good test-retest reliability ($r=.70$) in undergraduate samples from other reports (Hajcak, Huppert, Simons, & Foa, 2004). The PSWQ was internally consistent in the present sample ($\alpha=.96$), and showed good discriminant validity and excellent test-retest reliability ($r=.92$) in a previous report with a college sample (Meyer, Miller, Metzger, & Borkovec, 1990). The STAI-T (Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) is a measure of trait anxiety, and has adequate test-retest reliability ($rs = .81 -.95$; Barnes, Harp, & Jung, 2002). The STAI-T was internally consistent ($\alpha=.94$) in the present sample.

EEG Recording and Analyses

EEG was recorded from 64 Ag/AgCl electrodes using an ElectrodeArrays EEG cap (El Paso, Tx) and Neuroscan amplifiers (Charlotte, NC) for six minutes with alternating one minute segments of eyes-open or eyes-close; the order of eyes-open/eyes-close was counterbalanced across participants. EEG was recorded to an online reference electrode

between Cz and CPz in AC mode with an online bandpass filter (.5-100Hz), a sampling rate of 500Hz, and all impedances were below 10 k Ω . Additional sensors recorded electrical activity from the mastoids and around the eyes. One minute segments of EEG were segmented into 2.048s epochs, and these epochs were overlapped by 1.5s to compensate for the diminished weighting of the Hamming window for the Fast-Fourier Transformation (FFT). Artifact rejection was conducted in two steps: 1) artifacts due to amplifier clipping, line noise, or bad electrodes were identified visually and removed epoch-wise 2). Independent components analysis using EEGLAB (Delorme, & Makeig, 2004) and the semi-automatic ADJUST procedure (Mognon, Jovicich, Bruzzone, & Buiatti, 2010) were used to identify and remove remaining artifacts component-wise and no more than 15 components were removed for any participant. The artifact-free data were transformed using the Current-Source Density (CSD) toolbox for EEGLab (Kayser, 2009) based on the spherical spline approach summarized by Perrin, Pernier, Bertrand, and Echallier (1989, 1990). Then, an FFT was applied to all artifact-free Hamming-windowed epochs to extract the average power in the lower (8Hz–10Hz) and upper (10.5Hz – 12.5Hz) alpha bands, in agreement with previous findings that results may vary by spectral bins (Davidson, et al., 2000; Ischebeck et al., 2014; Oakes et al., 2004). Alpha power asymmetry scores were created by subtracting Ln-transformed alpha power at left hemisphere electrodes from Ln-transformed alpha power at right hemisphere electrodes (e.g., F4-F3). Internal consistency (Cronbach's alpha) of asymmetry scores was computed using 1-min segments (i.e., Allen, Urry, Hitt, & Coan, 2004), and Cronbach's alphas ranged from .94-.98 across electrodes.

Because laterality was of interest to the present hypotheses, in addition to the asymmetry score, a global-power-adjusted metric of alpha power was used to examine effects at individual electrodes. For example, an increase of relative left frontal activity using an asymmetry metric could result from a decrease in left frontal alpha or an increase in right frontal alpha or both. Examining single site alpha power can address this possibility, but this approach suffers from the fact that there are substantial individual differences in overall alpha power due to irrelevant factors such as skull thickness (Hagemann, Hewig, Walter, & Naumann, 2008). Thus, alpha power at every electrode was divided by the sum of alpha power over the entire head, and then this global-power-adjusted alpha power was Z-scored within-subjects to create a relativized measure of alpha power at each electrode (see Allen, Coan, & Nazarian, 2004). This global-power-adjusted alpha metric was also internally consistent using 1-min segments as test items (Cronbach's alphas ranged from .82-.97 across electrodes). Importantly, this global-power-adjusted alpha metric was interpreted similarly to the conventional

asymmetry score: left-lateralized activity was believed to index greater worry (i.e., Heller's model) and right-lateralized activity was believed to index greater avoidance motivation (i.e., Davidson's model) and anxious arousal (i.e., Heller's model).

Kruskal-Wallis tests of multiple independent groups were used to evaluate the differences in alpha metrics across groups. Wilcoxon rank-sum tests were used for post-hoc pairwise comparisons for any electrodes that had significant main effects identified by the Kruskal-Wallis test. All results $P \leq .10$ are reported below to mitigate Type II error. The supplemental materials include descriptive statistics for each electrode.

Results

First, results are presented for alpha asymmetry for three symptom-based anxiety groups and a healthy control group. Then, alpha asymmetry results are presented for two DSM-based anxiety groups compared to the same healthy control group. Following the alpha asymmetry results are the findings using the global-power-adjusted alpha power metric described above, first for the symptom-based groups, then for DSM-based groups.

Alpha Asymmetry

Three anxiety groups. Figure 1 shows median alpha asymmetry for each anxiety group at each electrode. Overall, activity was in predicted directions, but did not meet statistical thresholds in any case (see Figure 2, $P_s > .12$).

DSM groups. As can be seen in Figure 3, GAD participants were characterized by more leftward frontal activity than healthy controls. GAD participants also exhibited more leftward frontal activity than OCD participants.

A main effect of DSM group was observed in the high alpha band (10.5-12.5 Hz) at frontal sites ($\chi^2(2)=6.3$, $P=.04$ at F6/F5 and $\chi^2(2)=4.7$, $P=.09$ at FP2/FP1). Consistent with expectations, GAD participants exhibited more left-than-right frontal activity than the HC group ($W=217$, $Z=1.98$, $P=.05$ at F6/F5). GAD participants also exhibited more left-than-right frontal activity compared ($W=135$, $Z=2.02$, $P=.04$ at F6/F5 and $W=137$, $Z=2.19$, $P=.03$ at FP2/FP1) to OCD participants. OCD participants did not statistically differ from healthy controls ($W=81$, $Z=-1.62$, $P=.11$ at FP2/FP1).

There was a main effect of diagnostic category on low alpha (8Hz-10Hz) frontal asymmetry ($\chi^2(2)=8.1$, $P=.02$ at FP2/FP1, $\chi^2(2)=9.1$, $P=.01$ at AF4/AF3, and $\chi^2(2)=6.3$, $P=.03$ at F6/F5). Participants in the GAD group elicited more left

lateralized frontal activity than HC in the low alpha band at AF4/AF3 ($W=226$, $Z=2.37$, $P=.02$). GAD participants elicited more relative left activity ($W=136$, $Z=2.11$, $P=.04$ at F6/F5) than OCD participants. OCD participants did not statistically differ from controls at any frontal electrode ($Ps>.2$).

Main effects of group on parietal asymmetry in low (8Hz-10Hz) alpha ($\chi^2(2)=4.7$, $P=.10$, at P4/P3) revealed that participants with GAD symptomatology were characterized by more leftward parietal activity ($W=218$, $Z=2.02$, $P=.04$ at P4/P3) than controls. At P4/P3 the GAD group ($M=.23$, $MD=.35$, $SD=.43$) did not statistically differ ($W=125$, $Z=1.2$, $P=.23$) from the OCD group ($M=-.02$, $MD=.05$, $SD=.44$). GAD and OCD groups did not statistically differ at any other asymmetry site ($Ps>.20$), suggesting that GAD and OCD groups were characterized by similar levels of anxious arousal.

Global-Power-Adjusted Alpha Power

The global-power-adjusted alpha power approach used below allowed for the examination of the relationship between activity at specific sites and anxiety symptoms, by mitigating the effects of nuisance variables like skull thickness and global power differences.

Three anxiety groups. Alpha (10.5Hz-12.5Hz) varied with anxiety group at frontal ($\chi^2(3)=6.5$, $P=.09$ at F8) and frontal-central electrodes ($\chi^2(3)=7.3$, $P=.06$ at FC5 and $\chi^2(3)=6.8$, $P=.08$ at FC3). The Anxiety group exhibited less right frontal alpha (greater activity) than healthy controls at F8 ($W=176$, $Z=-2.24$, $P=.03$). Worry participants exhibited less left frontal-central alpha (greater activity) than the control group ($W=250$, $Z=-2.03$, $P=.04$ at FC5). Similar to the Worry group, and unexpectedly, participants in the OC group were characterized by less left frontal-central alpha (greater activity) than controls at FC5 ($W=704$, $Z=-2.48$, $P=.01$).

A main effect of group at parietal electrodes ($\chi^2(3)=16.03$, $P<.01$ at P6 and $\chi^2(3)=7.95$, $P=.05$ at P8) revealed that the Anxiety group was characterized by less right parietal 10.5Hz-12.5Hz power (greater activity) than HC ($W=187$, $Z=-1.84$, $P=.07$ at P6 and $W=179$, $Z=-2.13$, $P=.03$ at P8). In contrast, high OC participants demonstrated more right parietal alpha (less activity) than HC at P6 ($W=957$, $Z=2.43$, $P=.02$). High worriers did not statistically differ from controls ($W=286$, $Z=-.89$, $P=.38$ at P6; $W=280$, $Z=-1.08$, $P=.28$ at P8). OC participants ($M=.96$, $MD=.86$, $SD=.75$) were characterized by more right alpha power ($W=924$, $Z=2.59$, $P<.01$) than worriers ($M=.47$, $MD=.27$, $SD=.98$) at P6. OC participants ($M=2.1$, $MD=2.1$, $SD=1.0$) were also characterized by more ($W=885$, $Z=1.77$, $P=.08$) right alpha power than

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worriers ($M=1.5$, $MD=1.5$, $SD=1.1$) at PO6, suggesting that OC participants demonstrated less anxious arousal than worriers.

Low alpha (8Hz-10Hz) also varied with anxiety group at frontal electrodes ($\chi^2(3)=8.48$, $P=.04$ at F6 and $\chi^2(3)=6.40$, $P=.09$ at F8) and showed that the Anxiety group was characterized by less right frontal alpha than healthy controls at F8 ($W=185$, $Z=-1.91$, $P=.06$). Worry participants and OC participants did not differ from HC in terms of right frontal alpha ($P>.12$ at F6).

Low alpha activity (8Hz-10Hz) also varied across groups at parietal electrodes ($\chi^2(3)=10.0$, $P=.02$ at P6). The OC group showed more right parietal alpha ($W=974$, $Z=2.76$, $P=.01$) than healthy controls at P6. The anxiety and worry groups did not differ from healthy controls in regard to parietal asymmetry ($P>.23$ at P6). The OC and Worry group did not differ in regard to right parietal alpha power in the 8Hz-10Hz band at any site ($P>.14$).

DSM groups. For high alpha (10.5Hz-12.5Hz), a main effect of DSM group ($\chi^2(2)=6.0$, $P=.05$ at F7 and $\chi^2(2)=5.3$, $P=.07$ at F5) revealed that GAD participants demonstrated less left frontal alpha (greater activity) than healthy controls ($W=130$, $Z=-1.72$, $P=.09$ at F7, and $W=128$, $Z=-1.81$, $P=.07$ at F5), in line with predictions. OCD participants did not statistically differ from healthy controls at F7 ($P=.81$) or F5 ($P=.44$).

For the low (8Hz-10Hz) alpha band, there was a main effect of DSM group at F1 ($\chi^2(2)=5.5$, $P=.07$), yet post-hoc examination showed that neither the OCD nor GAD groups differed from healthy controls ($P>.13$).

GAD and OCD participants did not differ in regard to right parietal alpha power at any site for the 10.5Hz – 12.5Hz band ($P>.43$), or for right parietal sites in the 8Hz – 10Hz band ($P>.23$).

Discussion

The aim of this study was to test two theories of brain lateralization and anxiety. One model—the avoidance model of lateralization—proposes that participants high in avoidance show more relative rightward frontal activity. By comparison, another model of asymmetry—the worry model of lateralization—hypothesizes that a specific type of avoidance—worry—is related to more left-than-right activity. Results supported Heller's model of lateralization: participants high in worry (GAD and Worry groups) evidenced more left frontal activity. Participants high in non-specific anxiety showed more right-than-left frontal activity. Participants in the Anxiety group were also characterized by more

right parietal activity, supportive of Heller's model. Overall, Davidson's rightward-avoidance model held for non-specific anxiety in participants low on worry, whereas more specific types of anxiety—worry and anxious arousal—were related to distinct patterns of lateralization as predicted by Heller and others (1997).

Worry and Left-Lateralized Brain Activity

This is the first report to directly link worries to left frontal activity. This is also the first report to directly link GAD (a disorder characterized by excessive worry) with left frontal activity (cf. Carter et al., 1986). The present findings supports the neuropsychological formulation of Heller that worry is a disorder characterized by excessive verbalization and hyperactivity of speech production areas implemented in the left hemisphere (i.e., a verbal / visual model of lateralization). Interestingly, when accounting for worry in a sample of participants highly similar to the one used by Heller et al., (1997), anxiety was associated with more right-than-left activity across both frontal and parietal areas. This may suggest that reports finding non-specific anxiety with more left-than-right activity (Hofmann et al., 2005; Mathersul et al., 2008) may have been due to unassessed but elevated worry in their samples. The effect in the present study was especially pronounced when considering left frontal activity independently of right frontal activity (i.e., global-power-adjusted alpha power), suggesting that independent hyperactivity of the left hemisphere—rather than reciprocal inhibition between hemispheres—may be associated with worry instead of the relative contribution of each hemispheres as is often reported. Importantly, this global-power-adjusted alpha power is interpreted similarly to conventional asymmetry scores: more alpha power corresponds to more inhibition of activity, thus less left-frontal alpha power in worriers is indicative of more left hemisphere activity. Unexpectedly, greater left-lateralized activity was also apparent for participants in the OC group. As shown in Table 1, participants in the OC group reported similar levels of worry as participants in the Worry group, and a high level of worry is often coincident with OCD symptoms (Abramowitz & Foa, 1998). Previous reports however observed more right-than-left frontal activity in OCD patients (Ischebeck, et al., 2014; Kuskowski, et al., 1993), and OCD diagnosis was related to more right-than-left frontal activity at a trend-level in the present report, suggesting that diagnostic status, symptoms severity, or comorbid depression may moderate the relationship between worry and left-lateralized brain activity. Greater left-lateralized activity in a group of participants with high OC symptoms and coincident worries is also suggestive of a hyperactive verbalization process that is transdiagnostic, in accord with Heller (1993, 1997). When participants have high levels of non-specific trait anxiety (e.g., unpleasantness and/or distress) and low

worries, more right-lateralized activity is observed (i.e., Anxiety group), supportive of discriminant validity for worry and left-lateralized brain activity. Overall, the findings: a) reinforce a model of brain lateralization based on emotion-laden verbalization and attention (i.e., Heller, 1993); b) cast doubt on a theory of lateralization based solely on motivational direction; c) highlight the importance of assessing worries when evaluating EEG alpha asymmetry at-rest; and, d) suggest that worry is a distinct construct that cuts across DSM-based delineations and that is implemented in disinhibited left-frontal verbal-linguistic circuitry.

Strengths and Limitations

A strength of the present study included the use of a recording montage and processing approach that attenuated the contribution of distal sources of alpha power, and also attenuated the influence of skull thickness on alpha power, both of which may be unrelated to psychological phenomena. This approach also revealed the independent contributions of the left hemisphere to worry; by comparison, other reports have used asymmetry metrics that were indeterminate in regard to each hemisphere's unique contribution. The present study was limited by the single measurement of EEG: multiple EEG recordings at rest or during emotional induction can improve the reliability of EEG alpha asymmetry (Stewart, et al., 2014). The physiological indicator of arousal used in the present report—right parietal activity—revealed a pattern consistent with the hypothesis that Worry and OC groups were closely, but not *perfectly* matched in terms of anxious arousal (a potential confounding variable), and it would have been useful to carefully match Worry and OC groups in terms of physiological arousal (i.e., using a self-report measure of anxious arousal). Another limitation was the small sample sizes in the groups with DSM disorders and future studies should include comparisons with more participants to improve generalizability and statistical power. Also, the delay between symptom measurement and EEG recording may have resulted in additional variance if participants' symptoms spontaneously improved or declined between the time of completing the questionnaires and EEG recording.

Conclusion

The results from the present report showcase an emerging literature that brings the frontal lateralization debate back in line with classical neuropsychological and neurological formulations: enhanced left-lateralized activity in emotional/motivational paradigms may be associated with verbal-linguistic emotion-regulation (Mennin, et al., 2002;

Parvaz, et al., 2012) or problem-solving strategies (Davey, Hampton, Farrell, & Davidson, 1992; Harmon-Jones, et al., 2008; Stuss, 2011) that is future-oriented (Dien, 2008; Stuss, 2011), whereas enhanced right-lateralized activity may be associated with self-monitoring (Shackman, McMenamin, Maxwell, Greischar, & Davidson, 2009; Cohen & Cavanagh, 2011; Stuss, 2011) or enhanced attention to emotional stimuli (Beevers, Clasen, Enock, & Schnyer, 2015; Wiedemann et al., 1999). In fact, verbal fluency has been linked to relative leftward frontal activity (Hoptman & Davidson, 1998) and worry (Mohlman, 2013), and Heller's model of worry and lateralization was derived from a neuropsychological perspective on emotion (Heller, 1993). Enhanced left-lateralized activity in worriers is then indicative of a style of cognitive-emotional processing that is predominantly verbal-linguistic at rest, as has been suggested in clinical observations (Sibrava & Borkovec, 2006). Moreover, this cognitive style is not specific to participants selected for worry or GAD participants: participants selected for OC symptoms with coincident elevated worries also demonstrated a left-lateralized pattern, ostensibly reflecting enhanced verbal-linguistic processing at rest. These findings are also provocative inasmuch as they are incompatible with an influential and longstanding theory of brain lateralization that predicts less avoidance motivation in participants with more left-lateralized activity, despite worriers being characterized by more emotional avoidance. The results are also interesting in that they challenge the idea that a metric of brain activity typically believed to be an indicator of good mental health may in fact be maladaptive in certain cases (e.g., Harmon-Jones et al., 2010; Fortier et al., 2014). It is also apparent that researchers interested in investigating emotion-lateralization relationships would benefit from simultaneously considering participant worries as a potential moderator. Finally, the results suggest that worriers, and participants with OC symptoms, may in some cases have similar patterns of neural activity, which is somewhat at odds with the removal of OCD from the anxiety disorders section of the DSM-5, and showcases the importance of biomarkers and continuous measures of empirically delineated constructs for the ecologically valid investigation of emotion and psychopathology (Cuthbert & Insel, 2013; Nusslock, Walden, & Harmon-Jones, 2015).

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TABLE 1.
Descriptive statistics for symptoms scales for each group.

	Penn State Worry Questionnaire (PSWQ)	Obsessive Compulsive Inventory-Revised (OCI-R)	Spielberger Anxiety Inventory Trait Version (STAI-T)
	M [MD] (SD)	M [MD] (SD)	M [MD] (SD)
HC (N=19)	30.95 [31] (7.69)	5.37 [4] (3.74)	29.16 [27] (6.58)
ANXIETY (N=14)	50.64 [52.5] (8.75)	13.79 [15] (4.9)	53.64 [53.5] (3.52)
WORRY (N=17)	69.53 [69] (3.48)	9.76 [10] (5.38)	40.41 [41] (5.27)
OC (N=32)	64.84 [66] (9.2)	31.28 [29.5] (8.23)	53.44 [52] (7.3)
GAD (N=11)	71.91 [72] (3.86)	20.45 [16] (13.26)	48.09 [46] (9.41)
OCD (N=8)	62.89 [60] (8.63)	27.38 [23.5] (9.80)	52.25 [54] (5.6)

Note: PSWQ scores range from 16-80; OCI-R scores range from 0-72; STAI-T scores range from 20-80

TABLE 2.

Levels of independent variables across three anxiety groups and a healthy control group along with lateralization hypotheses

	Anxiety (N=14)	Worry (N=17)	OC (N=32)	Control (N=19)
Avoidance motivation	High	High	High	Low
Worry	Low	High	Low	Low
Davidson's prediction of brain lateralization	L<R	<u>L<R</u>	L<R	L=R
Heller's prediction of brain lateralization	L<R	<u>L>R</u>	L<R	L=R

Note: Descriptions of anxiety groups in regard to levels of avoidance motivation vs. worry (independent variables). Also, predictions for dependent variable (lateralization of activity) based on two competing models of brain lateralization for each anxiety group. L<R indicates the prediction that participants will show less left-than-right activity (less right-than-left alpha power). L>R indicates the prediction that participants will show more left-than-right activity (more right-than-left alpha power). The key test of the models is underlined: Heller and Davidson's theories make opposing predictions for participants high on worry.

TABLE 3.
Descriptions of anxiety groupings based on scores from three anxiety measures.

	Anxiety (N=14)	Worry (N=17)	OC (N=32)	Control (N=19)
OCI-R	Low	Low	High	Low
STAI-T	High	Low	Low	Low
PSWQ	Low	High	Low	Low

Note: Qualitative description of how groups were differentiated on three different components of anxiety: obsessive-compulsive symptoms, non-specific anxiety, and worry symptoms. The Worry group had to score above the clinical cutoff on the PSWQ (i.e. over 61; Behar, Alcaine, Zuellig, & Borkovec, 2003), below clinical cutoff on the OCI-R, and below the 80th percentile on the STAI-T. The Anxiety group included people that scored above the 80th percentile in the STAI-T and below the clinical cutoff of both the OCI-R and the PSWQ. The OC group was composed of people above the clinical cutoff on the OCI-R and above the median for PSWQ and STAI-T. The HC group included individuals that scored below the 50th percentile on the OCI-R, STAI-T, and the PSWQ, and did not meet criteria for any DSM-IV anxiety disorder. The scales used to differentiate the groups were the obsessive compulsive inventory-revised (OCI-R), the Spielberger State-Trait anxiety inventory-Trait (STAI-T), and the Penn-State Worry Questionnaire (PSWQ). The selection criteria are also described in detail in Zambrano-Vazquez & Allen, 2014.

Figure 1. Median alpha asymmetry scores for healthy control participants and three anxiety groups

Note: Median alpha asymmetry for each anxiety group. Alpha asymmetry near zero is shaded white. Warm colors—reds—indicate more left-than-right activity, whereas cool colors—blues—indicate less left-than-right activity. Results on head models are for graphical purposes only: data plotted on heads are interpolated and fitted to a head model. Please refer to supplemental materials for statistics at each electrode. HC=Healthy control group, Anxiety=Anxiety group, Worry=Worry group, OC=Obsessive-Compulsive group.

Figure 2. Main effects of anxiety group and pairwise comparisons of alpha asymmetry for healthy and anxious participants.

Note: Main effects of anxiety group are presented on the far left panels. Warm colors—yellows and reds—indicate smaller P -values. There was only one significant main effect of anxiety at C4/C3 for the low alpha band. All other main effects were statistically unreliable ($P_s > .10$). Pairwise Z-scores differences between anxiety participant groups and healthy controls are displayed on right-side panels. All Z-scores between 1 and -1 are shaded white. Warm colors—reds—indicate more left-than-right activity relative to healthy controls, whereas cool colors—blues—indicate less left-than-right activity relative to healthy controls. Results on head models are for graphical purposes only: data plotted on heads are interpolated and fitted to a head model. Please refer to supplemental materials for statistics at each electrode. HC=Healthy control group, Anxiety=Anxiety group, Worry=Worry group, OC=Obsessive-Compulsive group.

Figure 3. Main effects of DSM groups and pairwise comparisons of alpha asymmetry for healthy participants and participants meeting criteria for GAD or OCD.

Note: Main effects of DSM group are presented on the far left panels, $P_s > .10$ are shaded white. Warm colors—yellows and reds—indicate smaller P -values. There were significant main effects of DSM group at FP2/FP1 and F6/F5 for the high alpha band, and main effects of DSM group at FP2/FP1, AF4/AF3, F6/F5 and P4/P3 for the low alpha band. Pairwise Z-scores for differences between DSM groups and healthy controls are presented on right-side panels. Pairwise Z-scores between 1 and -1 are shaded white. Warm colors—reds—indicate more left-than-right activity relative to healthy controls, whereas cool colors—blues—indicate less left-than-right activity relative to healthy controls. Results on head models are for graphical purposes only: data plotted on heads are interpolated and fitted to a head model. Please refer to supplemental materials for statistics for each electrode. HC=Healthy control group, GAD=Generalized Anxiety Disorder, OCD=Obsessive-Compulsive Disorder.

Figure 4. Main effects of anxiety groups and pairwise comparisons of global-adjusted-alpha power for healthy and anxious participants.

Note: Main effects of anxiety group are presented on the left side panel, $P_s > .10$ are shaded white. Warm colors—yellows and reds—indicate smaller P -values. Main effects of anxiety group were apparent at FC5, FC3, and F8 (at the outermost right-frontal edge of the topoplot), and at P6 and P8 for the high alpha band. Main effects were apparent for F8 and F6, and at P6, for the low alpha band. On the right side of the panel, Z-scores are displayed for pairwise differences between groups. Z-scores between 1 and -1 are shaded white. Warm colors—reds—indicate more alpha power (less activity) relative to healthy controls, whereas cool colors—blues—indicate less alpha power (more activity) relative to healthy controls. Results on head models are for graphical purposes only: data plotted on heads are interpolated and fitted to a head model. Please refer to supplemental materials for statistics for each electrode. HC=Healthy control group, Anxiety=Anxiety group, Worry=Worry group, OC=Obsessive-Compulsive group.

Figure 5. Main effects of DSM groups and pairwise comparisons of global-adjusted-alpha power for healthy participants and participants meeting criteria for DSM-IV disorders.

Note: Main effects of DSM group are presented on the left side panel, P s > .10 are shaded white. Warm colors—yellows and reds—indicate smaller p -values. Main effects of anxiety group were apparent at F7 and F5 for the high alpha band. Main effects were apparent for F1 for the low alpha band. On the right side of the panel, Z-scores are displayed for pairwise differences between groups. Z-scores between 1 and -1 are shaded white. Warm colors—reds—indicate more alpha power (less activity) relative to healthy controls, whereas cool colors—blues—indicate less alpha power (more activity) relative to healthy controls. Results on head models are for graphical purposes only: data plotted on heads are interpolated and fitted to a head model. Please refer to supplemental materials for statistics for each electrode. HC=Healthy control group, GAD=Generalized Anxiety Disorder, OCD=Obsessive-Compulsive Disorder.