Supplementary Materials

Planning performance in schizophrenia patients: A meta-analysis of the influence of task difficulty and clinical and socio-demographic variables

Franziska Knapp[a], Wolfgang Viechtbauer[b],

Rainer Leonhart[c], Kai Nitschke[c,d,e,f,g], Christoph P. Kaller [d,e,f,g]

[a] Kliniken Schmieder, Allensbach, Germany

[b] Department of Psychiatry and Neuropsychology, Maastricht University, The Netherlands

[c] Dept. of Psychology, University of Freiburg, Germany

[d] Dept. of Neurology, Medical Center, University of Freiburg, Germany

[e] Medical Faculty, University of Freiburg, Germany

[f] Freiburg Brain Imaging Center, University of Freiburg, Germany

[g] BrainLinks-BrainTools Cluster of Excellence, University of Freiburg, Germany

S1 Handling of Multiple Data Sets and Specification of Covariances

Multiple effect size estimates were extracted from some studies as these reported estimates from more than one data set. Table S1-1 summarizes how many studies provided just one and how many studies provided multiple estimates.

Table S1-1. *Frequency of Estimates per Study*.

	# Data sets/Estimates				
	1	2	3	4	8
# Studies	17	4	3	6	1

The majority of studies (i.e., 17) provided only one estimate, but multiple estimates could be extracted from 14 studies. In one of these studies, results were given separately for men and women (Ayesa-Arriola et al., 2014), whereas in another study, results were given separately for three different genotypes (Tsuchimine, Yasui-Furukori, Kaneda, & Kaneko, 2013). Since there is no overlap in the data used to compute the effect size estimates within these studies, sampling errors can be assumed to be independent.

On the other hand, in four studies, multiple patient groups were compared against a common control group of healthy controls: Three studies with 2 patient groups (Braw et al., 2008; Greenwood, Wykes, Sigmundsson, Landau, & Morris, 2011; Tenjin et al., 2012) and one study with 4 patient groups (Braw, Benozio, & Levkovitz, 2012). Due to the repeated use of the control group data for the computation of the standardized mean differences, the estimates (or more accurately, the sampling errors of the estimates) are correlated. Using equations (19.18) and (19.19) from Gleser and Olkin (2009), the sampling variances and covariances of the standardized mean differences were computed for these studies.

In another eight studies, estimates for different tower tasks and/or different levels of task difficulty (i.e., minimum number of moves required for optimal solution) were reported for the same group of patients and the same group of controls: Two studies reported results separately for three different task difficulty levels (Morris, Rushe, Woodruffe, & M, 1995; Zhu et al., 2010), five studies

reported results separately for four different difficult levels (Joyce, 2002; Kontis et al., 2013; Langdon, Coltheart, Ward, & Catts, 2001; Langdon, 2002; Pantelis et al., 1997), and one study used two different tasks with four different difficulty levels each (Elliott, McKenna, Robbins, & Sahakian, 1998). Since the effect size estimates arising from these studies are based on the same group of study participants, the standardized mean differences (sampling errors) are again correlated. The sampling variances and covariances of the standardized mean differences were computed for these studies using equations (19.26) and (19.27) from Gleser and Olkin (2009).

In the computation of the covariances, we assumed that the correlation of the ability scores measured within studies examining the same type of task but with different number of moves is equal to 0.4 (cf. Table 2 in Kaller, Unterrainer, & Stahl, 2012). Furthermore, for different task types (i.e., variants of the Tower of London and Tower of Hanoi task) but with the same minimum number of moves, we assumed a correlation of 0.7. Finally, when the task type and minimum number of moves differed, we assumed a correlation of $0.4 \times 0.7 = 0.28$.

S2 Model Specification

For the analysis, we used a multilevel meta-analytic model (Konstantopoulos, 2011) of the form

$$y_{ij} = \mu + u_i + w_{ij} + \varepsilon_{ij} ,$$

where y_{ij} denotes the jth estimate from the ith study, μ is the (average) true standardized mean difference, $u_i \sim N(0, \hat{\sigma}_1^2)$ is a random effect at the study level, $w_{ij} \sim N(0, \hat{\sigma}_2^2)$ is a random effect at the effect size level, and $\varepsilon_{ij} \sim N(0, v_{ij})$ is the sampling error with (approximately) known sampling variance v_{ij}. For studies with multiple patient groups (and a common control group) and studies with multiple estimates for different tasks and/or levels of task difficulty, sampling errors are correlated with (approximately) known covariance $\text{cov}(\varepsilon_{ij},\varepsilon_{ij'})$, which was computed/estimated as described above.

The study-level random effects allow the true effects arising from the same study to be correlated. In particular, the model implies an intra-study correlation of

$$\rho = \frac{\sigma_1^2}{\sigma_1^2 + \sigma_2^2}$$

for multiple true effects corresponding to the same study.

S3 Identifiability of Variance Components

Profile likelihood plots for σ_1^2 and σ_2^2 were examined to ensure identifiability of the variance components and to obtain profile likelihood confidence intervals for these parameters (van Houwelingen, Arends, & Stijnen, 2002).

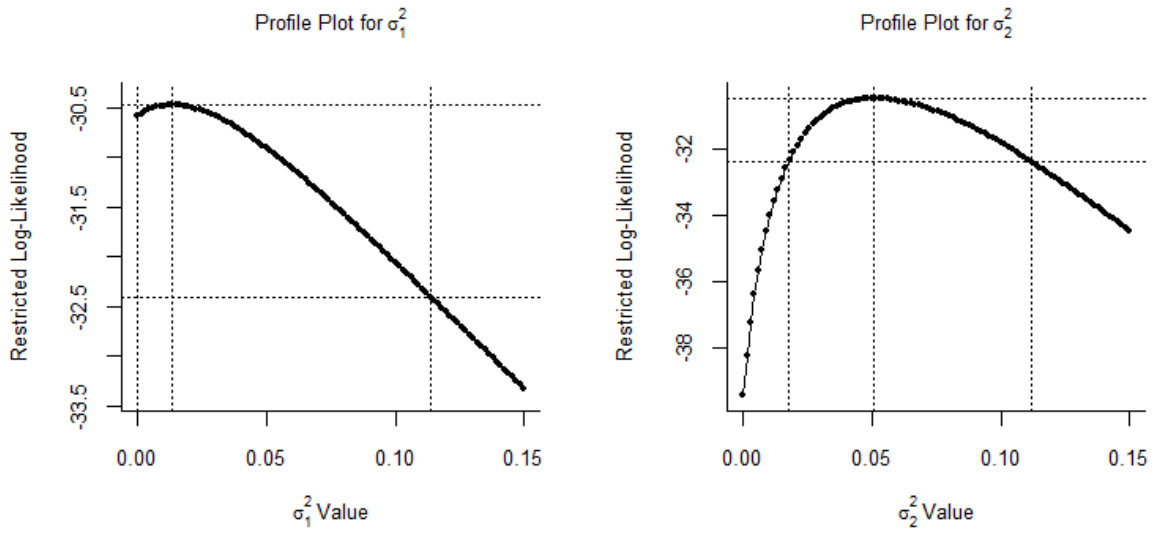

Figure S1. Profile of the restricted log-likelihood for each variance component.

As is evident from Figure S1, both profile plots are clearly peaked at the respective parameter estimates. The 95% profile likelihood CI for σ_1^2 has bounds of (0, 0.114). For σ_2^2, the profile likelihood CI has bounds of (0.018, 0.112).

S4 Moderator Analyses Using Meta-Regression

Table S4-1. *Moderating Effects of Task Difficulty*.

			Inferential Statistics			
Model	k (n)	Regressor	*b*	*SE*	*z*	*p*
Task Difficulty (Between + Within Studies)	57 (25)	*Intercept*	0.184	0.164	1.121	0.262
		Task Difficulty	0.124	0.038	3.284	0.001
Task Difficulty (Within Studies Only)	34 (8)	*Intercept*	0.066	0.150	0.436	0.663
		Task Difficulty	0.137	0.039	3.514	<.001

Abbr.: k, number of effect size estimates/data sets available; n, number of studies.

Table S4-2. *Summary Statistics of Between-Group Differences in Demographic Variables (Differences).*

Variables	*Min*	*1st Qu.*	*Median*	*Mean*	*3rd Qu.*	*Max*
Age	-0.5761	-0.2564	-0.0514	-0.0051	0.1813	0.8406
Sex	-0.3519	-0.1165	-0.0161	-0.0453	0.0000	0.2826
IQ	0.1020	0.3716	0.4833	0.5550	0.7152	1.2560
Education[a]	-0.1567	0.1921	0.4531	0.5640	0.7616	2.2300

Abbr.: Min, minimum; Qu., quartile; Max, maximum;

Note. For each variable, the patient group was subtracted from the control group.

[a] years of education

Table S4-3. *Moderating Effects of Sample Mismatch in Demographic Variables (Differences).*

			Inferential Statistics			
Model	k (n)	Regressor	*b*	*SE*	*z*	*p*
Age	58 (27)	*Intercept*	0.638	0.057	11.198	<0.001
		Age Mismatch	-0.045	0.180	-0.251	0.802
Sex	51 (24)	*Intercept*	0.662	0.069	9.596	<0.001
		Sex Mismatch	0.484	0.474	1.019	0.308
IQ	32 (14)	*Intercept*	0.707	0.164	4.323	<0.001
		IQ Mismatch	-0.074	0.289	-0.254	0.799
Education[a]	38 (20)	*Intercept*	0.540	0.099	5.453	<0.001
		Educ.Mismatch	0.117	0.134	0.873	0.383

Abbr.: k, number of effect size estimates/data sets available; n, number of studies.

Note. For each variable, the patient group was subtracted from the control group.

[a] years of education

Table S4-4. *Moderating Effects of Demographic Variables (Means).*

			Inferential Statistics			
Model	k (n)	Regressor	*b*	*SE*	*z*	*p*
Age	59 (28)	*Intercept*	0.836	0.291	2.872	0.004
		Age	-0.006	0.009	-0.636	0.525
Sex	51 (24)	*Intercept*	0.633	0.122	5.172	<0.001
		Sex	0.009	0.312	0.028	0.977
IQ	31 (13)	*Intercept*	0.223	1.936	0.115	0.908
		IQ	0.005	0.019	0.257	0.797
Education[a]	38 (20)	*Intercept*	1.048	0.716	1.463	0.143
		Education	-0.033	0.057	-0.584	0.559

Abbr.: k, number of effect size estimates/data sets available; n, number of studies.

[a] years of education

Table S4-5. *Moderating Effects of Clinical Variables*.

			Inferential Statistics			
Model	k (n)	Regressor	*b*	*SE*	*z*	*p*
Age at Disease Onset	39 (16)	*Intercept*	0.811	0.582	1.393	0.164
		Age at Disease Onset	-0.008	0.024	-0.321	0.748
Disease Duration	50 (22)	*Intercept*	0.614	0.117	5.251	<0.001
		Disease Duration	0.002	0.009	0.213	0.831
PANSS Negative	21 (11)	*Intercept*	0.271	0.347	0.781	0.435
		PANSS Neg.	0.020	0.017	1.188	0.235
PANSS Positive	21 (11)	*Intercept*	0.539	0.393	1.370	0.171
		PANSS Pos.	0.008	0.022	0.343	0.732
PANSS General	21 (11)	*Intercept*	0.198	0.378	0.525	0.600
		PANSS General	0.012	0.010	1.278	0.201
PANSS Total	21 (11)	*Intercept*	0.209	0.420	0.498	0.619
		PANSS Total	0.006	0.005	1.123	0.262
Medication (equivalent daily dose of chlorpromazine per 100 mg)	38 (16)	*Intercept*	0.834	0.156	5.347	<0.001
		Medication	-0.025	0.024	-1.058	0.290

Abbr.: k, number of effect size estimates/data sets available; n, number of studies.

References

Ayesa-Arriola, R., Rodriguez-Sanchez, J. M., Gomez-Ruiz, E., Roiz-Santiáñez, R., Reeves, L. L., & Crespo-Facorro, B. (2014). No sex differences in neuropsychological performance in first episode psychosis patients. *Progress in neuro-psychopharmacology & biological psychiatry*, *48*, 149–54. doi:10.1016/j.pnpbp.2013.09.009

Braw, Y., Benozio, A., & Levkovitz, Y. (2012). Executive functioning during full and partial remission (positive and negative symptomatic remission) of schizophrenia. *Schizophrenia research*, *142*(1-3), 122–8. doi:10.1016/j.schres.2012.10.011

Braw, Y., Bloch, Y., Mendelovich, S., Ratzoni, G., Gal, G., Harari, H., … Levkovitz, Y. (2008). Cognition in young schizophrenia outpatients: comparison of first-episode with multiepisode patients. *Schizophrenia bulletin*, *34*(3), 544–54. doi:10.1093/schbul/sbm115

Elliott, R., McKenna, P. J., Robbins, T. W., & Sahakian, B. I. (1998). Specific Neuropsychological Deficits in Schizophrenic Patients with Preserved Intellectual Function. *Cognitive Neuropsychiatry*, *3*(1), 45-69.

Gleser, L. J., & Olkin, I. (2009). Stochastically dependent effect sizes. In H. Cooper, L. V. Hedges, & J. C. Valentine (Eds.), The handbook of research synthesis and meta-analysis (2nd ed., pp. 357–376). New York: Russell Sage Foundation.

Greenwood, K. E., Wykes, T., Sigmundsson, T., Landau, S., & Morris, R. G. (2011). Tower of London versus real life analogue planning in schizophrenia with disorganization and psychomotor poverty symptoms. *Journal of the International Neuropsychological Society : JINS*, *17*(3), 474–84. doi:10.1017/S135561771100018X

Joyce, E., Hutton, S., Mutsatsa, S., Gibbins, H., Webb, E., Paul, S., … Barnes, T. (2002). Executive dysfunction in first-episode schizophrenia and relationship to duration of untreated psychosis: the West London Study. *The British Journal of Psychiatry*, *181*(43), 38–44. doi:10.1192/bjp.181.43.s38

Kaller, C. P., Unterrainer, J. M., & Stahl, C. (2012). Assessing planning ability with the Tower of London task: psychometric properties of a structurally balanced problem set. *Psychological assessment*, 24(1), 46–53. doi:10.1037/a0025174

Konstantopoulos, S. (2011). Fixed effects and variance components estimation in three-level meta-analysis. *Research Synthesis Methods*, *2*(1), 61-76.

Kontis, D., Theochari, E., Fryssira, H., Kleisas, S., Sofocleous, C., Andreopoulou, A., … Tsaltas, E. (2013). COMT and MTHFR polymorphisms interaction on cognition in schizophrenia: an exploratory study. *Neuroscience letters*, *537*, 17–22. doi:10.1016/j.neulet.2013.01.012

Langdon. (2002). Disturbed communication in schizophrenia : the role of poor pragmatics and poor mind-reading. *Psychological medicine, 32* (7), 1273–1284.

Langdon, R., Coltheart, M., Ward, P. B., & Catts, S. V. (2001). Mentalising, executive planning and disengagement in schizophrenia. *Cognitive Neuropsychiatry*, *6*(2), 81–108. doi:10.1080/13546800042000061

Morris, R. G., Rushe, T., Woodruffe, P. W. R., & Murray, R. M. (1995). Problem solving in schizophrenia : a specific deficit in planning ability, *Schizophrenia research*, *14*, 235–246.

Pantelis, C., Barnes, T. R. E., Nelson, H. E., Tanner, S., Weatherley, L., Owen, A. M., & Robbins, T. W. (1997). Frontal – striatal cognitive deficits in patients with chronic schizophrenia. *Brain, 120* (10), 1823–1843.

Tenjin, T., Miyamoto, S., Miyake, N., Ogino, S., Kitajima, R., Ojima, K., … Yamaguchi, N. (2012). Effect of blonanserin on cognitive function in antipsychotic-naïve first-episode schizophrenia. *Human psychopharmacology*, *27*(1), 90–100. doi:10.1002/hup.1276

Tsuchimine, S., Yasui-Furukori, N., Kaneda, A., & Kaneko, S. (2013). Differential effects of the catechol-O-methyltransferase Val158Met genotype on the cognitive function of schizophrenia patients and healthy Japanese individuals. *PloS one*, *8*(11), e76763. doi:10.1371/journal.pone.0076763

Van Houwelingen, H., Arends, L., & Stijnen, T. (2002). Advanced methods in meta-analysis: multivariate approach and meta-regression. *Statistics in medicine, 21*(4), 589–624.

Zhu, Y., Liu, X., Wang, H., Jiang, T., Fang, Y., Hu, H., … Zhang, K. (2010). Reduced prefrontal activation during Tower of London in first-episode schizophrenia: a multi-channel near-infrared spectroscopy study. *Neuroscience letters*, *478*(3), 136–40. doi:10.1016/j.neulet.2010.05.003