

Brief report

Autonomic reactivity to induced emotion as potential predictor of response to antidepressant treatment

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Abstract

Distinct factors have been identified as potential predictors of antidepressant treatment response. Although autonomic function changes have been described in depressive subjects, their value as predictors of antidepressant response has not been systematically evaluated. Eight un-medicated patients with major depressive disorder (MDD) have their skin conductance (SC) and heart rate variability (HRV) measured at basal condition and during four induced emotional states: happy, angry, sad and neutral. The high frequency (HF) and low frequency (LF) power parameters of HRV were assessed. Subsequently, patients were treated with fluoxetine 20 mg/day for 8 weeks. The antidepressant response was measured with the Beck Depression Inventory (BDI). The BDI percentage reduction correlated significantly with HRV responses during sad condition in LF power, and during happy condition with LF/HF ratio. The BDI percentage reduction also correlated significantly with HR responses in happy and in neutral conditions, and also with SC responses in neutral condition. These preliminary findings indicate that automatic responses to induced emotions may predict antidepressant response in MDD patients. Confirmatory studies are warranted.

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1. Introduction

Several studies have suggested the existence of a complex relationship between heart rate (HR), heart rate variability (HRV), skin conductance (SC) and depression. Patients with depression have shown increased baseline HR compared with non-depressed subjects (Dawson et al., 1985). In addition, studies have shown that the

relationship between HR and depression varies depending on the psychopathology and the cardiac parameter that have been evaluated. For example, studies focusing on apathy instead of the presence of a depressive disorder and measuring HR reactivity instead of HR at rest have reported an association of apathy with reduced HR reactivity (Andersson et al., 1999). Patients with major depression have also shown decreased HRV parameters (Carney et al., 1995) suggesting reduced cardiovagal activity (Agelink et al., 2002) and/or increased sympathetic cardiovascular activity (Agelink et al., 2002). In addition, increases in HRV component bands have been reported in response to treatment with antidepressants (Yeragani et al., 2002).

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Skin conductance is another measure of autonomic reactivity specifically related to the sympathetic branch of the autonomic nervous system. Decreased SC tone (Ward et al., 1983) and decreased amplitude of response (Iacono et al., 1983) have been associated with depression.

Despite these findings, the potential predictive value of autonomic physiologic measures at baseline and subsequent antidepressant treatment response has not been systematically investigated. The present study describes a preliminary investigation of patients with major depressive disorder (MDD), assessing whether HR, HRV, and SC responses to emotion induction are potential predictors of response to antidepressant treatment.

2. Methods

2.1. Participants

Eight unmedicated patients, three male and five female, with a mean age of 35 ± 12 (range, 26–62) years, diagnosed with MDD were recruited through the Depression Clinical and Research Program (DCRP) at Massachusetts General Hospital (MGH) in Boston, MA, as a subset of a larger study (Dougherty et al., 2004). A psychiatrist evaluated the patients with the Structured Clinical Interview for Axis I diagnosis in accordance with the Diagnostic and Statistical Manual of Mental Disorders—4th edition (SCID-DSM-IV) (First et al., 1995) and the Beck Depression Inventory (BDI) (Beck, 1961) at the time of the screening. Exclusion criteria included current or past Axis I diagnoses other than MDD, pregnancy, history of psychotic features, major medical or neurological disorder, head injury, and seizure disorder. All patients were free of psychotropic medication use or any medication that could affect the autonomic nervous system functioning for at least 2 weeks prior to beginning of the study evaluations. The MGH Human Research Committee approved the study, and all participants gave written informed consent.

2.2. Scripts

Scripts of past personal and emotional events were prepared according to previously published procedures (Rauch et al., 1996; Dougherty et al., 1999). Each subject provided a written description of the two life events corresponding to the two most angry, sad, and happy emotional experiences of their lifetimes plus two autobiographically neutral scripts (e.g., going for a walk, cooking dinner). Two scripts for each emotion were composed in the second person present tense and audio-

taped in a neutral voice by a study staff member for playback in the laboratory. All scripts were 30–40 s in duration. The participants were later exposed to each audiotaped recording of the autobiographical scripts as described below to induce four separate emotional states: Neutral, Happy, Sad, and Angry.

2.3. Autonomic measures

Physiologic data consisted of continuous HR, HRV, and SC recordings from the participants in supine position in a positron emission tomography (PET) imaging suite as part of a larger study (Dougherty et al., 2004). Physiologic recordings were made using ADInstruments PowerLab 8SP computer-based modular instrument system with Chart 4.2 Software (ADInstruments Inc., Sydney, Australia).

Following habituation to the PET suite environment, baseline physiologic data were collected for the 30 s prior to exposure to the autobiographical scripts. Immediately before each emotion induction script, participants were instructed as follows: “Close your eyes, listen carefully to the script, and imagine the event portrayed as vividly as possible, as if you are actually participating in the event rather than just watching yourself in it”. Participants were instructed to maintain the relevant emotion image for 60 s immediately after playback of the emotion induction script while physiologic parameters were collected.

Heart rate and HRV variables were extracted from the single lead chest EKG using commercially available software (Chart HRV Module Version 5.0, ADInstruments, Sydney Australia). The HRV variables were evaluated by means of frequency domain indices. The frequency domain components computed were: high-frequency power (HF: 0.15 to 0.40 Hz); low-frequency power (LF: 0.04 to 0.15 Hz); and the LF/HF ratio. The HR data is reported in beats per minute (bpm) while HF and LF results are reported in ms^2 . The SC level was recorded in microSiemens (μS) using Ag–AgCl electrodes on the distal palmar surface of the third and fourth digits of the non-dominant hand. Psychophysiological responses to the script induction protocol were quantified by subtracting 60-s baseline values of HR, HRV and SC prior to the relevant emotion from the values during the 60-s emotion imagery period.

2.4. Antidepressant treatment

Following the emotion induction protocol, participants were treated with fluoxetine 20 mg per day in an open label trial for 8 weeks in an outpatient clinic.

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