

ALCOHOL AND SUICIDALITY: COULD DEEP TRANSCRANIAL MAGNETIC STIMULATION (DTMS) BE A POSSIBLE TREATMENT?

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INTRODUCTION

The prevalence of alcohol abuse increased in the United States from 12.5% in men and 6.4% in women in 1994 (Kessler et al. 1994) to 24.6% in men and 11.5% in women in 2007 (Hasin et al. 2007). Alcohol use disorder is a widespread and serious personal and public health problem in the United States (Hasin et al. 2007). The lifetime prevalence of suicide attempts in patients with alcohol dependence is about 40% and mortality for suicide is 7% (Inskip et al. 1998). Alcohol abuse is linked to impulsivity, aggression, social norm transgression, poor judgment, abnormal speech, perceptual blunting, and increased pain threshold, which may all contribute to the suicide attempt. Mental disorders, particularly depression, are often associated with suicide (Inskip et al. 1998). However, suicide results from the interplay of complex socio-cultural factors; recently, the existence of suicidal syndromes independent from psychiatric illness has been proposed (Mann 2008). Pharmacotherapy for suicide prevention is only partially effective, supporting the need for new treatment modalities. Effective treatments should improve mood and reduce impulsiveness. Transcranial magnetic stimulation (TMS) has been shown to influence affective and cognitive states (George & Belmaker 2006) and may be considered as a potential treatment to reduce suicidality. Deep transcranial magnetic stimulation (dTMS), which showed efficacy in the treatment of drug-resistant depression (Bersani et al. 2013), might be effective in reducing suicidality through the modulation of associated mental health conditions. Prefrontal abnormalities have been documented in many substance abuse disorders and alcoholism (Moreno-López et al. 2012).

We provide dTMS in our alcohol service as part of the detoxification program, because it has shown effectiveness in reducing craving and depressive

symptoms (Rapinesi et al. 2013, Girardi et al. 2014). We describe a case of a patient who presented with alcohol use disorder and depression with suicidal ideation, who was treated with dTMS to benefit both substance abstinence and mood. Other than the expected effect on alcohol craving, we surprisingly observed improvement of suicidality independently from the effect on mood. The use of repetitive (r)TMS, but not dTMS, was recently shown to be associated with a stronger trend vs. sham rTMS towards a rapid reduction of suicidal ideation in patients with suicidal crisis (George et al. 2014).

The patient provided written informed consent for the collection of his data for research, participation in the study, and subsequent publication of study results. The Hospital's ethical board gave approval for carrying-out all therapeutic procedures.

CASE REPORT

A 56-year-old married state employee, the father of a 24-year-old girl, referred to our alcohol service day-hospital in October 2012 due to generalized anxiety and somatic symptoms, irritability, depressed mood, severe loss of libido, erectile impotence, and suicidal ideation. He manifested hopelessness, anhedonia, and social withdrawal. He had lost his mother one year ago after a long struggle with metastatic mammary carcinoma and following this, he had developed intolerable anxiety symptoms which he tried to soothe with drinking. He gradually increased his drinking to 1.5 Lt/day. Anxiety relief was only temporary; depressive symptoms mounted along with suicidal ideation. His problem-drinking had not affected his job.

He had no psychiatric history in his family, but ten years ago, after a traffic accident resulting in multiple fractures, chest injury, brain concussion, and residual-

dominant side motor deficit and pain, he manifested panic episodes during autumn to early winter, and this was repeated each year. He was prescribed serotonin transporter inhibitors and benzodiazepines with little benefit. One-year psychodynamically-oriented short-term psychotherapy produced little change. His psychiatric symptomatology had affected his marital life, with ensuing selective impotence and loss of libido towards his wife. After his mother's death, anxiety, depressive, and sexual symptoms generalised.

We subjected him to add-on dTMS (details about this procedure are available from the corresponding author) for twenty sessions spanning over one month (five weekly sessions). After the 7th session, anxiety and panic-like symptoms disappeared, and had no more craving; suicidal ideation subsided after the 11th session, while after the final session, the patient showed improved posture and reported improved pain and motor deficit, improved erectile symptoms and increased libido, and subsiding of depressive symptoms, hopelessness, anhedonia, and withdrawal. At the 6-month follow-up, he did not resume drinking, had no craving for alcohol, and does not think about suicide any more. His mood was stable and normal.

His suicidal ideation was confirmed at baseline by the score on the suicide item 3 of the 21-item Hamilton Depression Rating Scale (HDRS-21) (Hamilton 1960). The patient was assessed at baseline, after two weeks of dTMS, after the end of the dTMS cycle and at the 12-month follow-up with the HDRS-21, to evaluate depressive symptomatology, the Obsessive Compulsive Drinking Scale (OCDS) to evaluate craving (Anton et al. 1995), and the Clinical Global Impressions-Improvement Scale (CGI-s) (Guy 1976) to evaluate general psychiatric conditions. HDRS-21 dropped progressively from 25 at baseline to 16 at the 2nd week of dTMS, to 8 at the final dTMS session, finally to 1 at the 12-month follow-up, with the HDRS-21 suicide item dropping from 3 to 0 at the 2nd week of dTMS, and remaining at 0 through the entire observation period. OCDS dropped from 22 at baseline to 7 at the 2nd week of dTMS, to 3 at the final dTMS session, remaining stable thereafter. CGI-s showed clinical improvement, dropping from 6 to 2 at the 2nd week of dTMS, to 1 at the final dTMS session and at the 12-month follow-up.

DISCUSSION

We described a patient with recent onset alcohol use disorder comorbid with depressive symptoms and suicidal ideation who resisted to psychopharmacotherapy and psychotherapy, and who responded promptly to dTMS with disappearance of suicidal ideation and depression, abatement of alcohol craving, and general improvement of his psychiatric conditions. The effect was maintained at a 12-month follow-up. However, the disappearance of suicidal ideation was not

secondary to significant mood improvement, as it preceded it by two weeks.

It is possible that the different time course that depressive symptom and suicidal ideation improvement followed was due to different mechanisms. DLPFC stimulation could have ensued in reorganisation and better executive function performance, that may allow better planning and flexibility, better control of inhibition and reduced impulsiveness, possibly through improved plasticity, and reorganised thinking. In fact, improved cognitive task performance has been observed during DLPFC repetitive transcranial magnetic stimulation in patients with alcohol abuse (Herremans et al. 2013). Abnormal executive function has been shown in suicidal people (Raust et al. 2007) and abnormal DLPFC activation has been shown in suicidal adolescents as a reaction to angry faces (Pan et al. 2013); suicidal adults with depression show DLPFC thinning on T1-weighted MRI (Wagner et al. 2012) and suicide victims display abnormal prefrontal gene expression (Sequeira et al. 2012, Monsalve et al. 2014). Taken together, these data underline the importance of the DLPFC in suicidal behaviour; DLPFC stimulation through dTMS may counteract this prefrontal abnormality.

We used an antidepressant protocol that we showed to be effective in patients with dysthymia comorbid with alcohol use disorder, and the rapid disappearance of suicidal ideation emerged as a desirable side effect. Recently, a prospective, sham-controlled study conducted in two East-Coast centres in the US with the aim to reduce suicidality, used rTMS and obtained a rapid antisuicidal effect (George et al. 2014). Their method differs significantly from ours, in that they used a 3-day schedule with three daily rTMS sessions, with an 8-coil and 10 Hz stimulation at 120% of the measured motor threshold, 5-sec train duration, 10 sec intertrain interval for 30min, for a total of 6,000 pulses each session, while we used 55 18-Hz trains per session at 120% of the measured motor threshold, with 2-sec duration each 20 sec inter-train intervals, for a total of 1,980 pulses per session (details about this procedure are available from the corresponding author). Their regimen, as opposed to ours, was a "bolus" administration of TMS; furthermore, they rated suicidality with a specific scale, while we used the corresponding item of the Hamilton Depression Rating Scale. They obtained a rapid and lasting disappearance of suicidal thoughts, while the decline in suicidality in our patient was smooth, gradual, and persistent.

Chronic alcohol abuse is a risk factor for suicidality (Kessler et al. 1994). Alcohol diminishes the inhibitory control of the prefrontal cortex and increases pain threshold (Abernathy et al. 2010); as a consequence, it is possible that uncontrolled high-risk behaviour in some individuals may ensue. dTMS may be considered as a potential treatment to reduce craving and suicidality, as it is able to stimulate the prefrontal cortex,

thereby strengthening the mechanisms of self-control and planning.

This is a case study, therefore, it cannot be extended to the entire suicidal population. However, given the enormous social cost of suicide and the current lack of effective methods to counteract it, dTMS is a treatment modality that deserves further testing in a larger population.

CONCLUSIONS

Although alcohol abuse and suicide may be intimately linked, they are both complex, multifactorial phenomena. Suicidal ideation and attempts are relatively common findings among people with alcohol use, especially among those with comorbid major depression or bipolar disorder. Patients with alcohol abuse should be screened for psychiatric symptoms and for suicidality. Clinicians should assess the severity of suicidal symptoms and other depressive signs and symptoms in patients with alcohol abuse. Suicidal behaviour is a complex medical and social problem (Mann 2008), thus individual approaches lacking integration are unlikely to contribute to a significant, substantial decline in suicide rates. The potential of dTMS for reducing craving and suicide ideation in patients with substance use disorder deserves to be further investigated. Specific protocols to reduce suicidal ideation with dTMS have to be implemented and tested.

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Conflict of interest:

In the past two years, Paolo Girardi has received research support from Lilly, Janssen, and Springer Healthcare, and has participated in Advisory Boards for Lilly, Otsuka, Pfizer, Schering, and Springer Healthcare and received honoraria from Lilly and Springer Healthcare. Ruggero N. Raccach is scientific consultant to ATID Ltd, distributor of deep r-TMS (Brainsway) technology in Italy. All other authors of this paper have no relevant affiliations or financial involvement with any organization or entity with a financial interest in, or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties. This work has not been supported by any funding.

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