Title: Data extraction and statistical errors: a quantitative critique of Gumley, Braehler, & Macbeth, (2014)

Abstract

Objective: While oxytocin has been identified as having therapeutic properties for schizophrenia, the evidence has been mixed which has resulted in meta-analytic reviews. We identified several errors in one such meta-analysis. Here, we show the errors, demonstrate that the conclusions were incorrect, and state the importance of this report.

Methods: We reproduced the methods of Gumley, Braehler, & Macbeth, (2014): outcomes (positive symptoms, negative symptoms, general psychopathology, and total symptoms) and meta-analytic estimates for fixed and random effect models.

Results: While they reported oxytocin had significant effects on three of four outcomes, we show that all effects were non-significant.

 Conclusions: Based on these null results, we hope this report encourages a re-evaluation of oxytocin as a treatment for schizophrenia.

1. Introduction

Oxytocin is a neuropeptide that been used as an experimental therapeutic for various psychiatric disorders. In particular, randomized controlled trails have investigated the effects of intranasal oxytocin (IN-OT) on reducing symptoms in schizophrenia. As the extant literature has been mixed, meta-analyses have been published on this topic. One such meta-analysis was published in the British Journal of Clinical Psychology (Gumley, Braehler, & Macbeth, 2014). The authors concluded that IN-OT significantly improved overall symptoms, negative symptoms, and positive symptoms. We found several errors in this paper and suggest that the conclusions are incorrect. The aims of this report are threefold: (1) we will outline the errors; (2) we will perform a meta-analysis on the reported outcomes; and (3) we will conclude by stating the importance of our findings.

2. Data extraction errors

Gumley, Braehler, & Macbeth (2014) coded the effect estimates such that a positive value indicated a positive effect of IN-OT. Accordingly, all studies that reported a positive effect of IN-OT should have the same sign (±). However, in Table 2 of Gumley, Braehler, & Macbeth (2014) there are several coding mistakes. For total symptoms, for example, 3 out of 4 effects were misspecified. While Feifel et al. (2010) and Pedersen, Gibson, Rau, & Salimi (2011) reported a positive effect of IN-OT, they were coded as negative in the paper under question. In turn, while Lee et al. (2013) reported that the IN-OT group actually had higher symptom scores than the placebo group, Gumley, Braehler, & Macbeth (2014) coded this effect as though IN-OT had a positive effect on reducing symptoms. From the primary studies, we extracted the relevant data and found that 9 out of the 13 outcomes used to compute the meta-analytic estimates for each symptom type were incorrectly coded.

3. Statistical errors

Gumley, Braehler, & Macbeth (2014) fitted both fixed and random effects models. In their Table 2, both fixed and random effects estimates and corresponding confidence intervals (*CI*) were reported. By definition, the *CI* of a random effects estimate must be larger or equal to the CI of the fixed effects

estimate when both are based on the same data. This is because a random effects model has another variance source (variance in the true scores across studies), which increases uncertainty in the estimates and thus the *CI*s. However, Gumley, Braehler, & Macbeth (2014) consistently reported *smaller CI*s for the random effects estimates as compared to the fixed effects estimates. Due to heterogeneity between outcomes, their conclusions were based on the random effect estimates and where therefore incorrect.

4. Meta-analysis

To check whether the aforementioned errors changed the conclusions of the paper, we performed a meta-analysis based on the data reported in Table 2 in Gumley, Braehler, & Macbeth (2014). We attempted to replicate their procedures as closely as possible, including outcomes used and we report both fixed and random effect estimates.

5. Replication attempt

While Gumley, Braehler, & Macbeth (2014) reported significant effects for all outcomes excluding general psychopathology, the data in their Table 2 did not support this conclusion. Based on the random effects models, all meta-analytic estimates were non-significant (*CI*s included zero; Table 1): negative symptoms (SMD = 0.45, [-0.49, 1.39]), positive symptoms (SMD = 0.33, [-0.53, 1.19]), general psychopathology (SMD = 0.25, [-0.34, 0.83]), total symptoms (SMD = 0.47, [-0.46, 1.41]).

6. Discussion

Although Gumley, Braehler, & Macbeth (2014) is not a new article and they urged caution when interpreting their findings, there are several reasons this report deserves attention. First, while they reported IN-OT produced significant effects on all aspects of symptomology in schizophrenia, our analysis suggests that all effects were non-significant. Second, IN-OT research has become a very active field and ensuring accuracy in the publish literature is a mental health priority. For instance, recent publications cite Gumley, Braehler, & Macbeth (2014) in support of IN-OT reducing psychiatric symptoms (Hofmann, Fang, & Brager, 2015). Third, the evidence from animal studies supporting the role of oxytocin in psychiatric disorders is substantial, especially those comprised of social deficits (Lim,

Bielsky, & Young, 2005). By ensuring null results are represented in the literature, researchers can work towards improving current methods of delivery or dedicate more resources into developing pharmaceutical drugs that target oxytocin receptors. Together, we hope this report simultaneously results in a correction and moves the field towards effective treatments, which is especially important because of the difficulty in treating certain aspects (e.g., negative symptoms) of schizophrenia.

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Supplementary materials

Data and R code for analyses presented in this letter are publicly available at Donald R. Williams' Open Science Framework account (https://osf.io/mzcbr/)

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Table 1: Comparison of meta-analytic estimates for the data of Gumley et al. (2014)

Model type	Symptom type	Estimates computed by Gumley et al. (2014)		Estimates obtained by reanalyzing the data of Gumley et al. (2014)	
		SMD	*CI*	**SMD**	*CI*
Fixed	Negative	0.50	[0.07, 0.93]	0.49	[0.06, 0.92]
	Positive	0.39	[-0.04, 0.82]	0.38	[-0.04, 0.81]
	General	0.27	[-0.16, 0.70]	0.27	[-0.15, 0.70]
	Overall	0.70	[0.35, 1.05]	0.52	[0.15, 0.90]
Random	Negative	0.47	[0.17, 0.76]	0.45	[-0.49, 1.39]
	Positive	0.35	[0.04, 0.66]	0.33	[-0.53, 1.19]
	General	0.25	[-0.07, 0.57]	0.25	[-0.34, 0.83]
	Total	0.52	[0.34, 0.70]	0.47	[-0.46, 1.41]

Note: 3 out of 4 estimates for the fixed effects are similar between the two analyses. For the random effects models, however, the point estimates are similar but all confidence intervals include zero in our results. Accordingly, while Gumley, Braehler, & Macbeth (2014) reported significant effects for three outcomes, we show all meta-analytic estimates as non-significant.