Correspondence

EDITED BY KIRIAKOS XENITIDIS

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ECT and rTMS for depression

Schulze-Rauschenbach et al (2005) report an interesting study comparing electroconvulsive therapy (ECT) with repetitive transcranial magnetic stimulation (rTMS) for the treatment of major depression. They conclude that both are equally efficacious, but rTMS is associated with fewer cognitive side-effects.

Ultimately, a therapeutic plan that optimally helps a given individual cope with disability and recover can only be devised when the physician transcends the traditionally proven, generic insights about pathological anatomy, physiopathology and aetiology of disease, and identifies the unique characteristics of a specific patient. Therefore, therapeutic decisions should always consider the risk–benefit ratio of each treatment option for the specific patient and circumstances. The focus on differences in side-effect profile of rTMS and ECT in major depression by Schulze-Rauschenbach et al is thus most valuable.

In 2003 we conducted a similar study of which the authors appear to be unaware (O’Connor et al, 2003). We compared 14 patients with medication-refractory depression who underwent ECT with 14 who underwent rTMS. ECT had a significantly greater positive effect on mood than a 2-week trial of rTMS. The reason for this difference between our results and other published trials comparing rTMS with ECT (Janicak et al, 2002; Grunhaus et al, 2003; Schulze-Rauschenbach et al, 2005) is unclear. In our study, as in that of Schulze-Rauschenbach et al, ECT was applied unilaterally approximately three times per week for 2–4 weeks. We applied rTMS in sessions of 1600 stimuli at 10 Hz and 90% of motor threshold intensity to the left dorsolateral prefrontal cortex daily (Monday through Friday) for 2 consecutive weeks. Thus we employed ‘stronger’ parameters of rTMS than Schulze-Rauschenbach et al, who applied shorter trains and also limited stimulation to only 2 weeks. Nevertheless, in both studies ECT and rTMS may have been used at insufficient doses, since progression to bilateral ECT (UK ECT Review Group, 2003) or extension of daily rTMS to 3–4 weeks (Gershon et al, 2003; Rumi et al, 2005) were not considered.

In our study ECT exerted a deleterious but transient effect on various components of memory that was no longer detected 2 weeks after the end of treatment. However, there was evidence of persistent retrograde amnesia after ECT. Patients undergoing rTMS experienced only a modest reduction in the severity of depression but there was no evidence of anterograde or retrograde memory deficits and there was a remarkable suggestion of cognitive improvement even in those patients with no antidepressant benefits. These findings, as those of Schulze-Rauschenbach et al, suggest that the cognitive effects of rTMS might not be the consequence of the mood effects. The suggestion of independent effects of rTMS on mood and cognition also seems to be supported by a previous study of rTMS in major depression (Moser et al, 2002) and studies in patients with cerebrovascular (Rektorova et al, 2005) and Parkinson’s disease (Boggio et al, 2005). Boggio et al (2005) showed that 10 days of rTMS treatment (15 Hz, left dorsolateral prefrontal cortex) improved cognition and depression in patients with Parkinson’s disease, but this cognitive improvement was not correlated with mood change. Furthermore, there was no correlation between cognitive and motor function improvement. Thus, it appears that left prefrontal rTMS exerts differential effects on cognition, mood and motor function. Even in individuals without psychiatric illness, we have recently shown that suppression of the right hemisphere by slow rTMS can enhance verbal memory, while left-sided slow rTMS disrupts it (Kahn et al, 2005). Therefore, cognitive and antidepressant effects of rTMS may be the consequence of modulation of dissociable neural networks.

Effects of repetitive TMS and fluoxetine on cognitive function in patients with Parkinson’s disease and concurrent depression. Movement Disorders, in press.


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Authors’ reply: We are glad that Fregni et al share our interest in side-effect profiles of rTMS and ECT in major depression and thank them for their positive judgement of our work. They draw attention to their
related study (O’Connor et al, 2003), which we regretfully overlooked when we wrote our article. They point to similarities between the studies, but speculate about the reasons for the discrepant findings regarding the clinical efficacy of rTMS. We believe the following methodological differences might contribute.

First, in the study by O’Connor et al (2003), the level of baseline depression was different in the treatment groups: those receiving rTMS were significantly less depressed than those receiving ECT. Furthermore, those treated with rTMS were medication-free for at least 2 weeks but those receiving ECT continued to receive antidepressant medication. Finally, the duration of treatment – and the interval between initial and follow-up measurements – tended to be longer (2-4 weeks) in the ECT group than in the rTMS group (2 weeks). These features most likely contributed to the better clinical efficacy of unilateral ECT compared with rTMS in the study by O’Connor et al, where not a single patient treated with rTMS showed a clinically significant (50% reduction in the Hamilton Rating Scale for Depression) response.

In contrast, those treated with either rTMS or ECT in our study were matched for baseline levels of depression. They were treated for about 5 weeks on average. Antidepressant medication was kept constant in both ECT and rTMS treatment arms, and both treatments were clinically effective in about half of the patients. In principle, a comparative study of side-effects of two treatments only seems to be relevant when both modalities have a measurable clinical effect.

We agree that the effects of rTMS on mood and cognition may be independent of each other, and may point to different neural networks mediating these effects. However, the better retrograde memory performance after treatment, even in patients lacking an antidepressant response to rTMS, reported by O’Connor et al, is not necessarily suggestive of such a dissociation. It might also be explained by test repetition effects, which were masked in the ECT group because of enduring memory impairments. A healthy control group assessed repeatedly can be used to control for this confounding variable. We noted that patients receiving rTMS did not show stronger improvements over time than the control group for any objective cognitive measure, effectively ruling out a genuine memory-enhancing effect of rTMS as used in our study.

With the development of magnetic seizure therapy as possibly yet another form of brain stimulation for depression, the issue of relative benefits, side-effects and the duration of both will need further careful assessment. We have highlighted some of the methodological issues to be considered when studying the effects of different treatments on cognition.

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CBT for refractory psychotic symptoms

We read with interest the study of Valmaggia et al (2005), particularly noting that the interventions delivered were based on a comprehensive treatment manual and delivered by therapists specifically trained in the protocol.

By the authors’ admission, some aspects of the intervention showed only modest benefit over supportive counselling; indeed the only outcomes when examining the 95% CI that provide support for cognitive–behavioural therapy (CBT) are physical characteristics of hallucinations and cognitive interpretation of hallucinations. At the same time, the 95% CI for negative symptoms (Positive and Negative Syndrome Scale) suggest that supportive counselling is more effective than CBT. In addition, the effects of 16 sessions of highly structured CBT disappeared at follow-up. We were therefore very surprised at the authors’ conclusions that this therapy should be available within in-patient facilities. As experienced CBT clinicians and nurses, we are acutely aware that there is a serious shortage of CBT therapists and nursing staff available to provide therapist or ‘manualised’ CBT. Indeed, waiting lists of over 12 months are common for therapist-provided out-patient CBT. In turn, a very large number of in-patient wards rarely, if ever, see a psychologist, let alone have the capacity to train therapists and provide 16h of therapy! Should we not be more prudent when making claims on such scant resources by first ensuring that we have adequate evidence to support such claims? Perhaps the editor should consider making obligatory a section in every paper relating to real-world implications.


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Urban environment and schizophrenia

Selten et al (2003) cite two reasons for the increased risk of schizophrenia in Surinamese immigrants to The Netherlands. These are an increased base rate in the Surinamese population and exposure to an urban competitive Dutch society. These findings are of particular interest to researchers in Trinidad and Tobago because both countries share a similar mix of African and East Indian population and historically were simultaneously but independently developed by British and Dutch colonisers.

Interestingly, the authors noted that in their own study of Surinam and studies from Jamaica, Trinidad and Barbados no excess of schizophrenia was reported in the native countries. In addition, they argue that an overrepresentation of patients resident in Paramaribo points to an urban causation. The two reasons cited by the authors need further analysis.

The concept of urban environment causing disease is complex. Van Os (2004) proposes that the urban environment with a set of environmental factors acting between birth and the onset of illness is a risk factor for psychotic illness. However, Hutchinson & Morgan (2005) argue that the risk for psychosis is not specifically the urban environment but the social disadvantages and isolation experienced by vulnerable individuals in an urban society. These interact with perceptions of self, transgenerational expectations, cognitive processes and the urban environment to confer risk. Although both these views are tenable, it is not fair to assume that the variables described as associated with an urban environment will also be present in urban or rural environments? It appears, then, that the effect lies in the confounding variables described rather than the urban effect.
"Toxicity" of any environment is determined by the stability of the social framework that governs the lives of individuals. It is debatable whether the variables of racism, alienation, political discrimination, unemployment, lack of opportunity, crime and fear of crime are more common in urban areas in developing countries. There is often no means of rural living for urban dwellers in these countries and many opt to escape through migration to foreign lands. Migration from the native country is therefore associated with a release from these stressful factors, as is the case of some ethnic groups in the Caribbean. In societies where environmental factors confer greater stress either in the native or the receiving country, the rates of psychosis will be higher and should not be attributed only to the base rates of the native country as proposed by Selten et al. If a social model were to be developed, consideration must be given to the time between assault and disease manifestation with a formula for lag time, rather than equating disease with geographical location at the time of manifestation.

The degree of urbanisation cannot simply be judged by the number of households per square kilometre. In developing countries, the division of areas into urban and rural is arbitrary; consideration must be given to the availability of basic amenities, geographical distance from cities and towns, the availability of newspapers and electronic media, the degree of literacy, transportation systems and the presence of household amenities. The fact that all people in Surinam have access to psychiatric care except for two remote districts that are looked after by medical missions suggests a movement away from rurality, since access to psychiatric care is a good index of development. Nevertheless, in many rural communities there is a distrust of Western psychiatric services and, as pointed out by Selten et al, help is often sought from traditional healers. This can result in statistical inaccuracies in both directions, through leakage of cases and delay in first contact with the psychiatric services.

Our findings in Trinidad suggest that gender and ethnicity are important variables in "urbanisation". In more urbanised areas, more males aged between 15 and 29 years presented with schizophrenia than females. The affected young males were more likely to be of African descent. A neuroprotective effect of oestrogen in females could be responsible for their low rates of schizophrenia, and neuronal plasticity in response to exposure to a new environment and its effects on the disease process is another area of possible future research.

Selten et al and others have raised important questions that are relevant to Caribbean people and those who have migrated and settled abroad. Cross-cultural differences, environmental factors and gender affect the risk for the development of psychosis but the final common pathway of any disease is at the molecular level. Genetic factors must therefore also be taken into consideration.


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Authors' reply: We thank Dr Maharajh for his reaction. We agree with his observation that it is uncertain whether the urban effect is also operative in Surinam. The sample size of our study was too small for definitive conclusions and the possibility remains that some patients in rural areas do not see doctors.

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Advance directives and advance agreements

The paper by Amering et al (2005) adds to the growing literature on advance directives. The main difficulty with advance directives seems to be that with the available training programmes very few service users can be enthused to draft one. The authors recommend more training of service users and substantial administrative commitment from service providers.

The same could be said about advance agreements, another tool to empower patients to become partners in negotiating individualised treatment and care in time of crisis. Advance agreements (Behandlungsvereinbarungen) are widely used in German-speaking countries and according to a quick web search are offered routinely in at least 50 psychiatric hospitals in Austria, Switzerland and Germany.

Unfortunately no systematic research on advance agreements has been conducted in these countries; the only trial that has been published is from the UK (Henderson et al, 2004) and showed a significant reduction in the use of compulsory admission and treatment. Interestingly, advance agreements are seen as legally binding in Germany but not in the UK. Thomas & Cahill (2004) sceptically commented on the Henderson study that ‘Liberation cannot be handed to the oppressed by the oppressor’ Basaglia (1979) would probably answer that this is precisely what the psychiatrist is supposed to do: ‘to enter a dialogue with the patient, a dialogue not between subject and object, but between two human beings, who have become subjects. If we don’t accept this logic of contradictions between two individuals, we should better trade bananas than work as doctors’.

Advance agreements, from the experience in German-speaking countries, are usually initiated by nurses and doctors working in in-patient settings, who have perhaps the strongest incentive to reduce compulsory in mental health (as those who restrain, detain and enforce treatment). Negotiating job plans with senior and junior doctors, with ward managers and nurses where time is allocated to discuss and draft advance agreements might be a way forward.


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Authors' reply: In practice, rights are only as visible as the mechanisms put in place...
for their exercise. Formal recognitions – laws, regulations, policies – may assist but do not suffice on their own. The thrust of our exploratory report into the making of psychiatric advance directives was twofold. First, when presented with the opportunity and a modicum of support, many service users prove eager and able to participate in planning for future treatment eventualities: taking inventory, lining up support and laying out preferences. But second, the invitation to draft needs to be a credible one. At least in the context we studied, the system of care appears to be woefully out of step with that readiness and ability.

In line with the first, we would join Dr Zinkler in welcoming all manner of collaborative arrangements and shared decision-making that represent practical steps towards a progressively more transparent and reciprocally accountable service system. In line with the second, however, we would underscore the formal importance of one critical ingredient in the programme that Henderson et al (2004) studied: the appointment of a designated third party to ensure that crisis plans are faithfully integrated into treatment.

Such positions serve two purposes. They are strategic mechanisms for expediting the formal agreement to negotiate mutually acceptable treatment plans, bridging the power differential and ensuring that each side is heard. They are also the administrative equivalent of ‘earnest money’ – the collateral or upfront investment that ratifies an institutional commitment. Once standardised, that small modification has the potential to build the necessary momentum to alter ‘the way we do business here’, which makes for sustainable change.

**Doctors and lawyers**

Sarkar & Adshedd (2005) present important issues regarding the nature of the relationship between psychiatrists and patients in the process of judicial hearings, focusing particularly on the conflict that may arise from differing roles. There are two points I wish to add.

First, the outcome of hearings is very much a result of the behaviour of all players present, and there are ways as clinicians we may work to reduce harm that may arise from them. During reform of the Mental Health Act in New Zealand in the early 1990s, very similar dynamics emerged between judges, counsel for patients (always provided in New Zealand), review tribunal members and psychiatrists acting as responsible clinicians under the Act. To address these difficulties, the New Zealand Law Society recommended that counsel take on a ‘best outcomes’ approach, assisting the patient to achieve the best they could, rather than strictly following the letter of the patient’s instructions (McCarthy & Simpson, 1996). Such recommendations decreased damaging adversarial exchanges in committal and tribunal hearings, because of an awareness that ‘juridogenic’ harm could be long-lasting, and that such hearings were not criminal ones.

We also noted that the behaviour of clinicians could have a significant impact on how coercive or procedurally fair committal processes were for the patient. It came to be recommended that the psychiatrist shares their report to the tribunal with the patient and their counsel, and works through the issue of agreement or disagreement with the patient in advance of the hearing (Ministry of Health, 1997). This appears to have reduced possible negative impacts on the therapeutic relationship and may increase the patient’s satisfaction because of their sense of having received an opportunity to voice their opinion and scrutinise the basis of their detention. Such an outcome can be achieved if the process is managed openly by psychiatrists, and in an inquisitorial but non-confrontational manner by legal officers.

Second, civil committal is not simply a loss of liberty, but a focused loss of liberty whose purpose is the restoration or maximising of autonomy, for a person whose competence is lowered by mental illness. Liberty is therefore restored through detention and treatment, unlike other forms of state-mandated detention (e.g. detention that is motivated as punishment and public protection). Sadly, civil committal is increasingly being misused overtly or covertly for primary public protective purposes alone, in the absence of a competence-lowering disorder. One senses that some of Sarkar & Adshedd’s concern relates to the committal hearings for the latter group of ‘patients’. In ‘dangerous and severe personality disorder’ one is acting for security needs, with limited therapeutic health impact. In ‘dangerous and severe schizophrenia’ one is acting for the health needs of the patient, if the risk is symptom driven, and protecting the public is secondary. The due process protections necessary for these two different uses of civil committal may indeed need differing hearings.


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**One hundred years ago**

Dr. KRAFFT-EBING’S *Textbook of Insanity* [Textbook of Insanity. By Dr. von R. Krafft-Ebing, late Professor of Psychiatry and Nervous Diseases in the University of Vienna. Translated from the last German edition by Professor C. G. Chaddock, M.D., of St. Louis University, with introduction by Frederick Peterson, M.D., President of the New York State Commission in Lunacy. Philadelphia; F. A. Davis and Co. 1905. (Demy 8vo, pp. 654. 4 dollars.)] has enjoyed such wide popularity,
has run through so many editions, and has been for so many years the leading textbook of insanity in many Continental universities that an English translation cannot fail to be of great service to both English and American students. It is true that more modern writers, particularly Kraepelin and his school, are opening up fresh views, and bringing about gradual alterations in the classification of mental diseases, but Krafft-Ebing’s work still is, and is probably destined for many years to be, one of the standard clinical expositions of the facts of morbid psychology. An indefatigable worker, a lucid and convincing writer, a master in the art of clinical description, and the discoverer of many important psycho-pathological facts, his appointment to succeed Meynert at Vienna was well merited, and the thirteen years of his professorship, which ended on his death three years ago, bore golden fruit in his lectures and this book. Needless to say, some of the early chapters in Book I in which the subject and aids of its study are treated, would have been amended in so far as they related to the underlying neural changes in the insanities, had the author lived, but these have been ably brought up to date by the translator, Dr. Chaddock. Book I and Book II deal respectively with the general and special pathology of the insanities and their treatment. Under the heading of General Pathology are treated the elementary anomalies of cerebral function in the affective, intellectual, and psycho-motor spheres; the causes of insanity; the course and prognosis of mental diseases, and general diagnosis and therapy. The treatment of these subdivisions is admirably concise and finely didactic. Book III, the last, gives the special pathology and treatment of insanity arranged according to the author’s classification, which, like that of the Medico-Psychological Association of Great Britain, is partly aetiological and partly symptomatological. It is more complicated than ours, but is much more complete. Under the first main division of the “psycho-neuroses” are considered melancholia, mania, primary curable dementia (stupor), primary hallucinatory insanity and secondary insanity and terminal dementia. “Psychic Degenerations” come next under review, and this part contains most excellent accounts of paranoia and the periodic insanities. In Part II of the “Special Pathology” mental diseases arising out of constitutional neuroses are discussed at considerable length and thoroughly elucidated. It is impossible to do more here than outline the system of classification adopted, but attention may be drawn to the author’s masterly explication of this intricate subject, in which he evolves order from seeming chaos and knits up the ravelled sleave of overlapping symptoms. In this part, also, are considered imperative ideas which, it will be remembered, were first defined by Krafft-Ebing in 1876 and have, in most English textbooks, hardly been accorded their due importance. The chronic intoxications and the states of arrest of psychic development complete a work deservedly considered a classic. Illustrating footnotes and clinical records illustrate the text throughout, and theories and hypotheses have been, as far as possible, avoided. The clear style and comprehensible language of the author have been admirably translated into English by Dr. Chaddock, to whom are due the thanks of all students of psychiatry.

**REFERENCE**


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**Apology**

Who pays the piper? *BJP*, 187, 195. The letter by Dr Calton in the August issue of the *Journal* was inappropriately published and, contrary to *Journal* policy, the authors were given no right of reply. The *Journal*, and Dr Calton, would like to give an unreserved apology to Professors Owen and Craddock for giving the impression that the views expressed in their commissioned editorial were influenced by their occasional support from pharmaceutical companies.
Urban environment and schizophrenia
H. D. Maharajh
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References
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