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Does parasympathetic modulation prior to ECT treatment influence therapeutic outcome?

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ABSTRACT

Electroconvulsive therapy (ECT) is an established treatment option for major depressive disorder when other treatments have failed. However, the underlying mechanisms responsible for these therapeutical effects are insufficiently understood to date. Furthermore, treatment outcome is difficult to predict. Recent research suggested an important role of autonomic modulation for successful treatment.

We aimed to examine putative associations between autonomic modulation and response to ECT treatment and hypothesized a role for vagal modulation prior to therapy.

Twenty-four patients with MDD who received ECT were assessed by means of heart rate and blood pressure variability analysis as well as baroreflex sensitivity measurements before, during and after a course of ECT. Autonomic parameters from the complete study population revealed that ECT did not significantly alter basic autonomic modulation after six sessions. Analyses showed a significant association of the reduction of HAMD scores during therapy when compared with baseline autonomic function as reflected in $SDNN_{RR}$ ($p<0.004$), $Forbword_{RR}$ ($p<0.025$) and compression entropy Hc_{RR} ($p<0.0003$). A significant correlation was observed when overall HAMD reduction and changes of $LFnu_{RR}$ ($p<0.026$) or $HFnu_{RR}$ ($p<0.026$) during the course of therapy were analyzed.

Our findings suggest that high levels of parasympathetic modulation at baseline might be associated with a beneficial effect upon ECT treatment. Adding to this, levels of parasympathetic activity seemed to increase in patients who respond to ECT treatment. Given these findings can be confirmed in future studies, autonomic modulation might be used as a predictor for therapeutic efficacy of ECT.

Contents

Abbreviations: BBI, Beat-to-beat interval; BDI, Beck Depression Inventory; BDNF, Brain Derived Neurotrophic Factor; BPV, Blood pressure variability; BRS, Baroreflex sensitivity; DBP, Diastolic blood pressure; DSM, Diagnostic and Statistical Manual of Mental Disorders; ECT, Electroconvulsive therapy; Forbword, Forbidden words; HAMD, Hamilton Depression Rating Scale; Hc, Compression entropy; HF(nu), High frequency (normalized); LF(nu), Low frequency (normalized); MDD, Major depressive disorder; RR, "RR interval" (concerning heart rate variability); SBP, Systolic blood pressure; SDNN, Standard deviation of the average of normal to normal intervals; Sys, Systolic blood pressure; VLF, Very low frequency.

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1. Introduction

Major depressive disorder (MDD) is one of the most common psychiatric illnesses with a lifetime prevalence of approximately 16% (Kessler et al., 2003). While successful pharmacological and psychotherapeutic interventions are available, not all patients respond satisfactorily. In such cases, electroconvulsive therapy (ECT) represents an established and effective additional therapeutic option (Pagnin et al., 2004; Merkl et al., 2009). In this respect, approximately fifty percent of MDD patients who did not respond to psychopharmacological approaches have been shown to benefit from electroconvulsive treatment (Sackeim et al., 1990; Devanand et al., 1991). Despite the long history of clinical application of ECT and a large body of research dedicated to it, the exact underlying mechanisms responsible for its therapeutic effects remain unclear to date. For instance, some reports suggested changes of serum concentrations of Brain Derived Neurotrophic Factor (BDNF) or cortisol levels after administration of ECT (Bocchio-Chiavetto et al., 2006; Grønli et al., 2009). In animal models, electroconvulsive shocks appear to trigger neurogenesis and synaptic connectivity (Scott et al., 2000; Chen et al., 2009).

Furthermore, there is a growing body of evidence that ECT might alter the modulation of the autonomic nervous system. The administration of ECT induces profound short-lasting autonomic changes after each session. In particular, heart rate and blood pressure briefly decrease upon a seizure, followed by an immediate sympathetic counter-regulation (Welch and Drop, 1989). These effects might be of particular importance, since recent research detected disturbed autonomic modulation in patients with MDD which might add to the pathophysiology of the disease. These studies indicate an increase in sympathetic modulation in patients who suffer from major depression (Agelink et al., 2001; Udupa et al., 2007; Boettger et al., 2008; Koschke et al., 2009). In return, parasympathetic modulation of the autonomic nervous system seems to be reduced (Bär et al., 2004; Rottenberg et al., 2007; Koschke et al., 2009; Schulz et al., 2010). In this respect, findings of Nahshoni and coworkers which suggest that successful ECT treatment is accompanied by a long-term increase of cardiac vagal modulation in elderly depressed patients, thus indicating a normalization of autonomic balance, are of particular importance (Nahshoni et al., 2001, 2004).

Here, we hypothesized that a positive treatment response to ECT is associated with an increase in parasympathetic modulation of heart rate time series. In addition, we assumed that parasympathetic modulation before therapy might predict therapeutic outcome. To test these hypotheses we investigated 24 patients with MDD who underwent autonomic cardiac assessment prior to and during the course of ECT treatment. In particular, we studied changes of heart rate and blood pressure variability as well as baroreflex sensitivity. All values were analyzed by linear and novel non-linear methods. The obtained parameters were correlated to the severity of symptoms as assessed by the Hamilton Depression Rating Scale and Beck Depression Inventory.

2. Materials and methods

2.1. Participants

Twenty-four patients suffering from major depressive disorder were included in this study (Table 1). All of them fulfilled DSM-IV criteria for MDD. Diagnosis was confirmed by means of a structured clinical interview for DSM-IV Axis I disorders (SCID; First, 1997). In addition to physical examination, a routine electrocardiogram (ECG) and blood screening were performed. Any additional or interfering psychiatric condition (e.g. anxiety disorder) or other diseases led to the exclusion of participants (history of alcohol dependence: n = 3; diabetes mellitus: n = 1; schizoaffective disorder: n = 1).

Table 1
Characteristics of patients.

Demographic characteristics	
Women	21
Men	3
Age, mean in years (± standard deviation)	61.1 (± 16.8)
Youngest/oldest patient in years	18/72
Disease duration, mean in years (± standard deviation)	12 (± 11)
Smokers/non-smokers	6/18
Psychopharmacological characteristics	
Tricyclic antidepressants	2
Mirtazapine	
30 mg	N = 5
15 mg	N = 5
SSRI	
S-citalopram (10 mg)	N = 5
Sertraline (100 mg)	N = 1
NaSSRI	
Venlafaxine (150 mg)	N = 5
Venlafaxine (225 mg)	N = 6
Antipsychotics	
Risperidone	N = 8
Quetiapine	N = 7
Lithium	3
Antihypertensive medication	
Betablockers	N = 11
Calcium channel blocker	N = 5