



<sup>1</sup> Department of Clinical Neurosciences, University of Calgary,Canada

<sup>2</sup> Department of Bioethics, Medical University of Warsaw, Poland

<sup>3</sup> Department of Neurology, Complejo Asistencial Universitario of Burgos, Burgos, Spain

<sup>4</sup>Clinic of Psychiatry, Socialpsychiatry and Psychotherapy, Hannover Medical School,  
Hannover, Germany

Background and Aim

Methods

1. One previous meta-analysis by Cubo et al.<sup>1</sup> published 10 years ago systematically analyzed the magnitude of the placebo effect in randomized controlled trials (RCTs) including patients with tic disorders and demonstrated that there is a small, but relevant placebo effect in patients with tic disorders (Table 1).

2. The aim of this systematic review and meta-analysis was to update these results considering new data published recently.
1. We conducted a systematic review and meta-analysis to examine the magnitude of the placebo effect in RCTs including patients with tic disorders. Tic severity was measured using the total tic score of the Yale Global Tic Severity Scale (YGTSS-TTS).

2. The placebo effect was defined as an improvement of at least 30% over baseline scores in the YGTSS-TTS and was considered clinically relevant when at least 10% of patients in the placebo-arm met that benchmark.

Table 1. Meta-analysis of placebo effect in study by Cubo et a. <sup>1</sup>

Group	Mean scores ± SD		<i>P</i> value for baseline vs. follow-up scores: Comparison per group	Cohen's d for effect size
	Baseline score	First follow-up score		
Total tic scores				
Total sample	21.8±8.1	20.0±9.1	0.05	0.16
Children	21.0±7.7	19.6±9.1	0.08	0.18
Adults	23.8±8.3	23.1±8.7	0.30	0.08
Males	23.5±8.3	22.3±8.2	0.38	0.09
Females	20.7±6.6	18.2±11.1	0.18	0.37
Impairment scale				
Total sample	22.5±10.6	19.9±10.7	0.07	0.09
Children	22.0±12.0	18.0±12.2	0.08	0.19
Adults	12.2±10.9	11.1±11.6	0.34	0.00
Males	23.0±10.7	20.1±9.7	0.52	0.18
Females	20.4±10.3	18.6±16.8	0.68	0.19
Total YGTSS				
Total sample	42.0±18.5	37.3±19.2	0.11	0.21
Children	42.3±16.3	38.0±19.1	0.15	0.26
Adults	36.3±18.2	34.1±20.3	0.22	0.12
Males	48.2±17.2	39.6±16.6	0.67	0.13
Females	38.3±13.4	27.6±26.3	0.15	0.79

Abbreviations: SD, standard deviation; YGTSS = Yale Global Tic Severity score.

Results

1. In total, N=26 RCTs were included comprising N=961 patients randomized in the placebo group and N=1429 in respective intervention groups (Figure 1).

2. Tests for heterogeneity showed tolerable results (I<sup>2</sup>=28.41%).

3. According to YGTSS-TTS, there was a statistically significant improvement of tic severity after placebo administration (p<0.01), but the magnitude of the placebo effect was small (Cohen's d=0.35).

Conclusions

1. It can be concluded that there is a significant placebo effect in patients with tic disorders, but it is still small.

2. Our next analytic plan will be to further update the list of studies included in the meta-analysis.

3. New data considering the increasing number of large and well-designed RCTs should be constantly evaluated to better understand the relevance of the placebo effect in this group of patients, since this is of relevance for designing and interpreting results from RCTs.

