# The Psychomotor Retardation, a Marker of Response to rTMS Treatment in Patients with Major Depressive Disorder?

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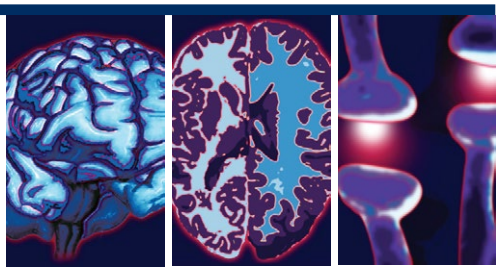
Commentary



# The Psychomotor Retardation, a Marker of Response to rTMS Treatment in Patients with Major Depressive Disorder?

Thibault Deschamps[1,†], Anne Sauvaget[2,3], Samuel Bulteau[2], Véronique Thomas-Ollivier[1]

**Abstract**

Now more than ever, let us continue to develop personalized medicine to improve the remission rate for treatment resistant depressed patients. Recent findings about psychomotor retardation - a core symptom of depression - provide new insights into the predictive efficiency of personalized treatments, such as rTMS.

**Keywords**

Psychomotor retardation, Depressive disorder, rTMS treatment, Cognitive and behavioral therapies

Repetitive transcranial magnetic stimulation (rTMS) is a therapeutic option often used in routine care plans for patients with major depressive disorder (MDD), especially for those who do not respond to treatment with medication or cognitive and behavioral therapies. Although clinically safe and quite efficient for medication-resistant major depression [1], this noninvasive neurostimulating technique is not without a certain cost [2]. In view of budget constraints related to healthcare strategies, providing attending psychiatrists with robust treatment moderators (i.e. patient's baseline characteristics with high predictive power of effectiveness of any specific treatment) may optimize the personalized treatment selection for MDD patients [3,4].

In this context of examination on specific dimensions of depression that can guide treatment selection, our current proposal is to advocate, or perhaps even better to reclaim the psychomotor retardation (PMR) - a core symptom of depression – whose importance in diagnostic, prognostic and personalized therapeutic issues is often understated, or even skipped. Not so much by its lack of relevant value in psychiatry, but mostly through the inconsistency of research evidence addressing these purposes. Here is the opportunity to shine light on the recent findings about PMR driving new insights into the predictive efficiency of personalized treatments, such as rTMS.

The PMR concern has been around for quite some time. From Widlöcher [5], this clinical symptom is considered to play a crucial role in depression. This "seniority" has resulted in the clinical use of interviewer-rated scales based on observations of behavior, such as the retardation item of the Hamilton Depression Rating Scale [6] and the Salpêtrière Retardation Rating Scale (SRRS) [5,7]; yet only few studies focused upon the prognostic dimension of PMR. Perhaps quite as rare, but more recent is the research examining

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the neuroanatomical substrates and the cortical mechanisms underlying depression-related PMR [8]. One reason can probably be ascribed to different methodological issues, starting with those related to the very nature of clinical scales and their relative sensitivity to subtle changes and robust prognostics. Besides this approach based on depression-focused questionnaires requires that MMD patients have reasonable insight into their symptoms. Yet there may be physical (motor), psychological (cognitive) or other changes that the patient is not aware of. That brings us to our first point to consider: a scientific and clinical interest for better characterization and independent outcomes measures of the PMR.

Based on the well-established definition, including many motor and cognitive components [9], the first step aimed to investigate the feasibility of a comprehensive battery of tests (e.g. 3-Meter Timed Up and Go test, dual-tasking postural control assessments, the handgrip strength test or verbal fluency tasks) assessing PMR for MDD patients after a 3-week protocol of rTMS. All these measures not only were feasible, free of adverse effects, and well tolerated by the MDD patients in naturalistic conditions before or after the rTMS protocol, but a preliminary insight emerged from improvements in some psychomotor assessments following the intervention, especially in balance performance [10]. Be that as it may, once this pre-requisite has been validated, the prognostic potential of PMR is ready to produce scientific evidence. That is our challenging conviction.

In that respect, we argue that the limited application of the PMR as a relevant treatment moderator in precision medicine can be explained not only by the few studies available in the literature about the neurostimulation-related effects on PMR in MDD patients, but also by their divergent results. Clearly, some studies have shown that rTMS significantly decreased PMR [11], whereas others found that rTMS did not influence PMR [12]. No firm conclusion could be drawn at this stage. Note also that these studies quantified the PMR either with one specific scale, or with only one item of a specific depression scale, but no cognitive, motor and behavioural assessments were specifically recorded. To overcome this second issue, Deschamps, *et al.* [13] recently investigated the interplay between the PMR scores and balance performance in MDD patients. The standing postural sway, particularly through the analysis of the center-of-pressure (COP) velocity based parameters, was easily measured by using a force platform during trials, with or without vision, and while backward counting (dual task). As a striking result, significant positive correlations were found between the PMR scores and the velocity-based COP variables, especially in the dual-task conditions. Hence, the study showed for the first time that the posture-cognitive dual tasking performance can be a good and reliable hallmark of depression-related PMR. In addition, some other explanatory results strongly suggest that this initial postural instability may be a consistent moderator that could predict positive outcomes in MDD patients after an rTMS intervention, such as significant improvements in PMR scores, depression (decrease in MADRS scores) and postural instability [13]. A more efficient postural control to rTMS stimulation marks substantively the motor component of PMR, even if an improved dual task performance is likely indicative of improvement in cognitive efficiency (i.e. lower attentional demands).

All else being equal, it's really time to produce neuroscientific evidence of these promising findings. We believe that this potential "dual postural moderator" deserves to be taken into consideration and specifically examined in a double-blind, sham-controlled trial to determine a prediction model, and if appropriate, to validate its clinical relevance on an independent cohort. Be convinced, and let us collectively enable this ambition.

As the last argument from these perspectives, far from being specific to neuropsychiatry, devising common and standardized measurements to assess motor-cognitive interactions may influence the future knowledge of the underlying mechanisms that can affect pathways to disability in mental disorders. Undoubtedly, the cognitive and motor aspects of everyday life for all human beings share behavioral and etiological factors that can drive new insights into (the best) treatment selection for individual patients. In that way, PMR-related dual postural performance seems to be a suitable candidate, by considering the cognitive and mobility dysfunction in MDD patients as a common problem. Mechanistically, changes in PMR-related brain networks probably arise from the alteration of limbic signals, at the interface of emotion, volition, higher-order cognitive function, and movement control

[8]. Combined with positive effects of rTMS treatment on the limbic system, a reduction of attention and cognitive deficits in MDD patients can be found [14], with positive impact on fine motor outcomes [15] and postural control [10,13]. However, a great deal of research still is needed to increase this functional anatomical specificity of PMR.

The potential benefits of evidence linking cognition/motor interaction in MDD patients may be clinically crucial. It may offer a reliable prognostic tool for detecting patients who are more likely to remit based on their response to rTMS treatment.

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## Disclosures

None.

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