



Dissociation, cognitive conflict and nonlinear patterns of heart rate dynamics in patients with unipolar depression

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ARTICLE INFO

Article history:

Received 20 September 2008
Received in revised form 3 November 2008
Accepted 8 November 2008
Available online 17 November 2008

Keywords:

Chaos
Cognitive conflict
Dissociation
ECG
Lyapunov exponent
Stress

ABSTRACT

Recent findings in cognitive neuroscience indicate that activation of anterior cingulate cortex (ACC) is related to detecting cognitive conflict. Conflict related ACC activation elicits responses in central autonomic network which can be assessed by psychophysiological measures such as heart rate variability (i.e. beat to beat R–R intervals – RRI). Recent findings in neuroscience also suggest that cognitive conflict is related to specific nonlinear chaotic changes of the signal generated by the neural systems. The present study used Stroop word-colour test as an experimental approach to the study of cognitive conflict in connection with RRI measurement, psychometric measurement of dissociation (DES) and calculation of largest Lyapunov exponents in nonlinear data analysis of RRI time series in 40 patients with unipolar depression and 35 healthy controls. Significant correlation 0.58 ($p < 0.01$) between largest Lyapunov exponents and DES found in depressive patients indicate that cognitive conflict related neural interference during conflicting Stroop task is closely related to dissociative processes. These results present first supportive evidence that degree of chaos could be related to dissociation.

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1. 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 (Baars, 1999, 2002). The higher cortical structures of ventrolateral prefrontal cortex probably play a key role in selection among competing stimuli (Hazeltine et al., 2000; Leung et al., 2000; Bunge et al., 2001) whereas higher activation of anterior cingulate cortex (ACC) is related to detecting cognitive conflict (MacDonald et al., 2000; Bunge et al., 2001; Ochsner et al., 2001; Raz et al., 2005; Egner et al., 2005; Yeung and Cohen, 2006). The aim of the selection among competing stimuli is to find whether these stimuli may fit into existing cognitive schemes. When the selection and attentional filtering is not momentarily possible, the competition leads to the cognitive conflict that needs great allocation of attention and may produce new adaptive response or a defense resolution and behavioral response leading to dissociated state (Bob, 2008).

Well-known experimental approach to neurophysiological study of cognitive conflict is Stroop word-colour test (Stroop, 1935). 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, sensory rejection and the Stroop task has been used as a model of the stress defense reaction in humans (Hoshikawa and Yamamoto, 1997; Freyschuss et al., 1988).

Conflicting streams of information lead to cognitive and neural interference that 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 calculated as beat to beat R–R intervals (RRI) or other psychophysiological measures (Critchley et al., 2003; Matthews et al., 2004). Recent neuroscience findings suggest the hypothesis that specific nonlinear chaotic changes of the signal generated by neural systems participating in response to stress are related to cognitive conflict and inhibitory deficits (Freeman, 2000; Korn and Faure, 2003; Bob, 2003, 2007; Bob et al., 2006). These chaotic changes are likely related to specific changes during development of mental disorders such as depression, schizophrenia or dissociative disorders (Korn and Faure, 2003; Huber et al., 1999; Paulus and Braff, 2003; Bob, 2003). However, chaotic neural process in principle must not be related only to pathological processing but may represent the potential existence of a new adaptive level in neurophysiological process that enable resolution of the cognitive conflict (Bob, 2007).

Similarly as in the case of cognitive conflict which reflects the competition and interference of many possible behavioral patterns and mental representations during “chaos in the mind”, a characteristic feature of neural chaotic states is that they lead to transient periods of

Abbreviations: ACC, Anterior Cingular Cortex; BDI-II, Beck Depression Inventory; DES, Dissociative Experiences Scale; HRV, Heart Rate Variability; LLE, Largest Lyapunov Exponents; RRI, beat to beat R–R intervals.

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high brain complexity during activity of independent areas and enable fast parallel information processing which runs in a distributed mode (Bob, 2003, 2007). It means that numerous processes from sensory and cognitive channels are executed simultaneously and this desynchronized neural state may be related to active information processing in the cortex (Tirsch et al., 2004). This enhanced parallel distributed mode of neural activity is probably typical for trauma related dissociative processes (Bob, 2003; Li and Spiegel, 1992). There is also relevant assumption that chaotic neural mechanism is related to concomitant chaotic psychological process (Pediaditakis, 1992; Sel, 1997; Putnam, 1997; Bob, 2003). According to Putnam (1997) retrieval of fragmentary, dissociated memories may lead to rapid changes of mental state. Specific characteristic of this neural dynamic might be chaotic shifts with extreme sensitivity to very small changes which lead to significantly different mental states and behavioral patterns (Bob, 2003, 2007; Putnam, 1997).

Dissociation as partial or total disconnection of certain competitive mental images, affects and memories which does not fit into current cognitive scheme is on the psychological level closely related to confusion and cognitive conflict, when a possible solution in a stressful situation is not found. This process manifests as a competition among very high number of prototype mental images representing a possible solution. These mental representations of possible solutions constitute different behavioral patterns and strategies. On neural level these processes are probably linked to a large number of complex and interlinked neural states which lead to extreme instability with respect to competition of many patterns of neural activity (Freeman, 1991, 2000; Korn and Faure, 2003; Bob, 2003, 2007).

In this study we have examined whether nonlinear chaotic changes as related to mental disorder in the case of depression, reflect cognitive conflict during Stroop test and whether this conflict related activity displays a significant relationship to dissociation.

2. Methods

2.1. Subjects

For empirical examination of suggested hypothesis the methods of ECG recording, nonlinear data analysis, Stroop test and psychometric measures of dissociation and depression were used in 40 outpatients of university hospital (mean of age 34.98, age range 20–55, SD=10.22) and 35 healthy controls (mean of age 34.09, age range 20–48, SD=7.06). Consecutively selected patients had diagnosis of unipolar depressive disorder (21 patients with depressive episode and 19 patients with recurrent depression with mean period of depression 2.8 years), confirmed by clinical interview according to DSM IV criteria (American Psychiatric Association, 1994) and were also assessed by structured psychiatric interview M.I.N.I. version 5.0.0 (Sheehan et al., 1998). In remission were 6 patients, 18 in partial remission and 16 were in relapse, with lasting depression less than 8 years and not more than 4 hospitalizations (average number of hospitalizations 1.8). Patients' treatment at the time of recruitment was based only on serotonergic antidepressant medication in usual recommended doses (paroxetine 10–40 mg; fluoxetine 20–40 mg; fluvoxamine 100–200 mg; sertraline 100–200 mg; citalopram 20–40 mg; escitalopram 10–20 mg). Exclusion criteria for both groups were organic illnesses involving the central nervous system, heart disease, any form of epilepsy and mental retardation [IQ Raven higher than 90], psychotic disorders, electroconvulsive therapy, bipolar disorder, alcohol and drug abuse. The reason for including unipolar depression among other types of depression was the aim to exclude patients with reactive depression that may be significantly influenced by momentarily psychosocial factors and on the other hand to exclude bipolar patients, who may have different pathogenic mechanisms caused by alterations between depressive and manic states in comparison to unipolar depressive states. Because high numbers of outpatients are

treated by serotonergic antidepressants we used this criterion for sample homogeneity. At this point the sample homogeneity was also criterion why we did not include unmedicated patients.

The healthy controls were selected from general population that included hospital and university staff members ($N=17$), university students ($N=14$) and other persons who responded to advertising ($N=4$). All the controls were psychiatrically healthy according to M.I. N.I. The patients were 16 men and 24 women and the control group involved 14 men and 21 women both predominantly with high-school education. All the patients and controls gave written informed consent and the clinical study was approved by the university ethical committee.

2.2. Stroop test and ECG measurement

Autonomic responses related to cognitive conflict and neural interference have been assessed during conflicting Stroop task (Stroop, 1935). 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, sensory rejection and the Stroop task has been used as a model of the stress defense reaction in humans (Hoshikawa and Yamamoto, 1997; Freyschus et al., 1988). The neural interference related to cognitive conflict predominantly occurs in the ACC and elicits autonomic responses in sympathetic as well as in parasympathetic nervous system that can be measured as heart rate variability calculated as beat to beat R–R intervals (RRI) or other psychophysiological measures (Hoshikawa and Yamamoto, 1997; Freyschus et al., 1988).

ECG measurement was performed 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 1000 Hz. After 5 min rest ECG measurement during three states was performed. The first was resting state (100 s); the second state was during non-conflicting Stroop task (four tables with words: green by green ink, red by red ink, blue by blue ink, yellow by yellow ink); the 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); with regularly changing questions: "name the colour", "name the word". Tables (A4, with types size 72 mm) with conflicting and non-conflicting stimuli were presented at distance about 50 cm. Subjects were required to complete 4 words with 5 s pause after each response with 20 s pause between non-conflicting and conflicting Stroop task.

2.3. Psychometric measures

For the screening of psychic dissociative symptoms the validated Czech version of the questionnaire Dissociative Experiences Scale (DES) was used (Bernstein and Putnam, 1986). DES represents 28 items self-reported questionnaire examining main dissociative phenomena such as absorption, amnesia, depersonalization, derealization, reality distortion, and others. Subjects indicate a degree of their experience on the continuum from 0% to 100%. Czech version of the DES displays (similarly as original English version) high convergent validity and reliability (Cronbach alpha 0.92, Split-half 0.94; test-retest $r=0.82$, $p<0.001$).

For the assessment of depressive symptoms Beck depression inventory BDI-II was used (Beck et al., 1996) (in validated Czech version) that represents 21-items questionnaire for assessing depression. Subjects indicate degree of their experience on 4-point Likert scale.

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