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Regional cerebral blood flow changes in depression after electroconvulsive therapy

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Abstract

A large number of studies have documented regional cerebral blood flow (rCBF) abnormalities in depression. A smaller yet significant number of studies have examined changes in rCBF before and after treatment. The findings, however, have been variable with regard to changes before and after electroconvulsive therapy (ECT). A consecutive series of patients ($n=10$) with drug-resistant major depressive episode according to DSM-IV with 17-item Hamilton Rating Scale for Depression (HRSD) scores greater than or equal to 14 gave their informed consent and were studied with technetium-99m ethyl cysteinate dimer single-photon emission computed tomography (^{99m}Tc-ECD SPECT) before and after a course of ECT. The results were analyzed with statistical parametric mapping version 99. No region showed significant positive correlations between rCBF patterns of changes and HRSD changes, but three clusters emerged as showing significant negative correlations. These regions corresponded with left frontopolar gyrus, left amygdala, globus pallidus and nucleus accumbens, and left superior temporal gyrus. It was speculated that ECT affected both the prefrontal cortex, commonly assumed to be involved in depression, and the amygdala, known to play a central role in the processing of emotional stimuli, through the limbic–cortical–striatal–pallidal–thalamic circuit.

Keywords: Depressive disorders; Electroconvulsive therapy; Single-photon emission computed tomography; Basal ganglia; Prefrontal cortex

1. Introduction

Functional neuroimaging techniques have helped to identify brain regions involved in the pathophysiology of several psychiatric disorders by measuring regional cerebral blood flow (rCBF) or regional cerebral metabolic rate (rCMR). For the last 20 years, many

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studies have revealed rCBF or rCMR changes in depressed patients, using neuroimaging techniques including single photon emission computed tomography (SPECT) or positron emission computed tomography (PET). Some studies have reported decreased rCBF or rCMR in the frontal or prefrontal regions (Austin et al., 1992; Bench et al., 1993; Mayberg et al., 1994; Awata et al., 2002), the temporal region (Austin et al., 1992; Mayberg et al., 1994), the parietal region (Austin et al., 1992; Bonne et al., 2003) and the cingulate gyrus (Bench et al., 1993; Mayberg et al., 1994). Others have reported no significant change (Maes et al., 1993) or increased rCBF in the frontal (Tutus et al., 1998; Abou-Saleh et al., 1999) and parietal (Abou-Saleh et al., 1999) cortical regions, the hippocampus (Videbech et al., 2001), the amygdala (Hornig et al., 1997), the thalamus (Drevets et al., 1992), the pallidum, the putamen (MacHale et al., 2000), and the cerebellum (Videbech et al., 2001).

Electroconvulsive therapy (ECT) is widely used to treat depressed patients and is considered to be a rapidly acting, effective therapy (UK ECT Review Group, 2003). It is especially indicated for patients who have not responded to conventional antidepressant therapies. A number of studies have examined the effect of a course of ECT on rCBF or rCMR, using SPECT or PET (Nobler et al., 1994; Bonne et al., 1996; Mervaala et al., 2001; Awata et al., 2002; Vangu et al., 2003), but the findings have been variable. Studies of the effect of ECT can be classified into three categories depending on the timing of CBF or CMR during the treatment course (Nobler and Sackeim, 1998): during seizure activity (ictal effect), seconds to several hours after the last ECT or a single ECT in a series (post-ictal effect or the short-term effect), and several days or more after the last ECT (the long-term effect). Studies of the ictal effect have reported differential regional increases and decreases in CBF or CMR (Elizagarate et al., 2001; Blumenfeld et al., 2003). Studies of the short-term effect have consistently reported CBF reductions (Scott et al., 1994; Nobler et al., 1994). However, studies of the long-term effect have resulted in inconsistent findings up to now. Nobler et al. demonstrated that their treatment-responsive patients showed greater reductions of rCBF (Nobler et al., 1994) and rCMR (Nobler et al., 2001) in some regions after a course of ECT. Awata et al. also showed that an rCBF reduction in some regions persisted for several weeks after ECT in voxel-by-voxel analyses (Awata et al., 2002). On the other hand, Bonne et al. reported that ECT increased blood flow in several regions of the brain (Bonne et al., 1996), and Mervaala et al. also reported increased perfusion after ECT in two cortices (Mervaala et al., 2001). According to Milo et al., only patients responsive to ECT showed changes toward normal in rCBF (Milo et al., 2001). In Vangu et al.'s study, all except one patient who responded to ECT showed increased cerebral perfusion as ascertained visually (Vangu et al., 2003). Finally Yatham et al. found no statistically significant differences between pretreatment and posttreatment in CMR (Yatham et al., 2000).

This much variability of findings in the changes of rCBF or rCMR in depressed patients receiving ECT treatment may stem from several sources, including differences in patients' diagnostic and demographic characteristics, differences in imaging techniques and the timing of the scan within the treatment course, and choices of control subjects. Differences in statistical analysis methods (region-of-interest vs. voxel-wise) seem to be another factor that may have contributed to variability of rCBF findings (Bonne et al., 2003). In recent years, statistical parametric mapping (SPM) (Friston et al., 1995) is increasingly used as an objective, whole-brain analysis technique. Among the studies on rCBF or rCMR after ECT reviewed above, only four studies used SPM analysis (Nobler et al., 2001; Awata et al., 2002; Blumenfeld et al., 2003; Bonne et al., 2003). This approach is preferable because it makes no assumptions about the location of significance and can compare cerebral perfusion between PET or SPECT scans on a voxel-by-voxel basis.

It is clinically important to measure rCBF changes in depressed patients before and after ECT because rCBF may provide important information about the brain regions involved in depression and the neural mechanisms of the action of ECT, and may identify specific biological markers capable of predicting therapeutic response. Based on these considerations, we studied a consecutive series of depressed patients who were referred for ECT in our Department of Psychiatry, with technetium-99m ethyl cysteinate dimer (^{99m}Tc-ECD) SPECT before and after a course of ECT, and with SPM99. The aims of the study were to examine the long-term effect of ECT, i.e. the association between the changes in rCBF patterns and the improvement of depressive symptoms after a course of ECT had been completed. Examining this association, a few studies found that a decrease in the CBF or CMR of the frontal region was positively correlated with the antidepressant effect of ECT (Nobler et al., 1994; Henry et al., 2001). However, previous findings were inconsistent regarding the laterality effect of rCBF changes in the frontal lobe