Title: A Pull to be Close: the Differentiating Effects of Oxytocin and Grief Stimulus Type on Approach Behavior in Complicated Grief

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Objectives:

Our first aim was to identify whether bereaved individuals would show different motivational responses depending on whether stimuli represented their deceased spouse, or were general reminders of the loss ("non-specific grief"). We hypothesized that participants overall would show an approach bias for stimuli depicting their spouse, but would not show an approach bias for "non-specific grief" stimuli. Our second aim was to investigate whether response bias differed between CG and non-CG participants. Specifically, we hypothesized that participants with CG would exhibit a greater approach bias for spouse stimuli, compared to non-CG participants. Our third aim proposed differential effects of intranasal oxytocin in CG and non-CG participants (i.e., a group x condition interaction), where oxytocin would specifically increase relative approach bias for the spouse in CG only. This is based on prior work supporting individual differences in socio-emotional functioning as likely moderators of oxytocin effects (Bartz et al., 2011; Seeley et al., 2018).

Study Protocol

Participants gave written informed consent and were compensated $200. Prior to their first session, participants provided three photos of their spouse, and three photos of a living loved one (identified via the WHOTO scale; Fraley & Davis, 1997). They completed self-report measures (e.g., demographics, health, length of relationship, time since the death), the Beck Depression Inventory-II (BDI-II; Beck et al., 1996), and Inventory of Complicated Grief (ICG; Prigerson et al., 1995). The ICG is a 19-item measure of complicated grief symptoms distinct from depression or anxiety and predictive of functional impairment, and showed high internal consistency in our sample ($\alpha = .92$).

Enrolled participants were categorized in the complicated grief (CG; n=17) or non- complicated grief (non-CG; n=22) group based on a clinical cutoff score of ≥ 25 on the ICG. A non-bereaved control group was not included in the current study because there was no available analogous stimulus to the deceased spouse for non-bereaved participants. Stratified sampling achieved representation of a full range of ICG scores ($M = 23.38$, $SD = 12.63$, range = 4-51).

Participants attended two experimental sessions 7-10 days apart. At each session, participants received a 24 IU dose of synthetic oxytocin (Syntocinon, Novartis, Switzerland) or placebo (all non-active ingredients of Syntocinon; Novartis, Switzerland) delivered via self- administered nasal spray. Participants and investigators were blind to condition until data analyses were complete. Order of oxytocin or placebo spray was randomized and counterbalanced across participants. After a 30-minute oxytocin rise-time, participants completed the AAT. They completed state measures before and after the task, and were debriefed after their second visit.

Task Description

Participants viewed three photos in each stimulus category: (1) deceased spouse, (2) living loved one, (3) stranger, (4) non-specific grief-related scenes such as a tombstone, casket, or hospital room, and (5) neutral scenes such as an outdoor picnic table or living room. Photos of a stranger were sex-matched to the spouse (for the living and deceased stimuli). Neutral environments (for the non-specific grief photos) were used to control for differences in person versus scene processing. Based on previous AAT designs (Derntl et al., 2011), photos were framed by a blue or yellow border. Participants were instructed to push or pull the joystick based on the frame color, not the photo's content. They completed the task twice per session, with reversed instructions on the second run (i.e., "*pull for yellow*" became "*push for yellow*"). Each seven-minute run of the task consisted of 144 2500ms trials (288 trials per visit, 576 trials total across runs/sessions; 500ms ITI). Order of instructions was randomized and counterbalanced across participants. Stimuli were presented via Inquisit 4 (2014), in a pseudorandomized order determined by genetic algorithm (Wager & Nichols, 2003).

Relative approach/avoidance bias was computed by subtracting median response time (RT; latency to joystick full extension) on PULL/approach trials in each stimulus category from PUSH/avoid trials in the same category (Rinck & Becker, 2007). Positive response bias values indicate relative approach bias; negative values indicate relative avoidance bias.

Statistical Analysis

Trials with RTs $\leq 1^{st}$ percentile (placebo: 463ms, oxytocin: 473ms) or $\geq 99^{th}$ percentile (placebo: 1717ms, oxytocin: 1711ms) were discarded as per previous AAT studies (Rinck & Becker, 2007). After discarding outliers and missed trials, none had >10% missing data except

for one participant (14% in the placebo condition). Data cleaning, visualization, and analysis were completed with R 3.6.3 using `dplyr`, 'ggplot2`, `afex`, `emmeans`, `nlme`, and `psych` packages (Lenth, n.d.; Pinheiro J, Bates D, DebRoy S, Sarkar D, R Core Team (2019), n.d.; Revelle, n.d.; Singmann, Bolker, Westfall and Aust, n.d.; Wickham, H., François, R., Henry, L., and Müller, K., n.d.).

Statistical analyses included repeated measures ANOVAs with tests of *a priori* contrasts on the estimated marginal means to predict bias scores. In addition, we repeated each analysis using mixed effects linear modeling. Mixed effects models yield higher power due to the larger number of observations at the trial level (288 observations per participant, per session) compared to the bias scores, which are computed from median RTs averaged across trials (five observations per participant, per session). The mixed effects linear models used individual PUSH/PULL trial RTs as the outcome rather than bias scores, and included joystick response direction (PUSH or PULL) as an additional fixed effect. Results did not change substantively using the mixed effects models, and are more difficult to interpret because of the added predictor. Further, an RT in one direction alone (rather than relative to the other direction) is a less direct index of response bias than bias scores, and thus, bias scores are easier to interpret. Therefore, we present the ANOVA results for ease of interpretation, and only report the mixed effects models when needed to demonstrate results requiring more power.