# Supplementary Motor Area as a Target for Non-Invasive Neuromodulation: A Systematic Review of the Clinical and Basic-Research Approaches

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Supplementary motor area (SMA) is a multifunctional cortical region, which is a promising target for neuromodulation in a wide range of neuropsychiatric disorders, affecting motor and cognitive domains [4]. Repetitive TMS (rTMS) of the SMA has been shown to improve motor symptoms in Parkinson's Disease, Obsessive-Compulsive Disorder, Tourette's syndrome etc. [5,1,2]. However, no systematic review has been conducted on this topic. A current study is dedicated to cover this lack of knowledge and to provide an overview of the SMA functional properties that were examined with rTMS.

This systematic review was conducted and reported according to the Cochrane and PRISMA guidelines (PROSPERO ID - 141289). All original articles published up to 27 July 2019, considering SMA rTMS were extracted from PubMed, Cochrane, and Scopus databases. The qualitative analysis was performed with narrative textual synthesis. Three investigators assessed the studies' quality with the Cochrane risk of bias tool [3]. Articles were divided into two categories: (1) studies in healthy volunteers and (2) studies including patients.

Literature analysis revealed the effect of SMA rTMS neuromodulation on a wide range of the motor control aspects (movement preparation, sequence processing, breathing control), emotions and time processing (Fig.1; Table 1). SMA is reported to have strong functional connectivity with the primary motor cortex, prefrontal cortex, secondary somatosensory cortex, insula, and cerebellum. rTMS of the SMA caused clinical improvement in Parkinson's Disease, Obsessive-Compulsive Disorder, and Tourette's Syndrome patients (Fig.1; Table 2).

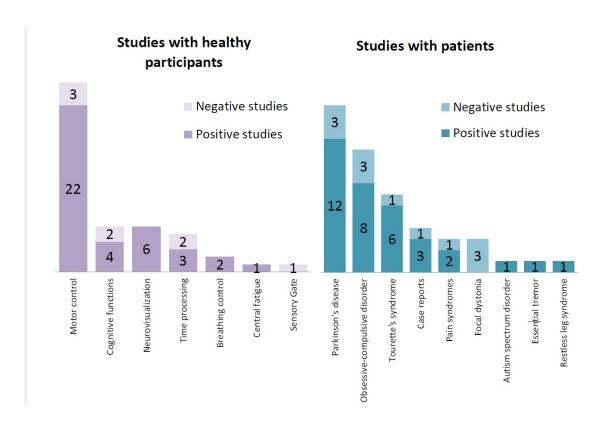
Analysis of the SMA rTMS studies showed that SMA is critically involved in motor and cognitive processes. In a clinical setup, SMA seems to be an effective target for neuromodulation in patients with diseases affecting the motor system. This review will be in help for the invention of new neuromodulatory protocols targeting SMA (e.g. catatonia).

#### Источники и литература

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#### Иллюстрации



**Puc. 1.** Figure 1: Representation of the SMA rTMS studies, with healthy volunteers and patients, reflecting positive/negative outcomes, number of studies examined function/disease

## Effects of neuromodulation in healthy participants

	Inhibitory rTMS	Excitatory rTMS		
	Motor control		Motor control	
SMA	Increase of success in:		Increase of success in:	
SIVIA	•motor inhibition task performance	6 1 Hz	•sequence learning task performance	20 Hz
	Decrease of success in:  • sequence learning task performance  • sequence production task performance  • bimanual coordination task performance  • movement preparation task performance  Decrease of:  • MEPs from diaphragm  • accuracy in time processing task	1 Hz 1 Hz 1 Hz 1 Hz 50 Hz 50 Hz	<ul> <li>mental rotation task performance</li> <li>action observation task performance</li> <li>Increase of MEPs from diaphragm</li> <li>Decrease in load-induced hyperventilation</li> <li>Decrease of success in bimanual coordination task performance</li> </ul>	10 Hz 10 Hz 5 Hz 5 Hz 5 Hz, 20 Hz
	Cognitive functions		Cognitive functions	
	Increase of:  • valence of emotionally negative faces perception	1 Hz		5 Hz
	valence of emotionally positive perception     phasic alertness     the reward perception	1 Hz 1 Hz 50 Hz		
Pre-	Motor control		Motor control	
SMA	Increase of success in : • motor inhibition task performance	1 Hz	•Increase of success in motor inhibition task performance	10 Hz
	motor inhibition task performance     sequence learning task performance	50 Hz 1 Hz	Cognitive functions Disturbance of happy	10 Hz
	periormance		faces recognition	

Рис. 2. Table 1: Representation of the SMA inhibitory and excitatory rTMS significant effects on motor and cognitive functions in healthy volunteers

### Effects of neuromodulation in patients

		Inhibitory rTMS	Excitatory rTMS
SMA	PD	Reduce:  • L-dopa-induced dyskinesia  • L-dopa-induced dystonia  • Other hyperkinetic symptoms	Reduce:  • PD symptoms (not specified);  • Freezing of gait;  • Bradykinesia;  • Mirror movements reduction. Improvement in:  • Self-initiated movements;  • Handwriting.
	OCD	OCD symptoms reduction	Was not applied
	TS	Tics reduction	Was not applied
	Other	ASD: increased movement preparation abilities in patients; UCPPS: decrease pelvic floor muscle tone; PLP: pain reduction; MM: mirror movements inducing.	UCPPS: increase pelvic floor muscle tone; BAF: lowering of seizure threshold for ECT
Pre- SMA	OCD	OCD symptoms reduction	Was not applied
	Other	Essential tremor reduction	Restless leg symptom reduction

PD – Parkinson's disease; OCD – obsessive-compulsive disorder; TS – Tourette's syndrome; ASD – Autism spectrum disorder; UCPPS: Urologic chronic pain syndrome; PLP – Phantom limb pain; MM – Mirror movements; BAF – Bipolar affective disorder; ECT – electroconvulsive therapy

**Рис. 3.** Table 2: Representation of the SMA inhibitory and excitatory rTMS significant therapeutical effects in patients with different nosologies