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Brief report

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

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

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

Results. Whereas (Gumley, Braehler, and Macbeth 2014) 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 intranasal oxytocin as a treatment for schizophrenia.

Oxytocin is a neuropeptide that has 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 *et al.*, 2014). The authors concluded that IN-OT significantly improved negative, positive, and overall symptoms. We found several errors in this report and suggest that the conclusions are incorrect. The aims of this report are threefold, in which we will: (1) outline the errors; (2) perform a meta-analysis on the data reported in Gumley *et al.* (2014); and (3) conclude by stating the importance of our findings.

Data extraction errors

Gumley *et al.* (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 *et al.* (2014), there are several coding mistakes. For total symptoms, for example, three of four effects were

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misspecified. While Feifel *et al.* (2010) and Pedersen, Gibson, Rau, and Salimi (2011) reported a positive effect of IN-OT, they were coded as negative in the paper under question. In turn, Lee *et al.* (2013) reported that the IN-OT group actually had higher symptom scores than the placebo group, but Gumley *et al.* (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 nine of the 13 outcomes used to compute the meta-analytic estimates were incorrectly coded (Table S1).

Statistical errors

Gumley *et al.* (2014) fitted both fixed and random effects meta-analytic models. In their table 2, both fixed and random effect estimates and corresponding confidence intervals (CIs) were reported. By definition, the CI of a random effects estimate must be larger than or equal to the CI of the fixed effects estimate when both are based on the same data. This is because a random effect model has another source of variation (variability in the true scores across studies), which increases uncertainty in the estimates and thus wider CIs. However, Gumley *et al.* (2014) consistently reported *smaller* CIs 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 were potentially incorrect.

Meta-analysis

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

Replication attempt

While Gumley *et al.* (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 (CIs included zero; Table 1): negative symptoms (SMD = 0.45, 95% CI = [−0.49, 1.39]), positive symptoms (SMD = 0.33, [−0.53, 1.19]), general psychopathology (SMD = 0.25, [−0.34, 0.83]), and total symptoms (SMD = 0.47, [−0.46, 1.41]).

Discussion

Although Gumley *et al.* (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 *et al.* (2014) in support of IN-OT reducing psychiatric symptoms (Hofmann, Fang, & Brager, 2015). Third, the evidence from animal and humans studies supporting the role of oxytocin in psychiatric disorders is substantial, especially for those comprised of social deficits (Lim,

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

		Estimates computed by Gumley *et al.* (2014)		Estimates obtained by reanalysing the data of Gumley *et al.* (2014)	
Model type	Symptom type	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

Notes. Three of four 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 (CIs) include zero in our results. Accordingly, while Gumley *et al.* (2014) reported significant effects for three outcomes, we show all meta-analytic estimates as non-significant.

Bielsky, & Young, 2005). By ensuring null results are represented in the literature (Williams & Bürkner, 2017), researchers can work towards improving current methods of intranasal 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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Supporting Information

The following supporting information may be found in the online edition of the article:

Table S1. 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/).