

Letters to the editor

An open trial of daily left prefrontal cortex repetitive transcranial magnetic stimulation for treating medication-resistant depression

While most depressive symptoms are eliminated by the current pharmacological treatment, as many as 50–60% have incomplete recovery [2]. Transcranial magnetic stimulation (TMS) for alleviating depression have recently garnered attention. We conducted a 2–4-week open trial of left dorso-lateral prefrontal rTMS (100% of MT, 5 Hz, 8 s, 40 trains per day, every weekday) on refractory depressed subjects ($n = 6$). After 2 weeks of treatment, scores of the 21-item Hamilton depression rating scale were reduced by 58%. Efficacy in two subjects, who were partially responsive to initial treatment, was increased by an additional 2 weeks of treatment. This finding supports the notion that more pulses can help some patients achieve full remission of their disease. Surprisingly, continuance of treatment in depressed patients with partial remission to rTMS has been rarely studied. Our results also showed a significant negative correlation between reductions of HDRS score after 2 weeks of rTMS treatment and patients' age ($r = -0.797$; $P = 0.029$), suggesting that younger patients might be more responsive to rTMS treatment, but this finding need to be further confirmed.

In comparison with the 41% [6] and 20% [1] improvement in HDRS scores previously reported, 58% improvement occurred in our study. All three studies used the same 10-day treatment course, but ours used 1600 stimulation pulses per session, the Triggs study used 2000 per session, and the George study only used 800 per session. Therefore, the fact that the results of Triggs' and ours studies differed from those of the George study may indicate a dose-related effect. Other parameters differing in these three studies might be the reason; we used 5 Hz for 8 s, whereas Triggs and George used 20 Hz for 2 s. In addition, the rTMS treatment response seemed to be influenced by the percent motor threshold intensity (our study: 100% vs. Triggs: 80%) or the medication status of the subjects (our study: on antidepressants vs. Triggs: drug-free). Further study of these factors is also needed. Although the sample size was small in this clinical open study, we were still able to see an age effect on rTMS response. This finding is consistent with those in previous reports [4,5]. The degree of brain atrophy, particularly prefrontal, might explain the relatively less antidepressant response to rTMS in older depressed subjects [3].

Our preliminary finding supports the notion that rTMS improves mood in medication-resistant depressed patients and further demonstrate more pulses can help some patients achieve full remission of their disease. Also, younger patients seemed to have better rTMS responses. However, more research is needed to optimize rTMS treatment delivery.

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Chih-Chia Huang

Department of Psychiatry,
Veterans General Hospital-Taipei, No. 201, Sec 2,
Shih-Pai Road, Taipei 112, Taiwan, ROC
Institute of Clinical Medicine,
National Yang-Ming University, Taipei, Taiwan, ROC

Tung-Ping Su *

Department of Psychiatry,
Veterans General Hospital-Taipei, No. 201, Sec 2,
Shih-Pai Road, Taipei 112, Taiwan, ROC
Division of Psychiatry, School of Medicine,
National Yang-Ming University,
Taipei, Taiwan, ROC

E-mail address: tpsu@vghtpe.gov.tw (T.-P. Su)

Ian-Kai Shan
Kelly Chang
*Department of Psychiatry,
Veterans General Hospital-Taipei, No. 201, Sec 2,
Shih-Pai Road, Taipei 112, Taiwan, ROC*

I.-Hua Wei
*Department of Anatomy and Cell Biology,
College of Medicine, National Taiwan University,
Taipei, Taiwan, ROC*

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* Corresponding author.

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Obsessive–compulsive disorder and treatment with clozapine in 200 patients with recent-onset schizophrenia or related disorders

Sir,

Clozapine has been associated with emergence of obsessive–compulsive symptoms in patients with schizophrenia [2,3,6,7]. However, this association is not unequivocally found [5].

We identified obsessive–compulsive disorder (OCD) according to DSM-IV criteria before and after initiation of treatment with clozapine or other antipsychotic medication in a chart study of 200 patients (158 male, mean age at admission 21.5 years (S.D. = 5.03) with recent-onset schizophrenia ($n = 152$), schizophreniform disorder ($n = 12$) or schizoaffective disorder ($n = 36$), randomly chosen from 900 first admissions from 1984 to 2000 to a first psychosis unit in the Academic Medical Center, Amsterdam.

Four out of 41 patients (9.8%) on clozapine had OCD before the start of treatment. During treatment their OCD symptoms reduced and at discharge OCD was no longer diagnosed. However, another four patients (9.8%) developed de novo OCD during clozapine therapy.

In the group treated with other antipsychotic medication 10 out of 154 (6.5%) showed OCD before treatment and this number was reduced to three at discharge (1.9%). None of the patients developed de novo OCD during treatment with other antipsychotic medication. Five patients refused medi-

cation. Clozapine therapy was associated with more OCD cases at discharge (Pearson chi-square = 6.0, $df = 2$, $P = 0.05$) and with less net reduction in OCD cases (Pearson chi-square = 18.2, $df = 4$, $P = 0.001$) compared to treatment with other antipsychotic drugs.

Our results suggest that a subgroup of patients with recent-onset schizophrenia or related disorders is susceptible for induction of OCD during treatment with clozapine and that clozapine is associated with reduction of OCD in another subgroup. Our findings underscore the response complexity concerning OCD to clozapine in patients with schizophrenic disorders. This response complexity may be related to 5-HT_{2A} receptor gene polymorphism's. Such polymorphism's are associated with clinical response to clozapine [1] and OCD [4], and could explain the differential effects of clozapine in our patients.

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Lieuwe De Haan *
Aygul Oekeneva
Therese Van Amelsvoort
Don Linszen

*Adolescent Clinic, Academic Medical Center, Department
of Psychiatry, University of Amsterdam, Post Box 22700,
1100 DE Amsterdam, The Netherlands*
E-mail address: l.dehaan@amc.uva.nl (L. De Haan).

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* Corresponding author.

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