The Ups and Downs of Brain Stress: Testing the Triple Network Hypothesis in a Largescale Biopsychological Sample

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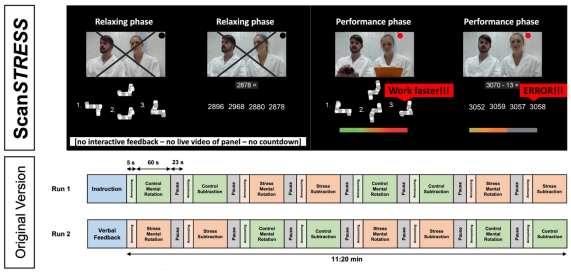
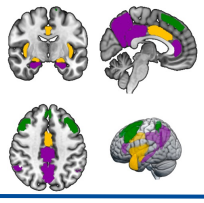
Background

- Many attempts have been made to determine neural response patterns to acute psychosocial stress exposure[1].
- Established and reliable laboratory stressors[2] were brought into the scanner environment: **Scan*STRESS***[3,4].



Psychosocial stress components (i.e., social-evaluative threat, negative feedback, forced failure) trigger distinct responses in the **triple network**[5,6]:

- ↑ **Salience Network, Default Mode Network**
- ↓ **Central Executive Network**



Salience Network (SN)	Frontoinsular Cortex (FIC)
	Dorsal Anterior Cingulate Cortex (dACC)
	Temporal Pole (TP)
	Amygdala
Default Mode Network (DMN)	Medial Prefrontal Cortex (mPFC)
	Precuneus/Posterior Cingulate Cortex (PCU/PCC)
	Inferior Parietal Lobule (IPL)
	(Para-)Hippocampus
Central Executive Network (CEN)	Dorsolateral Prefrontal Cortex (dlPFC)
	Posterior Parietal Cortex (PPC)
	Dorsomedial Prefrontal Cortex (dmPFC)

Methods

Using **ENIGMA HALFpipe**[7], neural responses to Scan*STRESS* were analyzed in a large-scale biopsychological sample.

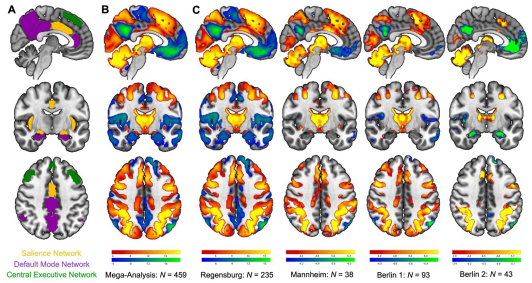
- **Activations & Deactivations** (stress > control, control > stress)
- **(Sex-specific) Associations** between stress-induced neural response and increases in Cortisol, Heart Rate, Negative Affect, and Task Performance (Error Rate)[1,4,8].
- **Psychophysiological Interactions** (gPPI)[9] – seeds: Fronto-insular Cortex (FIC), Dorsolateral Prefrontal Cortex (dlPFC), Precuneus/Posterior Cingulate Cortex (PCU/PCC)

Data set	Descriptives: *N*	Mean age	Sex ratio (women/men)	Site
Henze et al. (2020)	67	23.06	31/36	Regensburg
Konzok et al. (2021)	61	23.62	30/31	
Speicher & Henze et al. (2023)	40	23.85	0/40	
Giglberger et al. (2023)	111	21.96	70/41	
Bärtl et al. (2024)	116	41.24	56/60	
Streit et al. (2014)	42	28.00	20/22	Mannheim
Dahm et al. (2017)	86	27.70	50/36	Berlin 1
Nowak et al. (2020)	50	30.23	0/50	Berlin 2
	573	27.46	257/316	

Van Oort's hypothesis[5]:
Acute psychosocial stress processing involves structures of the SN and DMN at the expense of areas of the CEN.

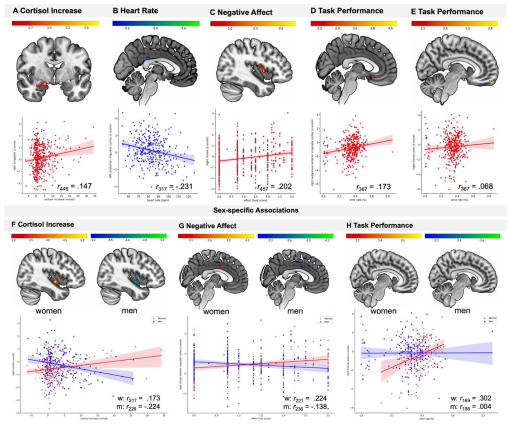
Results

Activations & Deactivations
(corrected for age, sex, site)

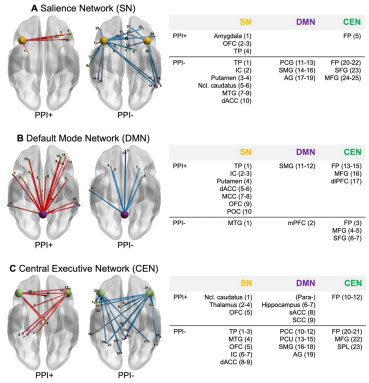


False Discovery Rate (FDR-)corrections were applied for all analyses.

(Sex-specific) Associations
(corrected for age, sex/menstrual cycle, site)



Psychophysiological Interactions
(corrected for age, sex, site)

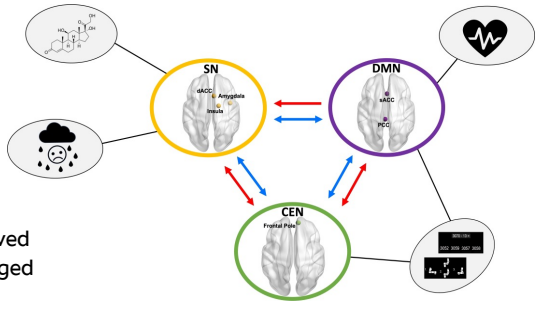


Abbreviations: OFC, Orbitofrontal Cortex; TP, Temporal Pole; IC, Insular Cortex; MTG, Middle Temporal Gyrus; dACC, dorsal Anterior Cingulate Cortex; MCC, Middle Cingulate Cortex; POC, Parietal Opercular Cortex; PCG, Paracingulate Gyrus; SMG, Supramarginal Gyrus; AG, Angular Gyrus; mPFC, medial Prefrontal Cortex; sACC, subgenual Anterior Cingulate Cortex; SCC, Subcallosal Cortex; PCC, Posterior Cingulate Cortex; PCU, Precuneus; FP, Frontal Pole; SFG, Superior Frontal Gyrus; MFG, Middle Frontal Gyrus; dPFC, dorsolateral Prefrontal Cortex; SPL, Superior Parietal Lobule.

Conclusion & Outlook

Triple Network Hypothesis[5,6]:

- **All networks** are responsive and show both increased (PPI+) and decreased (PPI-) functional connectivity with each other.
- **Quality of response** (activated vs. deactivated) differs within structures and within networks.
- **Contrary to Van Oort's hypothesis**: CEN is involved in acute stress processing, but is primarily engaged in processing the tasks of the paradigm.[5,10]



Extended Triple Network Hypothesis:

- Structures of **SN** and **DMN** orchestrate **central nervous stress responses**: (Sex-specific) Associations between stress-induced neural and cortisol, heart rate, and affective responses.
- Structures of **CEN** and **DMN** process the **tasks** during stress induction.

References
[1]Noack et al., *J. Neural Transm.* (2019); [2]Kirschbaum et al., *Neuropsychobiology* (1993); [3]Streit et al., *Stress* (2014) [4]Henze et al., *Biol. Psychiatry: Cogn. Neurosci. Neuroimaging* (2020); [5]Van Oort et al., *Neurosci. Biobehav. Rev.* (2017); [6]Menon, Trends Cogn. Sci. (2011); [7]Waller et al., *Human Brain Mapping* (2022); [8]Henze et al., *SCAN* (2021); [9]Corr et al., *Biol. Psychiatry: Cogn. Neurosci. Neuroimaging* (2022); [10]Zhang et al., NeuroImage (2019).

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