DESPERATELY SEEKING: EFFECTS OF COMPLICATED GRIEF AND INTRANASAL OXYTOCIN ON RESTING STATE NETWORKS IN WIDOWED OLDER ADULTS

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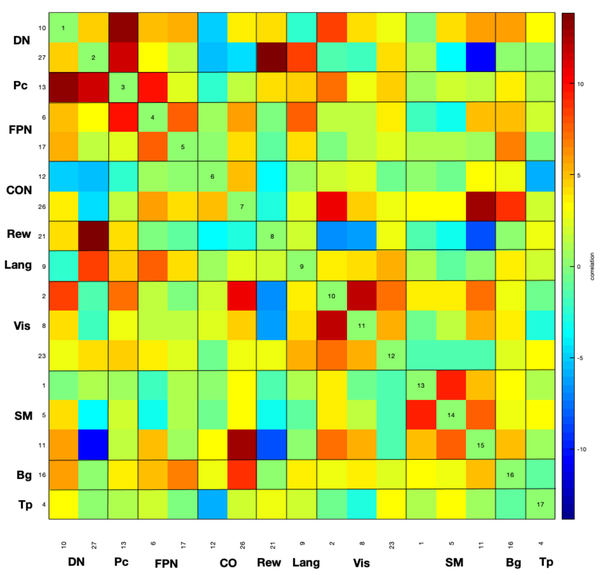
Participants and Procedure

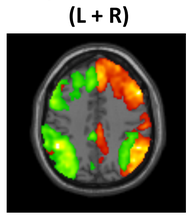
- 40 older adults (71% female, *M* age = 69 +/- 6.5 years).
  - Death of spouse/partner 6-36 months prior (*M* = 15.4 +/- 8.2 months).
  - Stratified sampling by Inventory of Complicated Grief scores.
- Attended two fMRI sessions as part of a larger parent study of oxytocin and complicated grief:
  - 24 IU intranasal oxytocin vs. placebo (double-blinded & counterbalanced).
  - Approach-avoidance task w/photos of the deceased spouse.
  - Six-minute resting state scan.

Data Preprocessing and Analysis

- 2 participants dropped after quality control via MRIQC.
  - Final *N* = 38
    - 15 met threshold for complicated grief (ICG >25)
- Preprocessing in fMRIPrep v1.1.8 + ICA-AROMA non-aggressive denoising.
- **Identify functional networks via group spatial ICA**, using GIFT v3.0b:
  - Subject-specific PCA (*c* = 45) → group-level reduction (*c* = 30).
  - Back-reconstruct single-subject/session spatial maps (GICA).
  - Detrend, despike, and low-pass filter timecourses at .15Hz.
  - ICASSO 10x to evaluate stability & reliability of estimates.
  - Component identification and labeling.
  - Select representative components from networks (relevant to theoretical model) for analysis.



Frontoparietal network (L + R)

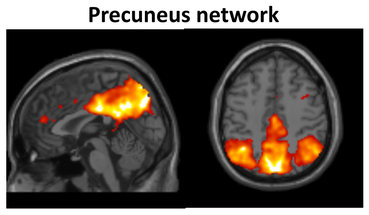


C17 C6

Reward network

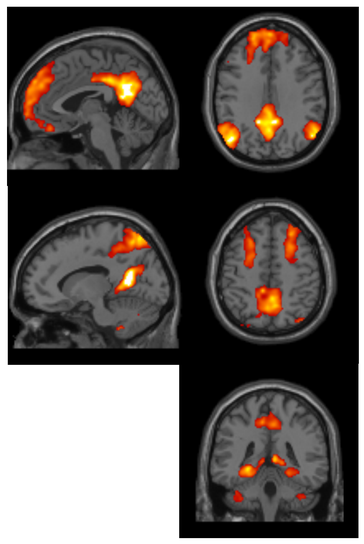
C21

Precuneus network



C13

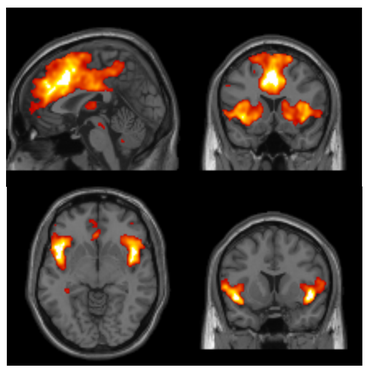
Default network



C27

C10

Cingulo-opercular network



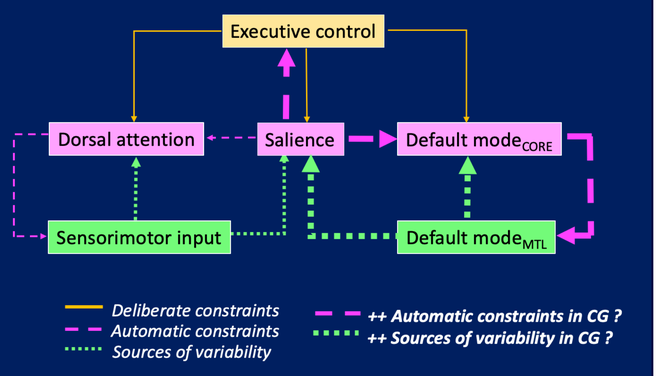
C26

C12

Complicated grief (CG) is an absence of typical adaptation following the death of a close loved one.

Internally-focused attention may be central to CG, in the forms of protracted ***yearning*** and grief-related ***rumination:***

- Separation distress
- Sustained attachment salience
- Intrusive memories
- Perseveration
- Counterfactuals
- Maladaptive cognitions



Adapted from Christoff et al. (2016) *Nat Rev Neurosci.*

Q1: Are complicated grief symptoms reflected in large-scale brain network interactions during rest?

Q2: Can we use intranasal oxytocin to test a theoretical model of network function in complicated grief?

Results suggest that both automatic and deliberate constraints may shape internally-focused attention in complicated grief – and that cingulo-opercular resting state functional connectivity with default and frontoparietal networks might be implicated.

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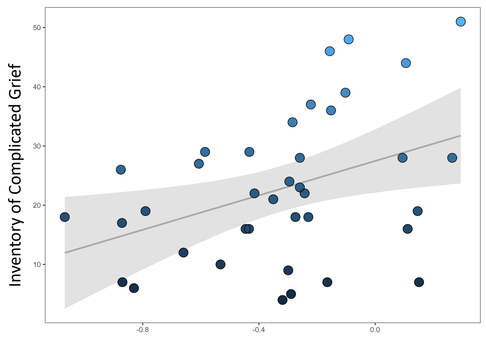
Q1: Is complicated grief symptom severity associated with resting state functional connectivity (placebo)?

In the placebo condition, only the midline default network (DN; C27) and cingulo-opercular network (CoN; C26) pair predicted complicated grief severity from rsFC values:

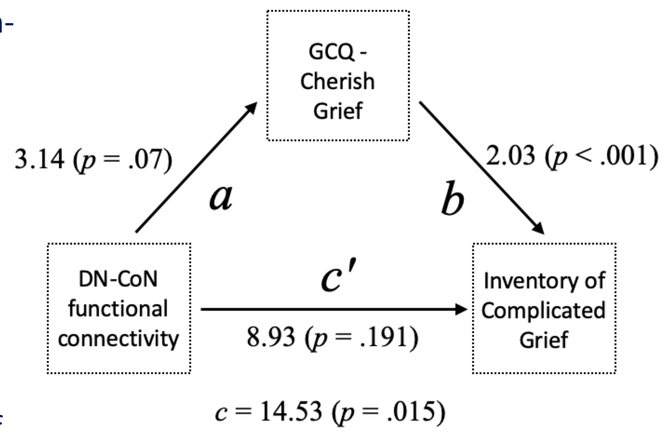


Predictors	Est.	95% CIs	*p*
(Intercept)	27.45	23.91, 30.99	<0.001
C27-C26 rsFC	8.48	1.02, 15.93	0.033
Age (centered)	0.04	-0.34, 0.41	0.852
Sex	6.48	2.64, 10.31	0.002
BDI (centered)	1.07	0.73, 1.41	<0.001
$F(4,33) = 16.76$, $p < .001$		$R^2 = 0.630$	adj. $R^2 = 0.670$

Z-scaled *r* of default network and cingulo-opercular components (C27-C26)

Q1b: Do maladaptive grief-related cognitions mediate the grief severity-rsFC relationship?

Exploratory non-parametric bootstrapped mediation analysis indicated that maladaptive cognitions mediated DN-CoN rsFC – but only the type of maladaptive cognitions characterized by efforts to remain in mourning in order to maintain the bond with the deceased.

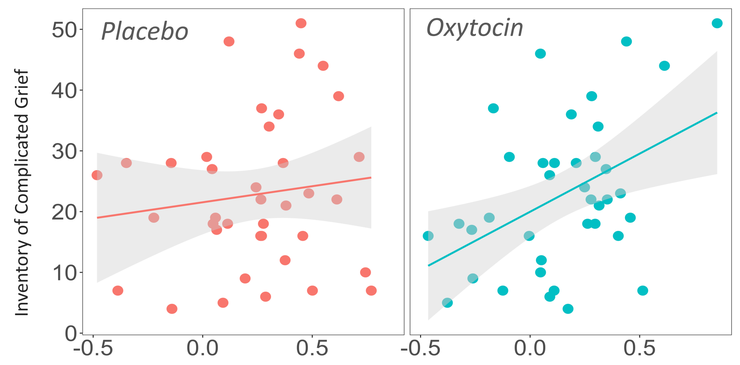


Proportion of spouse-related thought in post-scan reports was *not* related to DN-CoN rsFC.

Q2: Does complicated grief severity moderate effects of intranasal oxytocin on default network or cingulo-opercular rsFC?

Oxytocin increased rsFC between the retrosplenial/para-hippocampal DN component (C10) and the CoN component (C26), $F(1,36) = 7.02$, $p = .012$. Complicated grief severity did *not* moderate oxytocin effects.

There was a main effect of grief severity on rsFC between C26 and the right frontoparietal network component (C6). While no significant interaction, the effect of grief severity appeared to be primarily driven by the complicated grief severity—rsFC relationship in the oxytocin condition:



Z-scaled *r* of frontoparietal and cingulo-opercular components (C6-C26)