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Brief report

Changes in brain metabolism after ECT–Positron emission tomography in the assessment of changes in glucose metabolism subsequent to electroconvulsive therapy — Lessons, limitations and future applications

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Abstract

Background: Electroconvulsive therapy (ECT) has been used as an effective treatment option in severe and treatment resistant cases of depression for decades. However the mode of action of ECT is still not fully understood. Advances in neuroimaging created new possibilities to understand the functional changes of the human brain.
Methods: Literature review of studies assessing possible changes in cerebral glucose metabolism pre- and post-ECT by PET, identified by PubMed.
Results: Studies were limited by small sample size, inhomogeneous study population with uni- and bipolar depressive patients and methodological inconsistencies. Despite considerable variance, reduction in glucose metabolism after ECT in bilateral anterior and posterior frontal areas represented the most consistent findings.
Conclusions: Future research into this issue should include larger and more consistent cohorts of patients. Assessing clinical improvement of depression after ECT should allow to correlate changes in brain glucose metabolism with functional scores. Follow up PET scans after six or twelve months should be performed to test if changes in brain metabolism are persistent.

Keywords: Electroconvulsive therapy (ECT); Depression; Positron emission tomography (PET); Glucose metabolism

1. Introduction

A large body of evidence suggests electroconvulsive therapy (ECT) as an effective treatment especially for severe and treatment-refractory depression (Janicak et al., 1985; Pluijms et al., 2006; UK ECT Review Group, 2003; Prudic et al., 1996).

ECT-induced seizures propagate from the site of initiation to other specific brain regions and induce decreases in cerebral blood flow (CBF) in cingulate and left dorsolateral frontal cortex suggesting cortico-cortical or cortico-thalamo-cortical networks mainly involved in the mechanism of ECT (Enev et al., 2007; McNally and Blumenfeld, 2004).

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The use of Positron emission tomography (PET) as a probe of the cerebral metabolic glucose rate (CMR) in depressive patients appears especially promising, because depression per se has been shown to be associated with changes in CMR in different cerebral regions and can be used to display the "resting state" metabolism of the brain. Repeated PET provides an opportunity to explore changes in CMR associated with the use of ECT in vivo. Glucose represents the main source of energy for brain cells. Thus, persistent changes in glucose metabolism patterns are expected to provide a reliable estimate of neuroanatomic metabolism.

More or less consistently, specific regions have been implicated in the "functional neuroanatomy" of depression, such as the prefrontal cortex (left more than right), anterior temporal cortex and cingulate, amygdala, and related parts of the striatum, pallidum, thalamus and cerebellum (Holthoff et al., 2004). In acute depression, CBF and CMR decreases have been found especially in the dorsolateral prefrontal cortex in several PET studies (Baxter et al., 1985; Baxter et al., 1989; Martinot et al., 1990), while increases in CBF have been reported for the ventrolateral prefrontal cortex (Drevets et al., 1992).

2. Materials and methods

We performed a Medline search for studies in humans published between 1966 and June 2006 dealing with "electroconvulsive therapy", "positron emission tomography", "depression" and "cerebral glucose metabolism" or alternative wordings as "ECT", "PET", "glucose", "neuroimaging", and "tomography". Additional studies were identified from the references provided in the identified papers. We only included studies with a minimum of four patients, those providing complete description of the study population and precise details regarding type and intensity of intervention and neuroimaging. Studies further had to meet the following criteria: (1) ECT conducted as a series of acute treatment in severe or treatment resistant depression, (2) PET scans performed pre- and post-ECT series. These criteria were met only by five studies (Volkow et al., 1988; Guze et al., 1991; Yatham et al., 2000; Henry et al., 2001; Nobler et al., 2001), whereas several studies had to be excluded (Yuuki et al., 2005; Conca et al., 2003; Anghelescu et al., 2001; Sermet et al., 1998; Ackermann et al., 1986).

3. Results

A synopsis of all studies included is presented in Table 1. Considerable heterogeneity in the composition of the study cohorts and methodological differences in design and statistical analyses were noted. ECT was performed using both, standard bifrontotemporal and unilateral electrode placement. Number of treatments was based on clinical needs and varied between six and twenty-five sessions. All ECTs were administered under anesthesia, predominantly with methohexital and mild succinyl choline paralysis. Regional metabolic brain activity was measured using PET after i.v. administration of a 18F-Fluorodeoxyglucose (FDG) bolus. In all studies patients underwent the first PET scan before the first ECT session (pre-treatment). The timing of the second PET scan (post-treatment) varied between 45 min and 7 days after the last ECT session.

All studies were conducted on only small numbers (ranging from 4 to 10) of patients with a major depressive episode. Subjects had to be free of antidepressants, neuroleptics, and mood stabilizers. All studies defined regions of interest a priority and most of them concentrated on frontal, prefrontal and parietal regions. Changes in glucose metabolism were calculated by the observed or absolute metabolic rate (Henry et al., 2001; Nobler et al., 2001; Yatham et al., 2000) or the relative rate, where each region was compared to the glucose utilization averaged over all cortical regions pre- and post-ECT (Volkow et al., 1988; Nobler et al., 2001; Henry et al., 2001). A normalized rate was determined by dividing the weighted value by the ipsilateral cerebral hemispheric value (Guze et al., 1991).

3.1. Changes in glucose metabolism

Reduction in glucose metabolism after ECT in frontal areas represented the most consistent finding although it did not reach statistical significance in all studies (Volkow et al., 1988; Yatham et al., 2000). Significant decreases especially involved bilateral anterior and posterior frontal regions and bilateral parietal regions in the study of Henry et al. (2001). In addition, Nobler and colleagues found metabolic decreases after ECT in bilateral superior frontal, dorsolateral, medial prefrontal and parietal cortices, the posterior cingulate and the left medial and inferior temporal lobe. Relative rates showed decreases in the right anterior and posterior frontal region in comparison to the global brain glucose metabolism (Volkow et al., 1988; Henry et al., 2001; Nobler et al., 2001) whereas relative increases were observed in regions with known dopaminergic innervations as in the right basal ganglia, occipital lobe and brainstem (Henry et al., 2001; Nobler et al., 2001). Guze et al.'s study was negative but only focused on the