

Research Article

Right Dorsolateral Prefrontal Cortical Activity and Behavioral Inhibition

Alexander J. Shackman,^{1,2} Brenton W. McMenamin,³ Jeffrey S. Maxwell,^{1,4} Lawrence L. Greischar,^{1,2} and Richard J. Davidson^{1,2}

¹Laboratory for Affective Neuroscience, University of Wisconsin–Madison; ²Waisman Laboratory for Brain Imaging and Behavior, University of Wisconsin–Madison; ³Center for Cognitive Sciences, University of Minnesota–Twin Cities; and ⁴Army Research Laboratory, Aberdeen, Maryland

ABSTRACT—Individuals show marked variation in their responses to threat. Such individual differences in behavioral inhibition play a profound role in mental and physical well-being. Behavioral inhibition is thought to reflect variation in the sensitivity of a distributed neural system responsible for generating anxiety and organizing defensive responses to threat and punishment. Although progress has been made in identifying the key constituents of this behavioral inhibition system in humans, the involvement of dorsolateral prefrontal cortex (DLPFC) remains unclear. Here, we acquired self-reported Behavioral Inhibition System Sensitivity scores and high-resolution electroencephalography from a large sample ($n = 51$). Using the enhanced spatial resolution afforded by source modeling techniques, we show that individuals with greater tonic (resting) activity in right-posterior DLPFC rate themselves as more behaviorally inhibited. This observation provides novel support for recent conceptualizations of behavioral inhibition and clues to the mechanisms that might underlie variation in threat-induced negative affect.

Upon encountering a threat, mammals inhibit their ongoing behavior and marshal a response appropriate to the imminence and danger posed by the threat (McNaughton & Corr, 2004). Typically this entails increased anxiety combined with various defensive behaviors, including freezing, risk assessment, and

withdrawal or avoidance. Although this response is prototypical, there is striking variation in individuals' sensitivity to threat, or what has been termed their degree of *behavioral inhibition*.

Behavioral inhibition is thought to represent a fundamental dimension of temperament across phylogeny (Boissy, 1995) and is posited to underlie individual differences in trait anxiety, neuroticism, and related constructs in humans (Elliot & Thrash, 2002). Many theorists argue that individual differences in behavioral inhibition and its emotional and behavioral manifestations reflect variation in the neural system responsible for organizing responses to punishment, threat, and novelty (Elliot & Thrash, 2002). Among more inhibited individuals, a combination of genes and experience (Takahashi et al., 2007) sensitizes this *behavioral inhibition system* (BIS; Gray & McNaughton, 2000). Sensitization leads to exaggerated anxiety in the face of threat (Carver & White, 1994; Shackman et al., 2006) and quite likely accounts for inhibited individuals' heightened risk for psychopathology (Alloy et al., 2008).

On the basis of rodent work, the BIS has been conceptualized as a distributed neural circuit involving the periaqueductal gray (PAG), amygdala, anterior cingulate cortex (ACC), and dorsolateral prefrontal cortex (DLPFC; McNaughton & Corr, 2004). Direct support for the involvement of some of these regions comes from neuroimaging work showing that inhibited individuals exhibit greater activation in response to aversive images in the amygdala and PAG (Mathews, Yiend, & Lawrence, 2004). Studies using source-modeled electroencephalography (EEG) have also directly linked behavioral inhibition to task-evoked ACC activity (Amodio, Master, Yee, & Taylor, 2008).

By comparison, the contribution of DLPFC to behavioral inhibition remains ambiguous (McNaughton & Corr, 2004). Indirect evidence is provided by demonstrations that inhibited

Address correspondence to Alexander J. Shackman or Richard J. Davidson, Laboratory for Affective Neuroscience, University of Wisconsin–Madison, 1202 West Johnson St., Madison, WI 53706, e-mail: shackman@wisc.edu or rjdavids@wisc.edu.

individuals show greater tonic EEG activity at sensors overlying right PFC (Sutton & Davidson, 1997). Convergent support comes from work linking greater EEG activity over right PFC to trait anxiety and negative emotionality in adults (Coan & Allen, 2004) and measures of behavioral inhibition and distress in children and nonhuman primates (Buss, Davidson, Kalin, & Goldsmith, 2004). Moreover, individual differences in prefrontal EEG asymmetry possess a number of qualities required by BIS theory. They are predictive of threat-induced negative affect, psychometrically stable, and—particularly among women—heritable and associated with mood disorders (Buss et al., 2004; Coan & Allen, 2004; Smit, Posthuma, Boomsma, & De Geus, 2007).

Despite such evidence, the poor spatial resolution of prior EEG studies makes it difficult to infer which region of this large territory (~25% of the cerebral cortex) underlies individual differences in behavioral inhibition. Consequently, the degree to which behavioral inhibition is specifically related to DLPFC remains untested. This anatomical ambiguity also limits our ability to exploit regional heterogeneity in prefrontal function to understand the nature of its contribution to behavioral inhibition.

Here, we used high-resolution EEG (128 channels) and well-validated distributed source modeling techniques to test whether electrical activity generated in right DLPFC underlies individual differences in behavioral inhibition. Source modeling uses biophysical and neuroanatomical constraints to account for the spatial “blurring” imposed by the cerebrospinal fluid, skull and scalp (Pizzagalli, 2007). Particularly when combined with high-density recordings, this permits markedly greater resolution than conventional EEG analyses. In this study, tonic (i.e., resting) EEG and a well-validated measure of behavioral inhibition—the Behavioral Inhibition System (BIS) scale (Carver & White, 1994)—were acquired from a large sample ($n = 51$). Tonic activity was used because it is especially conducive to measuring features of temperament that involve the sustained maintenance of anticipatory goals or sets (Buckner & Vincent, 2007), such as those ascribed to DLPFC by BIS theory (e.g., risk assessment and vigilance; McNaughton & Corr, 2004).

METHOD

Participants

Seventy-three right-handed women were recruited from the University of Wisconsin–Madison as part of a larger investigation of the impact of temperament on cognitive performance. Given the challenges of collecting sufficiently large samples of artifact-free EEG for studying individual differences, the study was restricted to women in order to eliminate potential heterogeneity across the sexes (Smit et al., 2007) and maximize statistical power. Participants were paid \$10/hr. Participants with insufficient artifact-free data (<360 epochs) were excluded from

analyses, yielding a final sample size of 51 (mean age = 19.5 years, $SD = 1.9$).

Self-Report Measures

In accord with Gray’s theory (Gray & McNaughton, 2000), the 7-item Behavioral Inhibition System and 13-item Behavioral Activation System (BIS/BAS; Carver & White, 1994) scales were designed to index sensitivity to punishment and reward rather than traitlike levels of affect. Nevertheless, the BIS scale is highly correlated with measures of related constructs (e.g., neuroticism; Elliot & Thrash, 2002). BIS items include “I feel worried when I think I have done poorly at something” and “Even if something bad is about to happen to me, I rarely experience fear or nervousness” (reverse-scored). BAS items include “When I go after something, I use a ‘no holds barred’ approach” and “When good things happen to me, it affects me strongly.” Internal consistency and test-retest reliability of the BIS/BAS scales are good (α s and r s > .66). The BIS/BAS scales have been found to predict greater tonic EEG activity over right and left PFC, respectively (Sutton & Davidson, 1997).

Procedure

The procedure was similar to those that we employed in our prior work (Sutton & Davidson, 1997). Participants came to the laboratory on two occasions separated by several weeks. In the first session, participants provided consent and completed the BIS/BAS scales. During the second session, sensors were applied shortly after participants’ arrival. After ensuring adequate data quality (for 30–45 min), four or eight 60-s blocks of tonic EEG (half eyes open/half eyes closed; order counterbalanced) were acquired. Otherwise, procedures were identical across participants. Most participants also completed the State version of the State–Trait Anxiety Inventory (STAI; Spielberger, 1983) immediately following EEG collection.

EEG

In a procedure similar to that we employed in prior reports (e.g., McMenamin, Shackman, Maxwell, Greischar, & Davidson, 2009), EEG data were collected using a 128-channel Geodesic Sensor Net (GSN128; Electrical Geodesics Inc., Eugene, OR; <http://www.egi.com>) referenced to vertex (Cz), filtered (0.1–200 Hz), amplified, and digitized (500 Hz). Data were filtered (60 Hz), and artifact-contaminated epochs were rejected. Artifact-free data were rereferenced to an average montage, and power density ($\mu V^2/Hz$) was estimated for the alpha-1 band (8–10 Hz). Asymmetries were computed as $\log_{10}(\text{right})$ minus $\log_{10}(\text{left})$. Because alpha-1 represents an inverse measure of cerebral activity (Coan & Allen, 2004), we interpreted reductions in power as greater cerebral activity and negative asymmetry scores as relatively more right- than left-hemisphere activity.

Source Modeling

In accord with our previously described procedures (McMenamin et al., 2009), we used the low-resolution brain electromagnetic tomography (LORETA) algorithm (www.unizh.ch/keyinst/NewLORETA) to model cortical current density (A/m^2 ; 7-mm^3 voxels). The validity of LORETA for modeling neural activation has been repeatedly established (McMenamin et al., 2009). The forward model was based on a three-shell head model and probabilistic electrode locations normalized to the Montreal Neurological Institute's template (MNI305). Additional details are presented in the Supporting Information available on-line—see p. XXX.

Analytic Strategy

Analyses employed permutation-based significance testing, allowing correction for multiple comparisons. For each, 10,000 permutations were conducted. Details are presented in the Supporting Information available on-line.

Scalp Asymmetries

We used regressions to test whether individual differences in BIS sensitivity predicted asymmetries on the scalp overlying PFC. Scores on the BAS scale were included as a simultaneous predictor to ensure specificity. Correlations are reported as semipartial coefficients. Uncorrected p values for each electrode pair were derived from the distribution of coefficients across permutations of the predictor of interest (e.g., BIS scale scores). Analyses were restricted to previously identified regions of in-

terest (Coan & Allen, 2004): the midfrontal (F3/4) and lateral-frontal electrodes (F7/8) and their nearest neighbors. The correction for multiple comparisons was based on the distribution of minimum p values across pairs and permutations.

Source Modeling

For source modeling, the aim was to test whether tonic activity in right DLPFC predicts individual differences in BIS sensitivity. Consequently, regressions were restricted to areas 8, 9, 10, 44, 45, and 46 (www.unizh.ch/keyinst/NewLORETA). Permutation-based tests were used to calculate uncorrected p values. Correction for multiple comparisons employed a cluster extent threshold.

RESULTS

BIS/BAS Scale Scores

The mean and variance of scores on the BIS scale ($M = 19.3$, $SD = 2.9$) was comparable to those reported in prior EEG studies (Coan & Allen, 2004). Scores on the BAS scale were somewhat smaller than those in previous reports ($M = 40.5$, $SD = 3.8$). The two scales were uncorrelated, $r(49) = -.09$, $p > .50$.

Scalp Asymmetries

As shown in Figure 1, more inhibited individuals showed asymmetrically greater right midfrontal (F3/4) activity, $r(48) = -.47$, corrected $p = .007$. This effect was anatomically specific: No other sites demonstrated significant relations with BIS

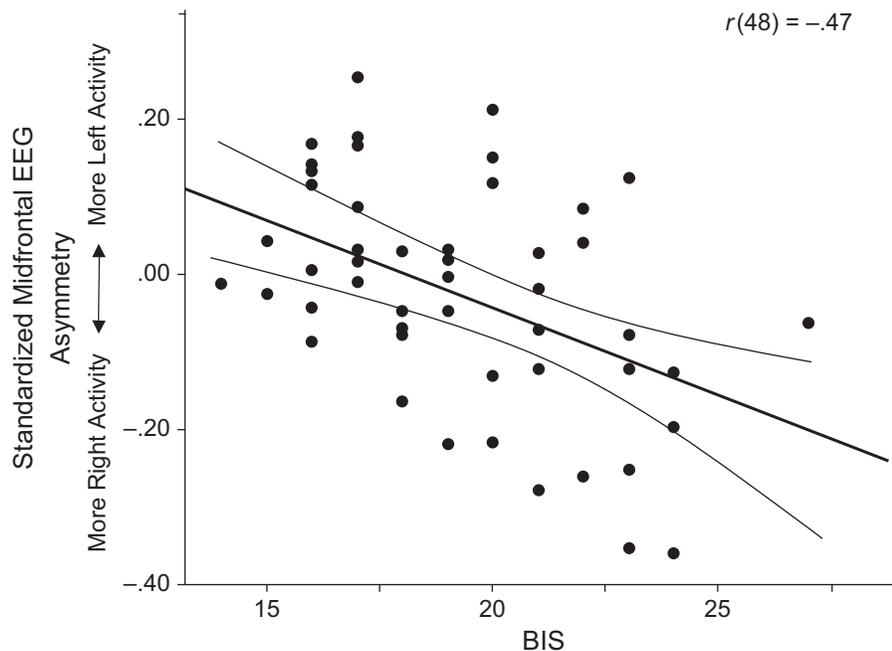


Fig. 1. Scatter plot showing the association between scores on the Behavioral Inhibition System (BIS) scale and midfrontal electroencephalographic (EEG) asymmetry (corrected $p = .007$). Asymmetry was computed as right minus left mean power density, $\log_{10}(\mu V^2/Hz)$, for the alpha-1 (8–10 Hz) band. Lines depict the regression line and 95% confidence envelope.

(corrected $ps > .09$). It was also psychologically specific: Relations between BAS and asymmetry were not reliable at any site (corrected $ps > .08$). Moreover, BIS, $r(49) = -.47$, was a significantly stronger predictor than BAS, $r(49) = -.09$, of mid-frontal asymmetry, $t(48) = -2.19, p = .03$.

It was possible that the effects ascribed to BIS represented a confound between BIS and state anxiety. To test this, we conducted an identical analysis using the 75% of participants who had completed the State version of the STAI (Spielberger, 1983). Contrary to this hypothesis, relations between BIS and mid-frontal asymmetry remained significant after we controlled for STAI, $r(34) = -.46, p = .003$. It was also possible that the effects ascribed to BIS represented a confound between BIS and muscle-tension artifacts (Shackman et al., 2009). Contrary to this hypothesis, BIS was unrelated to activity at extracerebral electrodes indexing ocular or muscular (e.g., temporalis and masseter) activity, $t(49) < .18$, uncorrected $ps > .11$.

Source Modeling

As displayed in Figure 2a, a 39-voxel cluster was identified in right DLPFC, lying predominantly in the right-posterior mid-frontal gyrus and inferior frontal gyrus pars opercularis (areas 9/46v, 8Av, 44; corrected cluster $p = .02$). As shown in Figure 2b, the more inhibited participants exhibited greater resting activity in this region with the peak lying in right-posterior DLPFC (53,24,29; area 9/46v), $r(48) = -.37$, uncorrected peak $p =$

.003. This effect was psychologically specific: No voxels in the lateral PFC demonstrated significant relations with BAS. Control analyses ruled out the possibility that this effect was an artifact of brain-behavior relations originating in the neighboring ACC (see the Supporting Information available on-line).

DISCUSSION

In agreement with prior work (Sutton & Davidson, 1997), we found that individuals with relatively greater EEG activity on the scalp overlying right PFC rated themselves as more behaviorally inhibited. Control analyses indicated that these relations were anatomically and psychologically specific. Mirroring results on the scalp, source modeling of the high-resolution EEG provided novel evidence that more behaviorally inhibited individuals are characterized by tonic activity in right-posterior DLPFC. Taken with work showing that activation in this region predicts variation in threat-evoked anxiety (Dalton, Kalin, Grist, & Davidson, 2005), this observation provides compelling support for the hypothesis that DLPFC is a key constituent of the BIS (McNaughton & Corr, 2004). Current models of the BIS argue that it is hierarchically organized along the dorsal-ventral axis of the brain (McNaughton & Corr, 2004). The lateralization observed in the present study and prior research suggests the need to incorporate hemispheric asymmetries as a second key organizing principle of the BIS. Although these findings provide

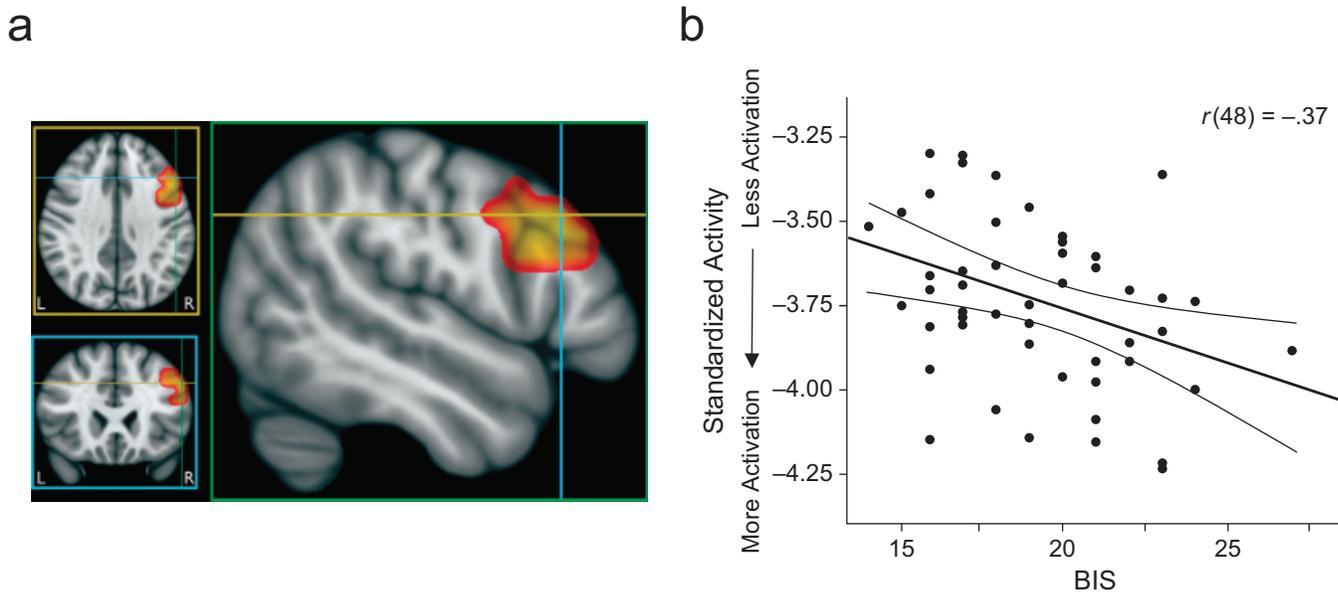


Fig. 2. Relations between individual differences in behavioral inhibition and tonic activity in right-posterior dorsolateral prefrontal cortex (DLPFC). The images in (a) depict the results of the electroencephalography source modeling analyses. The cluster lies at the intersection of the precentral and inferior frontal sulci, encompassing the right-posterior midfrontal and inferior-frontal gyri and including the inferior frontal junction (cluster-corrected $p = .02$). The crosshair shows the location in right-posterior DLPFC of the peak correlation in the sagittal (green outline), coronal (cyan outline), and axial (yellow outline) planes. The magnitude of voxel-wise correlations is depicted using a red-yellow scale; lighter shades of yellow indicate stronger correlations. “L” and “R” indicate the left and right hemispheres, respectively. The scatter plot (b) depicts the peak correlation between scores on the Behavioral Inhibition System (BIS) scale and standardized activity in right-posterior DLPFC (area 9/46v), $r(48) = -.37$, uncorrected $p = .003$. Standardized activity is in units of z-transformed cortical current density, $\log_{10}(A/m^2)$. Lines depict the regression line and 95% confidence envelope.

a clear association between right-posterior DLPFC activity and variability in behavioral inhibition, they do not address the issue of causation. Nevertheless, a causal role for right-posterior DLPFC seems plausible, given evidence that biofeedback manipulations of EEG activity over right PFC can attenuate negative affect elicited by aversive stimuli (Allen, Harmon-Jones, & Cavender, 2001).

Various theories suggest that temperament's impact on health and disease is mediated by individual differences in emotional susceptibility (Elliot & Thrash, 2002). In the face of threat, behaviorally inhibited individuals are prone to generate greater stress and anxiety, owing to alterations in the set point (e.g., reduced threshold or amplified peak output) of threat-sensitive neural circuitry: the BIS. Taken with other work in the cognitive and affective neurosciences, our findings suggest three hypotheses for how individual differences in right-posterior DLPFC activity could amplify threat-induced anxiety.

First, greater susceptibility could arise from dysfunctional anxiety regulation. This hypothesis stems from work showing that individuals with greater tonic EEG activity over right PFC are slower to recover from brief aversive challenges, indexed by a prolonged amplification of the fear-potentiated startle reflex (Jackson et al., 2003). This suggests that right-posterior DLPFC may play a role in the spontaneous regulation of negative emotions. Convergent support comes from studies directly implicating this region in the instructed regulation of negative affect (Ochsner & Gross, 2008).

Second, increased anxiety susceptibility could stem from increased vigilance. Neuroimaging research implicates the right DLPFC in vigilance and sustained attention (Robertson & Garavan, 2004). Although vigilance and other forms of risk assessment are a normative response across mammalian species to distal threats (Boissy, 1995; McNaughton & Corr, 2004), they are exaggerated among anxious individuals (MacLeod, Koster, & Fox, 2009; Poy, del Carmen Eixarch, & Avila, 2004). Likewise, electrophysiological markers of vigilance generated by PFC (e.g., mismatch negativity, P3a) are amplified by state anxiety (Cornwell et al., 2007) and trait anxiety (Hansenne et al., 2003). Heightened vigilance would tend to promote anxiety in situations where threat is ambiguous, remote, or task-irrelevant by increasing the likelihood that attention will be allocated to potential threats.

Third, increased susceptibility could reflect difficulties learning to resolve uncertainty. Right-posterior DLPFC is sensitive to uncertainty and ambiguity (Bach, Seymour, & Dolan, 2009; Huettel, Stowe, Gordon, Warner, & Platt, 2006; Vallesi, McIntosh, Shallice, & Stuss, 2009). Other research indicates that anxious individuals show difficulties learning to discriminate periods of threat from safety, presumably making it harder for them to determine when to relax. They show overgeneralization of threat-evoked anxiety to safety cues and to contexts in which conditioning occurred (Baas, van Ooijen, Goudriaan, & Kenemans, 2008). Indeed, elevated anxiety

during periods of overt safety is more discriminative of many anxiety disorders than that observed during periods of overt threat (Baas et al., 2008). Exaggerated right-posterior DLPFC activity could represent a locally generated uncertainty signal or an attempt to resolve uncertainty signals generated by other regions of the BIS network (e.g., amygdala or ACC). Regardless of the source of this signal, deficient uncertainty resolution can potentially account for both the enduring vigilance—representing an attempt to gather the information needed to resolve uncertainty—and the prolonged recovery from stressors characterizing threat-sensitive individuals.

Four limitations of this investigation represent key challenges for future research. First, our conclusions hinge on scores from a single self-report instrument acquired from an all-female sample. The degree to which these relations generalize to males or other measures of behavioral inhibition or anxiety is unclear. Caution is warranted by evidence of sex differences in prefrontal asymmetries (Smit et al., 2007) and the well-known limitations of ratings data (e.g., Sutton & Davidson, 1997). Ideally, future research will apply a multivariate approach, in which multiple measures of trait affect (e.g., neuroticism scales) and state affect (e.g., facial electromyography or momentary assessment) are collected from both sexes. This strategy would facilitate a stronger test of whether right-posterior DLPFC mediates or moderates individual differences in threat-evoked anxiety (Coan & Allen, 2004). Second, we did not replicate prior reports that more reward-sensitive individuals, indexed by the BAS, show relatively greater left-frontal EEG activity (e.g., Amodio et al., 2008). Nevertheless, null results have been reported elsewhere (e.g., Stewart, Levin-Silton, Sass, Heller, & Miller, 2008), which may simply indicate that the effect size of such relations is modest. Alternatively, this may reflect the truncated range of BAS scores in the present sample. Mass-screening combined with stratified sampling would help to resolve this issue. Third, our conclusions rest on a model, not a direct measurement, of the cerebral sources underlying the EEG. The use of an alternate algorithm or more complex head model might alter these results somewhat. This concern is partially ameliorated by the knowledge that the algorithm used here, LORETA, has received more extensive validation than have other algorithms (McMenamin et al., 2009) and has been shown to exhibit sufficient resolution ($\sim 1\text{--}2$ cm; Pizzagalli, 2007) for testing our key hypothesis. Fourth, the present study did not address the degree to which individual differences in behavioral inhibition reflect altered functional connectivity between right-posterior DLPFC and other structures thought to underlie the BIS (e.g., amygdala, PAG, or ACC). Future research designed to interrogate variation in connectivity is likely to yield substantial dividends for our understanding of behavioral inhibition.

Despite these challenges, our findings provide novel evidence linking right-posterior DLPFC to the BIS and a fresh source of insight into the contribution of PFC to threat-evoked anxiety and defensive behaviors. Such mechanisms may help to explain

why inhibited individuals are more vulnerable to a variety of physical and mental diseases. More generally, our results highlight the value of using neurophysiology to understand temperament.

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SUPPORTING INFORMATION

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Supplementary Method

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Supplementary Method

A.J. Shackman et al., “Right Dorsolateral Prefrontal Cortical Activity and Behavioral Inhibition”

EEG Acquisition and Reduction

EEG acquisition and reduction procedures were similar to our prior reports (Greischar et al., 2004; McMenamin, Shackman, Maxwell, Greischar, & Davidson, *in press*). EEG was measured using a 128-channel montage (<http://www.egi.com>) referenced to Cz, filtered (0.1-200Hz), amplified, and digitized (500Hz). Using EEGLAB (<http://scn.ucsd.edu/eeglab>) and in-house code, calibrated (μV) data were filtered (60-Hz), and epochs (1.024-s) contaminated by gross artifacts ($\pm 100\mu\text{V}$ for more than half an epoch or $\sigma^2 > 500$) or flat channels ($\sigma^2 < 0.25\mu\text{V}^2$) were rejected (Delorme, Sejnowski, & Makeig, 2007). Unusable channels were spline-interpolated (Greischar et al., 2004). Participants with fewer than 360 artifact-free epochs were excluded from analyses (Allen, Urry, Hitt, & Coan, 2004). Artifact-free data were re-referenced to an average montage¹ and mean spectral power density (μV^2) estimated for the alpha-1 band (8-10Hz) using 50% overlapped Hanning-windowed epochs.²

Asymmetries were computed as $\log_{10}(\text{right})$ minus $\log_{10}(\text{left})$. Because alpha represents an *inverse* measure of cerebral activity (Allen, Coan, & Nazarian, 2004; Davidson, Jackson et al., 2000; Laufs, *in press*; Oakes et al., 2004; Romei et al., 2007), we interpreted reductions in power as greater cerebral activity, and negative asymmetry scores as relatively less left than right activity (or relatively more right than left).

Source Modeling

Similar to our prior reports (McMenamin et al., *in press*; Pizzagalli et al., 2004), in-house code implementing the Low Resolution Brain Electromagnetic Tomography (LORETA) algorithm (Frei et al., 2001;

¹ Although there is evidence that measures of frontal EEG asymmetry differ across reference montages, when adequate spatial sampling of the scalp is achieved, as in the present experiment, an average reference montage is least biased and most reliable (Davidson, Jackson, & Larson, 2000; Dien, 1998; Gudmundsson, Runarsson, Sigurdsson, Eiriksdottir, & Johnsen, 2007).

² The decision to employ alpha-1 was (1) based on work indicating that it is more closely related to emotion constructs (Goncharova & Davidson, 1995) and resting cerebral metabolism (Oakes et al., 2004) than alpha (8-13Hz), and (2) in accord with prior reports by our laboratory (Davidson, Marshall, Tomarken, & Henriques, 2000) and others (Chavanon, Wacker, Leue, & Stemmler, 2007; Wyczesany, Kaiser, & Coenen, 2008).

Pascual-Marqui, 1999; Pascual-Marqui, Michel, & Lehmann, 1994) was used to model the distributed neuronal sources underlying the scalp-recorded voltage. LORETA has received more extensive cross-modal validation alternative modeling algorithms (McMenamin et al., *in press*; Pizzagalli, 2007).³ Voxelwise current densities (A/m^2) were generated for each participant using an inverse operator created using LORETA-Key (<http://www.unizh.ch/keyinst/NewLORETA>; $\lambda=10^{-5}$). The forward-model was comprised of a 3-shell (Ary, Klein, & Fender, 1981) head model and canonical electrode coordinates (<http://www.egi.com>) normalized (Towle et al., 1993) to the Montreal Neurological Institute's (MNI) probabilistic anatomical template (Collins, Neelin, Peters, & Evans, 1993) (MNI305). The source-space is restricted to the cerebral gray matter, hippocampi, and amygdalae (7-mm^3 voxels). Voxelwise source-estimates were \log_{10} -transformed (Thatcher, North, & Biver, 2005). Maps were exported using SPAMalize (<http://brainimaging.waisman.wisc.edu/~oakes>), normalized to the MNI template (trilinear interpolation) in FLIRT (<http://www.fmrib.ox.ac.uk/fsl/flirt>), and displayed using FSL (<http://www.fmrib.ox.ac.uk/fsl>). Final macroscopic (Duvernoy, 1999) and areal labels (Petrides, 2005) were then assigned. Our use of the term “inferior frontal junction” (IFJ) follows the convention established by Brass and colleagues (Brass, Derrfuss, Forstmann, & von Cramon, 2005).

Analytic Strategy

Analyses employed permutation-based nonparametric tests written in MATLAB (<http://www.themathworks.com>). For each, 10,000 permutations were conducted.

Scalp asymmetries. Multiple regressions were used to test whether BIS predicted asymmetries on the scalp overlying PFC. BAS was included as a simultaneous predictor to ensure specificity. Correlations are reported as semi-partial coefficients. Uncorrected p -values for each electrode-pair was estimated via

³ The validity of LORETA for modeling neural activation has been established using **(1) simulations** (Grova et al., 2006; Pascual-Marqui, Esslen, Kochi, & Lehmann, 2002; Phillips, Rugg, & Friston, 2002a, 2002b; Trujillo-Barreto, Aubert-Vazquez, & Penny, 2008; Yao & Dewald, 2005), **(2) verified epileptic foci** (Lantz et al., 1997; Worrell et al., 2000; Zumsteg, Friedman, Wennberg, & Wieser, 2005; Zumsteg, Wennberg, Treyer, Buck, & Wieser, 2005), **(3) intra-cerebral recordings** (Bai, Towle, He, & He, 2007; Seeck et al., 1998; Zumsteg, Friedman et al., 2005), **(4) positron emission tomography** (Pizzagalli et al., 2004; Zumsteg, Wennberg et al., 2005), and **(5) functional magnetic resonance imaging** (Bai et al., 2007; Duru et al., 2007; Eryilmaz, Duru, Parlak, Ademoglu, & Demiralp, 2007; Meltzer, Negishi, Mayes, & Constable, 2007; Mulert et al., 2004; Vitacco, Brandeis, Pascual-Marqui, & Martin, 2002). Given the enhanced resolution afforded by high-density recordings (Srinivasan, Tucker, & Murias, 1998), our results are likely to lie within $\sim 1\text{-}2\text{cm}$ of the true source (Pizzagalli, 2007). Further improvements in spatial resolution could be achieved using a more realistically complex finite element model (Fuchs, Wagner, & Kastner, 2007) or head-models derived from each participant's anatomy (but cf. Henson, Mattout, Phillips, & Friston, 2009).

permutation (ter Braak, 1992).⁴ To minimize the number of comparisons, analyses were restricted *a priori* (cf. Sutton & Davidson, 1997) to the mid- (F3/4) and lateral-frontal electrodes (F7/8) and their nearest neighbors (12 electrode-pairs total). Correction for multiple comparisons was performed using a minimum-*p* technique (Nichols & Holmes, 2002).⁵

LORETA source modeling. Here, the aim was to test whether tonic activity in right dlPFC predicts individual differences in BIS. Consequently, analyses were restricted to architectonic areas 8, 9, 10, 44, 45 and 46. The digitized atlas implemented in LORETA-Key (<http://www.unizh.ch/keyinst/NewLORETA>) was used to assign an architectonic label to each voxel, and the 410 voxels lying within the *a priori* region of interest (ROI) were included in analyses. A similar procedure was previously described by our laboratory (Pizzagalli, Peccoralo, Davidson, & Cohen, 2006).

Mirroring scalp analyses, intracerebral analyses relied upon voxelwise multiple regressions with BIS and BAS as simultaneous predictors of cortical current density at each voxel. Again, permutation-based nonparametric tests were employed to calculate uncorrected *p*-values. Multiple comparison correction was performed using a corrected cluster extent threshold with a preliminary intensity threshold of $p < .05$ (Nichols and Holmes, 2001).⁶

Supplementary Results

Post hoc analyses of ACC

Prior research indicates that behaviorally inhibited individuals exhibit greater event-related activity in dorsal ACC (dACC) during tasks that place heavy demands on conflict resolution (Amodio, Master, Yee, &

⁴ The predictor of interest (e.g., BIS) was randomly permuted (10,000 permutations)—while the values of the covariate (e.g., BAS) were fixed—to generate a coefficient-distribution at each electrode. The values demarcating the upper/lower 2.5th percentiles were used as the uncorrected *p*-values.

⁵ For each of the 10,000 permutations used to calculate the sampling distribution of regression parameters, the minimum *p*-value from the electrode-pairs of interest was recorded. This minimum-*p* distribution was used to transform the observed *p*-values into corrected *p*-values. Significance was achieved for corrected $p < .05$.

⁶ A primary threshold of uncorrected $p < .05$ was applied to the data and the volume of each contiguous cluster was recorded. Self-report data were permuted 10,000 times, and the volume of the largest cluster was recorded to create a distribution of maximal cluster volumes. Corrected *p*-values were calculated for each cluster on the basis of their volume using this distribution. Significance was achieved for clusters with a corrected $p < .05$.

Taylor, 2008). Given our ROI-based approach to hypothesis testing, it was therefore possible that the effect we ascribed to right-pdlPFC actually reflects the spread of a stronger effect peaking in the adjacent ACC. To test this possibility, we recomputed our analyses for voxels located within the dorsal and perigenual ACC (areas 24 and 32) ROIs described by Pizzagalli et al. (2006). The results were not consistent with this explanation. Individual differences in BI were unrelated to tonic activity in these regions, $r_s(48) < .14$, $p_s > .16$ (uncorrected).

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