ELSEVIER

Journal of Affective Disorders 106 (2008) 203–208

JOURNAL OF AFFECTIVE DISORDERS

www.elsevier.com/locate/jad

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

E.Z. Schmidt [a,*], B. Reininghaus [a], C. Enzinger [b], C. Ebner [a], P. Hofmann [a], H.P. Kapfhammer [a]

[a] *Department of Psychiatry, Medical University Graz, Auenbruggerplatz 31, 8036 Graz, Austria*
[b] *Department of Neurology and Section of Neuroradiology, Department of Radiology, Medical University Graz, 8036 Graz, Austria*

Received 5 April 2007; received in revised form 19 June 2007; accepted 20 June 2007
Available online 26 July 2007

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).

* Corresponding author. Tel.: +43 385 86214.
E-mail address: eva.schmidt@klinikum-graz.at (E.Z. Schmidt).

0165-0327/$ - see front matter © 2007 Elsevier B.V. All rights reserved.
doi:10.1016/j.jad.2007.06.009

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

Table 1
Synopsis of studies using FDG-PET of the brain to assess potential treatment effects of ECT on cerebral glucose metabolism

Authors	Number of patients; type of depression (responders)	Timing of 2nd PET scan (post-ECT) [a]	ECT: number of sessions, type of stimulation	Changes in glucose metabolism
Volkow et al. (1988)	4 UP (3)	24 h	6–11, bilateral	Reduction: n.s. (Bilateral frontal cortex) Increase: n.a.
Guze et al. (1991)	4 BP (4)	1 day in 3 patients, 112 days in one patient	6–11, unilateral	Reduction: No Increase: No (1 day) Middle frontal gyrus, parahippocampal gyrus (112 days)
Yatham et al. (2000)	6 UP (5)	7 days	8–12, unilateral/ bilateral	Reduction: n.s. Increase: n.s. Correlation with Hamilton Changes: No
Nobler et al. (2001)	6 UP and 4 BP (10)	5 days	6–25, bilateral	Reduction: 1. Bilateral superior frontal lobe, dorsolateral, medial prefrontal cortex 2. Parietal cortex 3. Postcingulate gyrus, left medial, inferior temporal lobe (all [a]) Frontal [b] Increase: Relative increase in occipital regions [b]
Henry et al. (2001)	6 UP and BP (3)	2–7 days	6–10, bilateral	Reduction: Frontal lobes, bilateral parietal regions [a] Right anterior and posterior frontal region [b] Increase: Right basal ganglia, occipital lobe and brainstem Correlation with Hamilton Changes: Decreases in the right parietal region, right anterior, left posterior frontal region

n.a. Not applicable; n.s. not statistically significant.
Bil.: bilateral; Unil.: unilateral.
BP: bipolar; UP: unipolar.
[a] Absolute rates: each region compared before and after ECT.
[b] Relative rates: each region compared to the average in glucose utilization in all cortical regions pre- and post-ECT.

middle frontal and parahippocampal gyrus (Guze et al., 1991).

3.2. Correlation of PET with behavioral changes

Interestingly, only two studies sought to determine changes in depressive symptoms and correlate these with changes in metabolism (Yatham et al., 2000; Henry et al., 2001). While Yatham et al. did not find any significant correlations, Henry et al. reported on an association between decreases in CMR in distinct brain regions (right parietal, right anterior and left posterior frontal) and improvements assessed with the Hamilton depression scale (Yatham et al., 2000; Henry et al., 2001).

4. Discussion

Reduced glucose metabolism after ECT in bilateral anterior and posterior frontal areas represented the most consistent finding. Single studies reported reductions in bilateral parietal regions, the posterior cingulated gyrus and the left medial and inferior temporal lobe (Volkow et al., 1988; Henry et al., 2001; Nobler et al., 2001).

Increases of glucose metabolism after ECT were found in areas with known dopaminergic innervation (right basal ganglia, occipital lobe and brainstem) (Henry et al., 2001; Nobler et al., 2001). Interestingly, a reduction in frontal glucose metabolism has been correlated with a decrease in the number and severity of depressive symptoms. Concurring with this observation, decreases in glucose metabolism in the ventrolateral prefrontal and the orbitofrontal cortex (parallel to a reduction in metabolism in amygdala and right subgenual anterior cingulate) have been found in responders to antidepressant psychopharmacological treatment with paroxetine and desipramine (Drevets et al., 2002; Brody et al., 1999; Brody et al., 2001). A normalization of frontal hypometabolism by sleep deprivation has been shown, while fluoxetine showed increased activity in the dorsolateral prefrontal cortex (Wu et al., 1992; Buchsbaum et al., 1997; Mayberg et al., 2000; Smith et al., 1999). More generally, a prominent role of a disruption of frontal metabolism is further emphasized by the increased incidence of depression in patients with neurological conditions with frontal lobe involvement (Vataja et al., 2001; House et al., 1990). A signal for a long-term effect of ECT on brain metabolism comes from a study by Guze et al., where an increase in glucose metabolism in the middle frontal lobe was observed in a single subject 112 days after ECT (Guze et al., 1991).

During this review, several limitations became apparent. First, different authors used different strategies for quantifying regional metabolism and for data analysis which renders comparisons difficult. Second, sample sizes were small and no distinction of gender, age (ranging between 19 and 84 years) and uni- or bipolar depression was made (despite considerable differences in pathophysiology) (Murphy et al., 1996; Lesser et al., 1994). Third, time intervals between the last ECT and the second PET scan ranged from 24 h to 7 days.

Different hypotheses might be relevant in the interpretation of the presented studies. The dopamine hypothesis indicates that the dopamine system strongly interacts with the norepinephrine and serotonergic systems in the pathophysiology in depression (Henry et al., 2001). Relative increases in glucose utilization were observed in regions with known dopaminergic innervation, consistent with animal studies (Lock and McCulloch, 1991). The finding that a course of ECT might reduce prefrontal CMR at first sight seems to be counterintuitive as pre-treatment deficits in similar regions can be found in depressed subjects. Postictal reduction in CBF and CMR has been reported after epileptic seizures and also after ECT (Silfverskiold et al., 1986; Prohovnik et al., 1986; Ackermann et al., 1986). In this context, short intervals between ECT and PET scan might be particularly problematic and anesthesia may have complicated estimation of metabolic rate because of a depression of brain metabolism (Brodersen et al., 1973; Engel et al., 1982; Pierce et al., 1962).

Differences in CMR between a pair of PET scans were also observed in healthy subjects without any intervention. Anxiety during the first scan has been proposed as an important confounder (Stapleton et al., 1997; Camargo et al., 1992). Difficulties in co-registration, assessing fluctuations in the amount and temporal decay of the administered radioagents, might represent further variation between PET sessions. The final image of FDG-PET represents a summary image over 20 min. Changes in neuroanatomic circuits not seen under resting conditions are missed and both time and spatial resolution are weak. Although there is a dynamic coupling of CMR and CBF, uncoupling phenomena have been reported (Fox et al., 1988; Iadecola and Reis, 1990; Conca et al., 2000). As such it may reflect glial activities (Herscovitch, 1993; Magistretti et al., 1993) and indicate transmitter action in cerebral microvessels and neurons (Podreka et al., 1987; Herscovitch, 1993; Dager and Swann, 1996).

Despite all the limits discussed FDG-PET represents a promising marker of neuronal cell functions and reflects an epiphenomenon of a complex and dynamic interaction of different neurobiochemical processes. Regardless of these methodological difficulties, research into this area highlights the potential of functional neuroimaging. Changes in metabolic patterns have been correlated with changes in behavioral variables reflecting the severity of the underlying disease and found a link between changes in frontal activity and improvements in clinical symptoms (Nobler et al., 2001).

Given the controversies outlined in this review, future research should focus on objectifying clinical improvement of depression after ECT to allow a correlation with possible changes in CMR. Follow up PET scans after six or twelve months should be performed to assess possible long-term effects (Guze et al., 1991). Clearly, a separation of patients with unilateral depression from patients with bipolar depression should be considered and larger samples of patients are needed to increase statistical power and to account for heterogeneity in study cohorts. Studying a group of healthy controls appears to be desirable to assess reproducibility of the system. Although such a study would be both cost-intensive and time-consuming, further research into this area using the approaches proposed appears particularly rewarding when considering the potential implications of these findings.

Role of funding source

All authors declare that there is no role of funding source in the writing of the report and in the decision to submit the paper for publication.

Conflicts of interest

All authors declare that there is no actual or potential conflict of interest including any financial, personal or other relationships with other people or organisations.

References

Ackermann, R.F., Engel Jr., J., Baxter, L., 1986. Positron emission tomography and autoradiographic studies of glucose utilization following electroconvulsive seizures in humans and rats. Ann. N.Y. Acad. Sci. 462, 263–269.

Anghelescu, I., Klawe, C.J., Bartenstein, P., Szegedi, A., 2001. Normal PET after long-term ECT. Am. J. Psychiatry 158, 1527.

Baxter Jr., L.R., Schwartz, J.M., Phelps, M.E., Mazziotta, J.C., Guze, B.H., Selin, C.E., Gerner, R.H., Sumida, R.M., 1989. Reduction of prefrontal cortex glucose metabolism common to three types of depression. Arch. Gen. Psychiatry 46, 243–250.

Baxter Jr., L.R., Phelps, M.E., Mazziotta, J.C., Schwartz, J.M., Gerner, R.H., Selin, C.E., Sumida, R.M., 1985. Cerebral metabolic rates for glucose in mood disorders. Studies with positron emission tomography and fluorodeoxyglucose F 18. Arch. Gen. Psychiatry 42, 441–447.

Brodersen, P., Paulson, O.B., Bolwig, T.G., Rogon, Z.E., Rafaelsen, O.J., Lassen, N.A., 1973. Cerebral hyperemia in electrically induced epileptic seizures. Arch. Neurol. 28, 334–338.

Brody, A.L., Saxena, S., Silverman, D.H., Alborzian, S., Fairbanks, L.A., Phelps, M.E., Huang, S.C., Wu, H.M., Maidment, K., Baxter Jr., L.R., 1999. Brain metabolic changes in major depressive disorder from pre- to post-treatment with paroxetine. Psychiatry Res. 91, 127–139.

Brody, A.L., Saxena, S., Stoessel, P., Gillies, L.A., Fairbanks, L.A., Alborzian, S., Phelps, M.E., Huang, S.C., Wu, H.M., Ho, M.L., Ho, M.K., Au, S.C., Maidment, K., Baxter Jr., L.R., 2001. Regional brain metabolic changes in patients with major depression treated with either paroxetine or interpersonal therapy: preliminary findings. Arch. Gen. Psychiatry 58, 631–640.

Buchsbaum, M.S., Wu, J., Siegel, B.V., Hackett, E., Trenary, M., Abel, L., Reynolds, C., 1997. Effect of sertraline on regional metabolic rate in patients with affective disorder. Biol. Psychiatry 41, 15–22.

Camargo, E.E., Szabo, Z., Links, J.M., Sostre, S., Dannals, R.F., Wagner Jr., H.N., 1992. The influence of biological and technical factors on the variability of global and regional brain metabolism of 2-[18F]fluoro-2-deoxy-D-glucose. J. Cereb. Blood Flow Metab. 12, 281–290.

Conca, A., Fritzsche, H., Peschina, W., Konig, P., Swoboda, E., Wiederin, H., Haas, C., 2000. Preliminary findings of simultaneous 18F-FDG and 99mTc-HMPAO SPECT in patients with depressive disorders at rest: differential correlates with ratings of anxiety. Psychiatry Res. 98, 43–54.

Conca, A., Prapotnik, M., Peschina, W., Konig, P., 2003. Simultaneous pattern of rCBF and rCMRGlu in continuation ECT: case reports. Psychiatry Res. 124, 191–198.

Dager, S.R., Swann, A.C., 1996. Advances in brain metabolism research: toward a moving picture of neural activity. Biol. Psychiatry 39, 231–233.

Drevets, W.C., Videen, T.O., Price, J.L., Preskorn, S.H., Carmichael, S.T., Raichle, M.E., 1992. A functional anatomical study of unipolar depression. J. Neurosci. 12, 3628–3641.

Drevets, W.C., Bogers, W., Raichle, M.E., 2002. Functional anatomical correlates of antidepressant drug treatment assessed using PET measures of regional glucose metabolism. Eur. Neuropsychopharmacol. 12, 527–544.

Enev, M., McNally, K.A., Varghese, G., Zubal, I.G., Ostroff, R.B., Blumenfeld, H., 2007. Imaging onset and propagation of ECT-induced seizures. Epilepsia 48, 238–244.

Engel Jr., J., Kuhl, D.E., Phelps, M.E., 1982. Patterns of human local cerebral glucose metabolism during epileptic seizures. Science 218, 64–66.

Fox, P.T., Raichle, M.E., Mintun, M.A., Dence, C., 1988. Nonoxidative glucose consumption during focal physiologic neural activity. Science 241, 462–464.

Guze, B.H., Baxter Jr., L.R., Schwartz, J.M., Szuba, M.P., Liston, E.H., 1991. Electroconvulsive therapy and brain glucose metabolism. Convuls. Ther. 7, 15–19.

Henry, M.E., Schmidt, M.E., Matochik, J.A., Stoddard, E.P., Potter, W.Z., 2001. The effects of ECT on brain glucose: a pilot FDG PET study. J. ECT 17, 33–40.

Herscovitch, P., 1993. Evaluation of the brain by positron emission tomography. Rheum. Dis. Clin. North Am. 19, 765–794.

Holthoff, V.A., Beuthien-Baumann, B., Zundorf, G., Trieme, A., Ludecke, S., Winiecki, P., Koch, R., Fuchtner, F., Herholz, K., 2004. Changes in brain metabolism associated with remission in unipolar major depression. Acta Psychiatr. Scand. 110, 184–194.

House, A.M., Dennis, M., Warlow, C., Hawton, K., Molyneux, A., 1990. Mood disorders after stroke and their relation to lesion location. A CT scan study. Brain 113, 1113–1129.

Iadecola, C., Reis, D.J., 1990. Continuous monitoring of cerebrocortical blood flow during stimulation of the cerebellar fastigial nucleus: a study by laser-Doppler flowmetry. J. Cereb. Blood Flow Metab. 10, 608–617.

Janicak, P.G., Davis, J.M., Gibbons, R.D., Ericksen, S., Chang, S., Gallagher, P., 1985. Efficacy of ECT: a meta-analysis. Am. J. Psychiatry 142, 297–302.

Lesser, I.M., Mena, I., Boone, K.B., Miller, B.L., Mehringer, C.M., Wohl, M., 1994. Reduction of cerebral blood flow in older depressed patients. Arch. Gen. Psychiatry 51, 677–686.

Lock, T., McCulloch, J., 1991. Local cerebral glucose utilization after chronic electroconvulsive shock: implications for the mode of action of electroconvulsive therapy. J. Psychopharmacol. 5, 111–119.

Magistretti, P.J., Sorg, O., Yu, N., Martin, J.L., Pellerin, L., 1993. Neurotransmitters regulate energy metabolism in astrocytes: implications for the metabolic trafficking between neural cells. Dev. Neurosci. 15, 306–312.

Martinot, J.L., Hardy, P., Feline, A., Huret, J.D., Mazoyer, B., Attar-Levy, D., Pappata, S., Syrota, A., 1990. Left prefrontal glucose hypometabolism in the depressed state: a confirmation. Am. J. Psychiatry 147, 1313–1317.

Mayberg, H.S., Brannan, S.K., Tekell, J.L., Silva, J.A., Mahurin, R.K., McGinnis, S., Jerabek, P.A., 2000. Regional metabolic effects of fluoxetine in major depression: serial changes and relationship to clinical response. Biol. Psychiatry 48, 830–843.

McNally, K.A., Blumenfeld, H., 2004. Focal network involvement in generalized seizures: new insights from electroconvulsive therapy. Epilepsy Behav. 5, 3–12.

Murphy, D.G., DeCarli, C., McIntosh, A.R., Daly, E., Mentis, M.J., Pietrini, P., Szczepanik, J., Schapiro, M.B., Grady, C.L., Horwitz, B., Rapoport, S.I., 1996. Sex differences in human brain morphometry and metabolism: an in vivo quantitative magnetic resonance imaging and positron emission tomography study on the effect of aging. Arch. Gen. Psychiatry 53, 585–594.

Nobler, M.S., Oquendo, M.A., Kegeles, L.S., Malone, K.M., Campbell, C.C., Sackeim, H.A., Mann, J.J., 2001. Decreased regional brain metabolism after ECT. Am. J. Psychiatry 158, 305–308.

Pierce Jr., E.C., Lambertsen, C.J., Deutsch, S., Chase, P.E., Linde, H.W., Dripps, R.D., Price, H.L., 1962. Cerebral circulation and metabolism during thiopental anesthesia and hyperventilation in man. J. Clin. Invest. 41, 1664–1671.

Pluijms, E.M., Birkenhäger, T.K., Mulder, P.G., Van den Broek, W.W., 2006. Influence of episode duration of major depressive disorder on response to electroconvulsive therapy. J. Affect. Disord. 90, 233–237.

Podreka, I., Suess, E., Goldenberg, G., Steiner, M., Brucke, T., Muller, C., Lang, W., Neirinckx, R.D., Deecke, L., 1987. Initial experience with technetium-99m HM-PAO brain SPECT. J. Nucl. Med. 28, 1657–1666.

Prohovnik, I., Sackeim, H.A., Decina, P., Malitz, S., 1986. Acute reductions of regional cerebral blood flow following electroconvulsive therapy. Interactions with modality and time. Ann. N.Y. Acad. Sci. 462, 249–262.

Prudic, J., Haskett, R.F., Mulsant, B., Malone, K.M., Pettinati, H.M., Stephens, S., Greenberg, R., Rifas, S.L., Sackeim, H.A., 1996. Resistance to antidepressant medications and short-term clinical response to ECT. Am. J. Psychiatry 153, 985–992.

Sermet, E., Gregoire, M.C., Galy, G., Lavenne, F., Pierre, C., Veyre, L., Lebars, D., Cinotti, L., Comar, D., Dalery, J., Bobillier, P., 1998. Paradoxical metabolic response of the human brain to a single electroconvulsive shock. Neurosci. Lett. 254, 41–44.

Silfverskiold, P., Gustafson, L., Risberg, J., Rosen, I., 1986. Acute and late effects of electroconvulsive therapy. Clinical outcome, regional cerebral blood flow, and electroencephalogram. Ann. N.Y. Acad. Sci. 462, 236–248.

Smith, G.S., Reynolds III, C.F., Pollock, B., Derbyshire, S., Nofzinger, E., Dew, M.A., Houck, P.R., Milko, D., Meltzer, C.C., Kupfer, D.J., 1999. Cerebral glucose metabolic response to combined total sleep deprivation and antidepressant treatment in geriatric depression. Am. J. Psychiatry 156, 683–689.

Stapleton, J.M., Morgan, M.J., Liu, X., Yung, B.C., Phillips, R.L., Wong, D.F., Shaya, E.K., Dannals, R.F., London, E.D., 1997. Cerebral glucose utilization is reduced in second test session. J. Cereb. Blood Flow Metab. 17, 704–712.

UK ECT Review Group, 2003. Efficacy and safety of electroconvulsive therapy in depressive disorders: a systematic review and meta-analysis. Lancet 361, 799–808.

Vataja, R., Pohjasvaara, T., Leppavuori, A., Mantyla, R., Aronen, H.J., Salonen, O., Kaste, M., Erkinjuntti, T., 2001. Magnetic resonance imaging correlates of depression after ischemic stroke. Arch. Gen. Psychiatry 58, 925–931.

Volkow, N.D., Bellar, S., Mullani, N., Jould, L., Dewey, S., 1988. Effects of electroconvulsive therapy on brain glucose metabolism: a preliminary study. Convuls. Ther. 4, 199–205.

Wu, J.C., Gillin, J.C., Buchsbaum, M.S., Hershey, T., Johnson, J.C., Bunney Jr., W.E., 1992. Effect of sleep deprivation on brain metabolism of depressed patients. Am. J. Psychiatry 149, 538–543.

Yatham, L.N., Clark, C.C., Zis, A.P., 2000. A preliminary study of the effects of electroconvulsive therapy on regional brain glucose metabolism in patients with major depression. J. ECT 16, 171–176.

Yuuki, N., Ida, I., Oshima, A., Kumano, H., Takahashi, K., Fukuda, M., Oriuchi, N., Endo, K., Matsuda, H., Mikuni, M., 2005. HPA axis normalization, estimated by DEX/CRH test, but less alteration on cerebral glucose metabolism in depressed patients receiving ECT after medication treatment failures. Acta Psychiatr. Scand. 112, 257–265.