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"Low standards, non-transparent reporting, and bias perpetuate the Mozart effect myth: A multiverse meta-analysis"

verfasst von / submitted by Sandra Oberleiter, BSc

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Ass.-Prof. Mag. Dr. Jakob Pietschnig, Privatdoz.

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In liebevoller Erinnerung an Max.

Abstract

In recent years, the Mozart effect has attracted extensive media and scientific attention in the context of epilepsy and other medically relevant conditions. It has been said, that the exposure to the first movement "allegro con spirito" of the Mozart sonata for two pianos in D major (KV448) would remarkably relive epileptic symptoms (e.g., seizure frequencies, interictal epileptiform discharges) and was proposed to supplement or replace drug treatment. The present paper represents an extensive review and meta-analysis on this topic, providing evidence for potential influences of dissemination biases and the adequacy of the evidential value. It was shown that the overall effect sizes are small in size (g range: 0.16 to 0.43) and statistically not significant (p range: .13 to .52), which, in the context of meta-analysis, indicates substantially underpowered primary studies. Moderator-, and multiverse-analyses as well as a series of publication bias detection methods indicate that a positive effect of the KV448 on epilepsy and other medically relevant conditions is not reproducible. Insufficient documentation of replication attempts and selective publication of seemingly successful but strikingly inadequately designed and underpowered ones can thus lead to unfounded assumption of a salient effect.

Keywords: Mozart effect, epilepsy, diseases, meta-analysis, multiverse-analysis, reproducibility.

Introduction

Over the past three decades, the Mozart effect has generated a lot of attention both in the scientific community and in popular media. The topic was introduced in the context of spatial task performance (Rauscher et al., 1993), which supposedly improved after subjects were exposed to the first movement "allegro con spirito" of Mozart's sonata KV448. This phenomenon was received with considerable skepticism in the scientific community and ultimately demonstrated to be a consequence of low study power and bias-related measurement artifacts (Pietschnig et al., 2010). However, claims about long-lasting intelligence-enhancing effects, especially in children, have popularized the Mozart effect in the public and given rise to an industry that sells customized selections of supposedly cognitive performance-enhancing classical music (e.g., Campbell, 2002). Up to this day, public interest in the Mozart effect and the supposed positive effect of Mozart's music on intelligence persists.

Perhaps as a consequence of this public interest, effects of listening to Mozart's music have been investigated in regard to other outcomes, with potentially symptom-alleviating effects in epilepsy being among the most frequently cited and generating considerable attention in public outlets (e.g., Cooney, 2021). Originally introduced in the late 1990s with some results suggesting that listening to KV448 leads to an acute decrease in both ictal and interictal epileptiform activity (Hughes et al., 1998), at least two studies successfully replicated this effect (Bodner et al., 2012; D'Alessandro et al., 2017).

A Mozart effect for epilepsy would be desirable because antiepileptic drugs often cause severe side effects and may have a negative impact on organ function, fertility, or blood counts (Donat, 2010); 30% of those affected, drug therapies are ineffective (Sesso & Sicca, 2020). In this vein, KV448 was suggested to be used to supplement or replace drug treatment when medication or surgery were ineffective or would not be accepted (Brackney & Brooks, 2018) because patients listening to KV448 were reported to experience fewer epileptic seizures and epileptic discharges compared to patients who wait in silence or listen to other music, whilst, e.g., *Haydn's Symphony No. 94* was even reported to be pro-epileptic (Maguire, 2022). Other studies contrasted these findings indicating no specific beneficial effect of KV448 on epilepsy (e.g., Coppola et al., 2017).

Two meta-analytic reviews are available to date which demonstrated positive effects of KV448 on epilepsy. However, they either included almost exclusively data from the same group of researchers (Brackney & Brooks, 2018) or used mere vote counting which does not

allow an evaluation of effect strength, bias, or meaningfulness (Sesso & Sicca, 2020), thus raising concerns about the validity of their conclusions.

Here, I present a systematic review and meta-analysis of KV448 effects on epilepsy and related medical conditions. Moreover, I provide evidence for potential influences of (i) dissemination biases, (ii) the adequacy of the evidential value as well as (iii) different ways about which data were analyzed and how this has been done by means of multiverse analyses.

Methods

The present study was preregistered prior to accessing the data. The preregistration protocol is available at the Open Science Framework (OSF; https://osf.io/sfvq5/), whereas any deviations from the preregistrations are documented in Appendix B. PRISMA checklist can be obtained from Table S1, see Appendix C. Primary study quality was assessed with the Newcastle-Ottawa Scale (NOS; Herzog et al., 2013), which is available in Appendix D, Table S2.

Literature search

I searched six databases for published studies (Google Scholar, PubMed, Scopus, ISI Web of Science, PsycInfo, PubPsych) and the Open Access Dissertation and Theses database to obtain grey literature (https://oatd.org). First, I used the following search string to identify relevant literature: ("mozart effect" AND epil*) OR ("mozart effect" AND brain) OR ("mozart effect" AND disease). Second, I screened the reference lists of studies that were eligible for inclusion in my synthesis for further potentially relevant hits. Finally, I conducted a cited reference search for the initial study that had been published on the Mozart effect (Rauscher et al., 1993) as well as the so far largest meta-analysis on this topic (Pietschnig et al., 2010). Non-English or -German titles, abstracts, and full texts were translated with the online translator DeepL (https://deepl.com/translator). Titles and abstracts of 1,573 potentially relevant articles were screened and subsequently full-texts of 64 studies were obtained (for a flowchart see Figure 1; references of excluded records according to exclusion reasons can be obtained of Appendix H). Literature search and screening were originally conducted from June to July 2022 and updated in October 2022.

Inclusion criteria

To be eligible for inclusion in the present meta-analysis, studies had to meet three inclusion criteria. First, they had to assess the effects of Mozart's sonata KV448, a musical stimulus, a non-musical stimulus (e.g., short story), or silence on a medically relevant condition (i.e., ICD-11 group-F-only conditions such as depression were not considered). Second, studies had to provide an appropriate measure for the symptoms of the respective medical condition, such as the number of epileptiform seizures experienced or interictal epileptiform discharges (IED) in case of epilepsy. Third, effect sizes or sufficient statistical information to calculate them needed to be available.

Coding

I conducted the coding of the studies twice, independently. Coding inconsistencies were discussed with an independent researcher [J.P.]. The following information were coded for individual studies: (i) study characteristics (publication status: published vs. unpublished; publication year; manuscript type: journal article vs. thesis; peer-reviewed: yes vs. no; funding: not reported vs. yes vs. no;), (ii) country of data collection, (iii) sample descriptors (sample size, mean age, sample type, percentage of men within sample), (iv) epilepsy or physical disease measurement (type of disease: epilepsy vs. other; seizure type: generalized and focal vs. other vs. mixed; type of control stimulus: other classical vs. non classical / scrambled; duration of exposure;), and (vi) statistical parameters (pre- and posttest means, standard deviations, effect sizes, *p*-values, reliabilities of dependent variables). In case of missing information, the primary studies' corresponding authors were contacted and reminders were sent after two and four weeks if no response had been received. If data were unavailable or the corresponding authors did not reply, the respective study was excluded from analyses. The coding file with all available study information can be found on the OSF (https://osf.io/t5wyb).

Data Analysis

Prior to all analyses, Hedges gs were calculated for group differences (Cooper et al., 2019). Data were synthesized according to (i) the different stimuli the experimental groups were exposed to and (ii) the study design that was applied. Three independent meta-analyses were conducted: First, I meta-analyzed primary studies that compared effects of listening to KV448 vs. silence in independent-groups pretest-posttest designs (henceforth: *independent MO-condition*; k = 3 study effects). Second, I once more meta-analyzed KV448 vs. silence studies but synthesized studies that used one-group pretest-posttest designs (henceforth: *dependent MO-condition*; k = 5 study effects). Third, I synthesized effects of listening to any other music vs. no stimulus at all in one-group pretest-posttest designs (*OM-condition*; k = 6 study effects).

If there is indeed a salient specific Mozart effect, a meaningful significant effect should be observable in both MO-conditions, but not in the OM-condition. Effect sizes of the samples are weighted by study precision (i.e., assigning higher weights to more precise studies according to the inverse standard errors of effect sizes) and synthesized in random-effects models. Potential effects of leverage points were assessed by means of leave-one-out analyses.

Heterogeneity was interpreted according to l^2 values (25%, 50%, and 75% representing the lower thresholds of small, moderate, and large heterogeneity; Higgins et al., 2003) and prediction intervals (Borenstein, 2021).

A series of subgroup analyses were conducted to assess potential influences of categorical moderator variables (see Table 1). Potential influences of continuous moderators were examined by means of linear-precision-weighted meta-regressions (for an overview, see Table 1; within-subgroup summary effect estimates and meta-regression effects are only provided if k > 1a and > 2, respectively).

To detect potential influences of confounding dissemination bias, I used different bias detection approaches (in all 10; see technical supplementary material available in Appendix F) following current recommendations from the literature (Siegel et al., 2022) to account for the different strengths and weaknesses of individual approaches. Only published studies were included in our publication bias analysis.

Because there are different (reasonable) ways of which studies to include and how to synthesize them in a meta-analysis, all of which may affect the results and interpretation of the outcomes (Voracek et al., 2019), multiverse analyses to account for potential differences according to different specifications were performed.

I used specification curve analyses to assess the effect of different reasonable combinations of which data to analyze and how to do this (so-called *which* and *how factors;* (see https://osf.io/nkv46/ for the R Code from Voracek et al., 2019). In this approach, it is assumed that all specifications that are based on the combination of any levels of different conceptually plausible moderators may be assumed to be equally reasonable (in other words: all summary effects are equally likely to reflect reality most accurately). Specification-relevant variables are presented in Table 1.

However, it could be argued that certain reasonable specifications may remain undetected by specification curve analyses, because not all reasonable specifications may be known. Therefore, I used combinatorial meta-analyses to assess potential systematic influences of any combination on effect syntheses (Olkin et al., 2012). Typically, due to the astronomical number of possible (unreasonable) combinations in a given meta-analysis, a sample of 100,000 ways to calculate summary effects is drawn from the data at random and resulting effect size patterns are visually inspected and distributional characteristics are interpreted. However, due to the low number of available data points in the present analyses, I was able to provide here an exhaustive analysis of all possible combinations. By calculating summary effects for $2^k - 1$ possible subsets of the available data, I obtained (i) $2^3 - 1 = 7$

combinations for the independent MO-condition, (ii) $2^6 - 1 = 63$ combinations for the dependent MO-condition, and (iii) $2^5 - 1 = 31$ combinations for the OM-condition.

All analyses were performed by means of the open-source software R (R Core Team, 2022), the online app MetaShine (Siegel et al., 2021), and the *p*-curve app (Simonsohn et al., 2015). Analysis-code is provided in Appendix G.

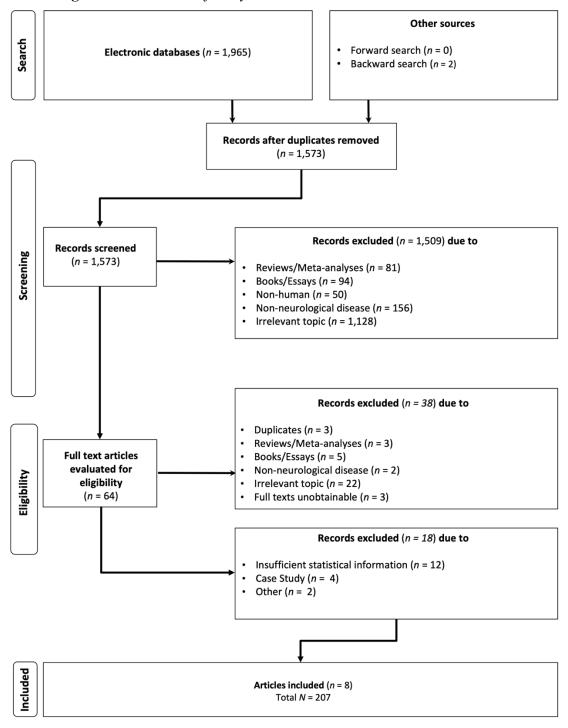


Figure 1. Flow-chart of study inclusion.

 Table 1. Moderator and specification-relevant variables for three independent meta-analyses.

Independent MO-condition	Dependent MO-condition	OM-condition		
	categorical moderators			
-	measurement method (seizure frequency vs. IED-EEG)	measurement method (seizure frequency vs. IED-EEG)		
-	funding (not reported / no vs. yes)	funding (not reported / no vs. yes)		
-	sample type (adults vs. mixed)	sample type (adults vs. children)		
-	seizure type (generalized and focal vs. not reported/mixed)	type of control music (other classical vs. non-classical / scrambled)		
	continuous moderators			
publication year	publication year	publication year		
age	age	age		
percentage of men in samples	percentage of men in samples	percentage of men in samples		
duration of exposure	duration of exposure	duration of exposure		
	specifications – which factors			
type of disease (epilepsy vs. other vs. either)	seizure type (generalized and focal vs. other vs. mixed vs. either)	seizure type (mixed vs. other vs. either)		
measurement method (other than EEG vs. either)	measurement method (IED-EEG vs. seizure frequency vs. either)	measurement method (IED-EEG vs. other vs. either)		
exposure (more than once vs. once vs. either)	sample type (adults vs. mixed vs. either)	exposure (more than once vs. either)		
sample type (children vs. adults vs. either)	funding (yes vs. not reported vs. either)	sample type (children vs. adults vs. either)		
funding (not reported vs. yes vs. no vs. either)		funding (yes vs. no vs. either)		
		type of control music (other classical vs. scrambled vs. either)		
	specifications – how factors			
effect size metric (Hedges g vs. Cohen d)	effect size metric (Hedges g vs. Cohen d)	effect size metric (Hedges g vs. Cohen d)		
meta-analytic approach (HO vs. HS vs. FE)	meta-analytic approach (HO vs. HS vs. FE)	meta-analytic approach (HO vs. HS vs. FE)		

Note. IED-EEG = interictal epileptic discharges measured with an electroencephalogram; scrambled = phase-scrambled version of KV448 representing a control piece with noise but no rhythmicity (Rafiee et al., 2020); HO = Hedges and Olkin-typed random-effects estimation (REML); HS = Hunter-Schmidt effect estimation; FE = fixed-effect model.

Results

Final sample

I identified 26 studies that conformed to my conclusion criteria. Six studies provided sufficient statistical information to calculate a summary effect size (D'Alessandro et al., 2017; Grylls et al., 2018; Paprad et al., 2020; Rafiee et al., 2020, Stillova et al., 2021; Vibrasiute, 2017). From the remaining 20 studies I had to exclude six because they represented single case reports, whose data cannot be formally meta-analyzed (see Table S3, Appendix E). Another study was excluded because no contact information for any of the authors was available (Hughes et al., 1998). I contacted all corresponding authors (k = 7) of the remaining 13 studies: Two authors provided sufficient summary data upon request for three studies (one of which had to be excluded due to being the only study in our entire analysis that compared KV448 to other music; Coppola et al., 2017) in personal communication (Bergomi et al., 2014; Coppola et al., 2015). One author indicated that data from six published studies were unavailable and further four corresponding authors did not respond at all (for an overview, see Table S3).

Consequently, I could formally meta-analyze data of k=8 (totaling N=207 participants) studies, which assessed the Mozart effect and its relation to either epilepsy (k=5), stroke (k=1), or other-reported premature infant pain (k=1). Studies observed patients' seizure frequency (k=3), evaluated interictal epileptic discharges by means of an electroencephalogram (IED-EEG; k=3), or used other methods to measure changes in the respective symptomatology (k=2). Study characteristics are detailed in Table 2.

Of the includable studies, k = 3 used two-group randomized controlled designs (RCT). Only one study investigated RCT-based effects on epilepsy, whilst the other two remaining RTC's investigated effects on other medically relevant conditions. Another four studies used two-group pre-post mirror- (k = 2) or one-group pre-post counterbalanced (k = 2) designs but did not control for potential carry-over effects by means of washout periods, i.e., between treatment and control condition, no time frame was allotted to eliminate potential effects of KV448. Carry-over effects would invalidate the respective studies. One further study used a one-group pretest-posttest design.

Table 2. Study characteristics of included studies.

Reference	N	Type	Medical condition	Measure	Condition	Study Design	Journal	ES (SE)	Data availability
Bergomi et al. (2014)	70	Children	Other- reported pain in premature infants	Premature infant pain profile (PIPP)	Independent MO	Randomized controlled	Research and Theory for Nursing Practice	$g = 1.655 (0.27)^{b}$	Summary data provided upon request.
Coppola et al. (2015)	11	Children	Epilepsy	Observation - seizure frequency	Dependent MO	One-group pretest-posttest	Epilepsy & Behavior	g = 0.743 (0.26)	Summary data provided upon request.
D'Alessandro et al. (2017)	12	Mixed	Epilepsy	Observation - seizure frequency	Dependent MO	Mirror-design (no washout) ^a	Psychiatria Danubina	$g1 = 0.083 (0.34)^{c}$ g2 = 0.197 (0.35)	Summary data available in paper.
Grylls et al. (2018)	45	Children	Epilepsy	EEG - interictal epileptiform discharges	Dependent MO; OM	One-group counterbalanced (no washout)	Seizure	g (MO-NM) = 0.045 (0.15) $g (OM-NM) = -0.03 (0.14)^{c}$	Summary data available in paper.
Paprad et al. (2020)	26	Children	Epilepsy	EEG - interictal epileptiform discharges	Independent MO	Randomized controlled	Epilepsy & Behavior	$g = 0.096 (0.38)^a$	Summary data available in paper.
Rafiee et al. (2020)	11	Adults	Epilepsy	Observation - seizure frequency	Dependent MO; OM	Mirror-design (no washout)	Epilepsia Open	g1(MO-NM) = 1.04 (0.48) $g2(MO-NM) = 0.06 (0.34)^{c}$ $g1(OM-NM) = 0.36 (0.38)^{c}$ g2(OM-NM) = -0.13 (0.35)	Primary data available in paper.
Stillova et al. (2021)	18	Adults	Epilepsy	EEG - interictal epileptiform discharges	Dependent MO; OM	One-group counterbalanced (no washout)	European Journal of Neurology	$g (MO-NM) = 0.30 (0.23)^{b}$ $g (OM-NM) = -0.21 (0.23)^{b, c}$	Summary data available in paper.
Vibrasiute (2017)	14	Adults	Stroke	Systolic blood pressure	Independent MO	Randomized controlled	Unpublished (bachelor's thesis)	g = -0.610 (0.52)	Primary data available in thesis.

Note. N = sample size; ES = Effect size; SE = standard error; positive signs indicate a beneficial effect of KV448 (MO) or other music (OM) compared to no music at all; a = formally, this had to be declared to be an RCT, but because no washout period was used, the study was assumed to be mirror designed in this analysis; b = mean and standard deviation for calculating effect sizes are based on median and interquartile ranges according to the approach of Shi et al. (2020) and Luo et al. (2018); b = mean and standard deviation for calculating effect sizes are based on median and interquartile ranges according to the approach of Shi et al. (2020) and Luo et al. (2018); b = mean and standard deviation for calculating effect sizes are based on median and interquartile ranges according to the approach of Shi et al. (2020) and Luo et al. (2018); b = mean and standard deviation for calculating effect sizes are based on median and interquartile ranges according to the approach of Shi et al. (2020) and Luo et al. (2018); b = mean and standard deviation for calculating effect sizes are based on median and interquartile ranges according to the approach of Shi et al. (2020) and Luo et al. (2018); b = mean and b = mean are the approach of Shi et al. (2020) and b = mean are the approach of Shi et al. (2020) and b = mean and

Main analyses

I obtained three independent random-effects analyses for each condition (see Figure 2; Table 3). First, the independent MO-condition yielded a non-significant summary effect of g = 0.43 (p = .52, 95% CI [-0.89, 1.76], k = 3), showing no beneficial effects of KV448 compared to other stimuli. Second, the dependent MO-condition yielded a non-significant summary effect of g = 0.16 (p = .13, 95% CI [-0.04, 0.36], k = 6). This conforms to the above finding of no beneficial influence of KV448 on medically relevant outcomes. Finally, the OM-condition yielded a non-significant summary effect of g = 0.09 (p = .58, 95% CI [-0.23, 0.40], k = 5), showing no benefit of listening to any vs. no stimuli in terms of medically relevant outcomes.

Sensitivity (i.e., leave-one-out) analyses did not show substantial evidence for summary effect size changes (see Table 3). However, regarding the independent MO-condition, excluding the study measuring other-reported pain in premature infants (Bergomi et al., 2014), the summary effect of KV448 on medically relevant conditions appears to become negative (g = -0.17, 95% CI [-0.84, 0.50).

Moderator analyses

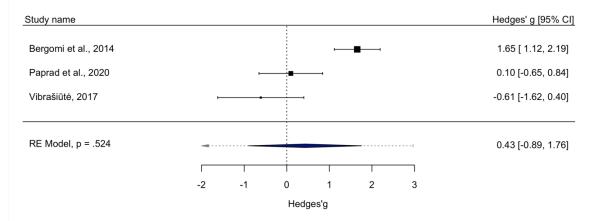
No nominally statistical significant group differences were identified in any of our analyses, most likely owing to the low power of the available data. Overall and within-subgroup summary effects are provided in Table 3.

Continuous moderator effects were examined by means of linear precision-weighted meta-regressions but did not yield any meaningful influences (see Table 5 for numerical outcomes).

Figure 2. Forest plots for three independent meta-analyses.

A

Independent MO-condition



B

Dependent MO-condition

Study name		Hedges' g [95% CI]
D'Alessandro et al., 2017 - Group A	-	0.08 [-0.59, 0.76]
D'Alessandro et al., 2017 - Group B	 	0.20 [-0.49, 0.88]
Rafiee et al., 2020 - Group A	·	1.04 [0.09, 1.99]
Rafiee et al., 2020 - Group B	· · · · · · · · · · · · · · · · · · ·	0.06 [-0.62, 0.73]
Grylls et al., 2018	⊢	0.04 [-0.24, 0.33]
Štillová et al., 2021		0.29 [-0.16, 0.75]
RE Model, p = .127	_	0.16 [-0.04, 0.36]
	-1 -0.5 0 0.5 1 1.5 2	
	Hedges'g	

 \mathbf{C}

OM-condition

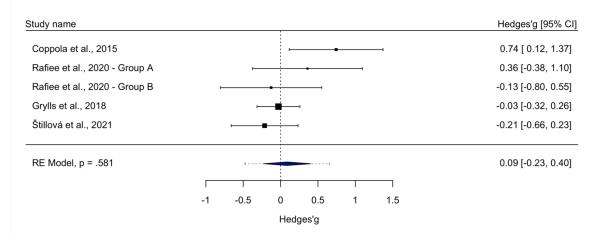


Table 3. Summary effects for overall and subgroup analyses.

	Summary effect	SE	<i>p</i> -value	95% CI	Q	τ^2 (SE)	I^2
Independent MO-condition							
Overall $(k = 3)$	g = 0.431	0.676	.524	[-0.89, 1.76]	20.485***	1.214 (1.374)	89.44%
	V	Depe	endent MO-con	dition		,	
Overall $(k = 6)$	g = 0.158	0.103	.127	[-0.45, 0.35]	4.384	< 0.001 (0.040)	< 0.001%
Measurement method	O						
Seizure freequency (observation; $k = 4$)	g = 0.246	0.185	.182	[-0.12, 0.60]	3.207	< 0.001 (0.111)	< 0.001%
IED (EEG; $k=2$)	g = 0.117	0.124	.346	[-0.13, 0.36]	0.836	< 0.001 (0.053)	< 0.001%
Funding	O						
Not reported / no $(k = 4)$	g = 0.121	0.110	.272	[-0.10, 0.39]	0.897	< 0.001 (0.043)	< 0.001%
Yes (k=2)	g = 0.490	0.487	.314	[-0.46, 1.44]	2.711	0.304 (0.680)	63.12%
Sample type	O					,	
Adults $(k=3)$	g = 0.332	0.178	.063	[-0.02, 0.68]	2.777	< 0.001 (0.107)	< 0.001%
Mixed(k=2)	g = 0.139	0.245	.057	[-0.34, 0.62]	0.054	< 0.001 (0.107)	< 0.001%
Seizure type	O						
Generalized and focal $(k = 3)$	g = 0.700	0.126	.580	[-0.18, 0.32]	0.165	< 0.001 (0.070)	< 0.001%
Not reported / mixed $(k = 3)$	g = 0.332	0.178	.063	[-0.18, 0.68]	2.777	< 0.001 (0.107)	< 0.001%
	- C		OM-condition	<u> </u>		,	
Overall $(k = 5)$	g = 0.088	0.160	.581	[-0.23, 0.40]	7.231	0.057(0.090)	46.44%
Measurement method							
Seizure freequency (observation; $k = 3$)	g = 0.337	0.262	.199	[-0.18, 0.85]	3.406	0.087 (0.207)	41.99%
IED (EEG; $k = 2$)	g = -0.083	0.123	.503	[-0.32, 0.15]	0.466	< 0.001 (0.052)	< 0.001%
Funding							
Not reported / no $(k = 3)$	g = 0.115	0.257	.664	[-0.39, 0.62]	6.255*	0.145 (0.200)	74.72%
Yes (k = 2)	g = 0.097	0.254	.704	[-0.40, 0.59]	0.909	< 0.001 (0.184)	< 0.001%
Sample type							
Adults $(k = 3)$	g = -0.075	0.170	.657	[-0.40, 0.26]	1.734	< 0.001 (0.094)	95.77%
Children $(k=2)$	g = 0.305	0.382	.425	[-0.44, 1.05]	4.799*	0.236 (0.421)	79.16%
Type of control music				_			
Other classical $(k = 2)$	g = 0.238	0.477	.618	[-0.69, 1.17]	5.921**	0.380 (0.647)	83.11%
Non-classical / scrambled $(k = 3)$	g = 0.003	0.127	.983	[-0.24, 0.25]	1.091	< 0.001 (0.074)	< 0.001%

Note. IED = interictal epileptic discharges; EEG = electroencephalogram; SE = standard error; 95% CI = 95% lower and upper bound of 95% confidence interval; Q = Cochran's Q test statistic for heterogeneity; τ^2 = between-studies variance; I^2 = ratio between true heterogeneity and total observed variation; *p < .05; **p < .01; ***p < .001.

Table 4. *Leave-one-out sensitivity analysis.*

Study name	Summary effect	SE	<i>p</i> -value	95% CI	Q	τ^2	I^2
•	•	Independent	MO-condition ((k=3)			
Bergomi et al. (2014)	g = -0.171	0.342	.617	[-0.84, 0.50]	1.209	0.043	17.30%
Paprad et al. (2020)	g = 0.565	1.132	.618	[-1.65, 2.18]	15.003***	2.393	93.34%
Vibrasiute (2017)	g = 0.898	0.779	.249	[-0.63, 2.43]	10.986**	1.104	90.90%
		Dependent	MO-condition (/	k=6			
D'Alessandro et al. (2017) – Group A	g = 0.164	0.108	.128	[-0.05, 0.38]	4.334	< 0.001	0.01%
D'Alessandro et al. (2017) – Group B	g = 0.153	0.108	.155	[-0.06, 0.36]	4.370	< 0.001	0.01%
Rafiee et al. (2020) – Group A	g = 0.115	0.105	.272	[-0.09, 0.32]	0.926	< 0.001	< 0.001%
Rafiee et al. (2020) – Group B	g = 0.166	0.108	.122	[-0.04, 0.38]	4.297	< 0.001	0.01%
Grylls et al. (2018)	g = 0.265	0.144	.066	[-0.02, 0.55]	3.234	< 0.001	< 0.001%
Stillova et al. (2021)	g = 0.123	0.115	.285	[-0.10, 0.35]	3.940	< 0.001	< 0.001%
		OM-c	condition $(k = 5)$				
Coppola et al. (2015)	g = -0.049	0.111	.662	[-0.26, 0.17]	1.778	< 0.001	< 0.001%
Rafiee et al. (2020) – Group A	g = 0.053	0.185	.773	[-0.30, 0.42]	6.425	0.074	56.11%
Rafiee et al. (2020) – Group B	g = 0.146	0.202	.470	[-0.25, 0.54]	6.987	0.096	61.65%
Grylls et al. (2018)	g = 0.161	0.234	.491	[-030, 0.62]	6.831	0.120	55.55%
Stillova et al. (2021)	g = 0.189	0.195	.332	[-0.19, 0.57]	5.709	0.072	47.98%

Note. SE = standard error; 95% CI = 95% lower and upper bound of 95% confidence interval; Q = Cochran's Q test statistic for heterogeneity; τ^2 = between-studies variance; I^2 = ratio between true heterogeneity and total observed variation; ** p <.01; ***p < .001.

Table 5. *Numeric outcomes of linear-precision-weighted meta-regressions.*

Predictor	b (SE)	R^2	<i>p</i> -value	95% CI	Q	τ(SE)	I^2
	Inc	dependent MC	O-condition (k	= 3)			
Publication year	-0.264 (0.276)	< 0.01%	.338	[-0.80, 0.28]	0.916	1.256 (2.080)	85.42%
Age	-0.023 (0.019)	23.73%	.220	[-0.06, 0.01]	1.508	0.926 (1.471)	89.07%
Percentage of men in samples	0.074 (0.019)	97.08%	<.001	[0.04, 0.11]	14.867***	0.035 (0.260)	19.27%
Duration of exposure	0.002 (0.003)	< 0.01%	.543	[-0.01, 0.01]	0.371	1.814 (2.849)	90.01%
•	De	ependent MO	-condition (k =	= 6)			
Publication year	0.072 (0.072)	< 0.01%	.316	[-0.07, 0.21]	1.006	< 0.001 (0.051)	< 0.001%
Age	0.007 (0.007)	< 0.01%	.299	[-0.01, 0.02]	1.080	< 0.001 (0.064)	< 0.001%
Percentage of men in samples	-0.006 (0.007)	< 0.01%	.411	[-0.02, 0.01]	0.676	0.003 (0.046)	4.01%
Duration of exposure	0.001 (0.001)	< 0.01%	.395	[-0.01, 0.01]	0.723	< 0.001 (0.073)	< 0.001%
•		OM-cond	ition $(k=5)$				
Publication year	-0.123 (0.066)	73.28%	.062	[-0.25, 0.01]	3.488	0.015 (0.064)	18.65%
Age	-0.007 (0.011)	< 0.01%	.549	[-0.03, 0.02]	0.360	0.105 (0.152)	57.21%
Percentage of men in samples	0.003(0.015)	< 0.01%	.851	[-0.03, 0.03]	0.035	0.094 (0.129)	62.38%
Duration of exposure	< 0.001 (< 0.001)	100.00%	.023	[< 0.001,< 0.001]	5.188*	< 0.001 (0.045)	< 0.001%

Note. $b = \text{unstandardized regression coefficient}; R^2 = \text{proportion of variance in the dependent variable explained by the independent variable}; SE = \text{standard error}; 95\% CI = 95\% lower and upper bound of 95% confidence interval}; Q = \text{Cochran's } Q \text{ test statistic for heterogeneity}; <math>\tau^2 = \text{between-studies variance}; I^2 = \text{ratio between true heterogeneity and total observed variation}; *p < .05; ***p < .001.$

Publication Bias

Publication bias analyses were conducted for published studies only (k = 7). Sample numbers had to exceed k = 2 for calculating funnel plot-, trim-and-fill, -Egger's regression-, and PET-PEESE-based methods. Numerical outcomes of all methods applied are provided in Table S4, see Appendix F.

In the light of the potentially includable studies, it was unexpected that the final study sets would result in such small sizes. As most of the methods for detecting potential publication bias performed rather poorly in simulation studies for small study sets (Carter et al., 2019), their application was not suitable for the present meta-analyses.

However, for the independent MO-condition, one of six methods indicated evidence for publication bias. Although the *p*-curve analysis included only a single study which examined the effects of KV448 on other-reported pain in premature infants (Bergomi et al., 2014), it indicated an evidential value.

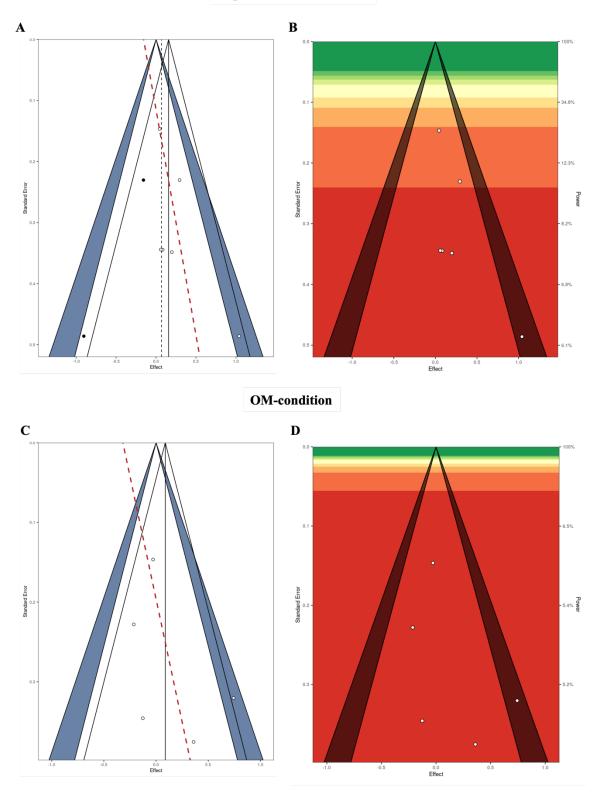
For the dependent MO-condition, four of seven methods indicated evidence for publication bias. *p*-curve analysis revealed no evidential value and an estimated power of 13% of the included study. Further, power enhanced funnel plot analysis showed that all study effects included were substantially underpowered (maximum power of 15%, see Figure 3B).

For the OM-condition, two of seven methods yielded evidence for publication bias. Power enhanced funnel plot analysis revealed a maximum power of 6% regarding all study effects included (see Figure 3D).

That several methods failed to detect a publication bias in the present study samples is attributable to (i) the limited number of effects available and (ii) the insufficient statistical power of the primary effects to represent an evidential value. Regardless of any outcome that we could have observed, the available evidence is too underpowered to conclude any salient effect.

Figure 3. Contour-enhanced funnel plots with imputed trim-and-fill values as well as Egger's regression line (left) and power-enhanced funnel plots (right) of published sample effect sizes for the dependent MO- (k = 6, panel A and B) and the OM-condition (k = 5, panel C and D). Study power is displayed from dark red (from 0 to 10 percent) to dark green (from 80 to 90 percent) in 10 percent increments.

Dependent MO-condition



Specification curve

Specification curve analyses are visualized in Figures 4 to 6.

Figure 4 indicates that virtually any reasonable specification in the independent MO-condition leads to unprecise estimates (i.e., effects with comparatively wide confidence intervals), which ranged from g = 0.40 to g = 1.30. The specified summary effects were mostly nominally non-significant (p > .05), as their 95%-confidence intervals included zero. Here, summary effect estimates were based on a maximum of three studies, whereof only one examined epilepsy. Specifications that included epilepsy yielded smaller effect sizes than those that included other medically relevant conditions only.

A similar picture of unprecise effect sizes emerged investigating reasonable specifications for the (i) dependent MO-condition (g range: 0.08 to 0.62; see Figure 5) and (ii) OM-condition (g range: -.10 to 0.48; see Figure 6). For both conditions, 2 out of 48 specifications yielded nominally significant outcomes, which would support positive effects of KV448 or other music on epilepsy or other medically relevant conditions.

Particularly, the large number of non-significant effects is surprising because, given the inherent large power of meta-analyses, non-significant summary effect sizes are sparse and typically indicate null effects.

Combinatorial meta-analyses

Combinatorial meta-analyses are visualized in Figure 7 (GOSH plots). In all conditions, results of sampled subsets of all possible combinations did not reveal evidence for any consistent effects.

For the independent MO-condition (panel A), effect sizes ranged from g = -0.61 to g = 1.65. Of note, individual combinations with the study providing the largest effect size (Bergomi et al., 2014; examining other-reported pain in premature infants) clearly exerted massive influences on effect strengths as well as heterogeneity. Effect sizes of subsets not including the outlier study ranged from g = -0.60 to g = 0.09.

For the dependent MO-condition (panel B), effect sizes ranged from g = 0.04 to g = 1.04. For the OM-condition (panel C), effect sizes ranged from g = -0.21 to g = 0.74.

In all conditions, larger effect sizes were associated with higher heterogeneity. Of some study combination in both the independent MO-condition as well as the OM-condition, negative summary effects resulted, which would indicate a negative effect of the KV448 or other music on epilepsy or other medically relevant conditions, compared to silence.

Figure 4. Descriptive meta-analytic specification plot of summary effects from all reasonable specifications for the independent MO-condition. The bottom panel indicates the "which" and "how" factors that were included for the estimated summary effects depicted in the top panel with respective 95% confidence intervals. The middle panel indicates the number of samples within the respective subsets.

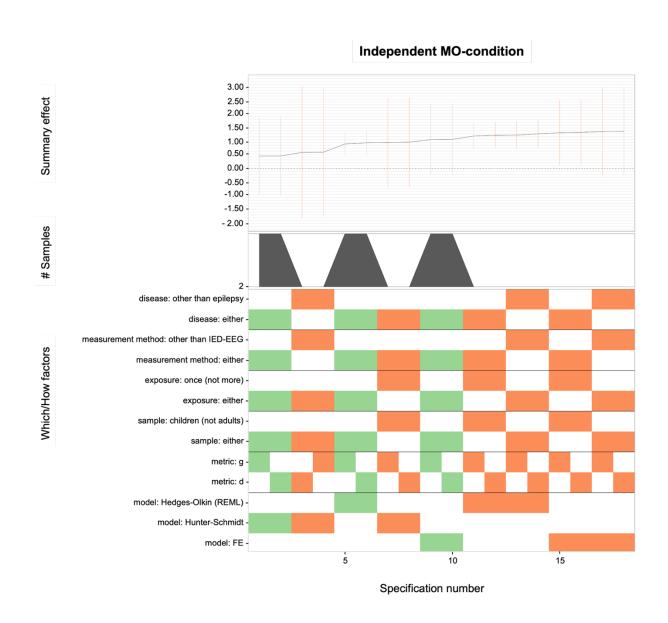


Figure 5. Descriptive meta-analytic specification plot of summary effects from all reasonable specifications for the dependent MO-condition. The bottom panel indicates the "which" and "how" factors that were included for the estimated summary effects depicted in the top panel with respective 95% confidence intervals. The middle panel indicates the number of samples within the respective subsets.

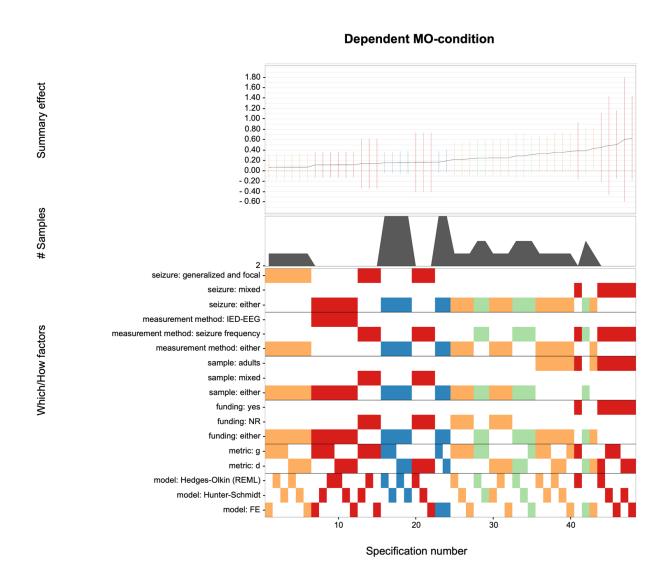


Figure 6. Descriptive meta-analytic specification plot of summary effects from all reasonable specifications for the OM-condition. The bottom panel indicates the "which" and "how" factors that were included for the estimated summary effects depicted in the top panel with respective 95% confidence intervals. The middle panel indicates the number of samples within the respective subsets.

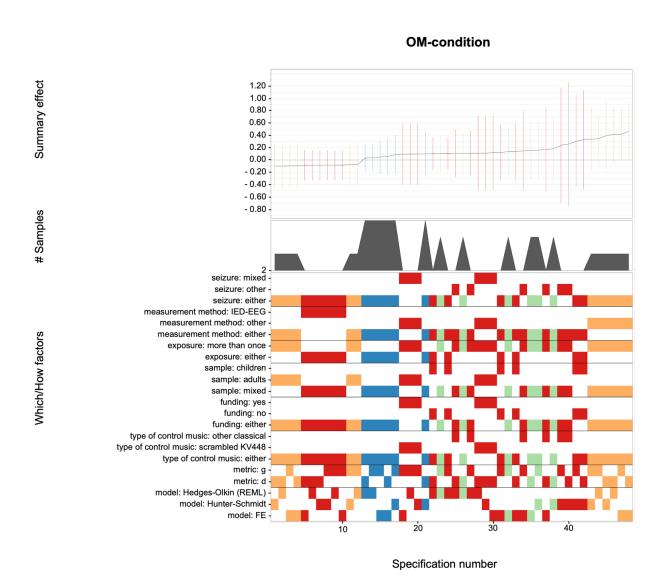
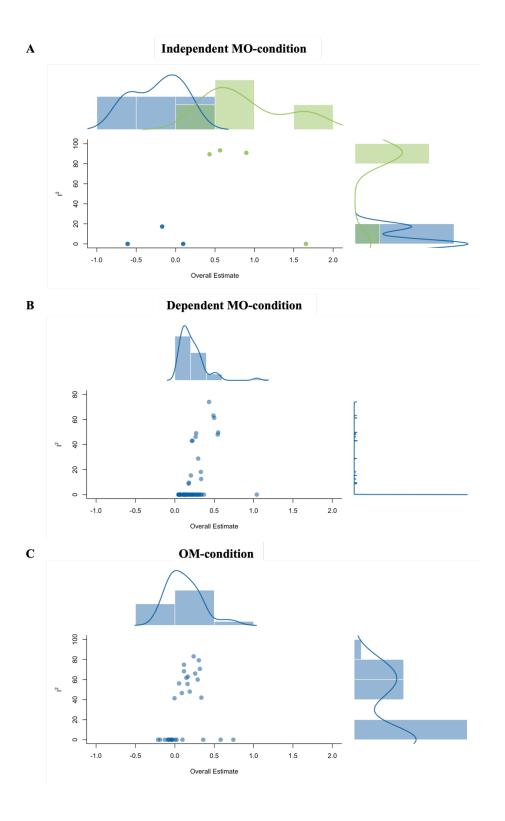


Figure 7. GOSH-plots of all possible combinations for each condition. Panel A shows all 7 possible combinations of k = 3 studies included in the independent MO-condition, whereas subset estimations including the study which reported the largest effect size (Bergomi et al., 2014; other-reported pain in premature infants) is highlighted in green. Panel B shows all 63 possible combinations of k = 6 studies included in the dependent MO-condition. Panel C shows all 31 possible combinations of k = 5 studies included in the OM-condition.



Discussion

The present meta-analysis shows, that there is only little evidence for any meaningful beneficial effect of listening to Mozart's sonata KV448 (or any other music) on epilepsy or other medically relevant conditions. Effect sizes of all conditions examined were small in size, statistically non-significant, and were based on qualitatively inadequate studies. These primary studies were substantially underpowered, suboptimal designed, and lacked of transparency. In general, it arises the impression of insufficient evidence for a salient effect and an unfounded authority.

Formal statistical syntheses of the Mozart effect on epilepsy or other medically relevant conditions compared to a non-musical stimulus did not yield any significant summary effects. Although some of the observed effects were non-trivial in term of strength, examination of the accumulated study power indicated that the available evidential value was insufficient. The maximal power of the studies included yielded 15%, whilst 80% is conventionally an acceptable level for power (Cohen, 1988). Also, the present results reveal that the effect is not moderated by characteristics such as age, sex, seizure type, or duration of exposure. Regardless *which* empirical studies are included in a formal meta-analysis and *how* they are analyzed, the lack of evidence leads to imprecise small effects. Therefore, no salient conclusions about a beneficial effect of the KV448 on epilepsy or other medically relevant conditions can be drawn.

This specific effect of KV448 is further challenged by the observation of similar, largely positive effects of the examination of any other musical stimulus compared with silence. Again, none of the observed summary effects were significant, suggesting a lack of study power. However, in terms of a salient specific effect of KV448, one would expect other musical stimuli to have no effect.

The available literature on the effect of Mozart's music on epilepsy or other medically relevant conditions does not follow the standards of experimental research. RCTs provide the strongest evidence among clinical trials and are therefore the state-of-the-art approach in experimental research (Held, 2010). In order to conclude about the success of a particular treatment, a control group (e.g., placebo) or at least two independent measurements are required. If this is not the case, no reliable conclusions can be drawn. Of the included studies in the present meta-analysis, a total of k = 3 studies were identified to meet these standards. Thereof, k = 1 addressed epilepsy. In mirror-designs, two independent groups undergo both the treatment and the control condition in a different order. To avoid bias, wash-out periods of

at least two weeks are crucial (Necdet, 2014). This was not considered in the eligible studies (k=2) that used such a mirror-design, through which the influence from one treatment phase on the other was uncontrolled. Therefore, a carry-over effect cannot be precluded, which in turn would invalidate the entire studies (Willan et al., 1986). Due to the absence of a control group as well as technical considerations (e.g., regression toward the mean), the one-group pretest-posttest is a very poor choice for testing the relationship between to variables (Knapp, 2016). However, a number of studies included in the present meta-analysis (k=3) applied this approach. Two of these studies added a counterbalanced design by directly exposing participants to another condition (i.e., other music). Instead of controlling for confounding variables, this reopens the issue of potential carry-over effects, questioning the validity of this investigations. Studies eligible for the present meta-analysis but excluded, e.g., because of data unavailability, were similarly poor designed (e.g., case studies, one-group pretest-posttest, lacking wash-out periods etc.). In the case studies identified (k=4), subjects suffered not only from epilepsy, but also from severe brain damage. These results cannot be generalized to patients in whom epilepsy is not comorbid.

In summary, of all literature available, four studies addressing the effect of the KV448 on epilepsy or other medically relevant conditions met experimental research standards (i.e., RCT). Of these, three studies found a non-trivial effect (Bodner et al., 2012; Paprad et al., 2020; Quon et al., 2021), but were based on small samples (treatment group n = 25; 12; 8, respectively) and unequal group sizes, through which they were substantially underpowered. Further, their results longer traceable.

Moreover, it is concerning that the primary data and even summary statistic that document the Mozart effect for epilepsy or other medically relevant conditions seem to be unavailable. Primary data of only one a single one (out of 26 studies) were accessible, summary statistics of only six studies were sufficiently documented within publications to calculate effect sizes. Upon request, another two authors provided the necessary statistical parameters which allowed the calculation of standardized effect sizes. However, for most of the studies effect size calculation was impossible, which resulted in another 14 studies having to be excluded. Personal communication with corresponding authors of these studies, which were predominantly cited, points out that they are related to poor data documentation (e.g., data repositories have become inaccessible). Open science practices (e.g., open access to data and code) are a common response to the replication crisis and sine qua non to implement scientific findings (Cashin et al., 2021). Given the present results, this claim cannot be fulfilled for research on the Mozart effect on epilepsy or other medically relevant conditions.

All in all, it arises the impression of an unfounded authority of the literature on which reports in science and popular media are based on. By citing this literature, which (i) in summary shows no salient effect and (ii) is built on a series of questionable research practices, information cascades can be generated that further reinforce the wrong impression of solid scientific evidence (Greenberg, 2009).

Limitations

Because the present analyses were based on a limited number of studies, the existence of the Mozart effect on epilepsy or other medically relevant conditions cannot be precluded with certainty. However, this is due to the fact that in regard to the question examined, too little evidence is available, extant studies are poorly documented, and not appropriately designed to draw reliable conclusions.

Conclusion

The present study shows that there is only little support for a specific Mozart effect or any other type of music on epilepsy or other medically relevant conditions considering the cumulative empirical evidence. Overall effects turned out to be small and non-significant. The available and useable literature is sparse, suboptimal designed, and substantially underpowered. A core value of science is transparency of methods and data (Kidwell et al., 2016), which is not the case in this regard. Studies would need to be conducted with larger samples on actual standards regarding design and research practices.

However, based on the literature available to date, no empirical evidence can be found to

confirm a salient effect of KV448 on epilepsy or other medically relevant conditions.

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factors that were included for the estimated summary effects depicted in the top panel with
respective 95% confidence intervals. The middle panel indicates the number of samples
within the respective subsets
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Appendix A

Abstracts in English and German

Abstract (English)

In recent years, the Mozart effect has attracted extensive media and scientific attention in the context of epilepsy and other medically relevant conditions. It has been said, that the exposure to the first movement "allegro con spirito" of the Mozart sonata for two pianos in D major (KV448) would remarkably relive epileptic symptoms (e.g., seizure frequencies, interictal epileptiform discharges) and was proposed to supplement or replace drug treatment. The present paper represents an extensive review and meta-analysis on this topic, providing evidence for potential influences of dissemination biases and the adequacy of the evidential value. It was shown that the overall effect sizes are small in size (g range: 0.16 to 0.43) and statistically not significant (p range: .13 to .52), which, in the context of meta-analysis, indicates substantially underpowered primary studies. Moderator-, and multiverse-analyses as well as a series of publication bias detection methods indicate that a positive effect of the KV448 on epilepsy and other medically relevant conditions is not reproducible. Insufficient documentation of replication attempts and selective publication of seemingly successful but strikingly inadequately designed and underpowered ones can thus lead to unfounded assumption of a salient effect.

Keywords: Mozart effect, epilepsy, diseases, meta-analysis, multiverse-analysis, reproducibility.

Abstract (German)

In den letzten Jahren hat der Mozart-Effekt im Zusammenhang mit Epilepsie und anderen medizinisch relevanten Erkrankungen sowohl in den Medien als auch in der Wissenschaft große Beachtung gefunden. Es wurde behauptet, dass die Exposition gegenüber dem ersten Satz "allegro con spirito" der Mozart-Sonate für zwei Klaviere in D-Dur (KV448) epileptische Symptome (z.B. Anfallshäufigkeit oder interiktale epileptoforme Entladungen) bemerkenswert lindern würde. Dabei wurde vorgeschlagen, die medikamentöse Behandlung der Epilepsie mit dem Hören der KV448 zu ergänzen oder gar zu ersetzen. Die vorliegende Studie stellt diesbezüglich eine umfangreiche Übersichtsarbeit und Meta-Analyse dar, die Hinweise auf mögliche Einflüsse von Publikationsverzerrungen und der Angemessenheit der Beweiskraft liefert.

Es wurde gezeigt, dass die kumulierten Effektgrößen klein (*g*-Bereich: 0,16 bis 0,43) und statistisch nicht signifikant (*p*-Bereich: .13 bis .52) sind, was im Rahmen einer Meta-Analyse auf deutlich unterpowerten Primärstudien hinweist. Moderatoren- und Multiversums-Analysen sowie einer Reihe von Methoden zur Erkennung von Publikationsverzerrungen deuteten darauf hin, dass ein positiver Effekt der KV448 auf Epilepsie und anderen medizinisch relevante Erkrankungen nicht reproduzierbar ist. Die mangelhafte Dokumentation von Replikationsversuchen und die selektive Publikation von scheinbar erfolgreichen, aber auffallend unzureichend konzipierten und unterpowerten Studien kann zu einer unbegründeten Annahme eines scheinbar herausragenden Effekts führen.

Schlüsselwörter: Mozart-Effekt, Epilepsie, Krankheiten, Meta-Analyse, Multiversum-Analyse, Reproduzierbarkeit.

Appendix B

Deviations from pre-registration

- 1. Stopping rule for Open Access Theses and Dissertations: No relevant paper on 3 pages in a row with 30 hits per page
- 2. If the sample mean was unavailable, the median value was used and interpreted as a mean. standard deviation was computed using *interquartile range* / 1.35:

Calculator produced by Shi (2020) and Luo (2018): http://www.math.hkbu.edu.hk/~tongt/papers/median2mean.html

Jiandong Shi, Dehui Luo, Hong Weng, Xian-Tao Zeng, Lu Lin, Haitao Chu and Tiejun Tong (2020), "Optimally estimating the sample mean and standard deviation from the five-number summary", arXiv:2003.02130 [stat.ME].

Luo D, Wan X, Liu J, Tong T. Optimally estimating the sample mean from the sample size, median, mid-range, and/or mid-quartile range. Statistical methods in medical research. 2018 Jun; 27(6):1785-805.

Studies affected:

- a. Bergomi et al., 2014 (used scenario: 3)
- b. Paprad et al., 2020 (used scenario: 2)
- c. Štillová et al., 2021 (used scenario: 1)
- **3.** The studies were not only divided into groups on the basis of the stimulus used (MO/OM/NM), but also on the basis of the study design used. Reason: Different study designs cannot be synthesized.
- **4.** Effect sizes for two-groups pretest-posttest designs were calculated using https://www.psychometrica.de/effect_size.html; variance and standard errors were calculated using formulas provided in Borenstein et al., 2021

- **5.** Effect sizes, variances and standard errors for one-group pretest-posttest designs were calculated using the formulas provided in Cooper et al., 2019; If the correlation between pre- and posttest was not available, it was estimated by r = 0.5
- 6. Studies with one-group and several measurement points (e.g., KV448 measurement no music measurement; KV448 measurement other music measurement): We have included the corresponding effect sizes in MO-NM or OM-NM. Potential carry-over effects in the samples are noted in the tables (D'Alessandro et al., 2017, Rafiee et al., 2020, Štillová et al., 2021, Grylls et al., 2018).
- 7. Vibrašiūtė (2017): Since several of the same samples cannot be synthesized with each other, we paid attention to the results concerning systolic blood pressure, since this was identified as the most meaningful.
- **8.** Additionally, combinatorial meta-analyses were conducted.
- **9.** Specification curve:

Due to unavailability of information, some *which* could not be investigated:

- Lab outside of Asia
- included in the previous meta-analysis (no previous meta-analysis available, which applied meta-analytical techniques)
- type of OM-condition: electronic, pop, techno, hip-hop, meditation, short story was not observed
- published vs. unpublished: we identified only one unpublished study
- sex: no study with women-only or men-only was identified

Appendix C

PRISMA checklist

Table S1. PRISMA checklist.

Section and Topic	Item #	Checklist item	Location where item is reported				
TITLE							
Title	1	ntify the report as a systematic review.					
ABSTRACT	1						
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	1				
INTRODUCTION	I						
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	2				
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	3				
METHODS							
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	4				
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the late when each source was last searched or consulted.					
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	4				
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	4				
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	4				
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	5				
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	5				
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	6				
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	6				
Synthesis methods	13a Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).						
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data	5				

Section and Topic	Item #	Checklist item	Location where item is reported					
		conversions.						
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	5					
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	5, 6					
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	6					
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	5					
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	6					
Certainty assessment	15	escribe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.						
RESULTS								
Study selection	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.							
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Table S1					
Study characteristics	17	Cite each included study and present its characteristics.						
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	17					
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	12, 13, 14					
Results of	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	17					
syntheses	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.						
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	12, 14					
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	12, 15					
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	17					
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	12-23					
DISCUSSION								
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	24					
	23b	Discuss any limitations of the evidence included in the review.	26					

Section and Topic	Item #	Checklist item						
	23c	iscuss any limitations of the review processes used.						
	23d Discuss implications of the results for practice, policy, and future research.							
OTHER INFORMA	TION							
Registration and 24a		Provide registration information for the review, including register name and registration number, or state that the review was not registered.						
protocol	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	4					
	24c	Describe and explain any amendments to information provided at registration or in the protocol.						
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	-					
Competing interests	26	Declare any competing interests of review authors.						
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	4-6					

Appendix D

Newcastle-Ottawa Scale adapted for cross-sectional studies

Selection: (Maximum 5 stars)

- 1) Representativeness of the sample:
- a) Truly representative of the average in the target population. * (all subjects or random sampling)
- b) Somewhat representative of the average in the target population. * (non-random sampling)
- c) Selected group of users.
- d) No description of the sampling strategy.
- 2) Sample size:
- a) Justified and satisfactory. *
- b) Not justified.
- 3) Non-respondents:
- a) Comparability between respondents and non-respondents characteristics is established, and the

response rate is satisfactory. *

- b) The response rate is unsatisfactory, or the comparability between respondents and non-respondents is unsatisfactory.
- c) No description of the response rate or the characteristics of the responders and the non-responders.
- 4) Ascertainment of the exposure (risk factor):
- a) Validated measurement tool. **
- b) Non-validated measurement tool, but the tool is available or described.* c) No description of the measurement tool.

Comparability: (Maximum 2 stars)

- 1) The subjects in different outcome groups are comparable, based on the study design or analysis. Confounding factors are controlled.
- a) The study controls for the most important factor (select one). *
- b) The study control for any additional factor. *

Outcome: (Maximum 3 stars)

- 1) Assessment of the outcome:
- a) Independent blind assessment. **
- b) Record linkage. **
- c) Self report. *
- d) No description.
- 2) Statistical test:
- a) The statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is presented, including confidence intervals and the probability level (p value). *
- b) The statistical test is not appropriate, not described or incomplete.

Table S2. *Quality of included primary studies assessed with the Newcastle-Ottawa Scale.*

	Sele	ection			Comparability	Outco	ome	
Study	1.	2.	3.	4.		1.	2.	Total (10)
Bergomi et al. (2022)	0	*	0	**	*	**	*	7
Coppola et al. (2015)	0	0	0	*	0	*	*	3
D'Alessandro et al. (2017)	0	0	0	*	0	*	*	3
Grylls et al. (2018)	0	0	0	**	0	**	*	5
Paprad et al. (2020)	0	0	0	**	*	**	*	6
Rafiee et al. (2020)	0	0	0	*	0	*	*	3
Stillova et al. (2021)	0	0	0	**	0	**	*	5
Vibrasiute (2017)	0	0	0	**	*	**	*	7

Herzog, R., Alvarez-Pasquin, M., Diaz, C., Del Barrio, J., Estrada, J., & Gil, A. (2013).

Newcastle-Ottawa Scale adapted for cross-sectional studies. *BMC Public Health*, *13*, 154.

Appendix E

Table S3: Study characteristics of excluded studies

Table S3. Study characteristics of excluded studies that are not traceable, poorly documented, or whose data are no longer available.

Reference	Sample size	Sample type	Disease	Conclusion	Journal	Exclusion reason	Data availability
Attanasio et al. (2012)	62	Adults	Tinnitus	Significant positive effect on the sound intensity of tinnitus after a single exposure to the KV448.	Acta Oto- Laryngologica	 Statistical information to calculate effect sizes was unavailable One-group pre-post design counterbalanced, no wash-out period 	Not reported and no author response.
Bedetti et al. (2019)	1	Adult	Epilepsy	Significant reduction of epileptic discharges and the frequency of seizures.	Psychiatria Danubina	 Case study Patient was affected by profound intellectual disability, autism spectrum disorder, intermittent explosive disorder, drug-resistant epilepsy, microcephaly, facial and limbs dysmorphisms 	-
Bodner et al. (2012)	n KV448 = 25 $n control = 11$	Mixed	Epilepsy	Significant reduction of seizures in subjects with a range of epilepsy and seizure types, in some cases complete cessation of seizures after exposure to KV448. The study was designed as an RCT.	PLOS one	- Statistical information to calculate effect sizes was unavailable	Not reported and no author response.

Coppola et al. (2017)	n KV448 = 9 $n control = 10$	Children	Epilepsy	Music therapy seems to be an effective treatment for patients with refractory epileptic seizures in childhood, even though the KV448 was not identified as more effective than other Mozart (i.e., other classical) music. The study was designed as an RCT.	Epilepsy & Behavior	- Only identified study with KV448 vs. other music condition, i.e., was not usable in the present meta-analysis	Summary data provided upon request.
Hughes et al. (1998)	29	Mixed	Epilepsy	Significant reduction of epileptiform activity in 23 of 29 patients, even if they were in coma, with status epilepticus, or with periodic lateralized epileptiform discharges.	Clinical EEG and Neuroscience	 Statistical information to calculate effect sizes was unavailable One-group design 	No contact information available.
Hughes et al. (1999)	1	Children	Epilepsy	Significant reduction of seizure frequency, generalized bilateral spike and wave complex over a 24-hour period while exposed to KV448 for ten minutes every hour during wakefulness.	Clinical Electroencephalo graphy	Case studyPatient suffered from Lennox-Gastaut Syndrome	-
Kuester et al. (2010)	1	Adults	Epilepsy	Reduction of epileptic discharges, recovering from coma after five days of exposure to KV448.	Epilepsy & Behavior	Case studyPatient had severe brain trauma	-
Lahiri & Ducan (2007)	1	Adults	Epilepsy	Complete cessation of secondarily generalized tonic-colonic seizures after three months of listening to Mozart's music for 45 minutes a day.	Epilepsy & Behavior	Case studySelf-report of the patient	-

Lin et al. (2010)	t0: 58 t1: 46	Children	Epilepsy	Reduction of epileptiform discharges in children with different seizure types after listening to KV448 once. No decrease in epileptiform discharge was observed when a computerized string version of the KV448 was used.	Epilepsy Research	 Statistical information to calculate effect sizes was unavailable One-group design 	Data requested, data unavailable.
Lin et al. (2011a)	11	Children	Epilepsy	After listening to KV448 once a day for six month, two patients were seizure free, six had a significant reduction in seizure frequency and in three patients a minimal or no effect was observed.	Epilepsy & Behavior	 Statistical information to calculate effect sizes was unavailable One-group design 	Data requested, data unavailable.
Lin et al. (2011b)	18	Children	Epilepsy	Long-term listening to KV448 decreases epileptiform discharge frequency. Seizure frequency was not measured, since all patients were seizure free for six months prior the study.	Epilepsy & Behavior	 Statistical information to calculate effect sizes was unavailable One-group design 	Data requested, data unavailable.
Lin et al. (2012)	N t0 = 39 N KV545 t1= 34 N KV448 t1 = 33	Children		Significant decrease in epileptiform discharges in children after listening to KV448 and KV545.	Evidence-Based Complementary and Alternative Medicine	 Statistical information to calculate effect sizes was unavailable Inaccurate reporting with regard to dropouts and group sizes One-group design counterbalanced, wash-out period one week only 	Data requested, data unavailable.

Lin et al. (2013)	n KV448 t0 = 41 n KV448 t1 = 34 n KV545 t0 = 23 n KV545 t1 = 19	Children	Epilepsy	Significant decrease of epileptiform discharges in children with epilepsy. During music (KV448 / KV545), an increased parasympathetic tone was observed.	Clinical Neurophysiology	 Statistical information to calculate effect sizes was unavailable Inaccurate reporting with regard to dropouts and group sizes 	Data requested, data unavailable.
Lin et al. (2014)	n KV448 t0= 22 n KV448 t1 = 11 n KV448 t2 = 10 n KV448 t3 = 8 n control t0= 24 n control t1= 10	Children	Epilepsy	Significant reduction of seizure recurrence rate and epileptiform discharged in children with first unprovoked seizures.	BMC Complementary Medicine and Therapies	 Statistical information to calculate effect sizes was unavailable Inaccurate reporting with regard to dropouts and group sizes Patients had experienced only a single seizure (unclear, if any of them experienced seizures ever again afterwards) 	Data requested, data unavailable.
Ren et al. (2019)	n KV448 = 11 $n control = 5$	Children	Epilepsy	Significant reduction of seizure recurrence rate and epileptiform discharged in children with first unprovoked seizures.	BMC – Complementary Medicine and Therapies	- Statistical information to calculate effect sizes was unavailable	Data requested, data unavailable.
Quon et al. (2021)	n1 = 8 $n2 = 8$	Adults	Epilepsy	Reduced interictal epileptiform discharges during the original version of KV448 after at least 30 seconds of exposure.	Scientific Reports	- Statistical information to calculate effect sizes was unavailable	Not reported and no author response.
Turner et al. (2004)	t0: = 4 t1: = 2 / 1	Children	Epilepsy	Significant decreases in interictal epileptiform discharges after exposure to KV448. No Effect for Beethoven's <i>Für Elise</i> .	Epilepsy & Behavior	 Statistical information to calculate effect sizes was unavailable Results from only one participants were reported 	-

Ziv et al. (2022)	n KV448 = 23	Children	Bronchiolitis	No significant difference in	Acta Pediatrica	- A patient could	Not reported and
	n control group 1			the severity score of children		participate in the study	no author
	= 22			hospitalized with		more than once, i.e.,	response.
	n control group 2			bronchiolitis after listening to		the study design is	
	= 25			the KV448.		unsuitable	

Note. Upper case *N* means that one sample underwent different conditions; lower case *n* means that different samples underwent different conditions; t: time of measurement.

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Appendix F

Description of publication bias detection methods and numeric results

Funnel plot (Light & Pillemer, 1984). Funnel plot was used to display the relationship between study size and effect size (Borenstein, 2021). It is expected, that less precise studies scatter considerably at the bottom of the plot, while more precise studies scatter less at the top due to smaller error variances of larger studies (Harrer et al., 2021). In absence of bias, distributions are symmetrical and shaped like an inverted funnel that is centered around the summary effect size. In the presence of bias, these distributions are non-symmetrical because unprecise estimates (i.e., those with high sampling errors) remain unpublished (Borenstein et al., 2021). In power-enhanced funnel plots (Kossmeier et al., 2020), the study-level statistical power is visualized by different colors (i.e., warmer colors indicating lower and colder colors indicating larger study power).

Trim-and-fill (Duval & Tweedie, 2000). In the trim-and-fill method (Duval & Tweedie, 2000), the number of study effects on the left and right of the summary effect size estimate are ranked according to their strength and subsequently compared by means of a Wilcoxon test (i.e., akin to the idea of assessing funnel plot asymmetry). In cases of asymmetry, the smallest studies of the funnel plot get removed in an iterative procedure, in which each removal is followed by a summary effect reestimation and asymmetry reassessment (Borenstein et al., 2021). Once no more asymmetry is detected, all trimmed study effects are reentered and the ostensibly missing effects are added around the re-estimated study effect (Duval & Tweedie, 2000). I assumed bias if the difference between the meta-analytic summary effects and the adjusted estimate exceeds 20% of the summary effect in either direction following current recommendations (Siegel et al., 2022). Because a minimum of k = 3 studies is required for its application, presently the trim-and-fill method was conducted only for the dependent MO-condition as well as the OM-condition.

Sterne and Egger's regression (Egger et al., 1997; Sterne & Egger, 2005). Sterne and Egger's regression corresponds to a linear regression of the effect size estimate on its standard error (i.e., the precision), weighted by the inverse variance of the effect estimate.

If the intercept differs significantly from zero, Egger's tests indicate funnel plot asymmetry, which may be indicative of dissemination bias or small-study effects (Harrer et al., 2021).

Rank correlation method (Begg & Mazumdar, 1994). The rank correlation approach is based on a non-parametric correlation of the standardized effect size and the variance of the study-specific effect estimate (by the means of Kendall's τ^2 ; Schwarzer & Rücker, 2010). In absence of bias, no systematic association should be observable between study precision and effect strength (i.e., p < .10 is assumed to be indicative of bias; Siegel et al., 2022).

PET-PEESE (Stanley & Doucouliagos, 2014). PET-PEESE can be viewed as an extension of Sterne and Egger's test and comprises two regressions (Cooper et al., 2019). In the first one, the a weighted regression of the effect size on the standard error with an intercept indicating the true effect if the standard error equals to zero represents the precision-effect test (PET; Stanley & Doucouliagos, 2014). If the intercept varies significantly from zero in PET, PEESE (precision-effect-estimate with standard error) is conducted, i.e., a weighted regression of the effect size on the squared standard error and its intercept is interpreted as an effect size estimate (Cooper et al., 2019). Evidence for bias is typically assumed if the difference between the meta-analytic summary effects and the adjusted estimate exceeds 20% of the summary effect in either direction (Siegel et al., 2022). Simulation studies indicate possible limitations of PET-PEESE in presence of small study numbers, small within-study sample sizes, and large heterogeneities (Carter et al., 2019).

Selection model approach (Vevea & Woods, 2005). Selection model approach by Vevea & Woods (2005) is based on four different study weight functions for *p*-values. By the means of this approach we assumed that effect sizes were selected either according to moderate vs. severe and one- vs. two tailed criteria (Pietschnig et al., 2015). In this vein, results would be indicative of publication bias if resulting summary effect estimates differed substantially (i.e., exceeding 20%) between the corrected and the uncorrected estimate (Siegel et al., 2022).

Test of Excess of Significance (Ioannidis & Trikalinos, 2007). Based on the Test of Excess of Significance we evaluate whether there is an excess of studies with statistically significant results, by comparing the expected number of significant studies (based on the assumption that the estimated summary effect corresponds to the true effect) and the observed number of included significant studies (Ioannidis & Trikalinos, 2007).

p-curve (Simonsohn et al., 2014), p-uniform (van Assen et al., 2015), and p-unform* (van Aert & van Assen, in press). p-curve is a diagnostic tool that assesses evidence for the

presence of both publication bias as well as p-hacking and shows the distribution of statistically significant p values (i.e., p < .05) within a study set (Harris et al., 2021). The shape of the p-curve depends on both the evidential value and the sample size of the included studies. Assuming the null hypothesis that small and large p-values are equally likely, a uniformly distributed p-curve is expected, indicating no evidential value. Under the alternative hypothesis, however, small and large p-values are expected to have unequal probabilities, resulting in a right-skewed curve, indicating the existence of an evidential value (Cooper et al., 2021). Right-skewness is tested by means of binomial tests, which compares the distribution of p-values > .025 with the distribution of p-values < .025. In order to avoid a loss of information, since binomial test require a dichotomization of the in fact continuous pvalues, additional continuous test (*Stouffer method*) are performed (Harris et al., 2021). Further, it is possible to assess the evidential value of the available studies by means of 33% power test. In case of a left-skewed curve, a publication bias or p-hacking can be assumed and indicates that the values just below .05 are overrepresented in the study set (Cooper et al., 2021). Thresholds of bias indication are based on the idea of combining full and half p-curve into a single analysis (Simonsohn et al., 2015), i.e., p-value of half p-curve > .05 or p-values of both half and full *p*-curves > .10 (Siegel et al., 2022).

Both *p*-uniform and *p*-uniform* are based on similar ideas as the *p*-curve method, but the former methods use different approaches to define the fit to the uniform distribution (Cooper et al., 2021). The effect estimation in *p*-uniform* is based on *p*-values of both significant and non-significant studies (Harris et al., 2021). All three methods estimate an adjusted summary effect size by means of published significant (*p*-curve and *p*-uniform) or published significant and non-significant *p*-values (*p*-uniform*). Furthermore, *p*-uniform and *p*-uniform* provide a means to calculate confidence intervals. Of note, it should be considered that *p*-value based methods for detecting publication bias tend to overestimate the effect size of the evidential value (Cooper et al., 2021).

Table S4. Numeric outcomes of publication bias detection methods except power-enhanced funnel-plots.

Method	Independent MO-	Dependent MO-condition	OM condition
	condition	(k=6)	(k=5)
	(k=2)		
Trim-And-Fill	NA	adjusted estimate = 0.068	adjusted estimate = 0.088
		unadjusted estimate =	unadjusted estimate =
		0.157	0.088
		56% change	0% change
Rank	$\tau = -1.00$	$\tau = 0.60$	au=0.40
correlation	p = 1.00	p = .136	p = .483
Egger's	NA	Z = 1.31	Z = 0.982
regression		p = .19	p = .326
PET-PEESE	NA	<u>PET</u>	<u>PET</u>
		intercept = -0.156	intercept = -0.317
		p = .503	p = .477
		<u>PEESE</u>	<u>PEESE</u>
		intercept = -0.014	intercept = -0.151
		p = .914	p = .556
Selection	moderate one tailed: 51%	moderate one tailed: 29%	moderate one tailed: 129%
Model	severe one tailed: 183%	severe one tailed: 66%	severe one tailed: 302%
	moderate two tailed: 7%	moderate two tailed: 13%	moderate two tailed: 15%
	severe two tailed: 15%	severe two tailed: 28%	severe two tailed: 32%
Test of Excess	p = .035	<i>p</i> = .458	p = .257
Significance			
<i>p</i> -curve	continuous tests yielded	continuous tests yielded p	NA
	p's < .001 for evidential	= .449 and $p = .699$ for	
	value indication and p's	evidential value indication	

	>.999 for <i>p</i> -hacking	and $p = .429$ and $p = .692$	
	indication;	p-hacking indication;	
	estimated statistical power:	estimated statistical power:	
	99%	13%	
<i>p</i> -uniform	Z = > 0.001	NA	NA
	p = .5		
p-uniform*	Z = 0.323	Z = 0.067	Z = 0.021
	p = .851	p = .410	p = .989

Note. NA = method was not feasible; results indicating publication bias are marked in red.

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Appendix G

R-Code

file needed: data final ME # libraries ---library(clubSandwich) library(data.table) library(plyr) library(dplyr) library(foreign) library(ggplot2) library(ggpubr) library(grid) library(gridExtra) library(gsl) library(haven) library(Matrix) library(metafor) library(metaviz) library(psychmeta) library(puniform) library(readx1) library(robumeta) library(SciViews) library(stringr) library(writex1) # import data ---data <- setDT(read xlsx(file.choose())) # prepare data ---data\$sample <- as.factor(data\$sample)</pre> data\$treatment condition <- as.factor <- data\$treatment condition data\$publication status <- as.factor(data\$publication status) data\$publisher <- as.factor(data\$publisher)</pre> data\$manuscript type<- as.factor(data\$manuscript type) data\$peer reviewed <- as.factor(data\$peer reviewed)</pre> data\$funding yn <- as.factor(data\$funding yn) data\$previously included <- as.factor(data\$previously included) data\(geographic \) location \(< - \) as factor(\(data\) geographic \) location) data\$sample type <- as.factor(data\$sample type)</pre> data\$measured disease <- as.factor(data\$measured disease) data\$epilepsy measurement <- as.factor(data\$epilepsy measurement) data\$seizure type <- as.factor(data\$seizure type)

data\$measurement method <- as.factor(data\$measurement method)

```
data$MO sonata <- as.factor(data$MO sonata)
data$OM kind <- as.factor(data$OM kind)
data$more than once <- as.factor(data$more than once)
data$state exposure <- as.factor(data$state exposure)</pre>
data$time of exposure <- as.factor(data$time of exposure)
# effect size calculation ----
## for studies with two groups
## calculated d with psychometrica ("3. Effect size for mean differences in groups with
unequal sample
## sizes within a pre-post control design"; https://www.psychometrica.de/effect_size.html)
## calculate variance for ES and transform into standard error (Cooper et al., 2019)
n1 <- #sample size 1
n2 <- #sample size 2
d <- #effect size in Cohen's d
V < -(n1+n2)/(n1*n2) + (d^2/(2*(n1+n2)))
se <- sqrt(V)
se
## for studies with one group + 2 measurement points pre-post (Cooper et al., 2019)
n <- #number of participants
mean1 <- #pre mean
S1 <- #pre sd
mean2 <- #post mean
S2 <- #post sd
SW <- sqrt((S1^2 + S2^2)/2) #calculate within standard deviation
SW
d <- (mean1 - mean2) / SW #Cohen's d
r <- 0.5 #correlation pre and post test (if not available - use imputed 0.5)
vd < -((1/n) + (d^2 / (2*n)))*(2*(1-r)) #variance d
vd
## to get an unbiased estimate (d has a slight bias, since it tends to overestimate the effect of
small samples):
## multiply d with correction factor (J) to get Hedges'g
df < -n-1
J <- 1 - (3/((4*df) - 1)) #correcter
g <- d * J #Hedges'g
g
```

```
vg <- J^2 * vd #variance Hedges'g
se <- sqrt(vg) #standard error Hedges'g
# extract data sets ----
two sample data <- data[sample %in% "two", ]
two sample data MONM <- two sample data[treatment condition %in% "MO-NM", ]
one sample data <- data[sample %in% "one", ]
one sample data MONM <- one sample data[treatment condition %in% "MO-NM", ]
one sample data <- data[sample %in% "one", ]
one sample data OMNM <- one sample data[treatment condition %in% "OM-NM", ]
## write spss files for meta shine (Siegel et al., 2021)
#write sav(two sample data MONM, path)
#write sav(one sample data MONM, path)
#write sav(one sample data OMNM, path)
# random-effects models ----
##RMA - two sample data MO-NM
two sample model <- rma(es, V, data = two sample data_MONM, method = "REML")
##forest plot
png(filename="TWO groups forest plot.png", res=350, width=3196, height=1648)
forest(two sample model,
    slab = two sample data MONM$author names,
    addcred = TRUE, #addcred: prediction interval
    col = "navyblue",
    xlab = "Hedges'g",
    mlab = expression("RE Model, p = .524"),
    steps = 5,
    cex = .9)
# Add column headings to the plot
text(-6.3, 4.2, "Study name", pos = 4, cex = .9)
text(6.9, 4.2, "Hedges' g [95\% CI]", pos = 2, cex = .9)
par(cex = .9, font = 2)
text(0, 6, "Independent MO-condition", pos = 1, cex = 1)
dev.off()
##RMA - one sample data MO-NM
```

```
one sample model MONM <- rma(es, V, data = one sample data MONM, method =
"REML")
##forest plot
png(filename="ONE group forest plot MONM.png", res=350, width=3196, height=1648)
forest(one sample model MONM,
    slab = one sample data MONM$author names,
    addcred = TRUE, #addcred: prediction interval
    col = "navyblue",
    xlab = "Hedges'g",
    mlab = "RE Model, p = .127",
    steps = 5,
    cex = .9
# Add column headings to the plot
text(-3.8, 7.4, "Study name", pos = 4, cex = .9)
text(5.2, 7.4, "Hedges' g [95\% CI]", pos = 2, cex = .9)
par(cex = .9, font = 2)
text(0.4, 9.5, "Dependent MO-condition", pos = 1, cex = 1)
dev.off()
##RMA - one sample data OM-NM
one sample model OMNM <- rma(es, V, data = one sample data OMNM, method =
"REML")
##forest plot
png(filename="ONE group forest plot OMNM.png", res=350, width=3196, height=1648)
forest(one sample model OMNM,
    slab = one sample data OMNM$author names,
    addcred = TRUE, #addcred: prediction interval
    col = "navyblue",
    xlab = "Hedges'g",
    mlab = "RE Model, p = .581",
    steps = 5,
    cex = .9
# Add column headings to the plot
text(-3.5, 6.3, "Study name", pos = 4, cex = .9)
text(4.05, 6.3, "Hedges'g [95\% CI]", pos = 2, cex = .9)
par(cex = .9, font = 2)
text(0.1, 8.5, "OM-condition", pos = 1, cex = 1)
dev.off()
```

robustness estimation leave-one-out ----

```
##LOO - two sample data MO-NM
leavelout(two sample model, digits = 3)
##LOO - one sample data MO-NM
leave1out(one sample model MONM, digits = 3)
##LOO - one sample data OM-NM
leave1out(one sample model OMNM, digits = 3)
# subgroup analysis ----
##SA - one sample data MO-NM
###measure
one sample data MONM measure SF <- one sample data MONM[reduction topic %in%
"seizure frequency", ]
rma(es, V, data = one sample data MONM measure SF, method = "REML", digits = 3)
one sample data MONM measure IED <- one sample data MONM reduction topic
%in% "epileptic discharges", ]
rma(es, V, data = one sample data MONM measure IED, method = "REML", digits = 3)
###funding
one sample data MONM NR <- one sample data MONM[funding yn %in% "NR" |
funding vn %in% "no". 1
rma(es, V, data = one sample data MONM NR, method = "REML", digits = 3)
one sample data MONM yes <- one sample data MONM[funding yn %in% "yes", ]
rma(es, V, data = one sample data MONM yes, method = "REML", digits = 3)
###sample type
one sample data MONM adult <- one sample data MONM[sample type %in% "adults", ]
rma(es, V, data = one sample data MONM adult, method = "REML", digits = 3)
one sample data MONM mixed <- one sample data MONM[sample type %in% "mixed",
rma(es, V, data = one sample data MONM mixed, method = "REML", digits = 3)
###seizure type
one sample data MONM gf <- one sample data MONM[seizure type %in%
"generalized focal", ]
rma(es, V, data = one sample data MONM gf, method = "REML", digits = 3)
one sample data MONM NR <- one sample data MONM[seizure type!=
"generalized focal", ]
rma(es, V, data = one sample data MONM NR, method = "REML", digits = 3)
```

```
##SA - one sample data OM-NM
###measure
one sample data OMNM measure SF <- one sample data OMNM[reduction topic %in%
"seizure frequency", ]
rma(es, V, data = one sample data OMNM measure SF, method = "REML", digits = 3)
one sample data OMNM measure IED <- one sample data OMNM reduction topic
%in% "epileptic discharges", ]
rma(es, V, data = one sample data OMNM measure IED, method = "REML", digits = 3)
###funding
one sample data OMNM NR <- one sample data OMNM[funding yn %in% "NR" |
funding yn %in% "no", ]
rma(es, V, data = one sample data OMNM NR, method = "REML", digits = 3)
one sample data OMNM yes <- one sample data OMNM[funding yn %in% "yes", ]
rma(es, V, data = one sample data OMNM yes, method = "REML", digits = 3)
###sample type
one sample data OMNM adult <- one sample data OMNM[sample type %in% "adults", ]
rma(es, V, data = one sample data OMNM adult, method = "REML", digits = 3)
one sample data OMNM children <- one sample data OMNM[sample type != "adults", ]
rma(es, V, data = one sample data OMNM children, method = "REML", digits = 3)
###type of control music
one sample data OMNM classic <- one sample data OMNM[OM kind %in% "set of
mozart music" | OM kind %in% "haydn's symphony no. 94", ]
rma(es, V, data = one sample data OMNM classic, method = "REML", digits = 3)
one sample data OMNM othercthanlassic <- one sample data OMNM[OM kind %in%
"scambled version KV448" | OM kind %in% "non classical", ]
rma(es, V, data = one sample data OMNM othercthanlassic, method = "REML", digits = 3)
# meta-regression ----
##MR - two sample data MO-NM
###publication year
py.two reg <- rma(es, V, mods = ~publication year, data = two sample data MONM,
method = "REML", digits = 3)
###age
age.two reg <- rma(es, V, mods = ~age mean overall, data = two sample data MONM,
method = "REML", digits = 3)
###sex
sex.two reg <- rma(es, V, mods = ~percentage male mean overall, data =
two sample data MONM, method = "REML", digits = 3)
###duration of exposure
dur.two reg <- rma(es, V, mods = ~dauration exposure sec 1, data =
two sample data MONM, method = "REML", digits = 3)
```

```
##MR - one sample data MO-NM
###publication year
py.oneMO reg <- rma(es, V, mods = ~publication year, data = one sample data MONM,
method = "REML", digits = 3)
###age
age.oneMO reg <- rma(es, V, mods = ~age mean overall, data = one sample data MONM,
method = "REML", digits = 3)
###sex
sex.oneMO reg <- rma(es, V, mods = ~percentage male mean overall, data =
one sample data MONM, method = "REML", digits = 3)
###duration of exposure
dur.oneMO reg <- rma(es, V, mods = ~dauration exposure sec 1, data =
one sample data MONM, method = "REML", digits = 3)
##MR - one sample data OM-NM
###publication year
py.oneOM reg <- rma(es, V, mods = ~publication year, data = one sample data OMNM,
method = "REML", digits = 3)
###age
age.oneOM reg <- rma(es, V, mods = ~age mean overall, data = one sample data OMNM,
method = "REML", digits = 3)
###sex
sex.oneOM reg <- rma(es, V, mods = ~percentage male mean overall, data =
one sample data OMNM, method = "REML", digits = 3)
###duration of exposure
dur.oneOM reg <- rma(es, V, mods = ~dauration exposure sec 1, data =
one sample data OMNM, method = "REML", digits = 3)
# publication bias ----
#inclusion of published studies only
two sample data <- data[sample %in% "two", ]
two sample data MONM <- two sample data[treatment condition %in% "MO-NM", ]
two sample data MONM PB <- two sample data MONM[publication status %in%
"published", 1
# write spss files for meta shine (Pietschnig et al., 2020)
#write sav(two sample data MONM PB, "/Users/sandroberleiter/Desktop/Master
Thesis/18 data/01 spss/two sample data MONM PB.sav")
one sample data <- data[sample %in% "one", ]
one sample data MONM <- one sample data[treatment condition %in% "MO-NM", ]
one sample data <- data[sample %in% "one", ]
one sample data OMNM <- one sample data[treatment condition %in% "OM-NM", ]
## one sample data MONM
```

```
one sample model MONM <- rma(es, V, data = one sample data MONM, method =
"REML")
###PET-PEESE
one sample data MONM$seq <- one sample data MONM$se^2
one sample data MONM$weights <- 1 / one sample data MONM$se^2
pet <- lm(es \sim se, weights = weights, data = one sample data MONM)
summary(pet)$coefficients
peese <- lm(es ~ seq, weights = weights, data = one sample data MONM)
summary(peese)$coefficients
###Test of Excess Significance
toe <- tes(one sample data MONM$es, one sample data MONM$V,
one sample data MONM$se)
summary(toe)
toe$sig
####study 3 identified as significant -> paired t-test for p-curve
#values: Raffiee et al., 2019 Group A
t0 \le c(11, 6, 20, 13, 5)
t1 < -c(4, 4, 7.5, 8, 0)
t.test(t0, t1, paired = TRUE)
###p-uniform ##ERROR
puniform(yi=one sample data MONM$es, vi = one sample data MONM$V,
ni=one sample data MONM$N, alpha=.05, side="left", method="P", plot = TRUE)
## one sample data OMNM
###PET-PEESE
one sample data OMNM$seq <- one sample data OMNM$se^2
one sample data OMNM$weights <- 1 / one sample data OMNM$se^2
pet <- lm(es \sim se, weights = weights, data = one sample data OMNM)
summary(pet)$coefficients
peese <- lm(es \sim seq, weights = weights, data = one sample data OMNM)
summary(peese)$coefficients
###Test of Excess Significance
tes(one sample data OMNM$es, one sample data OMNM$V,
one sample data OMNM$se)
```

```
###p-uniform ##ERROR
puniform(vi=one sample data OMNM$es, vi = one sample data OMNM$V,
ni=one sample data OMNM$N, alpha=.05, side="left", method="P", plot = TRUE)
# specification curve (Voracek et al., 2019) ----
data <- setDT(read xlsx(file.choose())) #data final SPECIFICATION
## prepare data
data$sample <- as.factor(data$sample)</pre>
data$treatment condition <- as.factor <- data$treatment condition
data\funding yn <- as.factor(data\funding yn)
data\sample type <- as.factor(data\sample type)
data$measured disease <- as.factor(data$measured disease)
data$seizure type <- as.factor(data$seizure type)
data$measurement method <- as.factor(data$measurement method)
data\( \)exposure more than once \( \)- as.factor(\( \)data\( \)exposure more than once \( \)
two sample data <- data[sample %in% "two", ]
two sample data MONM <- two sample data[treatment condition %in% "MO-NM", ]
one sample data <- data[sample %in% "one", ]
one sample data MONM <- one sample data[treatment condition %in% "MO-NM", ]
one sample data <- data[sample %in% "one", ]
one sample data OMNM <- one sample data[treatment condition %in% "OM-NM", ]
##one sample data MO-NM
x <- two sample data MONM
### "which" factors
measured disease <- c("epilepsy", "disease other", "disease either")
measurement_method <- c("EEG", "measurement_other", "measurement_either")
exposure more than once <- c("exposure yes", "exposure no", "exposure either")
sample type <- c("kids", "adults", "sample either")
funding <- c("NR", "yes", "no", "either")
### "how" factors
effect <- c("g", "d")
ma method <- c("FE", "HedgesOlkin(REML)", "HunterSchmidt")
### construct all possible combinations of internal and external factors
specifications <- expand.grid(measured_disease = measured_disease,</pre>
                 measurement method = measurement method,
                 exposure more than once = exposure more than once,
                 sample type = sample type,
                 funding = funding,
```

effect = effect,

```
ma method = ma method)
specifications <- data.frame(specifications,
                 mean = rep(NA, nrow(specifications)),
                  set = rep(NA, nrow(specifications)),
                  lb = rep(NA, nrow(specifications)),
                 ub = rep(NA, nrow(specifications)),
                 p = rep(NA, nrow(specifications)),
                  k = rep(NA, nrow(specifications)))
specifications
### conduct specification analyses
for(i in 1:nrow(specifications)) {
 dat <- x
 if(specifications\measured disease[i] == "epilepsy") {
  dat <- dat[dat$measured disease == "epilepsy", ]
 } else {
  if(specifications\measured disease[i] == "disease other") {
   dat <- dat[dat$measured disease == "other", ]
 if(specifications\measurement method[i] == "EEG") {
  dat <- dat[dat$measurement method== "EEG", ]
 } else {
  if(specifications\measurement method[i] == "measurement other") {
   dat <- dat[dat$measurement method == "other", ]
 if(specifications\exposure more than once[i] == "exposure no") {
  dat <- dat[dat$exposure more than once == "no", ]
 } else {
  if(specifications\exposure more than once[i] == "exposure_yes") {
   dat <- dat[dat$exposure more than once == "yes", ]
  }
 if(specifications\sample type[i] == "adults") {
  dat <- dat[dat$sample type == "adults", ]
 } else {
  if(specifications\sample type[i] == "kids") {
   dat <- dat[dat$sample type == "kids", ]
 if(specifications$funding[i] == "yes") {
  dat <- dat[dat$funding == "yes", ]
 } else {
  if(specifications\funding[i] == "no") {
   dat <- dat[dat$funding == "no", ]
   if(specifications\funding[i] == "NR") {
```

```
dat <- dat[dat$funding == "NR", ]
 ### only compute meta-analytic summary effects for specification subsets with at least two
studies/samples.
 if(nrow(dat) < 2) next
 ### save which study/sample IDs were selected by the "Which" factors for a given
specification.
 specifications$set[i] <- paste(rownames(dat), collapse = ",")
 if(specifications$effect[i] == "g") {
  if(specifications\ma method[i] == "HedgesOlkin(REML)") {
   mod <- rma(yi = dat$g, vi = dat$V g, method = "REML", control = list(stepadj=0.5,
maxiter = 2000)
  } else {
   if(specifications$ma method[i] == "HunterSchmidt") {
    mod <- rma(yi = dat\$g, vi = dat\$V_g, method = "HS", weights = dat\$N)
   } else {
    if(specifications$ma method[i] == "FE") {
      mod \le rma(yi = dat\$g, vi = dat\$V g, method = "FE")
   }
  specifications\mean[i] <- mod\b[[1]]
  specifications$lb[i] <- mod$ci.lb[[1]]
  specifications\ub[i] <- mod\u00e8ci.ub[[1]]
  specifications$p[i] <- mod$pval[[1]]
  specifications$k[i] <- nrow(dat)
 } else {
  if(specifications$effect[i] == "d") {
   if(specifications$ma_method[i] == "HedgesOlkin(REML)") {
    mod <- rma(yi = dat$d, vi = dat$V d, method = "REML", control = list(stepadj=0.5,
maxiter = 2000)
   } else {
    if(specifications$ma method[i] == "HunterSchmidt") {
      mod < -rma(yi = dat\$d, vi = dat\$V d, method = "HS", weights = dat\$N)
     } else {
      if(specifications$ma method[i] == "FE") {
       mod <- rma(yi = dat\$d, vi = dat\$V d, method = "FE")
   specifications$mean[i] <- mod$b[[1]]
   specifications$lb[i] <- mod$ci.lb[[1]]
   specifications\ub[i] <- mod\u00e8ci.ub[[1]]
   specifications$p[i] <- mod$pval[[1]]
```

```
specifications$k[i] <- nrow(dat)
specifications full <- specifications[complete.cases(specifications),]
### only keep unique study/sample subsets resulting from "Which" factor combinations.
specifications full <- specifications full[!duplicated(specifications full[, c("mean", "set",
"ma method", "effect")]), ]
#write xlsx(path = "specifications twoMONM.xlsx", x = specifications full)
##one sample data MO-NM
##one sample data MO-NM
x <- one sample data MONM
### "which" factors
seizure type <- c("generalized focal", "seizure mixed", "seizure either")
measurement method <- c("EEG", "seizure frequency observation", "measurement either")
sample type <- c("adults", "mixed", "sample either")
funding <- c("yes", "NR", "either")
### "how" factors
effect <- c("g", "d")
ma method <- c("FE", "HedgesOlkin(REML)", "HunterSchmidt")
### construct all possible combinations of internal and external factors
specifications <- expand.grid(seizure type = seizure type,
                  measurement method = measurement method,
                  sample type = sample type,
                  funding = funding,
                  effect = effect,
                  ma method = ma method)
specifications <- data.frame(specifications,
                 mean = rep(NA, nrow(specifications)),
                 set = rep(NA, nrow(specifications)),
                 lb = rep(NA, nrow(specifications)),
                 ub = rep(NA, nrow(specifications)),
                 p = rep(NA, nrow(specifications)),
                 k = rep(NA, nrow(specifications)))
specifications
### conduct specification analyses
for(i in 1:nrow(specifications)) {
 dat <- x
 if(specifications\seizure type[i] == "generalized focal") {
  dat <- dat[dat$seizure type == "generalized focal", ]
 } else {
```

```
if(specifications\seizure type[i] == "seizure mixed") {
   dat <- dat[dat$seizure type == "mixed", ]
 if(specifications\measurement method[i] == "EEG") {
  dat <- dat[dat$measurement method== "EEG", ]
 } else {
  if(specifications\measurement method[i] == "seizure frequency observation") {
   dat <- dat[dat$measurement method == "seizure frequency observation", ]
 if(specifications\sample type[i] == "adults") {
  dat <- dat[dat$sample type == "adults", ]
 } else {
  if(specifications\sample type[i] == "mixed") {
   dat <- dat[dat$sample type == "mixed", ]
 }
 if(specifications\funding[i] == "yes") {
  dat <- dat[dat$funding == "yes", ]
 } else {
  if(specifications\funding[i] == "NR") {
   dat <- dat[dat$funding == "NR", ]
  }
 ### only compute meta-analytic summary effects for specification subsets with at least two
studies/samples.
 if(nrow(dat) < 2) next
 ### save which study/sample IDs were selected by the "Which" factors for a given
specification.
 specifications$set[i] <- paste(rownames(dat), collapse = ",")
 if(specifications$effect[i] == "g") {
  if(specifications$ma method[i] == "HedgesOlkin(REML)") {
   mod <- rma(yi = dat$y, vi = dat$V g, method = "REML", control = list(stepadj=0.5,
maxiter = 2000)
  } else {
   if(specifications$ma method[i] == "HunterSchmidt") {
    mod < -rma(yi = dat\$g, vi = dat\$V g, method = "HS", weights = dat\$N)
    } else {
     if(specifications$ma method[i] == "FE") {
      mod \le rma(yi = dat\$g, vi = dat\$V g, method = "FE")
     }
  specifications\$mean[i] <- mod\$b[[1]]
```

```
specifications$lb[i] <- mod$ci.lb[[1]]
  specifications\ub[i] <- mod\u00e8ci.ub[[1]]
  specifications$p[i] <- mod$pval[[1]]
  specifications$k[i] <- nrow(dat)
 } else {
  if(specifications$effect[i] == "d") {
   if(specifications$ma method[i] == "HedgesOlkin(REML)") {
    mod <- rma(yi = dat$d, vi = dat$V d, method = "REML", control = list(stepadj=0.5,
maxiter = 2000)
   } else {
     if(specifications$ma_method[i] == "HunterSchmidt") {
      mod <- rma(yi = dat$d, vi = dat$V_d, method = "HS", weights = dat$N)
     } else {
      if(specifications\ma method[i] == "FE") {
       mod < -rma(yi = dat\$d, vi = dat\$V d, method = "FE")
   specifications\mean[i] <- mod\b[[1]]
   specifications$lb[i] <- mod$ci.lb[[1]]
   specifications\ub[i] <- mod\u00e8ci.ub[[1]]
   specifications$p[i] <- mod$pval[[1]]
   specifications$k[i] <- nrow(dat)
specifications full <- specifications[complete.cases(specifications),]
### only keep unique study/sample subsets resulting from "Which" factor combinations.
specifications full <- specifications full[!duplicated(specifications full[, c("mean", "set",
"ma method", "effect")]), ]
#Write xlsx(path = "specifications ONEMONM.xlsx", x = specifications full)
##one sample data OM-NM
##one sample data OM-NM
x <- one sample data OMNM
### "which" factors
seizure type <- c("seizure mixed", "other", "seizure either")
measurement_method <- c("EEG", "seizure_frequency_observation", "measurement_either")
exposure more than once <- c("exposure yes", "exposure either")
sample type <- c("kids", "adults", "sample either")
funding <- c("yes", "no", "either")
OM kind <- c("other classical", "scrambled KV448", "OM either")
### "how" factors
effect <- c("g", "d")
ma method <- c("FE", "HedgesOlkin(REML)", "HunterSchmidt")
```

```
### construct all possible combinations of internal and external factors
specifications <- expand.grid(seizure type = seizure type,
                  measurement method = measurement method,
                  exposure more than once = exposure more than once,
                  sample type = sample type,
                  funding = funding,
                  effect = effect,
                  ma method = ma method,
                  OM kind = OM kind)
specifications <- data.frame(specifications,
                 mean = rep(NA, nrow(specifications)),
                 set = rep(NA, nrow(specifications)),
                 lb = rep(NA, nrow(specifications)),
                 ub = rep(NA, nrow(specifications)),
                 p = rep(NA, nrow(specifications)),
                 k = rep(NA, nrow(specifications)))
specifications
### conduct specification analyses
for(i in 1:nrow(specifications)) {
 dat <- x
 if(specifications\seizure type[i] == "seizure mixed") {
  dat <- dat[dat$seizure type == "mixed", ]
 } else {
  if(specifications\seizure type[i] == "other") {
   dat <- dat[dat$seizure type == "other", ]
  }
 if(specifications\measurement method[i] == "EEG") {
  dat <- dat[dat$measurement method== "EEG", ]
 } else {
  if(specifications\$measurement_method[i] == "seizure_frequency_observation") {
   dat <- dat[dat\measurement method == "seizure frequency observation", ]
 if(specifications\exposure more than once[i] == "exposure yes") {
  dat <- dat[dat\exposure more than once == "yes", ]
 if(specifications\sample type[i] == "adults") {
  dat <- dat[dat$sample type == "adults", ]
 } else {
  if(specifications\sample type[i] == "kids") {
   dat <- dat[dat$sample type == "kids", ]
  }
 if(specifications\funding[i] == "yes") {
  dat <- dat[dat$funding == "yes", ]
```

```
} else {
  if(specifications\funding[i] == "no") {
   dat <- dat[dat$funding == "no", ]
 if(specifications$OM kind[i] == "scrambled KV448") {
  dat <- dat[dat$OM kind == "scrambled KV448", ]
 } else {
  if(specifications$OM kind[i] == "other classical") {
   dat <- dat[dat$OM kind == "other classical", ]
 }
 ### only compute meta-analytic summary effects for specification subsets with at least two
studies/samples.
 if(nrow(dat) < 2) next
 ### save which study/sample IDs were selected by the "Which" factors for a given
specification.
 specifications\set[i] <- paste(rownames(dat), collapse = ",")
 if(specifications$effect[i] == "g") {
  if(specifications$ma method[i] == "HedgesOlkin(REML)") {
   mod <- rma(yi = dat$g, vi = dat$V g, method = "REML", control = list(stepadj=0.5,
maxiter = 2000)
  } else {
   if(specifications$ma method[i] == "HunterSchmidt") {
    mod < -rma(yi = dat\$g, vi = dat\$V g, method = "HS", weights = dat\$N)
   } else {
    if(specifications$ma method[i] == "FE") {
      mod < -rma(yi = dat\$g, vi = dat\$V g, method = "FE")
   }
  specifications\$mean[i] <- mod\$b[[1]]
  specifications$lb[i] <- mod$ci.lb[[1]]
  specifications\ub[i] <- mod\u00e8ci.ub[[1]]
  specifications$p[i] <- mod$pval[[1]]
  specifications$k[i] <- nrow(dat)
 } else {
  if(specifications$effect[i] == "d") {
   if(specifications$ma method[i] == "HedgesOlkin(REML)") {
    mod <- rma(yi = dat$d, vi = dat$V d, method = "REML", control = list(stepadj=0.5,
maxiter = 2000)
   } else {
     if(specifications$ma method[i] == "HunterSchmidt") {
      mod < -rma(yi = dat\$d, vi = dat\$V d, method = "HS", weights = dat\$N)
     } else {
```

```
if(specifications\ma method[i] == "FE") {
       mod \le rma(yi = dat d, vi = dat V d, method = "FE")
     }
   specifications$mean[i] <- mod$b[[1]]
   specifications$lb[i] <- mod$ci.lb[[1]]
   specifications\ub[i] <- mod\u00e8ci.ub[[1]]
   specifications$p[i] <- mod$pval[[1]]
   specifications$k[i] <- nrow(dat)</pre>
specifications full <- specifications[complete.cases(specifications),]
### only keep unique study/sample subsets resulting from "Which" factor combinations.
specifications full <- specifications full[!duplicated(specifications full[, c("mean", "set",
"ma method", "effect")]), ]
#write xlsx(path = "specifications oneOMNM.xlsx", x = specifications full)
# plot specification curve (Voracek et al., 2019) ----
##two sample data MO-NM
### load data
specifications full <- read excel(file.choose()) #file: specifications twoMONM.xlsx
### "which" factors
measured disease <- c("disease other", "disease either")
measurement method <- c("measurement other", "measurement either")
exposure more than once <- c("exposure no", "exposure either")
sample type <- c("kids", "sample either")
### "how" factors
effect <- c("g", "d")
ma method <- c("FE", "HedgesOlkin(REML)", "HunterSchmidt")
x rank <- rank(specifications full$mean, ties.method = "random")
yvar <- rep(factor(rev(c(measured disease, measurement method,
exposure more than once, sample type, effect, ma method)),
           levels = rev(c(measured disease, measurement method,
exposure more than once, sample type, effect, ma method))),
       times = nrow(specifications full))
xvar \le rep(x rank, each = length(levels(yvar)))
spec <- NULL
### determine which specifications are observed and which are not
for(i in 1:nrow(specifications full)) {
 id <- as.numeric(levels(yvar) %in% as.character(unlist(specifications full[i, 1:7])))
```

```
spec <- c(spec, id)
plotdata <- data.frame(xvar, yvar, spec)
ylabels <- rev(c("disease: other than epilepsy", "disease: either",
           "measurement method: other than EEG", "measurement method: either",
          "exposure: once (not more)", "exposure: either",
          "sample: children (not adults)", "sample: either",
          "metric: g", "metric: d",
           "model: Hedges-Olkin (REML)", "model: Hunter-Schmidt", "model: FE"
))
plotdata$k <- rep(specifications full$k, each = length(levels(yvar)))
plotdata$fill <- as.factor(plotdata$k * plotdata$spec)</pre>
cols <- RColorBrewer::brewer.pal(min(11, length(levels(plotdata\fill)) - 1), "Spectral")
### create specification tile plot
p spec \leq- ggplot(data = plotdata, aes(x = xvar, y = as.factor(yvar), fill = fill)) +
 geom raster() +
 geom hline(yintercept = c(3, 5, 7, 9, 11) + 0.5) +
 scale x continuous(position = "bottom") +
 scale y discrete(labels = ylabels) +
 scale fill manual(values = c("white", c(cols[floor(seq(from = 1, to = length(cols), length.out
= length(levels(plotdata$fill)) - 1))]))) +
 labs(x = "Specification number", y = "Which/How factors") +
 coord cartesian(expand = F, xlim = c(0.5, nrow(specifications full) + 0.5)) +
 theme bw() +
 theme(legend.position = "none",
     axis.text = element text(colour = "black"),
     axis.ticks = element line(colour = "black"),
     plot.margin = margin(t = 5.5, r = 5.5, b = 5.5, l = 5.5, unit = "pt"))
### create summary forest plot
specifications full$xvar <- x rank
vrng <- range(c(0, specifications full$lb, specifications_full$ub))</pre>
vlimit < -c(vrng[1] - diff(vrng)*0.1, vrng[2] + diff(vrng)*0.1)
y_breaks_forest <- round(seq(from = round(ylimit[1], 1), to = round(ylimit[2], 1), by = 0.1),
y labels forest <- format(y breaks forest, nsmall = 2)
y breaks forest <- c(ylimit[1], y breaks forest)
y labels forest <- c(ylabels[which.max(nchar(ylabels))], y labels forest)
p forest <-
 ggplot(data = specifications full, aes(x = xvar, y = mean)) +
 geom errorbar(aes(ymin = 1b, ymax = ub, col = as.factor(k)), width = 0, size = 0.25) +
 geom_line(col = "black", size = 0.25) +
 geom hline(yintercept = 0, linetype = 2, size = 0.25) +
 scale x continuous(name = "") +
```

```
scale y continuous(name = "Summary effect", breaks = y breaks forest, labels =
y labels forest) +
 scale color manual(values = c(cols[floor(seq(from = 1, to = length(cols), length.out =
length(levels(as.factor(specifications full$k)))))) +
 coord cartesian(ylim = ylimit, xlim = c(0.5, nrow(specifications full) + 0.5), expand =
FALSE) +
 ggtitle("Independent MO-condition") +
 theme bw() +
 theme(legend.position = "none",
     axis.text.x = element blank(),
     axis.ticks.x = element blank(),
     axis.text.y = element text(colour = c("white", rep("black", times =
length(y labels forest) - 1))),
     axis.ticks.y = element line(colour = c("white", rep("black", times =
length(y breaks forest) - 1))),
    panel.grid.major.x = element blank(),
    panel.grid.minor.x = element blank(),
    panel.grid.major.y = element line(),
     panel.grid.minor.y = element blank(),
    plot.margin = margin(t = 5.5, r = 5.5, b = -15, l = 5.5, unit = "pt"))
### create subset size indicator
yrng <- range(c(2, max(specifications full$k)))
ylimit <- c(2, max(specifications full$k))
y breaks size <- round(seq(from = yrng[1], to = yrng[2], by = 100), 0)
y labels size <- format(y breaks size, nsmall = 0)
y breaks size <- c(ylimit[1], y breaks size)
y labels size <- c(ylabels[which.max(nchar(ylabels))], y labels size)
p size <-
 ggplot(data = specifications full, aes(x = xvar, y = k)) +
 geom area(fill = "gray35", color = "black", size = 0.25) +
 scale x continuous(name = "") +
 scale y continuous(name = "# Samples", breaks = y breaks size, labels = y labels size) +
 coord cartesian(ylim = ylimit, xlim = c(0.5, nrow(specifications full) + 0.5), expand =
FALSE) +
 theme bw() +
 theme(legend.position = "none",
     axis.text.x = element blank(),
     axis.ticks.x = element blank(),
     axis.text.y = element text(colour = c("white", rep("black", times = length(y labels size)
- 1))),
     axis.ticks.y = element line(colour = c("white", rep("black", times =
length(y breaks size) - 1))),
    panel.grid.major.x = element blank(),
    panel.grid.minor.x = element blank(),
    panel.grid.major.y = element line(),
    panel.grid.minor.y = element blank(),
```

```
plot.margin = margin(t = 5.5, r = 5.5, b = -15, l = 5.5, unit = "pt"))
### combine specification tile plot, subset size indicator and forest plot
p <- gridExtra::arrangeGrob(p spec, p size, p forest,
                 layout matrix = matrix(c(3, 3, 3, 2, 1, 1, 1, 1, 1), ncol = 1))
p <- ggpubr::as ggplot(p)</pre>
\#ggsave("twoMONM.jpg", p, width = 20, height = 20, dpi = 1200, units = "cm")
#ggsave("oneMONM.tiff", p, width = 16*1.2, height = 25*1.2, dpi = 1200, units = "cm",
compression = "lzw+p")
##one sample data MO-NM
### load data
specifications full <- read excel(file.choose()) #file: specifications oneMONM.xlsx
### "which" factors
seizure type <- c("generalized focal", "seizure mixed", "seizure either")
measurement method <- c("EEG", "seizure frequency observation", "measurement either")
sample type <- c("adults", "mixed", "sample either")
funding <- c("yes", "NR", "either")
### "how" factors
effect <- c("g", "d")
ma method <- c("FE", "HedgesOlkin(REML)", "HunterSchmidt")
x rank <- rank(specifications full$mean, ties.method = "random")
yvar <- rep(factor(rev(c(seizure type, measurement method, sample type, funding, effect,
ma method)),
           levels = rev(c(seizure type, measurement method, sample type, funding, effect,
ma_method))),
       times = nrow(specifications full))
xvar < -rep(x rank, each = length(levels(yvar)))
spec <- NULL
### determine which specifications are observed and which are not
for(i in 1:nrow(specifications full)) {
 id <- as.numeric(levels(yvar) %in% as.character(unlist(specifications full[i, 1:7])))
 spec <- c(spec, id)
plotdata <- data.frame(xvar, yvar, spec)</pre>
ylabels <- rev(c("seizure: generalized and focal", "seizure: mixed", "seizure: either",
          "measurement: IED-EEG", "measurement: seizure frequency", "measurement:
either",
          "sample: adults", "sample: mixed", "sample: either",
          "funding: yes", "funding: NR", "funding: either",
          "metric: g", "metric: d",
          "model: Hedges-Olkin (REML)", "model: Hunter-Schmidt", "model: FE"
```

```
))
plotdata$k <- rep(specifications full$k, each = length(levels(yvar)))
plotdata$fill <- as.factor(plotdata$k * plotdata$spec)</pre>
cols <- RColorBrewer::brewer.pal(min(11, length(levels(plotdata$fill)) - 1), "Spectral")
### create specification tile plot
p spec \leftarrow ggplot(data = plotdata, aes(x = xvar, y = as.factor(yvar), fill = fill)) +
 geom raster() +
 geom hline(yintercept = c(3, 5, 8, 11, 14) + 0.5) +
 scale x continuous(position = "bottom") +
 scale y discrete(labels = ylabels) +
 scale fill manual(values = c("white", c(cols[floor(seq(from = 1, to = length(cols), length.out
= length(levels(plotdata$fill)) - 1))]))) +
 labs(x = "Specification number", y = "Which/How factors") +
 coord cartesian(expand = F, xlim = c(0.5, nrow(specifications full) + 0.5)) +
 theme bw() +
 theme(legend.position = "none",
     axis.text = element text(colour = "black"),
     axis.ticks = element line(colour = "black"),
     plot.margin = margin(t = 5.5, r = 5.5, b = 5.5, l = 5.5, unit = "pt"))
### create summary forest plot
specifications full$xvar <- x rank
yrng <- range(c(0, specifications full$lb, specifications full$ub))
vlimit < -c(vrng[1] - diff(vrng)*0.1, vrng[2] + diff(vrng)*0.1)
y breaks forest <- round(seq(from = round(ylimit[1], 1), to = round(ylimit[2], 1), by = 0.1),
2)
y labels forest <- format(y breaks forest, nsmall = 2)
y breaks forest <- c(ylimit[1], y breaks forest)
y labels forest <- c(ylabels[which.max(nchar(ylabels))], y labels forest)
p forest <-
 ggplot(data = specifications full, aes(x = xvar, y = mean)) +
 geom errorbar(aes(ymin = 1b, ymax = ub, col = as.factor(k)), width = 0, size = 0.25) +
 geom line(col = "black", size = 0.25) +
 geom hline(vintercept = 0, linetype = 2, size = 0.25) +
 scale x continuous(name = "") +
 scale y continuous(name = "Summary effect", breaks = y breaks forest, labels =
y labels forest) +
 scale color manual(values = c(cols[floor(seq(from = 1, to = length(cols), length.out =
length(levels(as.factor(specifications_full$k)))))) +
 coord cartesian(ylim = ylimit, xlim = c(0.5, nrow(specifications full) + 0.5), expand =
FALSE) +
 ggtitle("Dependent MO-condition") +
 theme bw() +
 theme(legend.position = "none",
     axis.text.x = element blank(),
     axis.ticks.x = element blank(),
```

```
axis.text.y = element text(colour = c("white", rep("black", times =
length(y labels forest) - 1))),
     axis.ticks.y = element line(colour = c("white", rep("black", times =
length(y breaks forest) - 1))),
     panel.grid.major.x = element blank(),
     panel.grid.minor.x = element blank(),
     panel.grid.major.y = element line(),
     panel.grid.minor.y = element blank(),
     plot.margin = margin(t = 5.5, r = 5.5, b = -15, l = 5.5, unit = "pt"))
### create subset size indicator
yrng <- range(c(2, max(specifications full$k)))</pre>
ylimit <- c(2, max(specifications full$k))
y breaks size <- round(seq(from = yrng[1], to = yrng[2], by = 100), 0)
y labels size <- format(y breaks size, nsmall = 0)
y breaks size <- c(ylimit[1], y breaks size)
y labels size <- c(ylabels[which.max(nchar(ylabels))], y labels size)
p size <-
 ggplot(data = specifications full, aes(x = xvar, y = k)) +
 geom area(fill = "gray35", color = "black", size = 0.25) +
 scale x continuous(name = "") +
 scale y continuous(name = "# Samples", breaks = y breaks size, labels = y labels size) +
 coord cartesian(ylim = ylimit, xlim = c(0.5, nrow(specifications full) + 0.5), expand =
FALSE) +
 theme bw() +
 theme(legend.position = "none",
     axis.text.x = element blank(),
     axis.ticks.x = element blank(),
     axis.text.y = element text(colour = c("white", rep("black", times = length(y labels size)
- 1))),
     axis.ticks.y = element line(colour = c("white", rep("black", times =
length(y breaks size) - 1))),
     panel.grid.major.x = element blank(),
     panel.grid.minor.x = element_blank(),
     panel.grid.major.y = element line(),
     panel.grid.minor.y = element blank(),
     plot.margin = margin(t = 5.5, r = 5.5, b = -15, l = 5.5, unit = "pt"))
### combine specification tile plot, subset size indicator and forest plot
p <- gridExtra::arrangeGrob(p spec, p size, p forest,
                 layout matrix = matrix(c(3, 3, 3, 2, 1, 1, 1, 1, 1), ncol = 1))
p <- ggpubr::as ggplot(p)
\#ggsave("oneMONM.jpg", p, width = 20, height = 20, dpi = 1200, units = "cm")
#ggsave("oneMONM.tiff", p, width = 16*1.2, height = 25*1.2, dpi = 1200, units = "cm",
compression = "lzw+p")
```

##one sample data OM-NM

```
### load data
specifications full <- read excel(file.choose()) #file: specifications oneMONM.xlsx
### "which" factors
seizure type <- c("seizure mixed", "other", "seizure either")
measurement method <- c("EEG", "seizure frequency observation", "measurement either")
exposure more than once <- c("exposure yes", "exposure either")
sample type <- c("kids", "adults", "sample either")
funding <- c("yes", "no", "either")
OM kind <- c("other classical", "scrambled KV448", "OM either")
### "how" factors
effect <- c("g", "d")
ma method <- c("FE", "HedgesOlkin(REML)", "HunterSchmidt")
x rank <- rank(specifications full$mean, ties.method = "random")
yvar <- rep(factor(rev(c(seizure type, measurement method, exposure more than once,
sample type, funding, OM kind, effect, ma method)),
           levels = rev(c(seizure type, measurement method, exposure more than once,
sample type, funding, OM kind, effect, ma method))),
       times = nrow(specifications full))
xvar \le rep(x rank, each = length(levels(yvar)))
spec <- NULL
### determine which specifications are observed and which are not
for(i in 1:nrow(specifications full)) {
 id <- as.numeric(levels(yvar) %in% as.character(unlist(specifications full[i, 1:8])))
 spec <- c(spec, id)
plotdata <- data.frame(xvar, yvar, spec)</pre>
ylabels <- rev(c("seizure: mixed", "seizure: other", "seizure: either",
          "measurement: IED-EEG", "measurement: other", "measurement: either",
          "exposure: more than once", "exposure: either",
          "sample: children", "sample: adults", "sample: either",
          "funding: yes", "funding: no", "funding: either",
          "type of control music: other classical", "type of control music: scrambled KV448",
"type of control music: either",
          "metric: g", "metric: d",
          "model: Hedges-Olkin (REML)", "model: Hunter-Schmidt", "model: FE"
))
plotdata$k <- rep(specifications full$k, each = length(levels(yvar)))
plotdata$fill <- as.factor(plotdata$k * plotdata$spec)</pre>
cols <- RColorBrewer::brewer.pal(min(11, length(levels(plotdata$fill)) - 1), "Spectral")
### create specification tile plot
p spec \leftarrow ggplot(data = plotdata, aes(x = xvar, y = as.factor(yvar), fill = fill)) +
 geom raster() +
```

```
geom hline(yintercept = c(3, 5, 8, 11, 14, 16, 19) + 0.5) +
 scale x continuous(position = "bottom") +
 scale y discrete(labels = ylabels) +
 scale fill manual(values = c("white", c(cols[floor(seq(from = 1, to = length(cols), length.out
= length(levels(plotdata$fill)) - 1))]))) +
 labs(x = "Specification number", y = "Which/How factors") +
 coord cartesian(expand = F, xlim = c(0.5, nrow(specifications full) + 0.5)) +
 theme bw() +
 theme(legend.position = "none",
     axis.text = element text(colour = "black"),
     axis.ticks = element line(colour = "black"),
     plot.margin = margin(t = 5.5, r = 5.5, b = 5.5, l = 5.5, unit = "pt"))
### create summary forest plot
specifications full$xvar <- x rank
yrng <- range(c(0, specifications full$lb, specifications full$ub))
ylimit <- c(yrng[1] - diff(yrng)*0.1, yrng[2] + diff(yrng)*0.1)
y breaks forest <- round(seq(from = round(ylimit[1], 1), to = round(ylimit[2], 1), by = 0.1),
2)
y labels forest <- format(y breaks forest, nsmall = 2)
y breaks forest <- c(ylimit[1], y breaks forest)
y labels forest <- c(ylabels[which.max(nchar(ylabels))], y labels forest)
p forest <-</pre>
 ggplot(data = specifications full, aes(x = xvar, y = mean)) +
 geom errorbar(aes(ymin = 1b, ymax = ub, col = as.factor(k)), width = 0, size = 0.25) +
 geom line(col = "black", size = 0.25) +
 geom hline(yintercept = 0, linetype = 2, size = 0.25) +
 scale x continuous(name = "") +
 scale y continuous(name = "Summary effect", breaks = y breaks forest, labels =
y labels forest) +
 scale color manual(values = c(cols[floor(seq(from = 1, to = length(cols), length.out =
length(levels(as.factor(specifications full$k))))))) +
 coord cartesian(ylim = ylimit, xlim = c(0.5, nrow(specifications full) + 0.5), expand =
FALSE) +
 ggtitle("OM-condition") +
 theme bw() +
 theme(legend.position = "none",
     axis.text.x = element blank(),
     axis.ticks.x = element blank(),
     axis.text.y = element text(colour = c("white", rep("black", times =
length(y labels forest) - 1))),
     axis.ticks.y = element line(colour = c("white", rep("black", times =
length(y breaks forest) - 1))),
     panel.grid.major.x = element blank(),
     panel.grid.minor.x = element blank(),
     panel.grid.major.y = element line(),
     panel.grid.minor.y = element blank(),
     plot.margin = margin(t = 5.5, r = 5.5, b = -15, l = 5.5, unit = "pt"))
```

```
### create subset size indicator
yrng <- range(c(2, max(specifications full$k)))
ylimit <- c(2, max(specifications full$k))
y breaks size <- round(seq(from = yrng[1], to = yrng[2], by = 100), 0)
y labels size <- format(y breaks size, nsmall = 0)
y breaks size <- c(ylimit[1], y breaks size)
y labels size <- c(ylabels[which.max(nchar(ylabels))], y labels size)
p size <-
 ggplot(data = specifications full, aes(x = xvar, y = k)) +
 geom area(fill = "gray35", color = "black", size = 0.25) +
 scale x continuous(name = "") +
 scale y continuous(name = "# Samples", breaks = y breaks size, labels = y labels size) +
 coord cartesian(ylim = ylimit, xlim = c(0.5, nrow(specifications full) + 0.5), expand =
FALSE) +
 theme bw() +
 theme(legend.position = "none",
     axis.text.x = element blank(),
     axis.ticks.x = element blank(),
     axis.text.y = element text(colour = c("white", rep("black", times = length(y labels size)
- 1))),
     axis.ticks.y = element line(colour = c("white", rep("black", times =
length(y breaks size) - 1))),
     panel.grid.major.x = element blank(),
     panel.grid.minor.x = element blank(),
     panel.grid.major.y = element line(),
     panel.grid.minor.y = element blank(),
     plot.margin = margin(t = 5.5, r = 5.5, b = -15, l = 5.5, unit = "pt"))
### combine specfication tile plot, subset size indicator and forest plot
p <- gridExtra::arrangeGrob(p spec, p size, p forest,
                 layout matrix = matrix(c(3, 3, 3, 2, 1, 1, 1, 1, 1), ncol = 1))
p <- ggpubr::as ggplot(p)
ggsave("oneOMNM.jpg", p, width = 20, height = 20, dpi = 1200, units = "cm")
#ggsave("oneMONM.tiff", p, width = 16*1.2, height = 25*1.2, dpi = 1200, units = "cm",
compression = "lzw+p")
# combinatorial meta-analysis - GOSH plot ----
## two-sample-data MO-NM
png(filename="two group gosht plot MONM.png", res=350, width=3196, height=1648)
res.gosh twoMONM <- gosh(two sample model)
```

```
plot(res.gosh_twoMONM, cex = 1.5, out = 1, alpha = 0.9, col = c("#94C154","#0063A6"))

dev.off()

## one-sample-data MO-NM

png(filename="one_group_gosht_plot_MONM.png", res=350, width=3196, height=1648)

res.gosh_oneMONM <- gosh(one_sample_model_MONM)

plot(res.gosh_oneMONM, cex = 1.5, xlim = c(-1, 2), col = "#0063A6", alpha = 0.6)

dev.off()

## one-sample-data OM-NM

png(filename="one_group_gosht_plot_OMNM.png", res=350, width=3196, height=1648)

res.gosh_oneOMNM <- gosh(one_sample_model_OMNM)

plot(res.gosh_oneOMNM, cex = 1.5, xlim = c(-1, 2), breaks = 3.5, col = "#0063A6", alpha = 0.6)

dev.off()
```

Appendix H

References of excluded studies

Overview

A total of 7 databases were searched for relevant literature: *Google Scholar, PubMed, Isi Web of Science, PsycInfo, PubPsych, ProQuest, Open Access Thesis* and *Dissertations*. In deviation from the pre-registration, no literature search could be performed in *OpenGrey*. As pre-registered, a forward-search of Rauscher et al. (1993) as well as Pietschnig et al. (2010) was conducted. In addition, a backward search was performed using those studies that were identified as reviews/meta-analyses. All studies were searched as well as screened (titles and abstracts) from 06/22/2022 to 07/16/2022. In the following tables, the literature found is classified into different categories. Studies that were additionally considered in the individual phases of the literature search are marked with a "+" in the respective rows.

Classification of the found literature before coding full texts:

Total	1.967
Duplicates	394
Included	62
Included from forward search	0
Included from backward search	2
Reviews/Meta-analyses	81
Books/Essays	94
Non-human	50
Non-neurological disease	156
Irrelevant topic	1.128

Classification of the found literature after coding full texts:

Date: 12.08.2022

Total	1.967
Duplicates	394 + 3
Included	8
Excluded due to other reasons (see Appendix E)	18
Included from forward search	0
Reviews/Meta-analyses	81 + 3
Books/Essays	94 + 5
Non-human	50
Non-neurological disease	156 + 2
Irrelevant topic	1.128 + 22
Non accessible	3

Classification of the literature <u>after literature update:</u>

Date: 10.10.2022

Total	1.971
Duplicates	397
Included	8
Excluded due to other reasons (see Appendix E)	18
Included from forward search	0
Reviews/Meta-analyses	84 + 2
Books/Essays	99
Non-human	50
Non-neurological disease	158
Irrelevant topic	1.150 + 2
Non accessible	3

Documentation

1. Google Scholar

Date: 22.06.2022

Hits: 474

2. PubMed

Date: 22.06.2022

Hits: 54

3. Isi Web of Science

Date: 22.06.2022

Hits: 247

4. PsycInfo

Date: 22.06.2022

Hits: 63

5. PubPsych

Date: 22.06.2022

Hits: 30

Total	868
Duplicates	338
Included	63
Reviews/Meta-analyses	77
Books/Essays	94
Non-human	42
Non-neurological	76
Irrelevant topic	180

6. ProQuest

Database Not pre-registered Filter: Dissertations & Theses

Date: 15.07.2022

Hits: 977

Total	977
Duplicates	51
Included	0
Reviews/Meta-analyses	4
Books/Essays	0
Non-human	2
Non-neurological disease	80
Irrelevant topic	840

7. Open Access Theses and Dissertations

Date: 16.07.2022 Hits: 46.130

Not pre-registered stopping rule: No relevant paper on 3 pages in a row with 30 hits

per page

Resulting Hits: 120

Total	120
Duplicates	5
Included	1
Reviews/Meta-analyses	0
Books/Essays	0
Non-human	6
Non-neurological disease	0
Irrelevant topic	108

8. OpenGrey

Unfortunately, the service of Opengrey was terminated shortly before the time of my literature research. Accessing the OpenGrey MySQL file from DANS EASY Archive is also not possible, as EASY is out of service by the date of 07/17/2022.

9. Forward search:

Rauscher et al. (1993): 0 Pietschnig et al. (2010): 0

10. Backward search (Category Reviews/Meta-Analyses):

Additionally Included: 2:

Coppola, G., Operto, F. F., Caprio, F., Ferraioli, G., Pisano, S., Viggiano, A., & Verrotti, A. (2017). Mozart's music in children with drug-refractory epileptic encephalopathies: comparison of two protocols. *Epilepsy & Behavior*, 78, 100-103. https://doi.org/10.1016/j.yebeh.2017.09.028

Origin:

Dawit, S., & Crepeau, A. Z. (2020). When drugs do not work: alternatives to antiseizure medications. *Current Neurology and Neuroscience Reports*, 20(9), 1-8. https://doi.org/10.1007/s11910-020-01061-3:

De Bartolo, D., Morone, G., Giordani, G., Antonucci, G., Russo, V., Fusco, A., ... & Iosa, M. (2020). Effect of different music genres on gait patterns in Parkinson's disease. *Neurological Sciences*, 41(3), 575-582. https://doi.org/10.1007/s10072-019-04127-4

Origin

Victorino, D. B., Scorza, C. A., Fiorini, A. C., Finsterer, J., & Scorza, F. A. (2021). "Mozart effect" for Parkinson's disease: music as medicine. *Neurological Sciences*, 42(1), 319-320. https://doi.org/10.1007/s10072-020-04537-9:

Included Literature

- Bergomi, P., Chieppi, M., Maini, A., Mugnos, T., Spotti, D., Tzialla, C., & Scudeller, L. (2014). Nonpharmacological techniques to reduce pain in preterm infants who receive heel-lance procedure: A randomized controlled trial. *Research and theory for nursing practice*, 28(4), 335-348. https://doi.org/10.1891/1541-6577.28.4.335
- Coppola, G., Toro, A., Operto, F. F., Ferrarioli, G., Pisano, S., Viggiano, A., & Verrotti, A. (2015). Mozart's music in children with drug-refractory epileptic encephalopathies. *Epilepsy & Behavior*, *50*, 18-22. https://doi.org/10.1016/j.yebeh.2015.05.038
- D'Alessandro, P., Giuglietti, M., Baglioni, A., Verdolini, N., Murgia, N., Piccirilli, M., & Elisei, S. (2017). Effects of music on seizure frequency in institutionalized subjects with severe/profound intellectual disability and drug-resistant epilepsy. *Psychiatria Danubina*, 29(suppl. 3), 399-404.
- Grylls, E., Kinsky, M., Baggott, A., Wabnitz, C., & McLellan, A. (2018). Study of the Mozart effect in children with epileptic electroencephalograms. *Seizure*, *59*, 77-81. https://doi.org/10.1016/j.seizure.2018.05.006
- Paprad, T., Veeravigrom, M., & Desudchit, T. (2021). Effect of Mozart K. 448 on interictal epileptiform discharges in children with epilepsy: A randomized controlled pilot study. *Epilepsy & Behavior*, 114, 107177. https://doi.org/10.1016/j.yebeh.2020.107177
- Rafiee, M., Patel, K., Groppe, D. M., Andrade, D. M., Bercovici, E., Bui, E., ... & Valiante, T. A. (2020). Daily listening to Mozart reduces seizures in individuals with epilepsy: A randomized control study. *Epilepsia Open*, *5*(2), 285-294. https://doi.org/10.1002/epi4.12400
- Štillová, K., Kiska, T., Koriťáková, E., Strýček, O., Mekyska, J., Chrastina, J., & Rektor, I. (2021). Mozart effect in epilepsy: Why is Mozart better than Haydn? Acoustic qualities-based analysis of stereoelectroencephalography. *European Journal of Neurology*, 28(5), 1463-1469. https://doi.org/10.1111/ene.14758
- Vibrašiūtė (2017). Muzikos klausymo poveikis būdrumui, psichoemocinei būsenai, kognityviosioms funkcijoms ir judesų mokymuisi po galvos smegenų insulto.

Excluded Literature

Excluded due to reasons shown in Appendix E

- Attanasio, G., Cartocci, G., Covelli, E., Ambrosetti, E., Martinelli, V., Zaccone, M., ... & Cacciafesta, M. (2012). The Mozart effect in patients suffering from tinnitus. *Acta otolaryngologica*, *132*(11), 1172-1177. https://doi.org/10.3109/00016489.2012.684398
- Bedetti, Principi, M., Di Renzo, A., Muti, M., Frondizi, D., Piccirilli, M., D'Alessandro, P., Marchiafava, M., Baglioni, A., Menna, M., Gubbiotti, M., & Elisei, S. (2019). The Effect of Mozart's music in severe epilepsy: Functional and morphological features. *Psychiatria Danubina*, *31*(3), 467–474.
- Bodner, M., Turner, R. P., Schwacke, J., Bowers, C., & Norment, C. (2012). Reduction of seizure occurrence from exposure to auditory stimulation in individuals with neurological handicaps: A randomized controlled trial. PLOS ONE, 7(10), e45303. https://doi.org/10.1371/journal.pone.0045303
- Coppola, G., Operto, F. F., Caprio, F., Ferraioli, G., Pisano, S., Viggiano, A., & Verrotti, A. (2018). Mozart's music in children with drug-refractory epileptic encephalopathies: comparison of two protocols. *Epilepsy & Behavior*, 78, 100-103. https://doi.org/10.1016/j.yebeh.2017.09.028
- Hughes, J. R., Daaboul, Y., Fino, J. J., & Shaw, G. L. (1998). The "Mozart effect" on epileptiform activity. *Clinical Electroencephalography*, 29(3), 109-119. https://doi.org/10.1177/155005949802900301
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- Lahiri, N., & Duncan, J. S. (2007). The Mozart effect: encore. *Epilepsy & Behavior*, 11(1), 152-153. https://doi.org/10.1016/j.yebeh.2007.04.017
- Lin, L. C., Lee, W. T., Wu, H. C., Tsai, C. L., Wei, R. C., Jong, Y. J., & Yang, R. C. (2010). Mozart K. 448 and epileptiform discharges: effect of ratio of lower to higher harmonics. *Epilepsy research*, 89(2-3), 238-245. https://doi.org/10.1016/j.eplepsyres.2010.01.007

- Lin, L. C., Lee, W. T., Wang, C. H., Chen, H. L., Wu, H. C., Tsai, C. L., ... & Yang, R. C. (2011a). Mozart K. 448 acts as a potential add-on therapy in children with refractory epilepsy. *Epilepsy & Behavior*, 20(3), 490-493. https://doi.org/10.1016/j.yebeh.2010.12.044
- Lin, L. C., Lee, W. T., Wu, H. C., Tsai, C. L., Wei, R. C., Mok, H. K., ... & Yang, R. C. (2011b). The long-term effect of listening to Mozart K. 448 decreases epileptiform discharges in children with epilepsy. *Epilepsy & Behavior*, 21(4), 420-424. https://doi.org/10.1016/j.yebeh.2011.05.015
- Lin, L. C., Lee, M. W., Wei, R. C., Mok, H. K., Wu, H. C., Tsai, C. L., & Yang, R. C. (2012). Mozart k. 545 mimics mozart k. 448 in reducing epileptiform discharges in epileptic children. *Evidence-Based Complementary and Alternative Medicine*, 2012. https://doi.org/10.1155/2012/607517
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