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Psychiatry Research 137 (2005) 183–190

PSYCHIATRY RESEARCH

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Changes in plasma amino acids after electroconvulsive therapy of depressed patients

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Received 5 October 2004; received in revised form 1 July 2005; accepted 15 July 2005

Abstract

There are indications that mood disorders may be related to perturbations in the amino acid transmitters. The amino acids may thus be targets of treatment of depression. The purpose of this pilot study was to measure the acute effects of a single administration of electroconvulsive therapy (ECT) on the plasma levels of amino acids in depressed patients. ECT was administered to 10 patients with major depressive disorder. Altogether 23 plasma amino acids were analyzed before and at 2, 6, 24 and 48 h after ECT. The levels of glutamate and aspartate increased at 6 h after ECT compared with the baseline. Also the levels of total tryptophan increased 2–24 h after ECT. There were also elevations in other amino acids at 6 and 24 h. The levels of gamma-aminobutyric acid (GABA) decreased at 2 h. In this study the acute effects of single ECT were associated with changes in the levels of glutamate, aspartate, GABA, tryptophan and some other amino acids. The preliminary data suggest that the therapeutic effects of ECT in depression may be due to mechanisms involving these amino acid transmitters.

Keywords: Depression; Electroconvulsive therapy; Aspartate; Glutamate; GABA; Tryptophan

1. Introduction

The neurobiological action of electroconvulsive therapy (ECT) is not fully understood, but it is known that ECT has effects on several neurotransmitters and their receptors, neuropeptides, hormones and neurotrophic factors (Wahlund and von Rosen, 2003).

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0165-1781/$ - see front matter © 2005 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.psychres.2005.07.010

ECT is widely used and regarded as safe and effective in major depressive disorders and some other psychiatric syndromes such as catatonia and mania (American Psychiatric Association, 1990).

Several experimental and human studies indicate a role for the amino acid transmitters gamma-aminobutyric acid (GABA) and glutamate in the pathogenesis of mood disorders, especially depression; for reviews, see Krystal et al. (2002), Brambilla et al. (2003), and Tunnicliff and Malatynska (2003). In humans, reduced concentrations of GABA both in plasma and in cerebrospinal fluid (CSF) have been reported in depressed patients (Brambilla et al., 2003; Tunnicliff and Malatynska, 2003). Furthermore, decreased cortical GABA concentrations, demonstrated by proton magnetic resonance spectroscopy (MRS), have been associated with major depression (Sanacora et al., 1999, 2004). Alterations in the plasma levels of glutamate as well as those of aspartate, serine, glycine and taurine, have been observed in major depression (Altamura et al., 1993, 1995; Maes et al., 1998). A higher plasma serine concentration has been considered a possible marker for depression, but also for schizophrenia, paranoia and mania (Waziri et al., 1984; Maes et al., 1995; Sumiyoshi et al., 2004). Altered ratios of plasma levels of serine and glycine have been found in patients suffering from major depression, but also in subjects with schizophrenia (Altamura et al., 1995; Sumiyoshi et al., 2004). Recently, Sanacora et al. (2004) reported increased cortical concentrations of glutamate in depressed subjects.

GABA and glutamate may thus be targets of treatment of depression with drugs and ECT (Krystal et al., 2002; Brambilla et al., 2003; Ketter and Wang, 2003; Pfleiderer et al., 2003). The increase in occipital cortex GABA concentrations following ECT suggests possible GABAergic involvement in the positive actions of ECT (Sanacora et al., 2003). On the other hand, plasma GABA has been reduced after ECT for at least 1 h (Devanand et al., 1995). Reduced cortical glutamate/glutamine (Glx) levels have been measured in depressed patients. Glx concentrations have also correlated negatively with severity of depression. After successful treatment with ECT, Glx increased significantly in the amygdalar region, in the dorsolateral prefrontal cortex and in the left anterior cingulum (Pfleiderer et al., 2003; Michael et al., 2003a,b). However, data are scant on the effects of different treatments, especially those of ECT, on the plasma levels of these and other amino acids in patients with depression.

The purpose of this study was to measure the acute effects of a single administration of ECT on the plasma levels of amino acids in depressed patients. Altogether 23 plasma amino acids were analyzed before and up to 48 h after ECT.

2. Methods

The study was performed at the Department of Psychiatry, Tampere University Hospital, Finland. We included 10 patients, seven women and three men, with a mean age of 55.6 years (range 28–70 years). All the patients fulfilled the diagnostic criteria of DSM-IV major depressive disorder (MDD) (American Psychiatric Association, 1994); four of them showed psychotic features. The patients had no other medical or neurological disorders except for one patient (no. 7), who had ischemic heart disease and a history of a stroke 6 months before the treatment. The patients received a variety of psychotropic medications that were continued unchanged before and after ECT. The severity of depression was scored with the Montgomery–Åsberg Depression Rating Scale (MADRS) before and after the series of ECT. The mean MADRS scores were 29/60 before and 9/60 after ECT. Demographic data of the patients and their psychotropic medications are shown in Table 1.

Written informed consent to the blood samples was obtained from all patients. The study protocol was approved by the Ethics Committee of the Tampere University Hospital.

2.1. ECT procedure

ECT was administered with a Thymatron DGx (Somatics, Inc.) brief-pulse device. The initial stimulus dosage (millicoulombs) was adjusted to all patients with the age method being about five times their age (Swartz and Abrams, 1996). All patients were treated with bilateral ECT. Anesthesia was induced with propofol (5 patients) or methohexital (5 patients) and muscle relaxation with succinylcholine. The initial dosage was 1.5 mg/kg of propofol or 1 mg/kg of methohexital and 0.5 mg/kg of succinylcholine. The