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

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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-con-
licting (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 cogni-
tive conflict predominantly occurs in the ACC structures
and elicits autonomic responses in sympathetic as well
as in parasympathetic nervous system that can be mea-
sured as heart rate variability (HRV) calculated as beat
to beat R-R intervals (RRI) or other psychophysiological
measures [8,11,22]. Recent neuroscience findings sug-
gest the hypothesis that cognitive conflict is related to
specific nonlinear chaotic changes of the signal gener-
ated 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 hy-
pothalamic-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 oppos-
ing 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. avoid-
ance, 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 re-
fect 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

**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 stan-
dard ECG electrodes with electrolyte were attached to
the right flank (right hypogastrium), under the left col-
lar-bone and reference electrode to the left arm (upper
margin of left cubital fossa). ECG measurement was
performed with sampling frequency 1000Hz. During
ECG measurement three states have occurred. The first
was resting state (100 second); the second state was dur-
ing 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 dur-
ing 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 be-
tween 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 coefficients 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 embed-
ding dimension which determines reconstruction of

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underlying chaotic dynamics by means of Lyapunov exponents [16]. Largest Lyapunov exponents were calculated using the method of 7 s long sliding window (7000 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. Additionally, 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...
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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.

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