ORIGINAL ARTICLE

Chaotic neural response during conflicting Stroop task reflects the level of serum cortisol in patients with unipolar depression

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Submitted: 2007-02-13 *Accepted: 2007-02-25*

Key words: **depression; stress; HRV; Lyapunov exponent; chaos; cortisol**

Neuroendocrinol Lett 2007; **28**(2):106–109 **PMID:** 17435679 NEL280207A01 **www.nel.edu**

Abstract

OBJECTIVE: According to recent findings detecting a cognitive conflict is related to activation of anterior cingulate cortex (ACC) and central autonomic network. Several recent findings also suggest the hypothesis that the cognitive conflict is related to specific nonlinear chaotic changes of the neural signal. This conflict related activation elicits autonomic responses which can be assessed by psychophysiological measures such as heart rate variability calculated as beat to beat R-R intervals (RRI).
METHOD: The present study used Stroop word-colour test as an experimental approach to psychophysiological study of cognitive conflict in connection with RRI measurement, assessment of serum cortisol and calculation of largest Lyapunov exponents in nonlinear data analysis of RRI time series in 30 patients with unipolar depression.
RESULTS: Significant correlation –0.45 ($p<0.01$) between largest Lyapunov exponents during conflicting Stroop task and serum cortisol levels has been found.
CONCLUSIONS: The study indicates that a defect of neural inhibition during conflicting Stroop task is closely related to decreased serum cortisol levels which probably reflect defense psychological mechanisms.

INTRODUCTION

According to recent findings the higher cortical functions participating in attentional mechanisms may constitute a way of resolving cognitive and behavioral conflict by discrimination among mental events in accordance with dominant criteria for interpretation of perceptual information [2,3]. The higher cortical structures of ventrolateral prefrontal cortex probably play a key role in selection among competing stimuli [6,13,19] whereas higher activation of anterior cingulate cortex (ACC) is related to detecting cognitive conflict [6,9,20,25,28]. Well-known experimental approach to neurophysiological study of cognitive conflict is Stroop word-colour test [29]. In a typical Stroop experiment subject is

required to name the ink colour which may be non-conflicting (e.g. red is printed in red ink) or conflicting (e.g. red is printed in green ink). To perform the conflicting Stroop task it is necessary to ignore the meaning of the printed word. This process is related to response inhibition and sensory rejection which enables to use the Stroop task as a model of the stress defense reaction in humans [12,14]. The neural interference related to cognitive conflict predominantly occurs in the ACC structures and elicits autonomic responses in sympathetic as well as in parasympathetic nervous system that can be measured as heart rate variability (HRV) calculated as beat to beat R-R intervals (RRI) or other psychophysiological measures [8,11,22]. Recent neuroscience findings suggest the hypothesis that cognitive conflict is related to specific nonlinear chaotic changes of the signal generated by neural systems participating in response to stress related cognitive conflict [5,10,18]. These chaotic changes are likely related to specific changes during development of mental disorders such as depression, schizophrenia or dissociative disorders [5,15,18,26]. On the other hand mental disorders are often related to disturbances of hypothalamic-pituitary adrenal axis which lead to hormonal dysregulation [7,17,23,24,27]. One of the neuroendocrine changes related to chronic stress exposure is decreased cortisol level which probably reflects stress related defense mechanisms [21,30]. Recent findings in both animals and humans indicate, that cortisol levels reflect not only emotional arousal but also active defensive or antiarousal intrapsychic mechanisms and should be conceptualized in psychological perspective as a balance between opposing intrapsychic forces. These intrapsychic forces relate to excitatory and inhibitory influences and are experienced as engagement that represent active emotional response with high cortisol levels, and disengagement (e.g. avoidance, withdrawal or denial) related to response inhibition with low cortisol levels [21].

Because the chaotic nonlinear changes probably may reflect dynamical patterns of neural organization related to intensity of conflict response, it is possible to suggest the hypothesis, that specific dynamical changes may reflect also cognitive conflict during Stroop task and that lower levels of serum cortisol in patients with unipolar depression, likely linked to defense mechanisms, might be related to non-linear measures calculated from HRV.

METHODS

Participants

For empirical examination of suggested hypothesis the methods of ECG recording, nonlinear data analysis and assessment of serum cortisol levels were used in 30 consecutive inpatients, treated at the university hospital, Psychiatry department in the period from September to November 2006. The patients have diagnosis of unipolar depressive disorder (i.e. patients with recurrent depression or depressive period) in relapse, confirmed according to DSM IV criteria [1]. Exclusion criteria were organic illnesses involving the central nervous system, psychotic disorders, bipolar disorder, alcohol and/or drug abuse, hormonal medication, any form of epilepsy and mental retardation. The patients were 12 males and 18 females in average age 42.26±11.24 predominantly with high-school education. All the patients gave written informed consent and the clinical study was approved by university ethical committee.

ECG measurement

The ECG was recorded using SAM unit and Psylab software (Contact Precision Instruments) connected to computer in the room temperature 23 °C. Three standard ECG electrodes with electrolyte were attached to the right flank (right hypogastrium), under the left collar-bone and reference electrode to the left arm (upper margin of left cubital fossa). ECG measurement was performed with sampling frequency 1 000 Hz. During ECG measurement three states have occurred. The first was resting state (100 second); the second state was during procedure of non-conflicting Stroop task (four tables with words: green by green ink, red by red ink, blue by blue ink, yellow by yellow ink); and third state was during conflicting Stroop task (four tables with words: green by red ink, red by green ink, blue by yellow ink, yellow by blue ink); both with regularly changing questions: "name the colour", "name the word", with 20 second pause between the non-conflicting and conflicting Stroop task.

Biochemical assessment

For biochemical assessment, the blood samples of 5 ml volumes were collected in rest conditions according to common procedures at the time from 7:30 to 8 a.m. in laboratory of Psychiatry department (about 1 hour before ECG measurement and Stroop task experiment). The blood samples were carefully transferred (about 10 minutes) in icebox at the temperature of 4 °C to university biochemical department and immediately centrifuged at the temperature of 4 °C. After that cortisol serum levels have been assessed in biochemical laboratory according to common analytical procedures by chemiluminiscent immunoassay (CLIA) using analysator ADVIA (Centaur Bayer). The intra- and interassay coeficients of variance were 2.9 and 12.2%.

Data analysis

In nonlinear data analysis heart rate variability time series calculated as R-R intervals (RRI) from artifact-free ECGs were divided to three periods. Then 100 seconds long period before Stroop task and two approximately 20–30 seconds long periods during non-conflicting and conflicting Stroop task were processed by nonlinear data analysis using software package Dataplore. In the analysis mutual information, False Nearest Neighbours, embedding dimension and largest Lyapunov exponents were calculated [16]. False Nearest Neighbours technique utilizes geometric principles for the finding of embedding dimension which determines reconstruction of

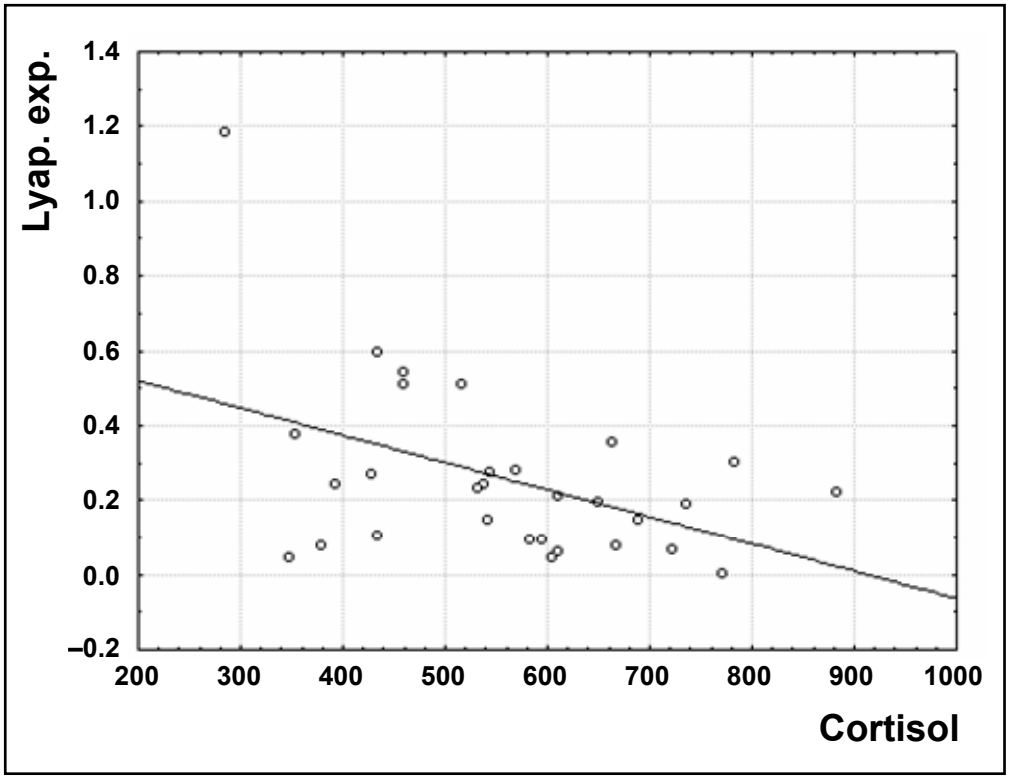

Figure 1. Dependency graph of cortisol serum levels [nmol/l] with largest Lyapunov exponents [bit/s] during conflicting Stroop task.

underlying chaotic dynamics by means of Lyapunov exponents [16]. Largest Lyapunov exponents were calculated using the method of 7 s long sliding window (7 000 datapoints, embedding dimension 3 for all calculated time series) which enables to approach to algorithmic criteria for signal stationarity.

In addition, the same analysis using the surrogate data was performed. The basic idea of the surrogate-data testing is to first perform the nonlinear analysis on the actual experimental time series. The resulting value of the nonlinear measure is then compared with the average value obtained from a set of suitably constructed control surrogate signals that are linearly filtered Gaussian white noises which have the same mean, the same variance, the same autocorrelation function and the same power spectrum as the original sequence but nonlinear phase relations are destroyed. The null hypothesis that the original data represent linearly filtered Gaussian white noises can be rejected if the actual and average-surrogate values are statistically significantly different. In this case the results cannot be understood as a consequence of the linear data properties. Surrogate data techniques thus permit the statistical testing of nonlinearities in neural dynamics [16].

Statistical evaluation for largest Lyapunov exponents and results of serum cortisol assessment included Pearson product moment correlation and t-test for independent samples.

RESULTS

Data obtained by nonlinear analysis of RRI time series display significant correlation between largest Lyapunov exponent during conflicting Stroop task and serum cortisol levels –0.45 (p=0.0062) (Figure 1). Largest Lyapunov exponents during rest and non-conflicting Stroop task did not display any significant correlations with serum cortisol.

Comparison between largest Lyapunov exponents calculated from original and surrogate time series by t-test confirmed with high statistical significance (t=5.722, p=0.0000003, df=58) that original data did not represent linearly filtered Gaussian white noises. In addition, correlation between largest Lyapunov exponent during conflicting Stroop task calculated from surrogate time series and serum cortisol levels is not statistically significant (r=–0.16, p=0.199) which strongly suggest that the results cannot be explained from the linear data properties and provide evidence for nonlinear dynamics in autonomic nervous system as measured by ECG.

DISCUSSION

Results of this study correspond to several recent findings which indicate that ACC activity is closely related to HRV and these findings also provide evidence that autonomic nervous system modulation by the ACC

is closely related to the cognitive processing of this structure [8, 13, 22]. ACC is a part of the central autonomic network which includes also insula and medial temporal lobe structures such as the amygdala, and hippocampus that integrate emotional and cognitive information and exert a modulatory role on lower brain centers that control autonomic nervous system and neuroendocrine response [4, 22]. Results of this study indicate that increase in largest Lyapunov exponents, likely linked to ACC activation during conflicting Stroop task, is closely related to decrease in levels of cortisol, which probably reflects defense reaction related to disengagement. Because conflicting Stroop task is related to response inhibition and failure of this inhibition leads to error information processing [22, 29], these findings suggest that the defects in complex functions of cognitive-emotional integration linked to response inhibition are particularly vulnerable to mental stress exposure and that disengagement related mental stress is closely related to lower cortisol levels.

ACKNOWLEDGEMENTS

Authors thank for support by research project of Ministry of Health IGA MZ NR 8824-4.

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