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Intermittent theta burst stimulation for major depression during pregnancy

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Dear Editor,

Major depression during pregnancy affects between 8.3% and 12.7% of women, but as few as 12% of these women receive formal psychiatric treatment [1]. Untreated, or incompletely treated, depression in pregnancy is associated with adverse pregnancy, infant and child outcomes. It is also associated with a heightened risk for postpartum depression and chronic maternal depression, which are linked to child socioemotional and behavioural problems across the lifespan [1].

While psychotherapy alone can be effective in mild cases, antidepressants are recommended for moderate and severe depression. Nonetheless, as many as 88% of pregnant women with depression do not seek treatment [2]. The stigma and uncertainty surrounding the safety of fetal exposure to antidepressants contribute to the low treatment rates [3]. Only a minority (23–33%) of pregnant women believe antidepressants are acceptable during pregnancy [3], and almost 60% who are treated with antidepressants before pregnancy stop taking them in the first trimester [4]. Although antidepressants pose risks to the fetus similar to gastrointestinal medications and antibiotics, 87% of women believe that the risk to the fetus is highest with antidepressants [5]. In this context, non-invasive brain stimulation strategies that locally stimulate the brain areas involved in depression but pose no theoretical fetal risk, such as repetitive transcranial magnetic stimulation (rTMS), are attractive treatment options for moderate and severe major depression during pregnancy [6].

Previous studies support the idea that rTMS is safe and effective in treating antenatal depression with minimal adverse effects. In a recently published randomized controlled trial, 22 women were treated with rTMS for depression during the second or third trimester of pregnancy (randomized to either active or sham rTMS,1:1 ratio). The protocol consisted of 20 sessions of 1 Hz to the right dorsolateral prefrontal cortex (single train, 900 pulses per session, 100% of the motor threshold), and the authors reported rTMS to be safe and superior to the sham stimulation [6]. In a case series, 29 depressed pregnant patients who underwent rTMS treatment reported a 41.4% and 20.7% response and remission rates, respectively [7], and the newborns had no abnormalities reported, all born at >36 weeks of gestational age, with a mean Apgar scores of 8.1/8.8. No abnormalities were reported during a mean follow-up of 3.7 years, and rTMS was not associated with the developmental scores [8].

Although rTMS has a favorable safety profile, it is time intensive. rTMS is approved by the US Food and Drug Administration (FDA), and the protocol requires 19–37.5 min of 10 Hz stimulation per session. Such long session lengths restrict treatment capacity and increase the cost per session. In addition, the long duration of the rTMS sessions represents a potential risk for supine hypotensive syndrome, which is caused by the compression of the inferior vena cava by the gravid uterus when in a supine position - usually adopted for subject positioning during rTMS treatments. Symptoms, including pallor, dizziness, low blood pressure, sweating, nausea, increased heart rate, and loss of consciousness, usually occur within 3–10 minutes after lying down [9].

A new rTMS technique called intermittent theta burst stimulation (iTBS) mimics endogenous theta rhythms, induces synaptic long-term potentiation, and can deliver 600 pulses in just 3 min [10]. A large trial recently demonstrated that 3-min iTBS sessions are noninferior to the standard FDA-approved 37.5-min 10 Hz sessions [10]. Correspondingly, the FDA approved, in 2018, the use of the 3-min iTBS sessions for the treatment of major depression. Herein we report a case of woman who received iTBS treatment for major depression during the third trimester of pregnancy.

“Ms. C” is a 38-year-old female patient (G2P1) diagnosed with recurrent major depressive disorder. In the period of 4 years, she received three complete courses of iTBS for depression, achieving remission of the depressive symptoms after 20 sessions in each successive course. She presented with a recurrence of the depressive episode during the third trimester of pregnancy. Due to the moderate nature of the depressive symptoms, her preference for not taking antidepressants due to poor tolerability and efficacy, and the history of achieving remission in the three previous courses of iTBS, a new course was recommended.

The treatment was delivered every weekday for four weeks (20 sessions) using 120% of her motor threshold, triplet 50 Hz bursts, repeated at 5 Hz, 2s on and 8s off, with a total of 600 pulses (3 min, 9 seconds) per session. Real time MRI-guided neuronavigation was used for coil positioning over the left dorsolateral prefrontal cortex using the MNI152 stereotaxic coordinates (x−38, y+44, z+26) (ANT Neuro, Enschede, Netherlands). All sessions were performed using the MagPro X100 equipped with a B70 fluid-cooled coil and high-performance cooler (MagVenture, Farum, Denmark) [10].

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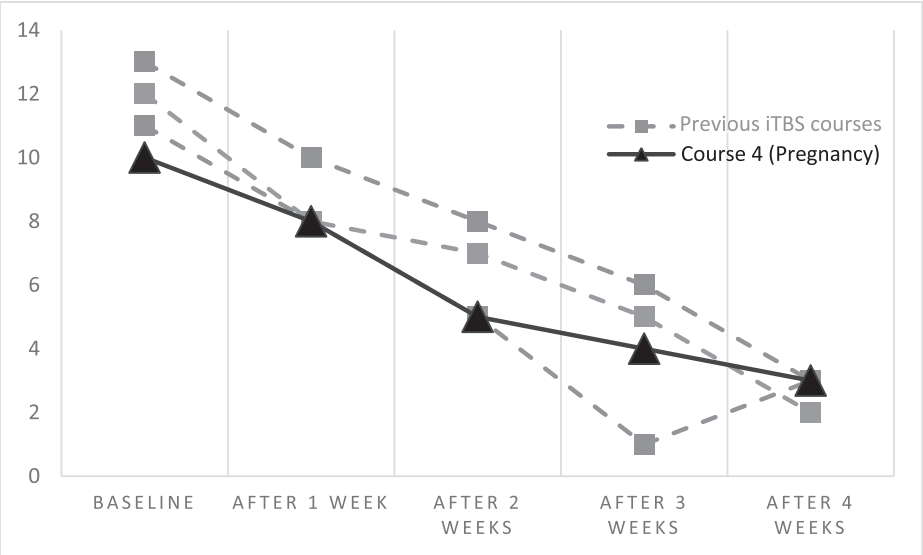

Fig. 1. Quick Inventory of Depressive Symptomatology *Self-Report* scores at baseline and during the 4-week course of iTBS.

Full remission was achieved following the 20 sessions of iTBS, as defined by a Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR) score of three after the treatment course (Fig. 1), and no adverse effects or complications during treatments were reported. The subject reported significant improvements in her mood, hedonic capacity, psychomotor symptoms, concentration, and future outlook, similar to the symptom improvements observed with the three previous courses. She still endorsed increased appetite, some excessive daytime sleepiness and fatigue, which she attributed to the pregnancy. She experienced no complications during her pregnancy, including hypertension and diabetes. A planned caesarean section was performed in the week following the end of the treatment (at 39 gestational weeks). The healthy full-term 7.8-pound neonate had no malformations, and no complications during childbirth (APGAR 9/9).

To our knowledge, this is the first report of iTBS for major depression during pregnancy. Given its high prevalence, the low rate of treatment-seeking and adherence to antidepressants, and the adverse consequences if left untreated, developing a safe treatment for moderate and severe depression during pregnancy remains a high public health priority. In this context, iTBS represents a promising treatment, reducing the risk of supine hypotensive syndrome during treatment sessions, and the unnecessary exposure – of both the fetus and the mother - to untreated depression or to medication treatment.

Conflicts of interest

AT reports no biomedical interests. SNV receives royalties from UpToDate Inc for chapters related to depression and pregnancy. ZJD has received within the last 3 years both research and equipment in-kind support for an investigator-initiated study through Brainsway Ltd. and Magventure. FVR receives research support from CIHR, Brain Canada, Michael Smith Foundation for Health Research, Vancouver Coastal Health Research Institute, and in-kind equipment support for an investigator-initiated trial from MagVenture. He has participated in an advisory board for Janssen. JD has received research support from CIHR, NIMH, Brain Canada, the Canadian Biomarker Integration Network in Depression, the Ontario Brain Institute, the Klarman Family Foundation, the Arrell Family Foundation, the Edgestone Foundation, a travel stipend from Lundbeck and from ANT Neuro, an advisor to BrainCheck and in-kind equipment support for this investigator-initiated trial from MagVenture. DMB has received research support from the CIHR, NIH, Brain Canada and the Temerty Family through the CAMH Foundation and the Campbell Research Institute. He received research support and in-kind equipment support for an investigator-initiated study from Brainsway Ltd., and he is the principal site investigator for three sponsor-initiated studies for Brainsway Ltd. He received in-kind equipment support from Magventure for investigator-initiated research. He received medication supplies for an investigator-initiated trial from Indivior.

References

[1] Vigod SN, Wilson CA, Howard LM. Depression in pregnancy. BMJ 2016;352:i1547. https://doi.org/10.1136/bmj.i1547.
[2] Marcus SM, Heringhausen JE. Depression in childbearing women: when depression complicates pregnancy. Prim Care 2009;36:151–65. https://doi.org/10.1016/j.pop.2008.10.011.
[3] Goodman JH. Women's attitudes, preferences, and perceived barriers to treatment for perinatal depression. Birth 2009;36:60–9. https://doi.org/10.1111/j.1523-536X.2008.00296.x.
[4] Ververs T, Kaasenbrood H, Visser G, Schobben F, de Jong-van den Berg L, Egberts T. Prevalence and patterns of antidepressant drug use during pregnancy. Eur J Clin Pharmacol 2006;62:863–70. https://doi.org/10.1007/s00228-006-0177-0.
[5] Bonari L, Koren G, Einarson TR, Jasper JD, Taddio A, Einarson A. Use of antidepressants by pregnant women: evaluation of perception of risk, efficacy of evidence based counseling and determinants of decision making. Arch Womens Ment Health 2005;8:214–20. https://doi.org/10.1007/s00737-005-0094-8.
[6] Kim DR, Wang E, McGeehan B, Snell J, Ewing G, Iannelli C, et al. Randomized controlled trial of transcranial magnetic stimulation in pregnant women with major depressive disorder. Brain Stimul 2018. https://doi.org/10.1016/j.brs.2018.09.005.
[7] Hizli Sayar G, Ozten E, Tufan E, Cerit C, Kagan G, Dilbaz N, et al. Transcranial magnetic stimulation during pregnancy. Arch Womens Ment Health 2014;17:311–5. https://doi.org/10.1007/s00737-013-0397-0.
[8] Eryilmaz G, Sayar GH, Ozten E, Gul IG, Yorbik O, Isiten N, et al. Follow-up study of children whose mothers were treated with transcranial magnetic stimulation during pregnancy: preliminary results. Neuromodulation 2015;18:255–60. https://doi.org/10.1111/ner.12231.
[9] Kim DR, Wang E. Prevention of supine hypotensive syndrome in pregnant women treated with transcranial magnetic stimulation. Psychiatr Res 2014;218:247–8. https://doi.org/10.1016/j.psychres.2014.04.001.
[10] Blumberger DM, Vila-Rodriguez F, Thorpe KE, Feffer K, Noda Y, Giacobbe P, et al. Effectiveness of theta burst versus high-frequency repetitive transcranial magnetic stimulation in patients with depression (THREE-D): a randomised non-inferiority trial. Lancet 2018;391:1683–92. https://doi.org/10.1016/S0140-6736(18)30295-2.

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