

Cortisol involvement in mechanisms of behavioral inhibition

MATTIE TOPS^{a,b,c} AND MAARTEN A.S. BOKSEM^{d,e}

^aExperimental and Work Psychology, University of Groningen, Groningen, The Netherlands

^bCentre for Child and Family Studies, University of Leiden, Leiden, The Netherlands

^cLeiden Institute for Brain and Cognition, Leiden University Medical Center, Leiden, The Netherlands

^dDonders Institute for Brain, Cognition and Behavior, Radboud University, Nijmegen, The Netherlands

^eRotterdam School of Management, Erasmus University, Rotterdam, The Netherlands

Abstract

We studied whether baseline cortisol is associated with post-error slowing, a measure that depends upon brain areas involved in behavioral inhibition. Moreover, we studied whether this association holds after controlling for positive associations with behavioral inhibition scores and error-related negativity (ERN) amplitudes that cortisol and post-error slowing may share. Healthy female volunteers performed a flanker task. Cortisol was independently positively associated with post-error slowing and the ERN, supporting hypotheses that cortisol is involved in behavioral inhibition. Additionally, cortisol mediated an association between ERN and more post-error slowing, which suppressed a direct association between ERN and less post-error slowing. The results are relevant, not only for researchers of behavioral inhibition, but also for researchers of the basic mechanisms of the ERN and post-error slowing, and may bring those literatures together.

Descriptors: Post-error slowing, Cortisol, Error-related negativity, Behavioral inhibition system

In humans, levels of the hormone cortisol have been related to punishment sensitivity (van Honk, Schutter, Hermans, & Putman, 2003), and it has been hypothesized that high levels of cortisol are involved in mechanisms of behavioral inhibition, perhaps by inhibiting dopaminergic approach (i.e., reward-seeking) systems (e.g., Tops, van der Pompe, et al., 2004; Tops, 2004). Behavioral inhibition, the inhibition of the initiation of behavior or behavioral responding in the context of novelty, signs of threat, or social evaluation (Fox, Henderson, Marshall, Nichols, & Ghera, 2005) may be part of a submissive behavioral repertoire that includes inhibition of aggression, which has also been linked to increased cortisol levels (e.g., Putman, Hermans, & van Honk, 2007; van Honk et al., 1998). At least in children, behavioral inhibition has been consistently related to high baseline cortisol levels (Fox et al., 2005). Effects of cortisol administration or stress-induced cortisol increases have been studied on behavioral and electroencephalographic (EEG) measures of approach-inhibition such as free recall positivity bias (Tops et al., 2003, 2004), frontal EEG asymmetrical activity (Schmidt, Fox, Goldberg, Smith, & Schulkin, 1999; Tops et al., 2005; Tops, van Peer, Wester, Wijers, & Korf, 2006), rotational behavior (Tops, Wijers, Koch, & Korf, 2006) and congruity between observed emotional

facial expressions and performed hand gestures (Roelofs, Elzinga, & Rotteveel, 2005; Roelofs et al., 2009; van Peer et al., 2007). The results have not been consistently affirmative across studies and measures, for instance, effects on facial expression–hand gesture congruity has been found to be absent (van Peer et al., 2007) or independent of facial valence (Roelofs et al., 2005).

Individual differences in punishment sensitivity and behavioral inhibition can be measured by the Behavioral Inhibition System (BIS) scale (Carver & White, 1994). This scale is derived from the theory postulated by Gray (1982, 1989) and proposes two interacting motivational systems: the behavioral approach system (BAS) and the behavioral inhibition system (BIS). According to Gray, the BIS is sensitive to signals of punishment and reward omission and inhibits behavior that may lead to aversive or harmful outcomes. In contrast, the BAS is proposed to be sensitive to positive signals of reward. In addition, these two motivational systems are proposed to depend on separate, but interacting, neural circuits: the BIS was proposed to comprise septal cholinergic projections that inhibit dopaminergic behavioral approach systems. In most recent formulations of the theory, BIS maintains vigilance for unexpected stimuli, conflict, and incongruity in the environment, directs attention to such stimuli when detected, and resolves conflict by inhibiting ongoing action in order to facilitate the processing of these stimuli and biasing action toward defensive behavior (Gray & McNaughton, 2000).

In this study, we investigated whether cortisol levels are related to a behavioral measure of inhibition: post-error slowing. Paradigms such as the flanker task produce such a post-error

This research was supported by a Veni grant of the Netherlands Organization for Scientific Research (NWO) (451-07-013).

Address correspondence to: Mattie Tops, Centre for Child and Family Studies, University of Leiden, Post Box 9555, 2300 RB Leiden, The Netherlands. E-mail: M.Tops@rug.nl

slowing effect; subjects typically slow down after committing an error to avoid making a subsequent mistake (Rabbitt, 1966), which has been suggested to reflect activity of the BIS (Kleider & Schwarzenbacher, 1989) and correlated positively to BIS scores (Boksem, Tops, Kostermaans, & De Cremer, 2008), trait distress reactivity (Larson, Fair, Good, & Baldwin, 2010; Luu, Collins, & Tucker, 2000), trait worry (Compton, Lin, et al., 2008) and, in adolescents, to ratings of behavioral inhibition obtained in childhood (Fox, 2010). Developmental and brain imaging research suggests that post-error slowing reflects a mechanism of response inhibition (Gupta, Kar, & Srinivasan, 2009; Marco-Pallarés, Camara, Münte, & Rodríguez-Fornells, 2008). Indeed, slowing after errors and after failures to inhibit responding have been related to right inferior frontal gyrus (IFG) activation (Hester, Barre, Mattingley, Foxe, & Garavan, 2007; Li et al., 2008; Marco-Pallarés et al., 2008) and lesions of the right inferior frontal sulcus reduced post-error slowing (Molenberghs et al., 2009). Areas of neural activation have been found in the right IFG, anterior insula (AI), and anterior cingulate cortex (ACC) that are common to inhibiting responses, approach, and emotions (Avila, Parcet, & Barrós-Loscertales, 2008; Shafritz, Collins, & Blumberg, 2006; Stone, Connolly, Wynne, Alhusaini, & Garavan, 2009). Of these areas the right IFG/AI, which is part of the BIS (McNaughton & Corr, 2004), has previously been shown to be critical for motor response inhibition (Aron, Robbins, & Poldrack, 2004; Chikazoe, Konishi, Asari, Jimura, & Miyashita, 2007).

The flanker task is also used in studies of the error-related negativity (ERN), which may reflect the BIS (Amodio, Master, Yee, & Taylor, 2008). The ERN is a negative event-related potential with a fronto-central scalp distribution, peaking 60–110 ms after an error response (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1990; Gehring, Coles, Meyer, & Donchin, 1990). Just like the BIS, the ERN is thought to reflect inhibition of dopaminergic systems in response to punishment, reward omission, and performance errors (Gray, 1982, 1989; Holroyd & Coles, 2002). Although associations between ERN and post-error slowing have not always been found, they have been reported in children, adolescents, and adults (Gehring, Goss, Coles, Meyer, & Donchin, 1993; Ladouceur, Dahl, & Carter, 2007; Scheffers & Coles, 2000; West & Travers, 2008) and in both between- and within-subject designs (Debener et al., 2005). The ERN is thought to be generated in the ACC, an area that is also involved in autonomic and hormonal control (Critchley, 2005). ERN amplitudes have been associated with BIS scores (Amodio et al., 2008; Boksem, Tops, Wester, Meijman, & Lorist, 2006; Boksem et al., 2008), cortisol levels (Tops, Boksem, Wester, Lorist, & Meijman, 2006) and cortisol responses to social evaluative threat in high BIS subjects (Cavanagh & Allen, 2008). Indeed, the ERN, BIS, and cortisol responses have all been related to social evaluative threat (Cavanagh & Allen, 2008; Hajcak, Moser, Yeung, & Simons, 2005). Moreover, adolescents who showed high behavioral inhibition in childhood displayed enhanced ERN amplitudes and post-error slowing; ERN amplitude moderated the relationship between early behavioral inhibition and later clinically significant anxiety disorders (Fox, 2010; McDermott et al., 2009).

In the present study, we investigated the relationship in healthy student subjects between basal salivary cortisol level and post-error slowing during a flanker task. We focused on basal levels just before the start of task performance because stress-induction and fatigue may impact on task performance in

unintended ways. Indeed, at least in children, behavioral inhibition has been consistently related to high baseline cortisol levels but less consistently to increased cortisol responses to stress (Fox et al., 2005). Similarly, in adults high BIS scores were related to decreased ERN amplitude and deficits in task performance during stress (Cavanagh & Allen, 2008). We studied whether cortisol is positively associated with post-error slowing. Moreover, we studied whether this association holds after controlling for positive associations with BIS scores and ERN amplitudes that cortisol and post-error slowing may have in common. Confirming this hypothesis would provide converging evidence of an association of cortisol with behavioral inhibition, using a measure that has the advantage over previously used measures that it has been shown to depend upon activity in brain areas that are known to be important in aspects of behavioral inhibition.

Methods

Subjects

Eighteen healthy right-handed female participants, between 18 and 27 ($M = 20$, $SD = 3.6$) years of age, were recruited from the university population. They were paid for their participation and had normal or corrected-to-normal vision. None of the subjects worked night shifts or used prescription medication. Written informed consent was obtained prior to the study.

Task

We used a version of the Eriksen Flanker Task (Eriksen & Eriksen, 1974). On each trial, a five-letter string was presented. The central letter was the target, the remaining letters the flankers. The stimuli used for targets and flankers were the letters H and S. The assignment of letter to response hand was balanced between participants. During the entire task, a fixation mark was displayed 0.14 degrees above the target letter. On congruent trials, the target letter was the same as the flankers (SSSSS or HHHHH); on incongruent trials the target letter differed from the flankers (SSHSS or HSHHH). Forty per cent of the trials consisted of incongruent stimuli, and 60% consisted of congruent stimuli. Congruent and incongruent trials were presented in random order.

The stimuli were presented on a 17-inch monitor. The letters were white against a black background, and each letter had a height and width of 0.24° visual angle. Eriksen and Eriksen (1974) showed that reaction times and error rates were highest when letters were presented close together. Therefore, we presented letters 0.05° apart. The complete five-letter string had a width of 1.43° visual angle.

In addition, flankers were presented 100 ms prior to target onset to maximize the expected flanker compatibility effect (Kopp, Rist, & Mattler, 1996). Target and flankers disappeared simultaneously at the moment a response was made. In case no response was given, targets and flankers disappeared after 1200 ms. The interstimulus interval was 3 s. Participants received seven blocks of 400 trials. Each block had a total duration of 20 min.

Questionnaires

Behavioral Inhibition System. We used the BIS subscale from the Dutch version (Franken, Muris, & Rassin, 2005) of the BIS/BAS-scale created by Carver and White (1994) to assess dispositional behavioral inhibition. This BIS scale (range: 7–28)

comprises seven items which subjects endorse on a 4-point scale from 1 ("very true for me") to 4 ("very false for me"). Cronbach's alpha was .76.

Salivary Cortisol

Saliva samples were taken with a Salivette (Sarstedt Inc., Rommelsdorf, Germany). Analyses of saliva cortisol were performed in the biochemical laboratory of the University of Trier. Saliva samples were stored at -20°C until analysis. Cortisol concentration in saliva was measured using a time-resolved fluorescence immunoassay, as described in detail in Dressendörfer, Kirschbaum, Rohde, Stahl, and Strasburger (1992).

Procedure

Subjects were instructed to abstain from alcohol 24 h before the experiment and from caffeine containing substances 12 h before the experiment. After arrival at the laboratory at 12.00 hours, subjects were given written task instructions where after they were trained in performing the task for 15 min. Following the application of the electrodes, subjects were seated in a dimly lit, sound-attenuated, electrically shielded room at 1.20 m from the screen. Their index fingers rested on touch-sensitive response boxes. Subjects were instructed to lift their finger from the response button as quickly as possible when a target was presented, maintaining a high level of accuracy. Immediately before task performance, on average 45 min after arriving in the laboratory, a saliva sample was collected.

Electrophysiological Recording and Data Reduction

The EEG was recorded using 60 Sn electrodes attached to an electro cap (Electro-Cap International, Inc., Eaton, OH). All electrodes were referenced to averaged earlobes. The electro-oculogram (EOG) was recorded bipolarly from the outer canthi of both eyes and above and below the left eye, using Sn electrodes. Electrode impedance was kept below 5 k Ω . EEG and EOG were amplified with a 10-s time constant and a 200-Hz low pass filter, sampled at 1000 Hz, digitally low pass filtered with a cut-off frequency of 70 Hz, and online reduced to a sample frequency of 250 Hz.

All ERP analyses were performed using the Brain Vision Analyzer software (Brain Products, Gilching, Germany). ERPs were averaged off-line. The data was further filtered with a 0.53-Hz high-pass filter and a slope of 48 dB/oct and a 40-Hz low-pass filter with a slope of 48 dB/oct. Out-of-range artefacts were rejected and eye movement artefacts were corrected, using the Gratton, Coles, and Donchin method (Gratton, Coles, & Donchin, 1983). A baseline voltage over the 100-ms interval preceding the response was subtracted from the averages.

Data Analysis

Performance. For the different stimulus conditions, mean reaction times were calculated. Correct reactions occurring within a 150–1000-ms interval after stimulus presentation were considered as hits. Erroneous reactions occurring within this interval were considered as errors. Responses outside of this interval (also non-responses) were considered misses. To investigate strategic changes after error detection, we analyzed reaction times on correct trials following an error minus reaction times on correct trials following a correct response (i.e., post-error slowing; Kleiter & Schwarzenbacher, 1989; Rabbit, 1966). As we found no difference in post-error slowing for congruent

and incongruent n–1 trials, our measure of post-error slowing includes both.

ERPs. Mean ERN amplitudes were calculated at Cz, where visual inspection showed this component was maximal. We quantified the ERN on error trials as the most negative peak occurring in the 100 ms following an erroneous response. For statistical analyses, we used the average amplitude of the ERN in a time window starting 20 ms before the peak until 20 ms after the peak. Measuring the amplitude as an area around the peak makes the data more reliable, as it reduces the impact of extreme data-points. We processed the ERP elicited by correct trials in exactly the same manner. In addition, to arrive at a measure that reflects activity associated with error-processing only, we created difference waves by subtracting amplitudes elicited on correct trials from those elicited by incorrect trials, creating a 'difference ERN,' which we will refer to as ERN.

Statistical Analyses

For the present analysis, we used data from a study of time-on-task effects on task engagement that we present elsewhere (Tops & Boksem, 2010). To study time-on-task effects, the subjects had to perform the flanker task for an exceptionally long time (2.5 h). Because from previous studies we know that performance and ERN amplitudes deteriorate quickly during prolonged performance of the present task (Boksem, Meijman, & Lorist, 2006; Tops, Boksem, et al., 2006), as do associations between ERN and measures of individual differences (Luu et al., 2000) and, indeed, post-error slowing was only significant in the first block, we analyzed and report only data from the first block. Only the first block is comparable to other studies that do not study time-on-task effects; it does not show fatigue effects that may interfere with behavioral inhibition processes, and it is closest in time to the cortisol measurement. We performed regression analyses of cortisol level as dependent variable and post-error slowing, BIS, and ERN amplitude as independent variables. In an additional analysis, we used post-error slowing as dependent variable and cortisol, BIS, and ERN amplitude as independent variables. We did not assume directionality of relationships, but merely used the regression analyses to investigate which variables independently related to cortisol levels and post-error slowing. All statistical tests of significance were two-tailed.

Results

Reaction times on incongruent flanker trials ($M = 488$ ms, $SD = 56$) were longer than on congruent trials ($M = 428$, $SD = 64$; $F(1,17) = 130.95$, $p < .001$). Also, error rates were lower on congruent trials (3.1%) compared to incongruent trials (10.4%; $F(1,17) = 20.07$, $p < .001$). The overall error rate was 6.7%, which amounts to 26.8 ($SD = 15$) erroneous responses on average per subject. Almost all of these error-trials (18.2 on average, $SD = 9.5$; range 7–35) were also included in the ERN analyses, indicating a very low loss of data in the ERN analysis due to signal artefacts. Reaction times and errors were not related to BIS scores, ERN amplitude, or cortisol levels. Misses were very rare, 0.8% = 3.2 trials on average per subject, and not included in the analyses.

Mean post-error slowing was 23 ms ($SD = 35$; $t(17) = 2.82$, $p < .05$). Mean BIS score was 21.8 ($SD = 3.6$). Mean ERN amplitude was $-7.59 \mu\text{V}$ ($SD = 6.57$); mean ERN amplitude on

error trials was $-9.8 \mu\text{V}$ ($SD = 8.4$). Mean cortisol level was 7.3 nmol/l ($SD = 3.4$).

Higher cortisol was associated with more post-error slowing (Table 1; Figure 1), higher BIS scores (trend level), and a more negative ERN amplitude (Table 1; Figures 1 and 2). Figure 1A shows that individuals with higher cortisol levels showed post-error slowing, while individuals with low cortisol levels showed no post-error slowing; Figure 1b shows that individuals with higher cortisol levels showed clear ERNs, while some individuals with low cortisol levels evidenced no ERN. We performed a regression analysis of cortisol level as dependent variable and post-error slowing, BIS, and ERN amplitude as independent variables. We did not assume directionality of relationships, but merely investigated which variables independently related to cortisol levels. Table 1 shows that only ERN and post-error slowing remained related to cortisol levels, while the original trend-level correlation of BIS score with cortisol level no longer approaches significance. Similarly, to also study association of ERN and BIS with post-error slowing, we performed a regression analysis of post-error slowing as dependent variable and cortisol, BIS, and ERN amplitude as independent variables. Table 1 shows that the ERN but not BIS was associated with slowing. Larger ERN amplitudes were associated with less post-error slowing.

Figure 3A presents a depiction of the relationships between cortisol, post-error slowing, and ERN in terms of Pearson's and partial correlations. The similarities of the partial correlations in this figure with those in Table 1 shows that BIS score has little influence on those relationships. The partial correlations in Figure 3A show that ERN amplitude appears significantly associated with both post-error slowing and cortisol, even though this association between ERN and post-error slowing did not show up using only Pearson's correlations. Apparently, the positive path through cortisol cancels out the significant negative direct association between ERN and post-error slowing, observed when partialling out this correlation with cortisol. We tested the significance of this inconsistent mediator/suppressor effect of cortisol on the relationship between ERN and post-error slowing (MacKinnon, Krull, & Lockwood, 2000) using the MacKinnon, Lockwood, Hoffman, West, and Sheets (2002) distribution of products method. As cortisol proved to be significantly related to both ERN amplitude and post-error

Table 1. Regression Analyses with Cortisol Level or Post-Error Slowing as Dependent Variable

	Beta	<i>t</i>	<i>p</i>	<i>r</i>	Partial <i>r</i>
Dependent: Cortisol	$R^2 = .70, F(3,14) = 9.36, p < .01$				
Post-error slowing	.53	3.25	.007	.55*	.69
ERN	-.68	-4.15	.001	.66*	.77
BIS	-.07	-0.40	.694	.39 [†]	.12
Dependent: Slowing	$R^2 = .50, F(3,14) = 4.01, p < .05$				
ERN	.65	2.37	.035	-.02	-.56
Cortisol	.88	3.25	.007	.55*	.69
BIS	.20	0.92	.376	.23	.26

Note: *p*-values apply to both *t*-tests and partial correlations; *r*: Pearson's correlation between independent variable and cortisol level (* $p < .05$; [†] $p < .10$); Partial *r*: partial correlation between independent variable and cortisol level after partialling out the variance of cortisol that is explained by the other independent variables. ERN: amplitude on error trials minus on correct trials, inversely signed such that higher positive values mean larger amplitude.

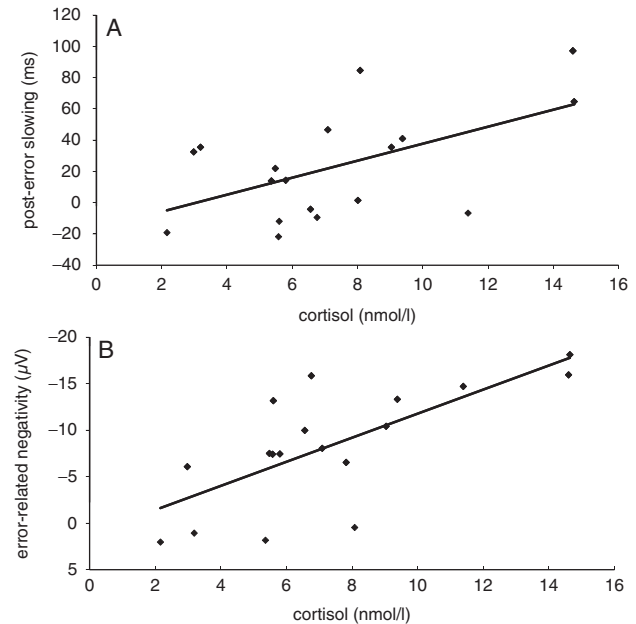


Figure 1. Scatterplots of (A) post-error slowing as a function of cortisol; (B) ERN amplitude as a function of cortisol. Note that the y-axis in (B) has been inverted, so that up denotes larger ERN amplitude (amplitude on error trials minus on correct trials).

slowing, this mediation test provides a good balance of Type I error and statistical power in small samples (MacKinnon et al., 2002). This analysis showed that cortisol mediates a positive association between ERN and post-error slowing, while the direct relation between ERN and slowing is actually negative ($P = -13.28, p < .05$).

Based on MacKinnon et al. (2000), a suppressor is a third variable that increases the predictive validity of another variable (or set of variables) by its inclusion in a regression equation. A suppressor effect would be present when the direct and mediated effects of an independent variable have opposite signs. If the opposite direct and mediated effects are of similar magnitude, then they will cancel each other out in the overall relationship (e.g., the Pearson's correlation will be close to zero). However, including the third suppressor variable in the regression equation will make the direct effect evident and at the same time demonstrate that the third variable mediated an opposite, suppressor effect. This is the situation described above and depicted in the top diagram of Figure 3, where including cortisol as a predictor made the direct association between larger ERN and less post-error slowing evident; mediation analysis showed that cortisol is a suppressor of a negative association between ERN amplitude and post-error slowing. Statistically, suppression is equivalent to inconsistent mediation and confounding, and differs from "negative confounding" only on conceptual grounds (i.e., it depends on the hypotheses studied; MacKinnon et al., 2000).

Many studies relating ERN amplitude to individual differences measures of temperament or emotionality used the ERN on error trials, instead of the difference between the ERN on error and correct trials (e.g., Boksem, Tops, et al., 2006, 2008; Hajcak, McDonald, & Simons, 2004; Luu et al., 2000; McDermott et al., 2009; Tops, Boksem, et al., 2006). It has been suggested that measures of temperament relate better to the ERN on error trials than to the difference ERN because such measures

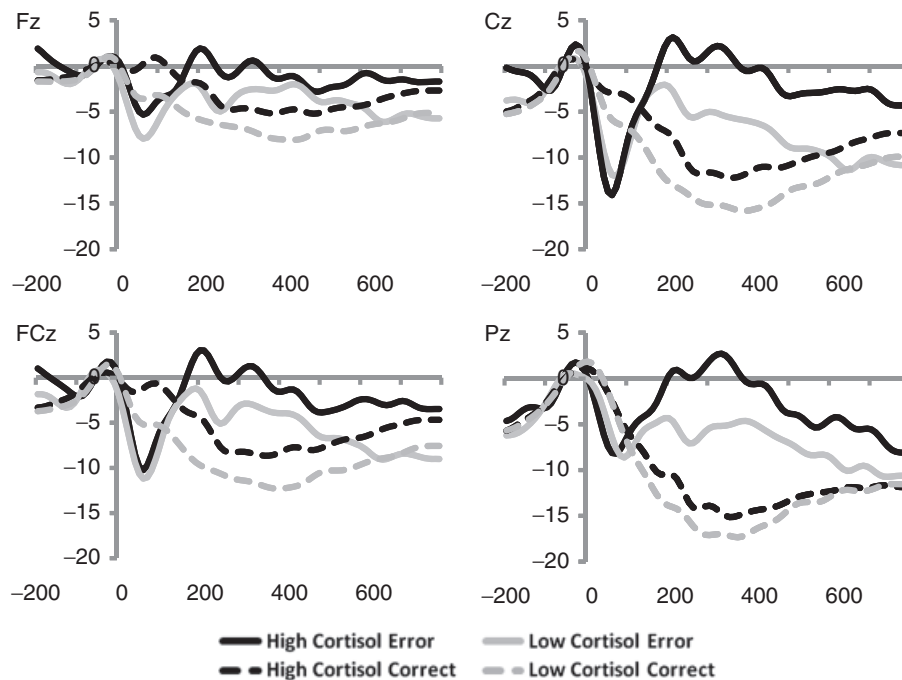


Figure 2. Response-locked ERP waveforms in μV over time (ms) at Fz, FCz, Cz, and Pz for groups with low or high cortisol levels as a function of correctness of responses (solid lines = error responses; dashed lines = correct responses). The results are based on analyses using cortisol as a continuous variable, but only for the purpose of this figure, the subjects were divided in a low and high cortisol group based on median split. At Cz, where the ERN was maximal in magnitude, higher cortisol levels related to a larger ERN amplitude.

tend to relate to larger ERN amplitudes on correct trials, as well (Endrass, Klawohn, Schuster, & Kathmann, 2008; Hajcak et al., 2004; Tops, Boksem et al., 2006). Indeed, in the present study BIS score correlated with ERN magnitude on error trials ($r = .53, p < .05$) but tended to correlate in the same direction to the ERN on correct trials ($r = .34, p > .10$) which rendered the correlation with the difference ERN nonsignificant ($r = .27, p > .10$). The ERN on error trials was highly correlated to the difference ERN ($r = .82, p < .001$) and related to the other measures similarly but less strongly compared to the difference ERN. However, Figure 3B shows that the ERN on error trials appears to mediate the relationship between BIS and cortisol: it is associated with both, and including it as predictor in the analyses almost completely abolishes the trend-level association between BIS and cortisol. However, because most of the associations in Figure 3B do not reach significance, we only present this pattern of associations so that larger studies in the future may investigate whether the ERN on error trials really mediates an association between BIS and cortisol. This particular association may be important but is not the main interest in the present study.

Discussion

We found that cortisol related positively to post-error slowing and ERN amplitude. The association between cortisol and post-error slowing was independent from the association between cortisol and ERN amplitude, while a positive trend-level association between BIS scores and cortisol seemed to be mediated by their associations with a larger ERN on error trials. Although we cannot really address this suggested mediation by ERN of an association between BIS and cortisol because of lack of power, we note mounting evidence that attention or error monitoring

mediates the relation between behavioral inhibition and stress (Cavanagh & Allen, 2008; Fox, 2010; McDermott et al., 2009). The association between BIS and the ERN on error trials replicates previous studies in which BIS scores were related to error-trial ERN amplitude (Amodio et al., 2008; Boksem, Tops, et al., 2006, 2008) and also to the ERN in response to performance feedback (Balconi & Crivelli, 2010; De Pascalis, Varriale, & D'Antuono, 2010). In addition, trait low behavioral control has been related to smaller ERN amplitude (Stahl & Gibbons, 2007). Most importantly, the positive association between cortisol and post-error slowing is consistent with hypotheses that cortisol is involved in behavioral inhibition (e.g., Tops et al., 2005).

The present results suggested an association between ERN amplitude and *decreased* post-error slowing. The ERN is thought to be generated in areas of the ACC related to adaptive post-error changes in response behavior, such as improvement in response speed following an error, which suggests increases in cognitive control (Kerns et al., 2004). However, the literature on ACC activity in relation to post-error changes in behavior is inconsistent (Hester et al., 2007). Similarly, many studies found no association between the ERN and post-error slowing, although positive associations have been reported in children, adolescents, and adults (Gehring et al., 1993; Ladouceur et al., 2007; Scheffers & Coles, 2000; West & Travers, 2008) and in both between- and within-subject designs (Debener et al., 2005), indicating that a relation exists between ERN amplitude and *increased* post-error slowing. The present results suggest that a mechanism of cortisol-related post-error slowing may suppress the relationship between ERN amplitude and decreased slowing: an association between ERN and decreased slowing was only revealed after controlling for cortisol levels. Cortisol mediated a positive association between ERN amplitude and post-error slowing.

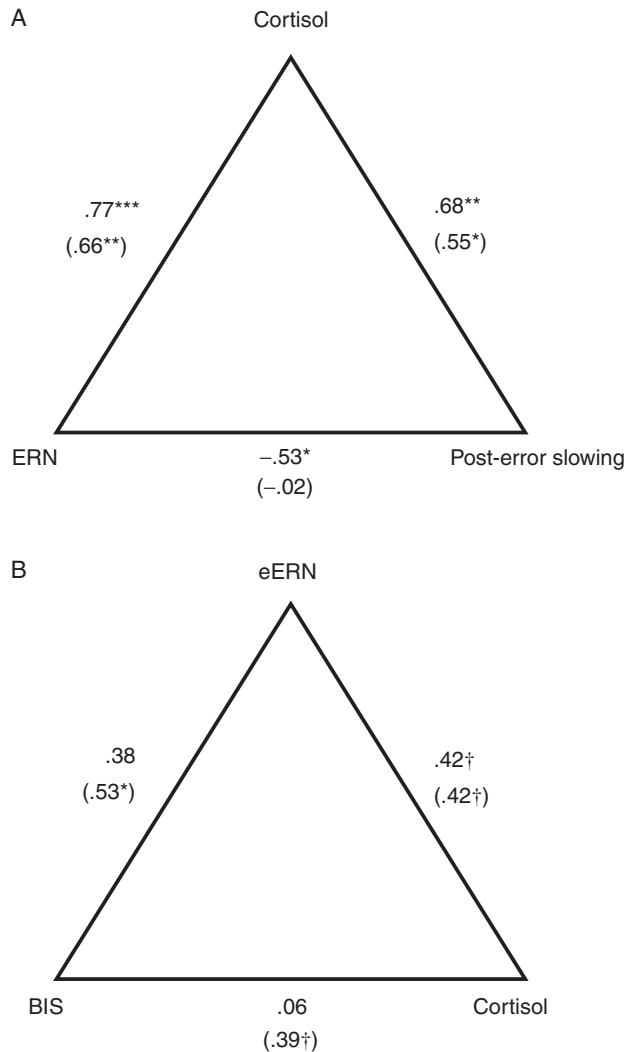


Figure 3. Pearson correlations (in parentheses) and partial correlations ($df = 15$) controlling for the effect of the third variable, between (A): ERN (amplitude on error trials minus on correct trials, inversely signed such that higher positive values mean larger amplitude), post-error slowing, and salivary cortisol; (B): BIS, salivary cortisol, and ERN amplitude on error-trials (eERN; inversely signed such that higher positive values mean larger amplitude). * $p < .05$; ** $p < .01$; *** $p < .001$; † $p < .10$.

Consistent with post-error speed being controlled or influenced not only by ACC but also by other mechanisms, post-error slowing often is not related to better accuracy; indeed, it has even been related to less efficient performance (e.g., Carp & Compton, 2009; Compton, Robinson, et al., 2008; Notebaert et al., 2009). There are indications that post-error slowing is related to orienting and arousal responses to errors, and to failure to disengage from the error (e.g., Carp & Compton, 2009; Compton, Robinson, et al., 2008). For instance, slowing occurs after unexpected events whether they are correct or erroneous responses (Notebaert et al., 2009; Núñez Castellar, Kühn, Fias, & Notebaert, 2010). Errors are followed by increased autonomic arousal (Hajcak, McDonald, & Simons, 2003; Kleiter & Schwarzenbacher, 1989), potentiated defensive startle reflex (Hajcak & Foti, 2008), and increased cortical arousal, as measured by changes in EEG alpha power (Carp & Compton, 2009). The results by Carp and

Compton (2009) indicated that, whereas after correct responses subjects transiently disengage during the intertrial period, after errors they failed to disengage, and this predicted increased post-error slowing. Indeed, depression is associated with a decrease in accuracy, increased slowing and inability to disengage after errors (Compton, Lin, et al., 2008; Tucker, Luu, Frishkoff, Quiring, & Poulsen, 2003), and ERN amplitude predicted post-error slowing only among depressed participants in a Stroop task condition involving negative words (Compton, Lin, et al., 2008). In addition, post-error slowing dramatically increased and performance became more error prone with a decreasing response stimulus interval (Dudschig & Jentsch, 2009), providing further evidence for the idea that error evaluation can produce substantial interference with subsequent trial processing, particularly when there is insufficient time between the error and the subsequent event. In contrast, in a task in which an error on a difficult “lure” trial predicted that the same lure would be repeated between two and seven trials later, such that effects of post-error failure to disengage were unlikely to interfere with performance on the next lure trial, post-error slowing was related to increased accuracy on the next lure trial (Hester et al., 2007).

By what mechanisms may cortisol increase post-error slowing and ERN amplitude? One possibility is that individuals who began the task with greater levels of cortisol were also more aroused or engaged in the task itself, which may be reflected in larger ERN amplitudes and more post-error slowing (Tops, Boksem, et al., 2006). Second, the ability of cortisol to increase dopaminergic activity may be implicated (Pruessner, Champagne, Meaney, & Dagher, 2004; Tops, van Peer, Wijers, & Korf, 2006). The ERN is thought to be generated by dopaminergic mechanisms, and ERN amplitude is increased and decreased by dopaminergic stimulants and blockers, respectively¹ (de Bruijn, Hulstijn, Verkes, Ruigt, & Sabbe, 2004; de Bruijn, Sabbe, Hulstijn, Ruigt, & Verkes, 2006; Zirnheld et al., 2004). As these manipulations left performance and post-error speed largely unaffected, they may abolish relationships between ERN amplitude and post-error slowing. At the same time, at the cortical control level, dopamine is thought to be involved in behavioral constraint and inhibition (Sallet & Rushworth, 2009; Tops, Boksem, Luu, & Tucker, 2010; Tops & Boksem, 2010; Tucker, Luu, & Pribram, 1995) and in the looping and iterative processing of old, redundant, or threatening information thought to cause post-error slowing (Kleiter & Schwarzenbacher, 1989; Tucker, Luu, & Pribram, 1995). We suggest the hypothesis that cortisol may stimulate behavioral inhibition by facilitating cortical dopaminergic function.

Alternatively, along the line of suggestions that trait ERN amplitude relates to stress reactivity or susceptibility to developing social anxiety (Cavanagh & Allen, 2008; McDermott et al., 2009), trait ERN amplitude may relate to cortisol levels. Such a relationship could be explained by the involvement of ACC and IFG/AI areas in autonomic and hormonal regulation (e.g., Critchley, 2005; Liberzon et al., 2007; Suzuki et al., 2009; Wang et al., 2005). However, those suggestions that trait ERN amplitude relates to stress reactivity or susceptibility to developing social anxiety (Cavanagh & Allen, 2008; McDermott et al., 2009) are inconsistent with a study in which ERN amplitude and error correction predicted less emotional reactivity to stress in daily life

¹It should be noted that dopaminergic agonists and antagonists appear to acutely increase and decrease plasma cortisol levels, respectively (Fuller et al., 1983; Kitchen, Kelly, & Turner, 1988).

(Compton, Robinson, et al., 2008). Perhaps relations between adaptive cognitive control and decreased emotional reactivity to stress may have higher likelihood of being detected in studies using the difference ERN measure, which reflects efficient error detection (Compton, Robinson, et al., 2008). In contrast, the likelihood of finding relations between post-error slowing, ERN, and increased stress susceptibility may be increased by differentiating individuals on the basis of variables such as behavioral inhibition or cortisol level, and by using the ERN on error trials (Cavanagh & Allen, 2008; McDermott et al., 2009). Individual differences in negative affectivity, stress reactivity, and obsessive compulsive symptom severity appear not to relate strongly to the difference ERN because they tend to relate to the ERN on correct trials as well (Endrass et al., 2008; Hajcak et al., 2004; Tops et al., 2006). Perhaps this relationship with the ERN on correct trials reflects a similar mechanism as proposed above for post-error slowing, such as a failure to disengage mechanisms of error-processing and increased accuracy bias triggered or primed by errors on previous trials. The adaptive performance monitoring function best reflected in the difference ERN may reflect the activity of cognitive dorsal ACC and related network areas implicated in proactive action control and emotion regulation, while the emotional reactive and inhibitory function best reflected in the ERN on error trials may reflect the activity of ventral/rostral ACC and related ventral networks including the IFG/AI implicated in reactive motor control (Critchley, 2005; Tops, Boksem, et al., 2010; Tucker et al., 1995).

It has been reported that post-error slowing (Jentsch & Leuthold, 2006) and ERN amplitude (Gehring et al., 1993) were larger when instruction stressed accuracy rather than speed. Post-error slowing is usually explained by strategic control adjustments towards a more conservative response threshold (Jentsch & Dudshig, 2009). Using functional magnetic resonance imaging (fMRI), Ivanoff, Branning, and Marois (2008) showed that emphasizing the speed of a perceptual decision at the expense of its accuracy lowers the amount of perceptual evidence-related activity in the IFG/AI that is gathered before responding. Moreover, this speed-accuracy difference in activity correlated with a behavioral measure of speed-accuracy difference in decision criterion. The IFG seems involved in withholding responses when increased processing is needed for accurate responses (Leitman et al., 2010), which may also be its role in slowing processes such as post-error slowing. Indeed, right IFG activation is related to post-error slowing after errors (Marco-Pallarés et al., 2008) and failures to inhibit responding (Li et al., 2008), and lesions of the right inferior frontal sulcus reduced post-error slowing (Molenberghs et al., 2009). In the study in which an error on a difficult "lure" trial predicted that the same lure would be repeated between two and seven trials later, such that effects of post-error failure to disengage were unlikely to interfere with performance on the next lure trial, post-error slowing was related to increased accuracy on the next lure trial; the slowing and the increased accuracy were predicted by activity in right IFG/AI, middle frontal gyrus, and ACC (Hester et al., 2007).

Neuroimaging studies implicate the IFG/AI in behavioral inhibition and anxiety. Authors have argued that this area is involved in the restraining of inappropriate responses (Garavan, Ross, & Stein, 1999) and judging the appropriateness of facial affect (Kim et al., 2005). Left IFG/AI has additionally been associated with dopamine release in response to negative emotional stimuli (Badgaiyan, Fischman, & Alpert, 2009). Avila

et al. (2008) presented infrequent stop signals after generating a dominant response set for reward and found activation of right IFG that seemed to antagonize activity in dopaminergic areas (the dorsal striatum and the mesial prefrontal cortex). In a reinforcement learning task, activation of IFG/AI was more pronounced for risk-averse participants, suggesting that this region also serves to inhibit risky choices (d'Acromont, Lu, Li, Van der Linden, & Bechara, 2009). The right IFG/AI has also been consistently associated with social anxiety disorder, and the AI with anxiety in general (Etkin & Wager, 2007). Of note, the insula has been implicated in the regulation of automatic arousal and neuroendocrine responses to psychological stress (Craig, 2005; Liberzon et al., 2007; Suzuki et al., 2009; Wang et al., 2005). The right IFG/AI may have an alarm function as part of its critical role in the switching between internally and externally oriented control modes (Sridharan, Levitin, & Menon, 2008) and consistently shows error-related activity (Wittfoth, Küstermann, Fahle, & Herrmann, 2008) consistent with an alarm function of error-related brain signals (Tucker et al., 2003). In short, the IFG/AI may be the interface where behavior inhibition including post-error slowing, error-processing, and cortisol regulation interact.

Starting from the developmental research by Jerome Kagan and colleagues, the physiological parameters that have classically been associated with behavioral inhibition are high cortisol levels and relative right frontal EEG activity asymmetry (Fox et al., 2005). The tendency for right lateralization of inhibition-related activity in the IFG/AI may underlie these associations. BIS scores and behavior inhibition in adults (Balconi & Mazza, 2009; Harmon-Jones & Allen, 1997; Peterson, Gable, & Harmon-Jones, 2008; Shackman, McMenamin, Maxwell, Greischar, & Davidson, 2009; Wacker, Chavanon, Leue, & Stemmler, 2008) and behavioral inhibition in children (see Fox et al., 2005) have been related to relative right frontal activity. It has been suggested that this frontal asymmetry reflects asymmetrical AI/IFG activity (Craig, 2005; Tops & Boksem, 2010; Tucker et al., 2003) and a meta-analysis of emotional faces processing found a relation between approach vs. avoidance dimensions and left vs. right IFG (Fusar-Poli et al., 2009). Indeed, a recent study using source modeling found support for activity in right IFG explaining the association between BIS scores and relative right frontal EEG activity (Shackman et al., 2009). Moreover, frontal asymmetrical activity has been related to cortisol levels (see Tops et al., 2005), and exogenous cortisol has even been found to affect this asymmetry (Tops et al., 2005; Tops, Wijers, et al., 2006; Tops, van Peer, et al., 2006).

The present study has obvious limitations and should be regarded as preliminary. All results are correlational, and no causality can be inferred. The number of subjects was small, and replication in a larger sample is warranted before firm conclusions can be drawn. Cortisol measurement depended on one saliva sample, limiting its reliability as a measure of individual differences. Moreover, associations with stress-induced cortisol responses or other measures of hypothalamus-pituitary-adrenal cortex function were not addressed. The inclusion of only female students as subjects prevents generalization to other groups such as males or childhood behavioral inhibition. On the other hand, the present study was guided by theory and replicates previous findings; furthermore, it extends and sheds new light on previously reported associations by demonstrating an association between cortisol and post-error slowing, a measure of behavioral inhibition of which brain substrates have recently been discov-

ered, and suggesting opposing influences on the relationship between the ERN and post-error slowing. Moreover, suggesting a link between cortisol, behavioral inhibition, and this brain mechanism may help integrating this literature including associations with frontal asymmetrical activity, and suggest directions for further research.

Heightened orienting towards and decreased disengagement from threat, more post-error slowing, and larger ERN magnitude seem to characterize people who stay behaviorally inhibited from childhood into adulthood and have an increased likelihood of developing a social anxiety disorder (Fox, 2010). Fox (2010) proposed that behaviorally inhibited individuals are highly concerned over making mistakes, and that this overconcern (and perhaps their history in receiving negative feedback in certain

situations) contributes to the emergence of heightened anxiety. Individual differences in concern over mistakes has been related to social concerns, increased attention focused on the mistake, a sense of pressure to overcome the mistake, difficulty disengaging from the mistake, and difficulty concentrating (see Frost et al., 1997). The associations between cortisol, post-error slowing, ERN, and BIS warrant further investigation of the involvement of brain systems of behavioral inhibition that may include the IFG/AI. Better understanding of such systems may generate options for treatment and prevention of anxiety disorders (McDermott et al., 2009). Moreover, we think the results are relevant, not only for researchers of behavioral inhibition, but for researchers of the basic mechanisms of the ERN and post-error slowing as well, and may bring those literatures closer together.

REFERENCES

- Amodio, D. M., Master, S. L., Yee, C. M., & Taylor, S. E. (2008). Neurocognitive components of the behavioral inhibition and activation systems: Implications for theories of self-regulation. *Psychophysiology*, *45*, 11–19.
- Aron, A. R., Robbins, T. W., & Poldrack, R. A. (2004). Inhibition and the right inferior frontal cortex. *Trends in Cognitive Science*, *8*, 170–177.
- Avila, C., Parcet, M. A., & Barrós-Loscertales, A. (2008). A cognitive neuroscience approach to individual differences in sensitivity to reward. *Neurotoxicity Research*, *14*, 191–203.
- Badgaiyan, R. D., Fischman, A. J., & Alpert, N. M. (2009). Dopamine release during human emotional processing. *NeuroImage*, *47*, 2041–2045.
- Balconi, M., & Mazza, G. (2009). Lateralisation effect in comprehension of emotional facial expression: A comparison between EEG alpha band power and behavioral inhibition (BIS) and activation (BAS) systems. *Laterality*, *17*, 1–24.
- Balconi, M., & Crivelli, D. (2010). FRN and P300 ERP effect modulation in response to feedback sensitivity: The contribution of punishment-reward system (BIS/BAS) and behavior identification of action. *Neuroscience Research*, *66*, 162–172.
- Boksem, M. A., Meijman, T. F., & Lorist, M. M. (2006). Mental fatigue, motivation and action monitoring. *Biological Psychology*, *72*, 123–132.
- Boksem, M. A. S., Tops, M., Wester, A. E., Meijman, T. F., & Lorist, M. M. (2006). Error related ERP components and individual differences in punishment and reward sensitivity. *Brain Research*, *1101*, 92–101.
- Boksem, M. A. S., Tops, M., Kostermans, E., & De Cremer, D. (2008). Sensitivity to punishment and reward omission: Evidence from error-related ERP components. *Biological Psychology*, *79*, 185–192.
- Carp, J., & Compton, R. J. (2009). Alpha power is influenced by performance errors. *Psychophysiology*, *46*, 336–343.
- Carver, C. S., & White, T. L. (1994). Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: The BIS/BAS scales. *Journal of Personality and Social Psychology*, *67*, 319–333.
- Cavanagh, J. F., & Allen, J. J. (2008). Multiple aspects of the stress response under social evaluative threat: An electrophysiological investigation. *Psychoneuroendocrinology*, *33*, 41–53.
- Chikazoe, J., Konishi, S., Asari, T., Jimura, K., & Miyashita, Y. (2007). Activation of right inferior frontal gyrus during response inhibition across response modalities. *Journal of Cognitive Neuroscience*, *19*, 69–80.
- Compton, R. J., Lin, M., Vargas, G., Carp, J., Fineman, S. L., & Quandt, L. C. (2008). Error detection and posterror behavior in depressed undergraduates. *Emotion*, *8*, 58–67.
- Compton, R. J., Robinson, M. D., Ode, S., Quandt, L. C., Fineman, S. L., & Carp, J. (2008). Error-monitoring ability predicts daily stress regulation. *Psychological Science*, *19*, 702–708.
- Craig, A. D. (2005). Forebrain emotional asymmetry: A neuro-anatomical basis? *Trends in Cognitive Science*, *9*, 566–571.
- Critchley, H. D. (2005). Neural mechanisms of autonomic, affective, and cognitive integration. *Journal of Comparative Neurology*, *493*, 154–166.
- d'Acremont, M., Lu, Z. L., Li, X., Van der Linden, M., & Bechara, A. (2009). Neural correlates of risk prediction error during reinforcement learning in humans. *NeuroImage*, *47*, 1929–1939.
- Debener, S., Ullsperger, M., Siegel, M., Fiehler, K., von Cramon, D. Y., & Engel, A. K. (2005). Trial-by-trial coupling of concurrent electroencephalogram and functional magnetic resonance imaging identifies the dynamics of performance monitoring. *Journal of Neuroscience*, *25*, 11730–11737.
- de Bruijn, E. R., Hulstijn, W., Verkes, R. J., Ruigt, G. S., & Sabbe, B. G. (2004). Drug-induced stimulation and suppression of action monitoring in healthy volunteers. *Psychopharmacology*, *177*, 151–160.
- de Bruijn, E. R., Sabbe, B. G., Hulstijn, W., Ruigt, G. S., & Verkes, R. J. (2006). Effects of antipsychotic and antidepressant drugs on action monitoring in healthy volunteers. *Brain Research*, *1105*, 122–129.
- De Pascalis, V., Varriale, V., & D'Antuono, L. (2010). Event-related components of the punishment and reward sensitivity. *Clinical Neurophysiology*, *121*, 60–76.
- Dressendörfer, R. A., Kirschbaum, C., Rohde, W., Stahl, F., & Strasburger, C. J. (1992). Synthesis of a cortisol-biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. *Journal of Steroid Biochemistry and Molecular Biology*, *43*, 683–692.
- Dudschig, C., & Jentsch, I. (2009). Speeding before and slowing after errors: Is it all just strategy? *Brain Research*, *1296*, 56–62.
- Endrass, T., Klawohn, J., Schuster, F., & Kathmann, N. (2008). Overactive performance monitoring in obsessive-compulsive disorder: ERP evidence from correct and erroneous reactions. *Neuropsychologia*, *46*, 1877–1887.
- Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of target letters in visual search. *Perception and Psychophysics*, *16*, 142–149.
- Etkin, A., & Wager, T. D. (2007). Functional neuroimaging of anxiety: A meta-analysis of emotional processing in PTSD, social anxiety disorder, and specific phobia. *American Journal of Psychiatry*, *164*, 1476–1488.
- Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1990). Effects of errors in choice reaction tasks on the ERP under focused and divided attention. In C. H. M. Brunia & A. W. K. Gaillard (Eds.), *Psychophysiological brain research* (pp. 192–195). Tilburg: Tilburg University Press.
- Fox, N. A., Henderson, H. A., Marshall, P. J., Nichols, K. E., & Ghera, M. M. (2005). Behavioral inhibition: Linking biology and behavior within a developmental framework. *Annual Review of Psychology*, *56*, 235–262.
- Fox, N. A. (2010). Factors contributing to the emergence of anxiety among behaviorally inhibited children: The role of attention. In H. Gazelle & K. H. Rubin (Eds.), *Social anxiety in childhood: Bridging developmental and clinical perspectives*. *New Directions in Child and Adolescent Development*, *127*, 33–49.

- Franken, I. H. A., Muris, P., & Rassin, E. (2005). Psychometric properties of the Dutch BIS/BAS scales. *Journal of Psychopathological Behavioral Assessment, 27*, 25–30.
- Frost, R. O., Lynn Trepanier, K., Brown, E. J., Heimberg, R. G., Juster, H. R., Makris, G. S., & Leung, A. W. (1997). Self-monitoring of mistakes among subjects high and low in perfectionistic concern over mistakes. *Cognitive Therapy and Research, 21*, 209–222.
- Fuller, R. W., Snoddy, H. D., Mason, N. R., Clemens, J. A., & Bemis, K. G. (1983). Elevation of serum corticosterone in rats by dopamine agonists related in structure to pergolide. *Neuroendocrinology, 36*, 285–290.
- Fusar-Poli, P., Placentino, A., Carletti, F., Allen, P., Landi, P., Abbamonte, M., et al. (2009). Laterality effect on emotional faces processing: ALE meta-analysis of evidence. *Neuroscience Letters, 452*, 262–267.
- Garavan, H., Ross, T. J., & Stein, E. A. (1999). Right hemispheric dominance of inhibitory control: An event-related functional MRI study. *Proceedings of the National Academy of Sciences, 96*, 8301–8306.
- Gehring, W. J., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1990). The error-related negativity: An event-related brain potential accompanying errors. *Psychophysiology, 27*, S34.
- Gehring, W. J., Goss, B., Coles, M. G. H., Meyer, D. E., & Donchin, E. (1993). A neural system for error detection and compensation. *Psychological Science, 4*, 385–390.
- Gratton, G., Coles, M. G., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. *Electroencephalography and Clinical Neurophysiology, 55*, 468–484.
- Gray, J. A. (1982). *The neuropsychology of anxiety*. New York: Oxford University Press.
- Gray, J. A. (1989). Fundamental systems of emotion in the mammalian brain. In D. S. Palermo (Ed.), *Coping with uncertainty: Behavioral and developmental perspectives* (pp. 173–195). Hillsdale, NJ: Lawrence Erlbaum.
- Gray, J. A., & McNaughton, N. (2000). *The neuropsychology of anxiety*. Oxford, England: Oxford University Press.
- Gupta, R., Kar, B. R., & Srinivasan, N. (2009). Development of task switching and post-error-slowness in children. *Behavioral and Brain Functions, 5*, 38.
- Hajcak, G., McDonald, N., & Simons, R. F. (2003). To err is automatic: Error-related brain potentials, ANS activity, and post-error compensatory behavior. *Psychophysiology, 40*, 895–903.
- Hajcak, G., McDonald, N., & Simons, R. F. (2004). Error-related psychophysiology and negative affect. *Brain and Cognition, 56*, 189–197.
- Hajcak, G., Moser, J. S., Yeung, N., & Simons, R. F. (2005). On the ERN and the significance of errors. *Psychophysiology, 42*, 151–160.
- Hajcak, G., & Foti, D. (2008). Errors are aversive: Defensive motivation and the error-related negativity. *Psychological Science, 19*, 103–108.
- Harmon-Jones, E., & Allen, J. J. (1997). Behavioral activation sensitivity and resting frontal EEG asymmetry: Covariation of putative indicators related to risk for mood disorders. *Journal of Abnormal Psychology, 106*, 159–163.
- Hester, R., Barre, N., Mattingley, J. B., Foxe, J. J., & Garavan, H. (2007). Avoiding another mistake: Error and posterror neural activity associated with adaptive posterror behavior change. *Cognitive Affective and Behavioral Neuroscience, 7*, 317–326.
- Holroyd, C. B., & Coles, M. G. (2002). The neural basis of human error processing: Reinforcement learning, dopamine, and the error-related negativity. *Psychological Review, 109*, 679–709.
- Ivanoff, J., Branning, P., & Marois, R. (2008). fMRI evidence for a dual process account of the speed-accuracy tradeoff in decision-making. *PLoS One, 3*, e2635.
- Jentsch, I., & Leuthold, H. (2006). Control over speeded actions: A common processing locus for micro- and macro-trade-offs? *Quarterly Journal of Experimental Psychology, 59*, 1329–1337.
- Jentsch, I., & Dudschig, C. (2009). Why do we slow down after an error? Mechanisms underlying the effects of posterror slowing. *Quarterly Journal of Experimental Psychology, 62*, 209–218.
- Kerns, J. G., Cohen, J. D., MacDonald, A. W. 3rd, Cho, R. Y., Stenger, V. A., & Carter, C. S. (2004). Anterior cingulate conflict monitoring and adjustments in control. *Science, 303*(5660), 1023–1026.
- Kim, J. W., Kim, J. J., Jeong, B. S., Ki, S. W., Im, D. M., Lee, S. J., & Lee, H. S. (2005). Neural mechanism for judging the appropriateness of facial affect. *Brain Research Cognitive Brain Research, 25*, 659–667.
- Kitchen, I., Kelly, M., & Turner, M. (1988). Dopamine receptor modulation of corticosterone secretion in neonatal and adult rats. *Journal of Pharmacy and Pharmacology, 40*, 580–581.
- Kleider, G. D., & Schwarzenbacher, K. (1989). Beyond the answer: Post-error processes. *Cognition, 32*, 255–277.
- Kopp, B., Rist, F., & Mattler, U. (1996). N200 in the flanker task as a neurobehavioral tool for investigating executive control. *Psychophysiology, 33*, 282–294.
- Ladouceur, C. D., Dahl, R. E., & Carter, C. S. (2007). Development of action monitoring through adolescence into adulthood: ERP and source localization. *Developmental Science, 10*, 874–891.
- Larson, M. J., Fair, J. E., Good, D. A., & Baldwin, S. A. (2010). Empathy and error processing. *Psychophysiology, 47*, 415–424.
- Leitman, D. I., Wolf, D. H., Ragland, J. D., Laukka, P., Loughead, J., Valdez, J. N., et al. (2010). “It’s not what you say, but how you say it”: A reciprocal temporo-frontal network for affective prosody. *Frontiers in Human Neuroscience, 4*, 19. Retrieved from <http://www.ncbi.nlm.nih.gov/pubmed>.
- Li, C. S., Huang, C., Yan, P., Paliwal, P., Constable, R. T., & Sinha, R. (2008). Neural correlates of post-error slowing during a stop signal task: A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 20*, 1021–1029.
- Liberzon, I., King, A. P., Britton, J. C., Phan, K. L., Abelson, J. L., & Taylor, S. F. (2007). Paralimbic and medial prefrontal cortical involvement in neuroendocrine responses to traumatic stimuli. *American Journal of Psychiatry, 164*, 1250–1258.
- Luu, P., Collins, P., & Tucker, D. M. (2000). Mood, personality, and self-monitoring: Negative affect and emotionality in relation to frontal lobe mechanisms of error monitoring. *Journal of Experimental Psychology General, 129*, 43–60.
- MacKinnon, D. P., Krull, J. L., & Lockwood, C. M. (2000). Equivalence of the mediation, confounding and suppression effect. *Prevention Science, 1*, 173–181.
- MacKinnon, D. P., Lockwood, C. M., Hoffman, J. M., West, S. G., & Sheets, V. (2002). A comparison of methods to test mediation and other intervening variable effects. *Psychological Methods, 7*, 83–104.
- Marco-Pallarés, J., Camara, E., Münte, T. F., & Rodríguez-Fornells, A. (2008). Neural mechanisms underlying adaptive actions after slips. *Journal of Cognitive Neuroscience, 20*, 1595–1610.
- McDermott, J. M., Perez-Edgar, K., Henderson, H. A., Chronis-Tuscano, A., Pine, D. S., & Fox, N. A. (2009). A history of childhood behavioral inhibition and enhanced response monitoring in adolescence are linked to clinical anxiety. *Biological Psychiatry, 65*, 445–448.
- McNaughton, N., & Corr, P. J. (2004). A two-dimensional neuropsychology of defense: Fear/anxiety and defensive distance. *Neuroscience and Biobehavioral Reviews, 28*, 285–305.
- Molenberghs, P., Gillebert, C. R., Schoofs, H., Dupont, P., Peeters, R., & Vandenbergh, R. (2009). Lesion neuroanatomy of the Sustained Attention to Response task. *Neuropsychologia, 47*, 2866–2875.
- Notebaert, W., Houtman, F., Opstal, F. V., Gevers, W., Fias, W., & Verguts, T. (2009). Post-error slowing: An orienting account. *Cognition, 111*, 275–279.
- Núñez Castellar, E., Kühn, S., Fias, W., & Notebaert, W. (2010). Outcome expectancy and not accuracy determines posterror slowing: ERP support. *Cognitive Affective and Behavioral Neuroscience, 10*, 270–278.
- Peterson, C. K., Gable, P., & Harmon-Jones, E. (2008). Asymmetrical frontal ERPs, emotion, and behavioral approach/inhibition sensitivity. *Social Neuroscience, 3*, 113–124.
- Pruessner, J. C., Champagne, F., Meaney, M. J., & Dagher, A. (2004). Dopamine release in response to a psychological stress in humans and its relationship to early life maternal care: A positron emission tomography study using [¹¹C]raclopride. *Journal of Neuroscience, 24*, 2825–2831.
- Putman, P., Hermans, E. J., & van Honk, J. (2007). Exogenous cortisol shifts a motivated bias from fear to anger in spatial working memory for facial expressions. *Psychoneuroendocrinology, 32*, 14–21.
- Rabbitt, P. M. A. (1966). Errors and error correction in choice-response tasks. *Journal of Experimental Psychology, 71*, 264–272.
- Roelofs, K., Elzinga, B. M., & Rottevel, M. (2005). The effects of stress-induced cortisol responses on approach-avoidance behavior. *Psychoneuroendocrinology, 30*, 665–677.
- Roelofs, K., van Peer, J., Berretty, E., Jong, P., Spinhoven, P., & Elzinga, B. M. (2009). Hypothalamus-pituitary-adrenal axis hyperresponsive-

- ness is associated with increased social avoidance behavior in social phobia. *Biological Psychiatry*, *65*, 336–343.
- Sallet, J., & Rushworth, M. F. S. (2009). Should I stay or should I go: Genetic bases for uncertainty-driven exploration. *Nature Neuroscience*, *12*, 963–965.
- Scheffers, M. K., & Coles, M. G. H. (2000). Performance monitoring in a confusing world: Error-related brain activity, judgments of response accuracy, and types of errors. *Journal of Experimental Psychology: Human Perception and Performance*, *26*, 141–151.
- Schmidt, L. A., Fox, N. A., Goldberg, M. C., Smith, C. C., & Schulkin, J. (1999). Effects of acute prednisone administration on memory, attention and emotion in healthy human adults. *Psychoneuroendocrinology*, *24*, 461–483.
- Shackman, A. J., McMenamin, B. W., Maxwell, J. S., Greischar, L. L., & Davidson, R. J. (2009). Right dorsolateral prefrontal cortical activity and behavioral inhibition. *Psychological Science*, *20*, 1500–1506.
- Shafritz, K. M., Collins, S. H., & Blumberg, H. P. (2006). The interaction of emotional and cognitive neural systems in emotionally guided response inhibition. *NeuroImage*, *31*, 468–475.
- Sridharan, D., Levitin, D. J., & Menon, V. (2008). A critical role for the right fronto-insular cortex in switching between central-executive and default-mode networks. *Proceedings of the National Academy of Sciences*, *105*, 12569–12574.
- Stahl, J., & Gibbons, H. (2007). Dynamics of response-conflict monitoring and individual differences in response control and behavioral control: An electrophysiological investigation using a stop-signal task. *Clinical Neurophysiology*, *118*, 581–596.
- Stone, A., Connolly, C., Wynne, C., Alhusaini, S., & Garavan, H. (2009). Common and unique aspects of impulsivity: The neural correlates of inhibiting rewards, responses and emotions. Poster presented at the Organization of Human Brain Mapping 15th Annual Meeting, June 18–23, 2009, San Francisco, California.
- Suzuki, H., Watanabe, S., Hamaguchi, T., Mine, H., Terui, T., Kanazawa, M., Oohisa, N., Maruyama, M., Yambe, T., Itoh, T., & Fukudo, H. S. (2009). Brain activation associated with changes in heart rate, heart rate variability, and plasma catecholamines during rectal distention. *Psychosomatic Medicine*, *71*, 619–626.
- Tops, M., van der Pompe, G., Baas, D., Mulder, L. J. M., den Boer, J. A., Meijman, T. F., & Korf, J. (2003). Acute cortisol effects on immediate free recall and recognition of nouns depend on stimulus valence. *Psychophysiology*, *40*, 167–173.
- Tops, M., van der Pompe, G., Wijers, A. A., den Boer, J. A., Meijman, T. F., & Korf, J. (2004). Free recall of pleasant words from recency positions is especially sensitive to acute administration of cortisol. *Psychoneuroendocrinology*, *29*, 327–338.
- Tops, M. (2004). *Inhibition of approach: Cortisol-mediated mechanisms in affect and depression*. Doctoral thesis, University of Groningen.
- Tops, M., Wijers, A. A., van Staveren, A. S. J., Bruin, K. J., den Boer, J. A., Meijman, T. F., & Korf, J. (2005). Acute cortisol administration modulates EEG alpha asymmetry in volunteers: Relevance to depression. *Biological Psychology*, *69*, 181–193.
- Tops, M., Wijers, A. A., Koch, T., & Korf, J. (2006). Modulation of rotational behavior in healthy volunteers by cortisol administration. *Biological Psychology*, *71*, 240–243.
- Tops, M., van Peer, J. M., Wester, A. E., Wijers, A. A., & Korf, J. (2006). State-dependent regulation of cortical activity by cortisol: An EEG study. *Neuroscience Letters*, *404*, 39–43.
- Tops, M., Boksem, M. A. S., Wester, A. E., Lorist, M. M., & Meijman, T. F. (2006). Task engagement and the relationships between the error-related negativity, agreeableness, behavioral shame proneness and cortisol. *Psychoneuroendocrinology*, *31*, 847–858.
- Tops, M., van Peer, J. M., Wijers, A. A., & Korf, J. (2006). Acute cortisol administration reduces subjective fatigue in healthy female subjects. *Psychophysiology*, *43*, 653–656.
- Tops, M., Boksem, M. A. S., Luu, P., & Tucker, D. M. (2010). Brain substrates of behavioral programs associated with self-regulation. *Frontiers in Psychology*. DOI:10.3389/fpsyg.2010.00152.
- Tops, M., & Boksem, M. A. S. (2010). Absorbed in the task: Personality measures predict engagement during task performance as tracked by error negativity and asymmetrical frontal activity. *Cognitive Affective and Behavioral Neuroscience*, in press.
- Tucker, D. M., Luu, P., & Pribram, K. H. (1995). Social and emotional self-regulation. *Annals of the New York Academy of Sciences*, *769*, 213–239.
- Tucker, D. M., Luu, P., Frishkoff, G., Quiring, J., & Poulsen, C. (2003). Frontolimbic response to negative feedback in clinical depression. *Journal of Abnormal Psychology*, *112*, 667–678.
- van Honk, J., Tuiten, A., van den Hout, M., Koppeschaar, H., Thijssen, J., de Haan, E., & Verbaten, R. (1998). Baseline salivary cortisol levels and preconscious selective attention for threat. A pilot study. *Psychoneuroendocrinology*, *23*, 741–747.
- van Honk, J., Schutter, D. J., Hermans, E. J., & Putman, P. (2003). Low cortisol levels and the balance between punishment sensitivity and reward dependency. *NeuroReport*, *14*, 1993–1996.
- van Peer, J. M., Roelofs, K., Rotteveel, M., van Dijk, J. G., Spinhoven, P., & Ridderinkhof, K. R. (2007). The effects of cortisol administration on approach-avoidance behavior: An event-related potential study. *Biological Psychology*, *76*, 135–146.
- Wacker, J., Chavanon, M. L., Leue, A., & Stemmler, G. (2008). Is running away right? The behavioral activation-behavioral inhibition model of anterior asymmetry. *Emotion*, *8*, 232–249.
- Wang, J., Rao, H., Wetmore, G. S., Furlan, P. M., Korczykowski, M., Dinges, D. F., & Detre, J. A. (2005). Perfusion functional MRI reveals cerebral blood flow pattern under psychological stress. *Proceedings of the National Academy of Sciences USA*, *102*, 17804–17809.
- West, R., & Travers, S. (2008). Tracking the temporal dynamics of updating cognitive control: An examination of error processing. *Cerebral Cortex*, *18*, 1112–1124.
- Wittfoth, M., Küstermann, E., Fahle, M., & Herrmann, M. (2008). The influence of response conflict on error processing: Evidence from event-related fMRI. *Brain Research*, *1194*, 118–129.
- Zirnheld, P. J., Carroll, C. A., Kieffaber, P. D., O'Donnell, B. F., Shekhar, A., & Hetrick, W. P. (2004). Haloperidol impairs learning and error-related negativity in humans. *Journal of Cognitive Neuroscience*, *16*, 1098–1112.

(RECEIVED April 19, 2010; ACCEPTED July 23, 2010)

[Correction added after online publication September 29, 2010: an incorrect version of Figure 2 was published. The corrected version appears here.]