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No evident neuronal damage after electroconvulsive therapy

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Abstract

Electroconvulsive therapy (ECT) is regarded as one of the most effective treatments for major depressive disorder but has also been associated with cognitive deficits possibly reflecting brain damage. The aim of this study was therefore to evaluate whether ECT induces cerebral damage as reflected by different biochemical measures. The concentrations in the cerebrospinal fluid (CSF) of three established markers of neuronal/glial degeneration, tau protein (tau), neurofilament (NFL) and S-100 beta protein, were determined in nine patients who fulfilled DSM-IV criteria for major depression. CSF samples were collected before and after a course of six ECT sessions. The CSF/serum (S) albumin ratio reflecting potential blood-brain barrier (BBB) dysfunction was also determined at these time points. The treatment was clinically successful with a significant decline of depressive symptoms in all patients as assessed by the Montgomery-Åsberg Rating Scale for Depression. Several patients had signs of BBB dysfunction and/or neuronal damage before the start of treatment. Levels of CSF-tau, CSF-NFL and CSF-S-100 beta levels were not significantly changed by ECT. Also the CSF/S albumin ratio was found to be unchanged after the course of ECT. In conclusion, no biochemical evidence of neuronal/glial damage or BBB dysfunction could be demonstrated following a therapeutic course of ECT.

Keywords: Electroconvulsive therapy; Depression; Cerebrospinal fluid; Tau; Neurofilament; S-100 beta

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1. Introduction

Electroconvulsive therapy (ECT) is regarded as one of the most effective treatments for major depressive disorder, both of the unipolar and bipolar subtypes (American Psychiatric Association, 1990; Abrams, 1992; Potter and Rudorfer, 1993). The onset of action and the response rate compare favorable to those for treatment with antidepressant medication. ECT is also effective in mania, mixed affective states, catatonia and schizoaffective disorder associated with perplexity (Dodwell and Goldberg, 1989) and in some cases of Parkinson's disease (Andersen et al., 1987; Fall, 1999). The treatment has, however, been associated with cognitive deficits which could possibly reflect brain damage (Friedberg, 1977; Breggin, 1993), causing concern among professionals and in the public.

As the intercellular space in the brain is in direct contact with the cerebrospinal fluid (CSF), biochemical changes in brain tissue may be reflected in the CSF. Different types of brain damage may therefore be evaluated by measuring brain-derived proteins in the CSF. In this study we investigated whether ECT might induce brain damage as reflected by blood–brain barrier (BBB) disruption or increased levels of CSF-tau, CSF-NFL and CSF-S-100 beta proteins.

Evaluation of BBB integrity can be performed by calculating the ratio between CSF-albumin/serum (S)-albumin (Tibbling et al., 1977). Older studies have often used CSF total protein as a measure of BBB function. Elevated CSF protein levels have frequently been found in patients with affective disorders. Males have been shown to have higher levels relative to females (Pitts et al., 1990; Samuelson et al., 1994; Pazzaglia et al., 1995).

Tau is a microtubule-associated protein predominantly localized at axons of neurons (Goedert, 1993; Pei et al., 1998), and is proposed as a powerful marker of the neuronal physiological state (Delacourte and Buee, 1997). CSF-tau has been used as a marker of axonal damage and is a positive biochemical marker in discriminating neurodegenerative disorders such as Alzheimer disease from normal aging (Blennow et al., 1995; Blennow and Vanmechelen, 1998). An increase in CSF-tau has also been observed after cerebral ischemia, stroke and head trauma (Dewar and Dawson, 1995; Irving et al., 1996; Zemlan et al., 1999). In head trauma, a relationship between clinical improvement and decreased CSF-tau levels has furthermore been observed. The CSF-tau concentration has thus been proposed as a clinically useful parameter for quantifying the axonal injury associated with head trauma and for monitoring efficacy of neuroprotective agents (Zemlan et al., 1999). The neurofilament protein (NFL) is a major structural protein of neurons. Increased concentration of the light subunit of the neurofilament triplet protein in CSF is thought to reflect ongoing neuronal degeneration, affecting mainly the axonal component (Holmberg et al., 1998), and has been suggested as a useful marker of neurodegeneration (Rosengren et al., 1996). Increased CSF concentrations have been shown in dementia disorders (Rosengren et al., 1999), multiple sclerosis (Lycke et al., 1998), normal-pressure hydrocephalus (Tullberg et al., 1998), disc herniation and sciatica (Brisby et al., 1999), and held to reflect disease activity in several of these conditions.

S-100 beta is an astroglial protein and a cytokine released from activated astroglial cells. It has neurotrophic properties and stimulates glial cell proliferation in vitro and in vivo (Schmidt, 1998). S-100 beta has been associated with a variety of intra- and extra-cellular calcium-mediated functions, including learning and memory (Kubista et al., 1999). Increased levels in CSF have been reported after brain damage such as infarction (Aurell et al., 1991) and in dementia (Sheng et al., 1994).

The aim of the present study was to evaluate whether ECT given to patients with major depression induces cerebral damage as reflected by BBB dysfunction or in changes of the neuronal/glial biochemical markers in CSF.

2. Methods and materials

2.1. Patients

Patients admitted to a psychiatric hospital for treatment of depression were considered for the