Available online at www.sciencedirect.com

SCIENCE DIRECT®

International Journal of Psychophysiology 55 (2005) 127–129

INTERNATIONAL JOURNAL OF PSYCHOPHYSIOLOGY

www.elsevier.com/locate/ijpsycho

Letter to the Editor

Salivary cortisol levels and the coupling of midfrontal delta–beta oscillations

Sir:

Experts in the field of electroencephalography (EEG) have suggested that different frequency bands are related to distinct functional processing properties of the brain (e.g., Başar et al., 2001; Gruzelier, 2001). Interestingly in this respect, recent publications in the *International Journal of Psychophysiology* on evolutionary accounts of human brain development have suggested phylogenetically distinct subcortical and cortical brain systems (Maclean, 1985) that relate to delta (1–3 Hz) and beta (13–30 Hz) oscillations in the EEG spectrum. In these frameworks, enhanced subcortical–cortical coupling reflecting increased inter-regional cross-talk predicts behavioral inhibition and anxiety (Knyazev and Slobodskaya, 2003; Knyazev et al., 2004). Moreover, Knyazev and co-workers have repeatedly demonstrated this hypothesized relationship between stress-related indices of behavior (i.e., behavioral inhibition and anxiety) and enhanced subcortical–cortical cross-talk as indexed by brain oscillations in the EEG spectrum. Neuro-endocrinological support for the framework was recently provided by Schutter and Van Honk (2004), who demonstrated subcortical–cortical (beta–delta) decoupling after administering testosterone to healthy volunteers. This decoupling is in line with the behavioral disinhibitory and anxiolytic properties of the steroid hormone testosterone, as it reflects a shift in motivational brain state from behavioral inhibition towards behavioral activation. Notably, testosterone is the end-product of the hypothalamic–pituitary–gonadal (HPG) axis, while cortisol, the steroid hormone directly associated with behavioral inhibition and anxiety, is the end-product of the hypothalamic–pituitary–adrenal (HPA) axis. Notably, Viau (2002) has postulated an antagonistic endocrine system in which cortisol and testosterone inhibit activity of the HPG and HPA axis, respectively. Steroid hormones can evidently influence neural cross-talk (Hausmann and Güntürkün, 2000; Schutter and Van Honk, 2004), and as mentioned cortisol is an endocrinological marker for behavioral inhibition and anxiety. From the framework above, it can therefore be hypothesized that high levels of cortisol should be associated with enhanced cortical–subcortical cross-talk. To investigate this hypothesis, a salivary sample was collected from 30 non-smoking healthy volunteers (19–25 years)[1] between 1300 and 1700 h to assess baseline cortisol levels. The issue whether cortisol measured at a single point in time can reflect a baseline tonic level has been debated, because of the diurnal rhythm of this steroid hormone. In the present study, the samples were collected in the above noted time window to minimize the effect of circadian hormonal rhythm. This method has abundantly been applied and proven successful in revealing relations between cortisol and emotional behavior (e.g., Putman et al., 2004; Van Honk et al., 1998). After collecting the salivary sample, participants were prepared for the EEG

[1] The subject sample was used in an earlier study (Van Honk et al., 2002) and drawn from a large population comprising of 525 students at the Utrecht University. The selection of this subject sample was based upon the self-reported behavioral inhibition and behavioral activation scales (Carver and White, 1994). Since statistical analyses revealed no relationship whatsoever between these self-reports and basal cortisol levels [$r(30)=0.74$: $p=0.72$], which supports the notion that phenomenological and endocrinological indices of behavior occupy different dimensions in the motivational space (Schultheiss and Rhode, 2002; Van Honk et al., 2004), the present report only addresses the hypothesized relationship between cortisol and cortical–subcortical cross-talk.

0167-8760/$ - see front matter
doi:10.1016/j.ijpsycho.2004.07.003

recording and seated in a comfortable chair in a dimly lit room. A 4-min resting EEG baseline recording from the frontal, Fp1, Fp2, F3, F4 and Fz electrode sites was obtained (impedance: <5000 Ω, sampling rate: 250 Hz, amplification: 20000). Raw EEG data were corrected for horizontal and vertical eye movements using linear regression. EEG signals containing residual muscle movements, or other forms of artifacts, greater than −50 and +50 μV were rejected prior to further analysis. The designation of an artifact in one of the leads resulted in removal of that epoch for all channels in order to ensure that the remaining data were identical for all sites in time. Next, 1024-s chunks of averaged artifact-free EEG were extracted through a Hamming window (length 10%) to reduce spurious estimates of spectral power (μV^2) in the 1 Hz frequency bins for each electrode site. For the Fz electrode, spectral power values were averaged across all epochs within a single baseline and were then transformed to power density values for the delta (1–3 Hz) and beta (13–30 Hz) frequency bands.

Salivary cortisol levels were determined without extraction at the Department of Endocrinology of Utrecht University using an in-house competitive radio-immunoassay (RIA) employing a polyclonal anticortisol-antibody (K7348). Following chromatographic verification of its purity, 1,2-^{3}H(*N*)-hydrocortisone (NET 185, NEN-Dupont, Dreiech, Germany) was used as a tracer. The lower limit for detection is 0.5 nmol/l and reference values for adults are 4–28 nmol/l. Due to apparatus failure, EEG data of one subject was lost. In addition, baseline cortisol levels of three subjects could not be determined due to contaminated salivary samples. A median split on baseline cortisol levels was applied and the non-parametric Spearman rank-order correlation between delta and beta power was calculated for the low and high baseline cortisol groups and tested for significant group difference. Alpha level of significance was set at 0.05 (two-tailed) throughout. In accordance with the hypothesis, midfrontal delta–beta coupling was significant for the high cortisol group [rho(13)=0.76: p=0.002], whereas midfrontal delta–beta decoupling was observed in the low cortisol group [rho(13)=0.06: p=0.84]. For the neuroendocrinological measurements, the difference between the delta–beta coupling and decoupling reached statistical significance [Z=2.10: p<0.02]. In Fig. 1, the midfrontal delta–beta decoupling and coupling for the low and high cortisol groups, respectively, are depicted.

The present findings suggest that cortisol enhances the overall information exchange between subcortical and cortical brain regions. The interdependence of the delta and beta oscillations we observed seems to reveal steroid hormone-mediated electrophysiological properties associated with functional motivational brain states. Cortisol defensibly strengthens cortical control over subcortical drives, which provides an explanation for the recently observed relationship between cortisol and anxious non-risky decision-making strategies (Van Honk et al., 2003). Testoster-

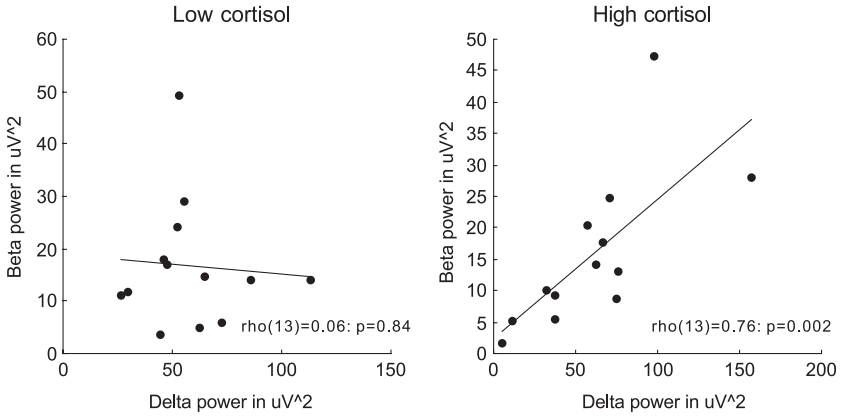

Fig. 1. Significant midfrontal delta–beta coupling in the high cortisol group, whereas the low cortisol group displays midfrontal delta–beta decoupling.

one might in this respect be associated with non-anxious risky decision-making strategies, and this was in fact recently observed in a placebo-controlled testosterone administration design (Van Honk et al., 2004). Knyazev and Slobodskaya (2003) furthermore argued that the anxious or behavioral inhibited personality style goes accompanied by so-called descending inhibition (DI), wherein the cortical systems control the subcortical systems. The concept of DI fits with Davidson (2002) suggestion that the prefrontal cortex inhibits the amygdala in states of behavioral inhibition or anxiety. Neuroimaging studies by Phillips et al. (2003) have indeed provided evidence for cortical regulation of subcortical affective circuits, stressing the notion that the higher-order brain regions constrain the lower in an attempt to control inappropriate affect. In conclusion, the current findings indicate an important role for steroid hormones in modulating cortical–subcortical cross-talk and add to the evidence for Knyazev's evolutionary account on the relations between motivation, emotion and brain oscillations.

Acknowledgment

This work was sponsored by an Innovational Research Grant (#016-005-060) from the Netherlands Organization for Scientific Research (NWO).

References

Başar, E., Başar-Eroglu, C., Karakaş, S., Schürmann, M., 2001. Gamma, alpha, delta, and theta oscillations govern cognitive processes. Int. J. Psychophysiol. 39, 241–248.

Carver, C.S., White, T.L., 1994. Behavioral inhibition, behavioral activation, and affective responses to impending reward and punishment: the BIS/BAS scale. J. Pers. Soc. Psychol. 67, 319–333.

Davidson, R.J., 2002. Anxiety and affective style: role of the prefrontal cortex and amygdala. Biol. Psychiatry 51, 68–80.

Gruzelier, J.H., 2001. New advances in EEG and cognition. Int. J. Psychophysiol. 24, 1–5.

Hausmann, M., Güntürkün, O., 2000. Steroid fluctuations modify functional cerebral asymmetries: the hypothesis of progesterone-mediated interhemispheric decoupling. Neuropsychologia 38, 1362–1374.

Knyazev, G.G., Slobodskaya, H.R., 2003. Personality trait of behavioral inhibition is associated with oscillatory systems reciprocal relationships. Int. J. Psychophysiol. 48, 247–261.

Knyazev, G.G., Savostyanov, A.N., Levin E.A., 2004. Alpha oscillations as a correlate of trait anxiety. Int. J. Psychophysiol. 53, 147–160.

Maclean, P.D., 1985. Brain evolution relating to family, play, and the separation call. Arch. Gen. Psychiatry 42, 405–417.

Phillips, M.L., Drevets, W.C., Rauch, S.L., Lane, R., 2003. Neurobiology of emotion perception: I. The neural basis of normal emotion perception. Biol. Psychiatry 54, 504–514.

Putman, P., Van Honk, J., Kessels, R.P.C., Mulder, M., Koppeschaar, H.P.F., 2004. Salivary cortisol and short and long-term memory for emotional faces in healthy young women. Psychoneuroendocrinology 29, 953–960.

Schultheiss, O.C., Rhode, W., 2002. Implicit power motivation predicts men's testosterone changes and implicit learning in a contest situation. Horm. Behav. 41, 195–202.

Schutter, D.J.L.G., Van Honk, J., 2004. Decoupling of midfrontal delta–beta oscillations after testosterone administration. Int. J. Psychophysiol. 53, 71–73.

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., Hermans, E.J., Putman, E., Montagne, B., Schutter, D.J.L.G., 2002. Defective somatic markers in sub-clinical psychopathy. NeuroReport 13, 1025–1027.

Van Honk, J., Schutter, D.J.L.G., Hermans, E.J., Putman, P., 2003. Low cortisol levels and the balance between punishment sensitivity and reward dependency. NeuroReport 14, 1993–1996.

Van Honk, J., Schutter, D.J.L.G., Hermans, E.J., Putman, P., Tuiten, A., Koppeschaar, H.P.F., 2004. Testosterone shifts the balance between sensitivity for punishment and reward in healthy young women. Psychoneuroendocrinology 29, 937–943.

Viau, V., 2002. Functional cross-talk between the hypothalamic–pituitary–gonadal and –adrenal axes. J. Neuroendocrinol. 14, 506–513.

Dennis J.L.G. Schutter*
Jack van Honk
Affective Neuroscience Section, Department of Psychonomics, Helmholtz Research Institute, Utrecht University, Heidelberglaan 2, 3584 CS Utrecht, The Netherlands
E-mail address: D.Schutter@fss.uu.nl.
*Corresponding author. Tel.: +31 30 2534369; fax: +31 30 2534511.

1 June 2004