Transcranial Magnetic Stimulation for the Treatment of Non-Motor Symptoms of Parkinson's Disease – A Review

Gomes-Pereira, E ¹; Guedes, R ¹; Reis, C ¹

¹ Clinic of Psychiatry and Mental Health of São João University Hospital Centre, Porto

Background

Parkinson's Disease (PD) is a neuropsychiatric disorder with both motor and non-motor symptoms. The latter include depression, anxiety, apathy and psychosis, among others. Treatment of these symptoms is often challenging due to poor efficacy and side effects of the available drugs. Transcranial Magnetic Stimulation (TMS) is a non-invasive brain stimulation treatment that is considered safe and has been studied in several psychiatric disorders.

Objectives

To review the potential role of TMS on the treatment of non-motor symptoms of PD.

Methods

A search for English-written papers in the past 5 years was conducted in the PubMed database. The keywords used were *Parkinson's Disease*, *TMS*, *depression*, *anxiety*, *apathy*, *psychosis* and *non-motor*. Titles and abstracts of the resulting articles were reviewed and selection was made based on its relevance to the subject.

Results

Eighteen articles were selected. All of the included articles focused on the use of TMS for treatment of depression, either as a primary or secondary outcome. No data were found regarding anxiety, apathy or psychosis.

- **Anderková & Rektorová, 2017**
“(…) rTMS has beneficial and long-lasting antidepressant effects in PD populations, particularly when high-frequency stimulation is targeted over the left DLPFC and when repeated session protocols are used. (...) similar to that of antidepressant medication, with considerably fewer side effects.”
- **Zhou et al., 2019**
“rTMS has a significant positive pre-post anti-depressive effect over PFC in patients with depression, especially by using 5.0 Hz frequency with 90% RMT intensity in discontinuous days (...)”
- **Bomasang-Layno et al., 2015**
“Use of rTMS in this population looks promising but requires further study.”
- **Brys et al., 2016**
“(…) we found benefit of M1 rTMS for motor symptoms of PD but no benefit of left DLPFC rTMS for mood symptoms and no benefit of combined M1 1 DLPFC rTMS for motor or mood symptoms.”
- **Dinkelbach et al., 2017**
“Beneficial effects on both mood and cognitive dysfunctions were observed in PD patients treated with high-frequency rTMS over prefrontal cortices.”
- **Lesenskyj et al., 2018**
“Combining study groups that specifically examined rTMS to the DLPFC yielded an even higher treatment efficacy. (...) these findings suggest that rTMS may be an effective treatment for depression in patients with PD.”
- **Makkos et al., 2016**
“Our results demonstrate the beneficial effects of high-frequency bilateral M1 rTMS on depression and health-related quality of life in PD.”
- **Martin et al., 2017**
“(…) evidence in support of modest task-specific cognitive enhancing effects of repeated rTMS treatments when administered to the prefrontal cortex in depressed patients.”
- **Qin et al., 2018**
“In summary, our meta-analysis failed to demonstrate a beneficial effect of HF-rTMS for the treatment of depression in PD patients (...)”
- **Pal et al., 2010**
“(…) a 10-day left DLPFC rTMS had an antidepressant effect on mild or moderate depression in PD (...)”
- **Randver, 2018**
“Nearly all studies included in this review that applied high-frequency rTMS over prefrontal brain regions found beneficial effects on mood, thereby alleviating depression associated with PD (...)”
- **Elder & Taylor, 2014**
“Several trials incorporated treatment and placebo combinations of anti-depressant medication and TMS, generally showing comparable improvements in mood to those observed using anti-depressant medication with sham TMS.”
- **Schrag & Taddei, 2017**
“While there was no clear evidence of an improvement of mood symptoms when compared to sham-TMS, others concluded some beneficial effect of TMS on depression. Further large-scale studies are needed.”
- **Shin et al., 2016**
“(…) the HF-rTMS of the left DLPFC was an effective treatment for depressive symptoms in MDD patients with PD (...)”
- **Torres et al., 2015**
“In conclusion, dTMS is a strong predictor of improvements in PD symptoms. (...) significant improvements in motor and non-motor symptoms, ADL, gait, posture, balance, risk of fall, gait speed, autonomic and depressive symptoms.”
- **Wang et al., 2018**
“(…) rTMS over DLPFC can improve depression in PD patients, similar to treatment with SSRIs.”
- **Xie et al., 2015**
“(…) rTMS was superior to sham-rTMS and possessed same antidepressant efficacy as SSRIs (...)”
- **Yokoe et al., 2017**
“(…) the application of HF-rTMS over the M1 or the SMA was able to significantly ameliorate the motor symptoms, but it did not clearly ameliorate the mood disturbances in the PD patients.”

Conclusions

Despite conflicting results, unilateral high-frequency rTMS over the left dorsolateral-prefrontal cortex has the most consistent evidence on the treatment of depressive symptoms in patients with PD. This technique seems to be, at least, as effective as SSRIs, with some studies showing that the antidepressive effect may persist for several weeks. Reported side effects are generally mild and usually restricted to headaches and facial pain. In conclusion, TMS seems to be a valid treatment option for depression in PD, with the perks of few side effects and no drug interactions. However, further large-scale, randomized, control studies with well-defined TMS protocols are needed, in order to make clear recommendations.