

Results for YODA Project 2021-4568 (Motor side effects and antipsychotic efficacy of antipsychotic drugs: An individual participant meta-analysis)

## Abstract

**Objective:** The primary objective of this study was to investigate the relationship between motor side effects and treatment efficacy of antipsychotic drugs in individuals with schizophrenia. The study aimed to measure whether the effectiveness of antipsychotic treatment in alleviating psychotic symptoms is interrelated with the propensity for these treatments to induce motor side effects such as tardive dyskinesia, parkinsonism, and akathisia.

**Methods Used:** Consistent with the original proposal, this study conducted a meta-analysis using participant-level data from placebo-controlled randomized clinical trials. Data were sourced from the YODA Project to evaluate antipsychotics' impact on schizophrenia-related acute psychosis. Analysis focused on the interaction term “time treatment motor side effect liability” using a mixed model analysis for repeated measures. However, during the progression of the analysis, it became apparent that some data did not contain sufficient participant-level characteristics for a comprehensive evaluation of all motor side effects. Consequently, resource constraints inhibited a complete analysis of all initially proposed variables.

**Results:** The pooled data analysis revealed no significant interaction between treatment efficacy and any of the measured motor side effects, namely tardive dyskinesia (Figure 2), parkinsonism (Figure 3), and akathisia (Figure 4). Despite initially established hypotheses, the time by group interaction in clinical trials (Figure 1) indicated no substantial variances in treatment outcomes attributable to motor side effect liability. As such, the anticipated correlation between motor side effects and treatment efficacy was not supported by the data.

**Conclusions:** While the hypothesis regarding the relationship between antipsychotic efficacy and motor side effect liability was not confirmed, this work contributed valuable insights into the complex interactions of antipsychotic treatments with motor responses. Challenges encountered, such as insufficient specific data variables, underscore the importance of access to comprehensive datasets for future research. Although the findings did not yield the expected results, this exercise highlights critical methodological considerations for similar studies in the field. Future research should endeavor to address these challenges by ensuring a broader spectrum of participant-level data and supporting continued exploration of antipsychotic drug effects.

Table 1. Population characteristics of included trials

	ANTIPSYCHOTIC	PLACEBO
n	3305	1101
Sex = Male (%)	2102 (63.6)	693 (62.9)
Age (mean (SD))	38.94 (12.18)	39.41 (12.76)
PANSS_Total (mean (SD))	92.36 (12.70)	92.32 (12.75)
PANSS_Positive (mean (SD))	23.48 (5.06)	23.52 (5.24)
PANSS_Negative (mean (SD))	23.23 (5.32)	23.12 (5.36)
PANSS_General (mean (SD))	45.65 (7.14)	45.68 (7.23)
Dose (mean (SD))	3.67 (1.74)	0.00 (0.00)
Tardive Dyskinesia = 1 (%)	71 ( 2.1)	22 ( 2.0)
Parkinsonism = 1 (%)	190 ( 5.7)	56 ( 5.1)
Akathisia = 1 (%)	336 (10.2)	85 ( 7.7)
Max AIMS at a single visit (median [IQR])	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]
Max SARS at a single visit (median [IQR])	0.00 [0.00, 2.00]	0.00 [0.00, 2.00]
Max BARS score at a single visit (median [IQR])	0.00 [0.00, 0.00]	0.00 [0.00, 0.00]
Study (%)		
PSY-3003	292 ( 8.8)	95 ( 8.6)
PSY-3004	387 (11.7)	124 (11.3)
PSY-3007	487 (14.7)	164 (14.9)
SCA-3001	234 ( 7.1)	107 ( 9.7)
SCA-3002	216 ( 6.5)	95 ( 8.6)
SCH-201	163 ( 4.9)	84 ( 7.6)
SCH-3015	319 ( 9.7)	79 ( 7.2)
SCH-302	76 ( 2.3)	38 ( 3.5)
SCH-303	502 (15.2)	127 (11.5)
SCH-305	493 (14.9)	123 (11.2)
SCH-4012	136 ( 4.1)	65 ( 5.9)

Figure 1. Pooled efficacy reflected as the time by group interaction in clinical trials of antipsychotics compared to placebo in individuals with schizophrenia and acute psychosis

**Meta-analysis of time by placebo interaction on total PANSS**

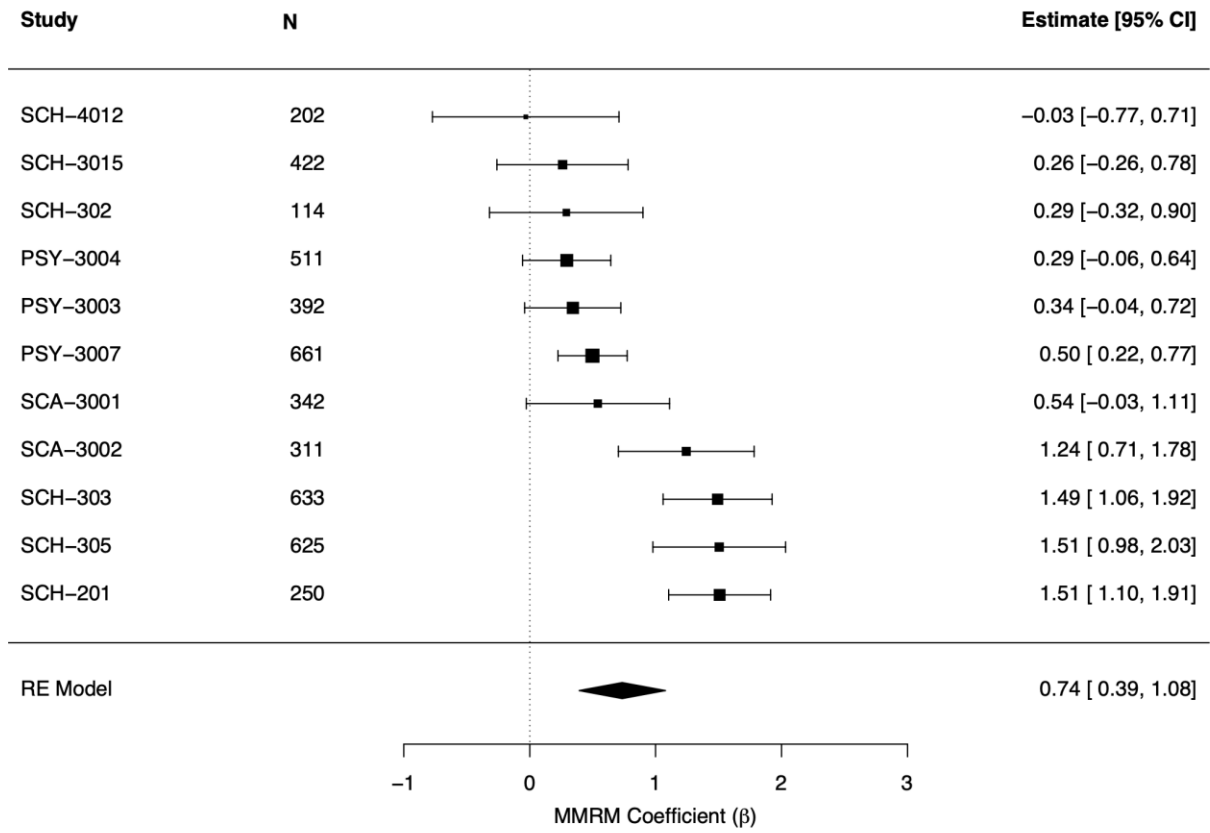


Figure 2. Pooled interaction of tardive dyskinesia on treatment response (i.e., time by group interaction)

**Meta-analysis of time by placebo randomization by tardive dyskinesia interaction on total PANSS**

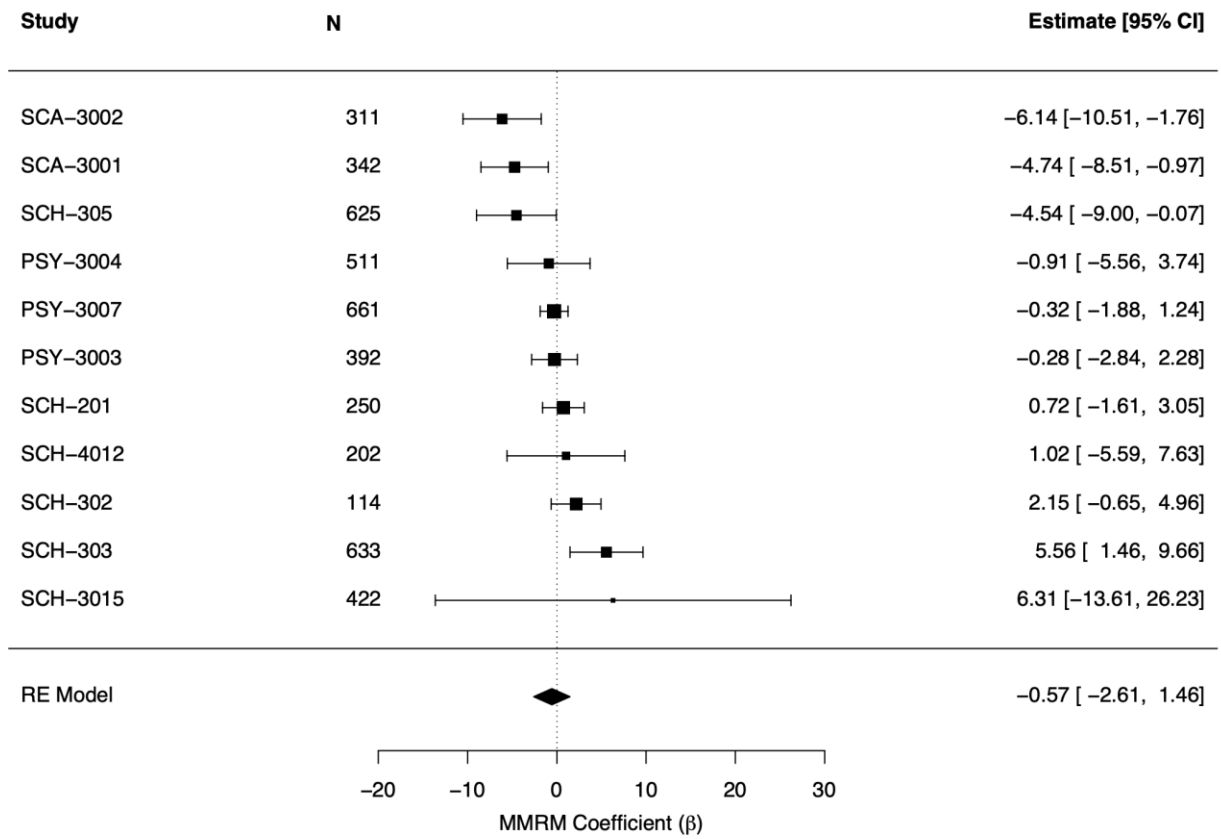


Figure 3. Pooled interaction of parkinsonism on treatment response (i.e., time by group interaction)

**Meta-analysis of time by placebo randomization by parkinsonism interaction on total PANSS**

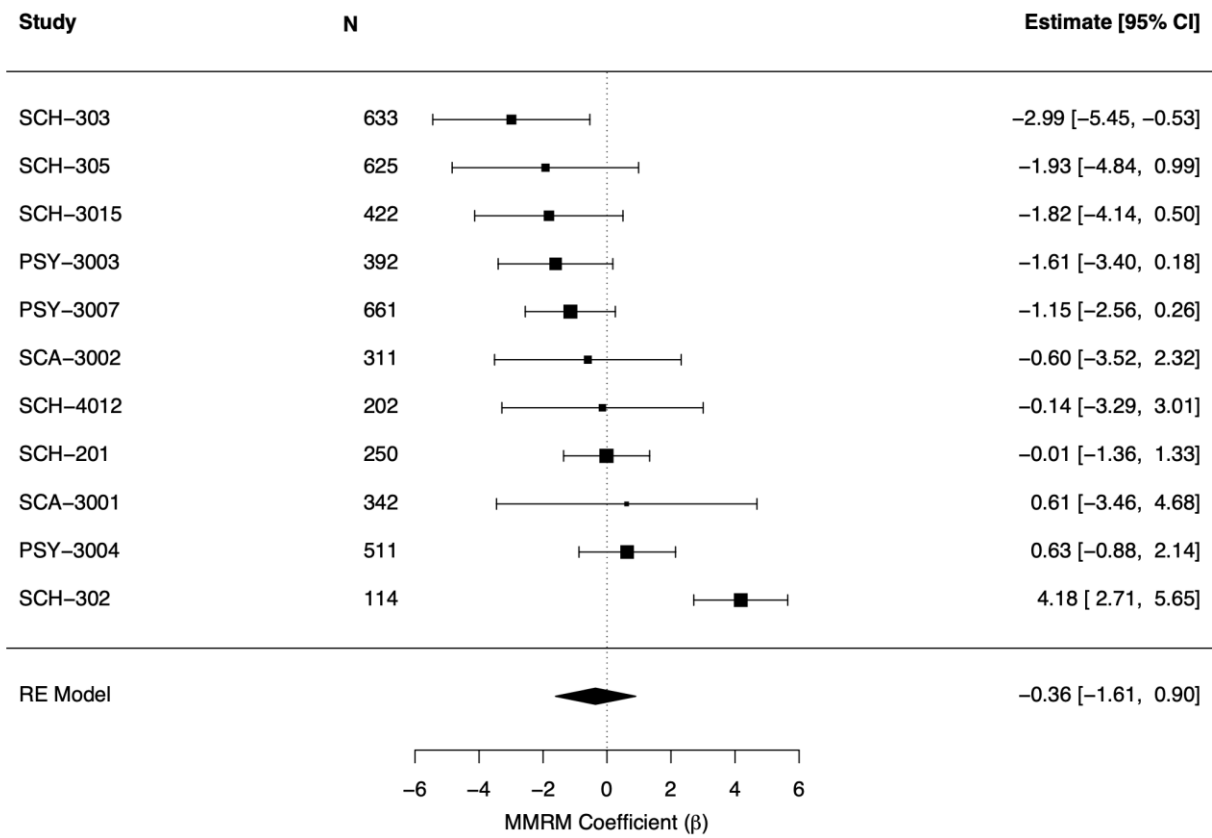


Figure 4. Pooled interaction of akathisia on treatment response (i.e., time by group interaction)

**Meta-analysis of time by placebo randomization by akathisia interaction on total PANSS**

