Salience, Default Mode and Central Executive Network Activity during Fear Generalization in PTSD

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Fear Generalization in PTSD

Fear generalization is the process by which fear of a threat cue transfers to similar but safe cues.

Overgeneralization of acquired fear is a core feature of PTSD: intense distress or arousal to cues that resemble an aspect of the traumatic event. (DSM-5)

Understanding overgeneralization and its and neural correlates will help to inform conceptualization and treatment of PTSD.

Stimulus Generalization Paradigm

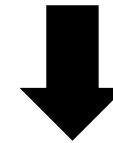(Kaczkurkin et al. 2017, *Am J Psychiat*)

Participants:
58 US combat veterans
  ➢ 20 with PTSD
  ➢ 19 with subthreshold PTSD symptoms
  ➢ 19 trauma-exposed controls
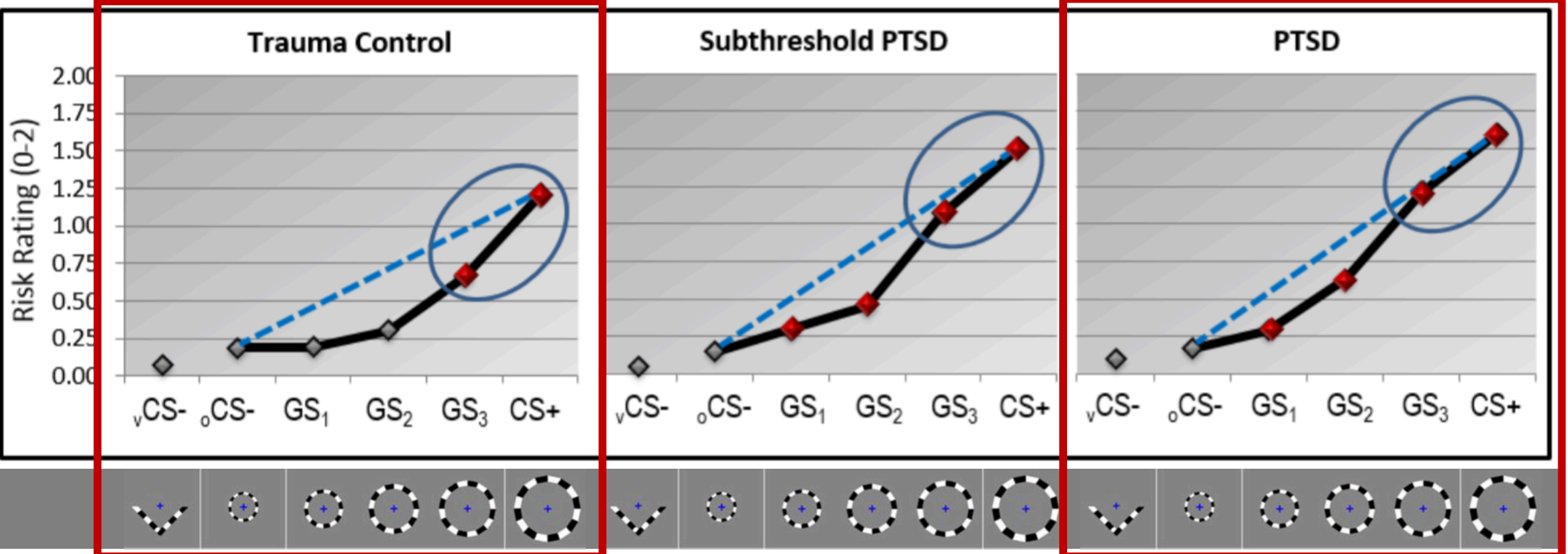
ACQUISITION

15 oCS-, 15 vCS-, 15 CS+
12 of 15 CS+ ⚡

GENERALIZATION

20 of each stimulus type
10 additional CS+ ⚡

Stimulus Generalization: Self-Report Findings

◆ sig. different from vCS- after Hochberg adjustment, p<.05

(Kaczkurkin et al. 2017, *Am J Psychiat*)

Stimulus Generalization: fMRI Findings

FIGURE 2. Group Differences in Positive Neural Gradients of Generalization in a Study of Neural Substrates of Overgeneralized Conditioned Fear[a]
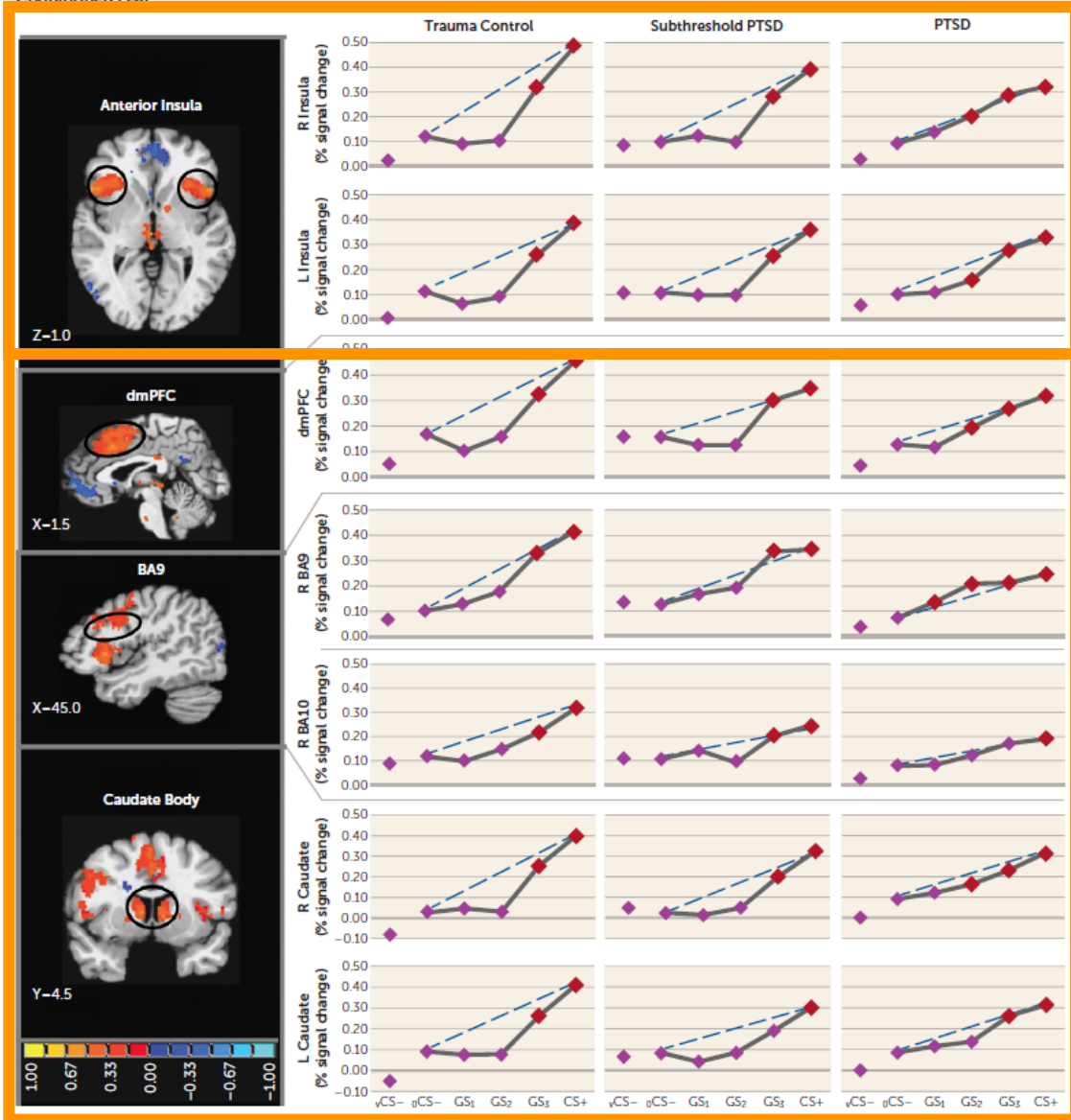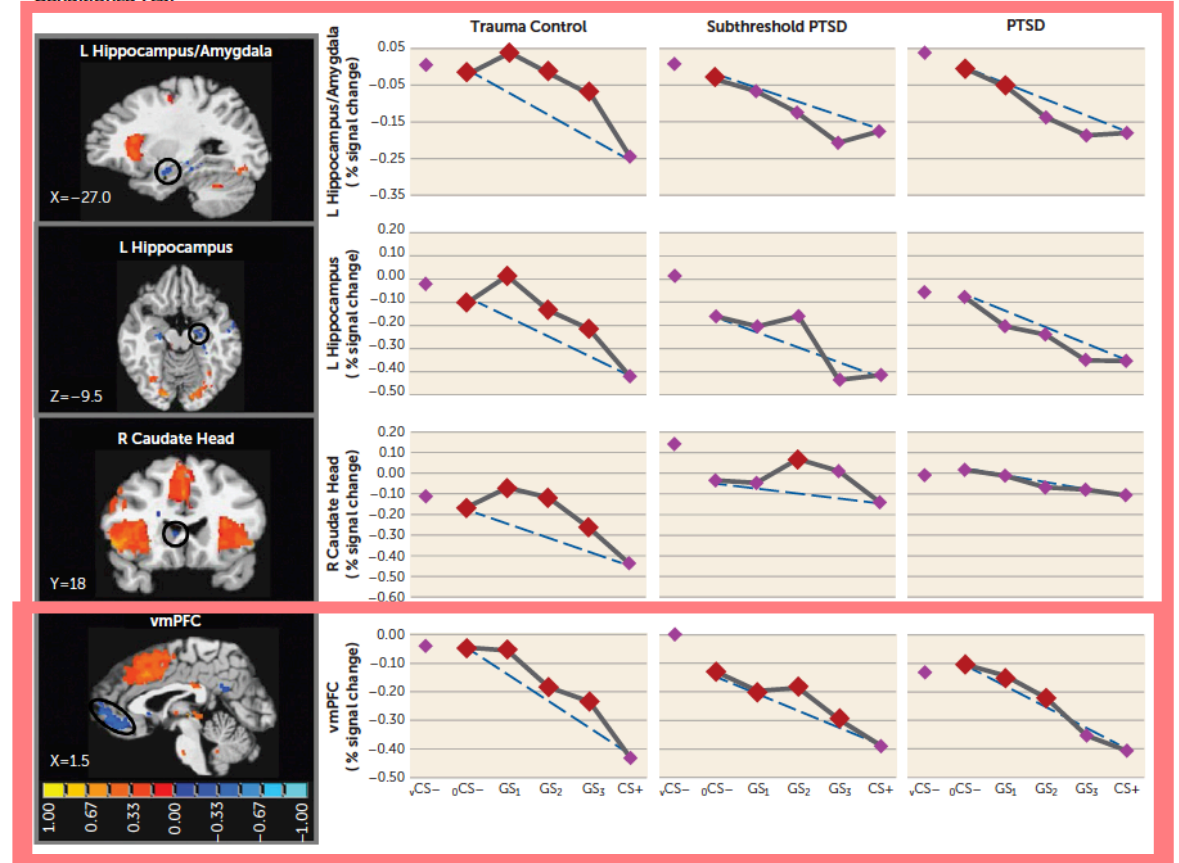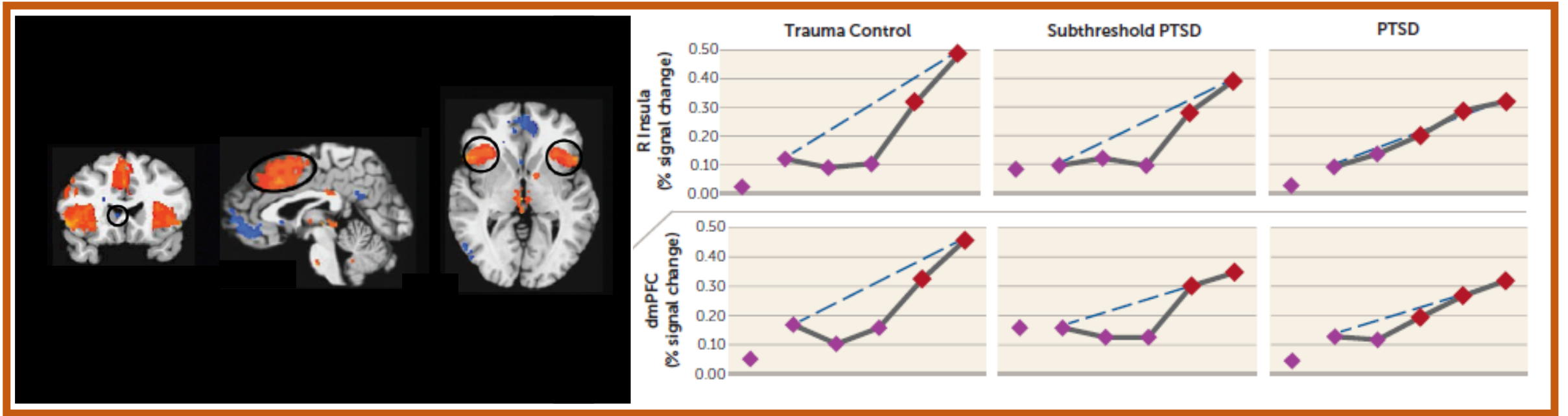
FIGURE 3. Group Differences in Negative Neural Gradients of Generalization in a Study of Neural Substrates of Overgeneralized Conditioned Fear[a]
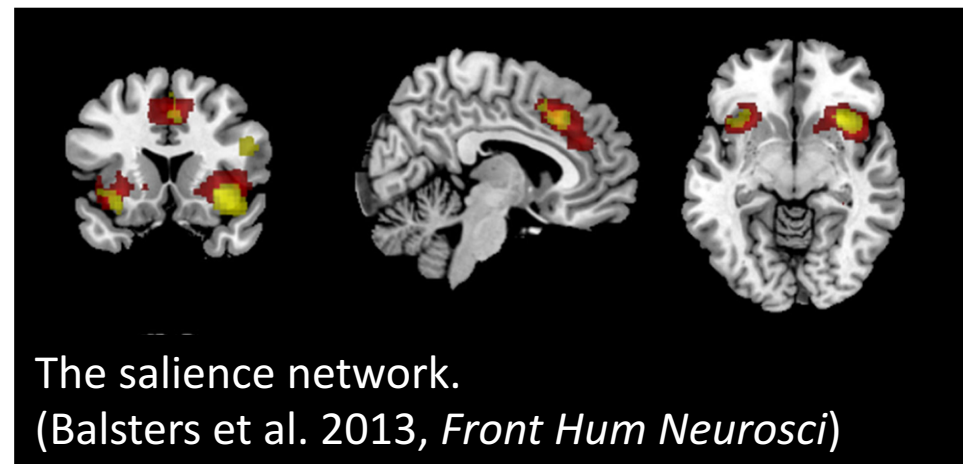
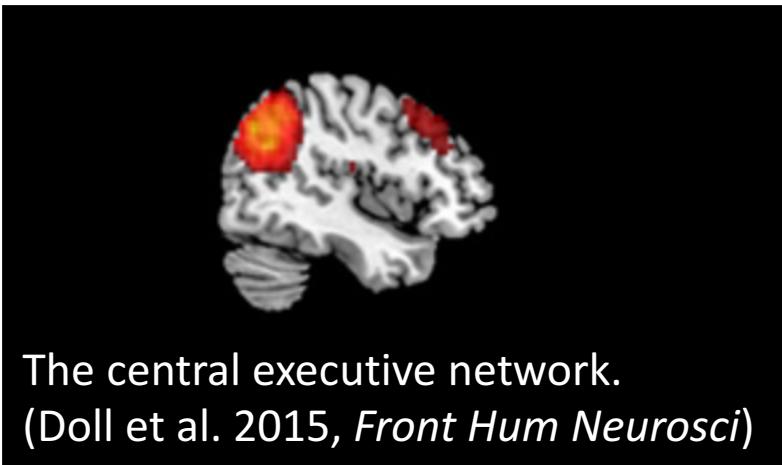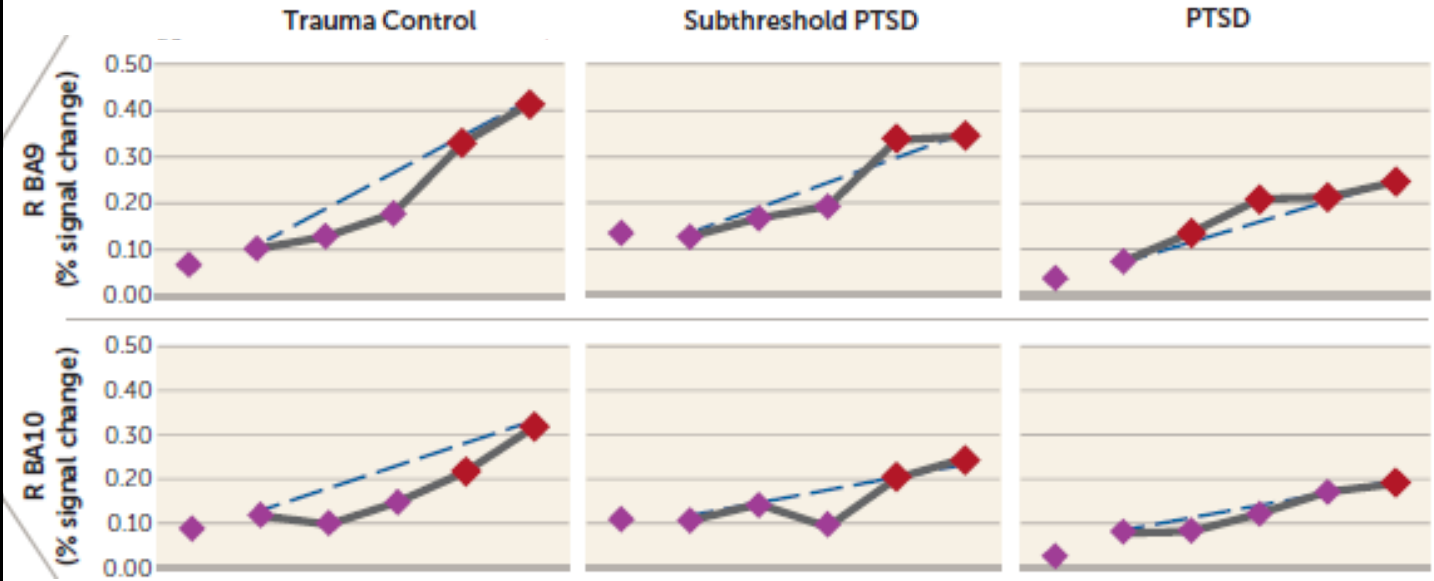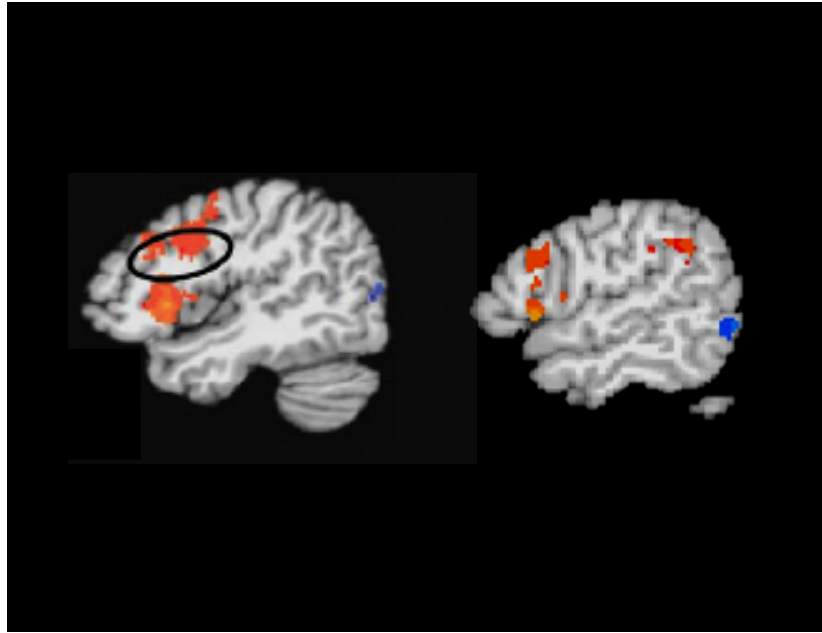(Kaczkurkin et al. 2017, *Am J Psychiat*)

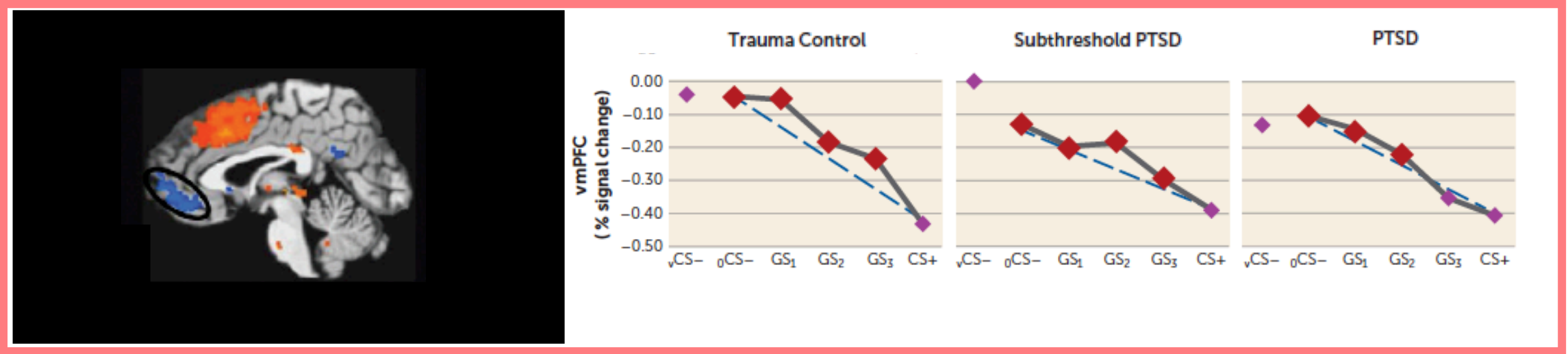# The Salience Network

(Kaczkurkin et al. 2017, *Am J Psychiat*)

The salience network.
(Balsters et al. 2013, *Front Hum Neurosci*)

The Central Executive Network

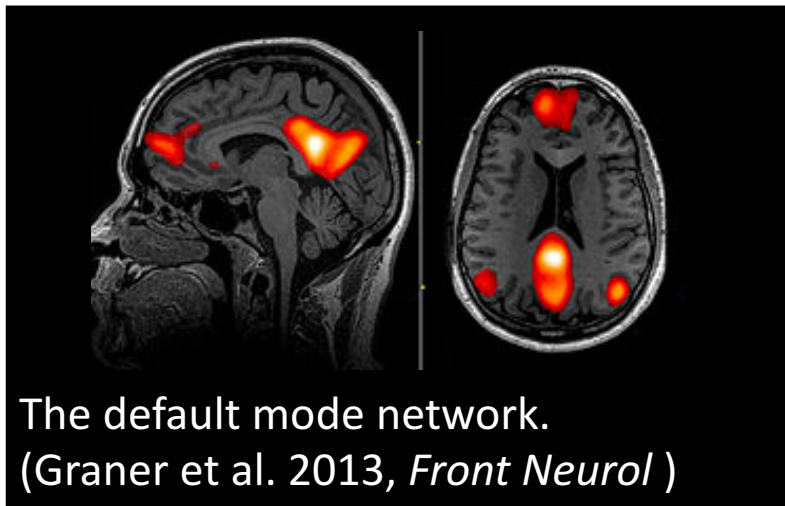(Kaczkurkin et al. 2017, *Am J Psychiat*)

The central executive network.
(Doll et al. 2015, *Front Hum Neurosci*)

The Default Mode Network

(Kaczkurkin et al. 2017, *Am J Psychiat*)
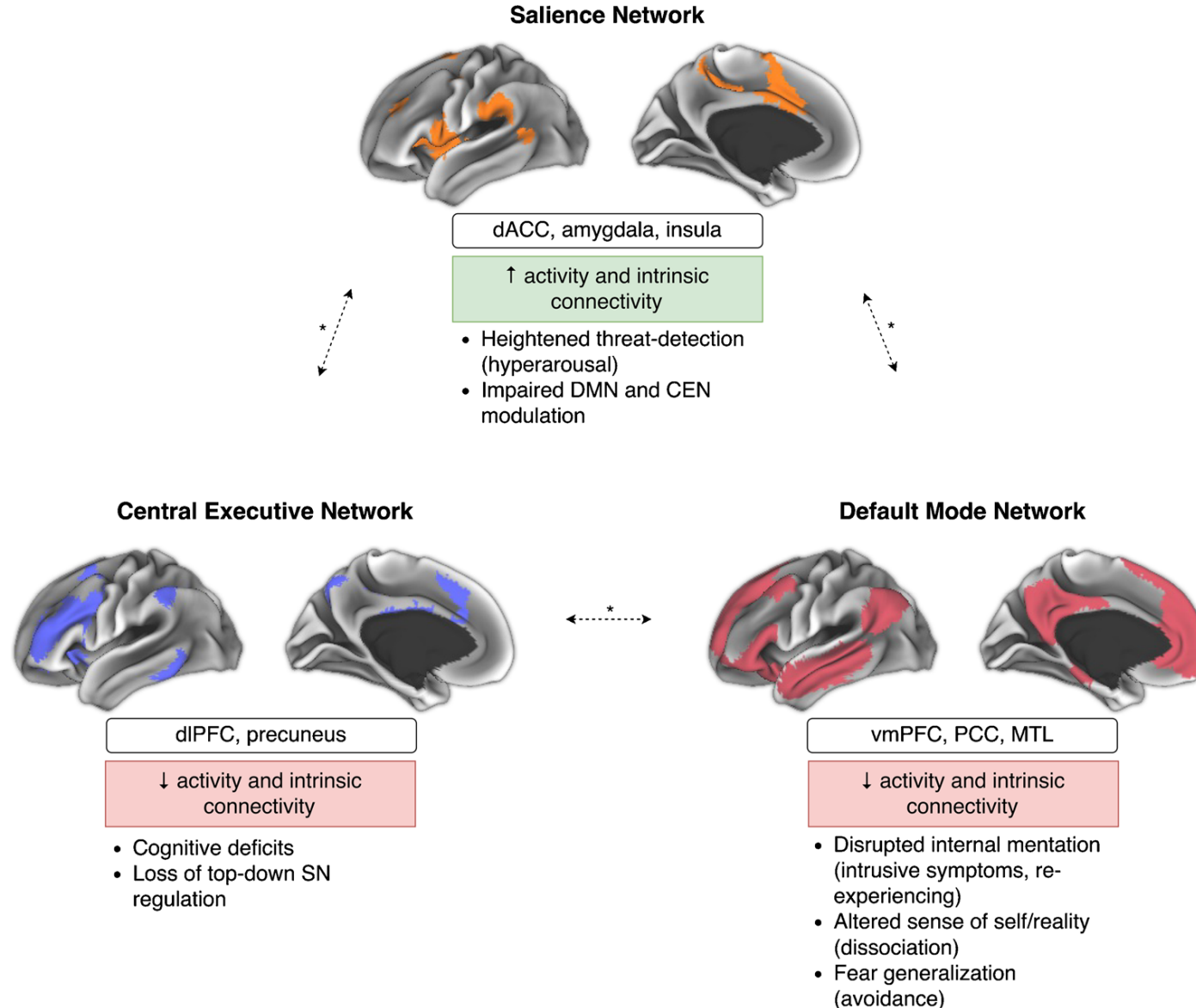

The default mode network.
(Graner et al. 2013, *Front Neurol*)

Neural Substrates of Generalization

Study	Positive gradients						Negative gradients		
	AI	dmPFC[a]	Caud	Thal	dlPFC[b]	IPL[c]	vmPFC[d]	VPc	HPC
Dunsmoor et al., 2011	X		X	X					
Greenberg et al., 2013a	X	X	X				X	X	
Greenberg et al., 2013b	X	X	X				X	X	
Kaczkurkin et al., 2017	X	X	X	X	X	X	X	X	X
Lange et al., 2017	X	X		X	X	X	X	X	X
Lissek et al., 2014	X	X			X	X	X	X	X
Onat & Büchel, (2015)	X						X	X	X
Network	Salience		Salience (subcortical)		Central Executive		Default mode		

[a]dmPFC includes Brodmann areas (BA) 6 and 8 and dorsal ACC; [b]BA 9 and 10; [c]BA 40; [d]BA 11

PTSD Pathology and the Triple-Network Model

Salience Network

dACC, amygdala, insula

↑ activity and intrinsic connectivity

- Heightened threat-detection (hyperarousal)
- Impaired DMN and CEN modulation

Central Executive Network

dlPFC, precuneus

↓ activity and intrinsic connectivity

- Cognitive deficits
- Loss of top-down SN regulation

Default Mode Network

vmPFC, PCC, MTL

↓ activity and intrinsic connectivity

- Disrupted internal mentation (intrusive symptoms, re-experiencing)
- Altered sense of self/reality (dissociation)
- Fear generalization (avoidance)

(Akiki et al. 2017, *Curr Psychiatry Rep*)

The Present Study

Hypotheses

For those with PTSD, **salience** and **central executive** networks will form less-steep upward-sloping gradients of generalization.

For those with PTSD, **default mode** network will form less-steep downward-sloping gradients of generalization.

For those with PTSD, SN will be more strongly connected with CEN and more weakly connected with DMN during generalization.
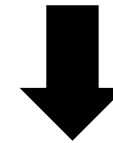
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Representing Brain Networks

Intrinsic connectivity networks (ICN's) reflect patterns of synchronized fluctuations in neural activity, and characterize the brain's inherent functional organization. (Abram et al 2015, Laird et al. 2010)

Resting-state ICN's show high correspondence across diagnostic groups and brain states (Griffanti et al. 2016, Mennes et al. 2010, Smith et al. 2009)

We used ICN's derived from a large (n=218) resting-state sample.

Task-Related Activation of ICN's

PREPROCESSING

OBSERVED ACTIVITY OF COMPONENTS
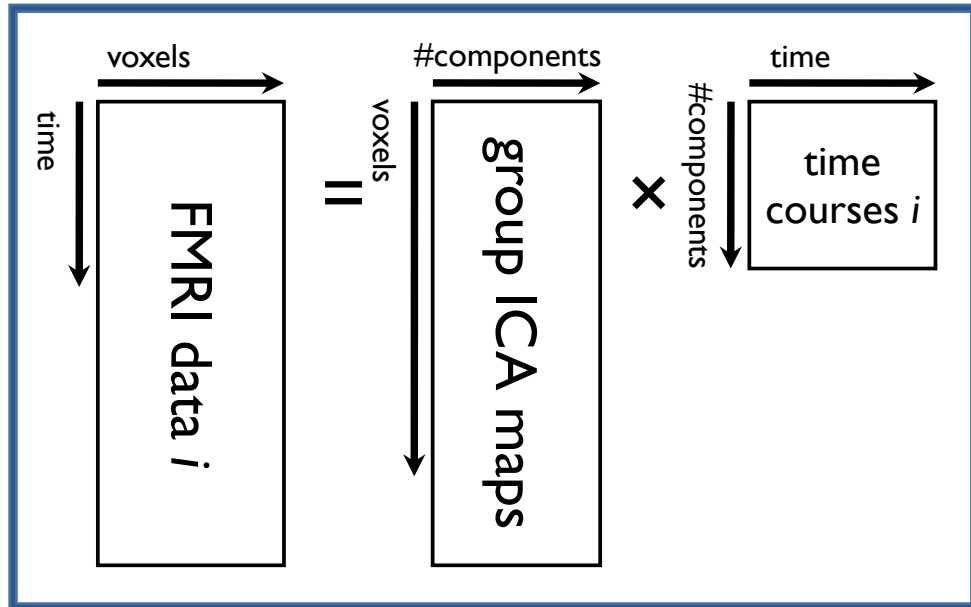
TASK-RELATEDNESS OF COMPONENTS
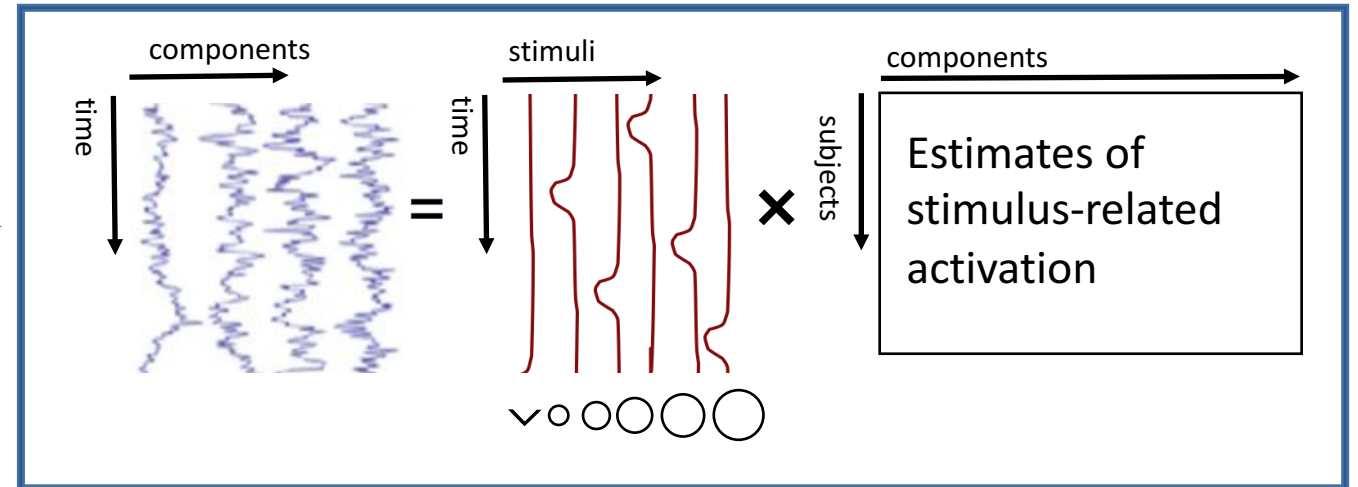
(adapted from Beckmann et al. 2009, *Neuroimage*)

Standardized betas

Selecting ICN's of Interest

Contain brain areas instantiating group differences in generalization → Display significant main effect of stimulus → Display gradient upon visual inspection → **ICN of Interest**
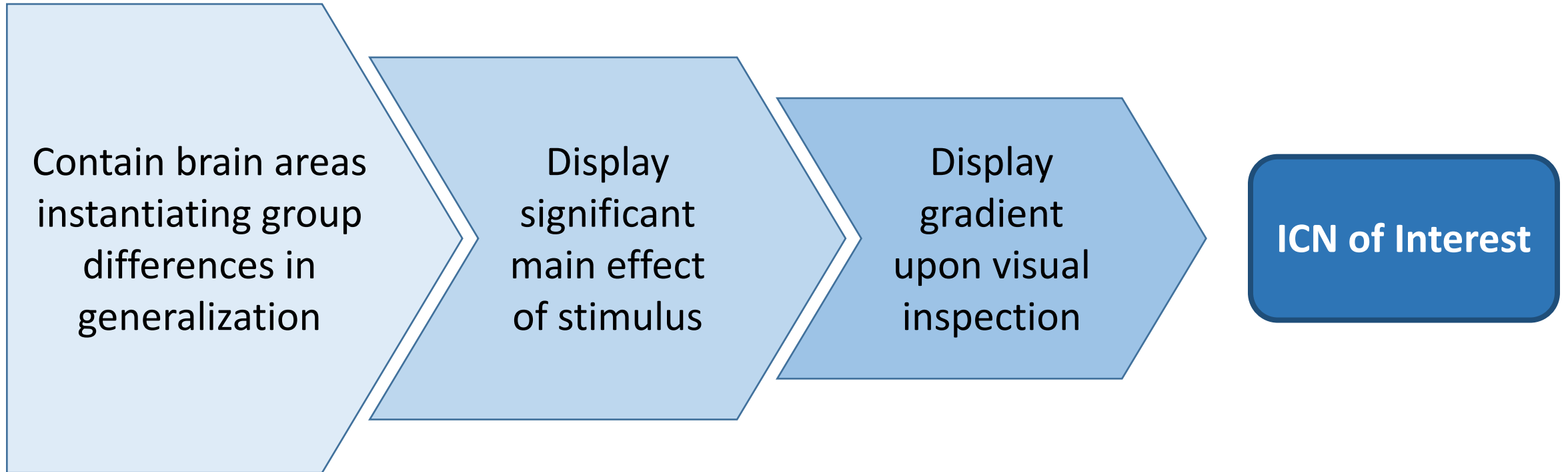
Results

The Salience Network
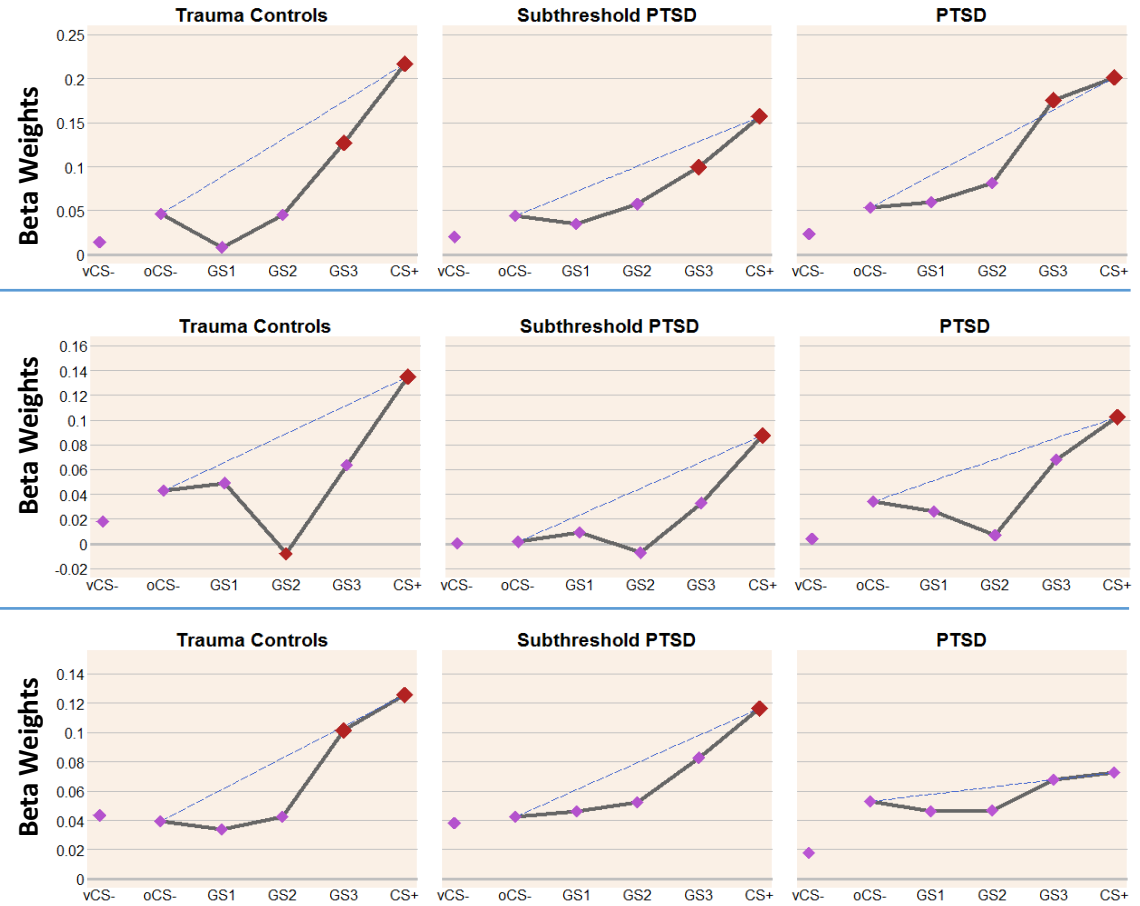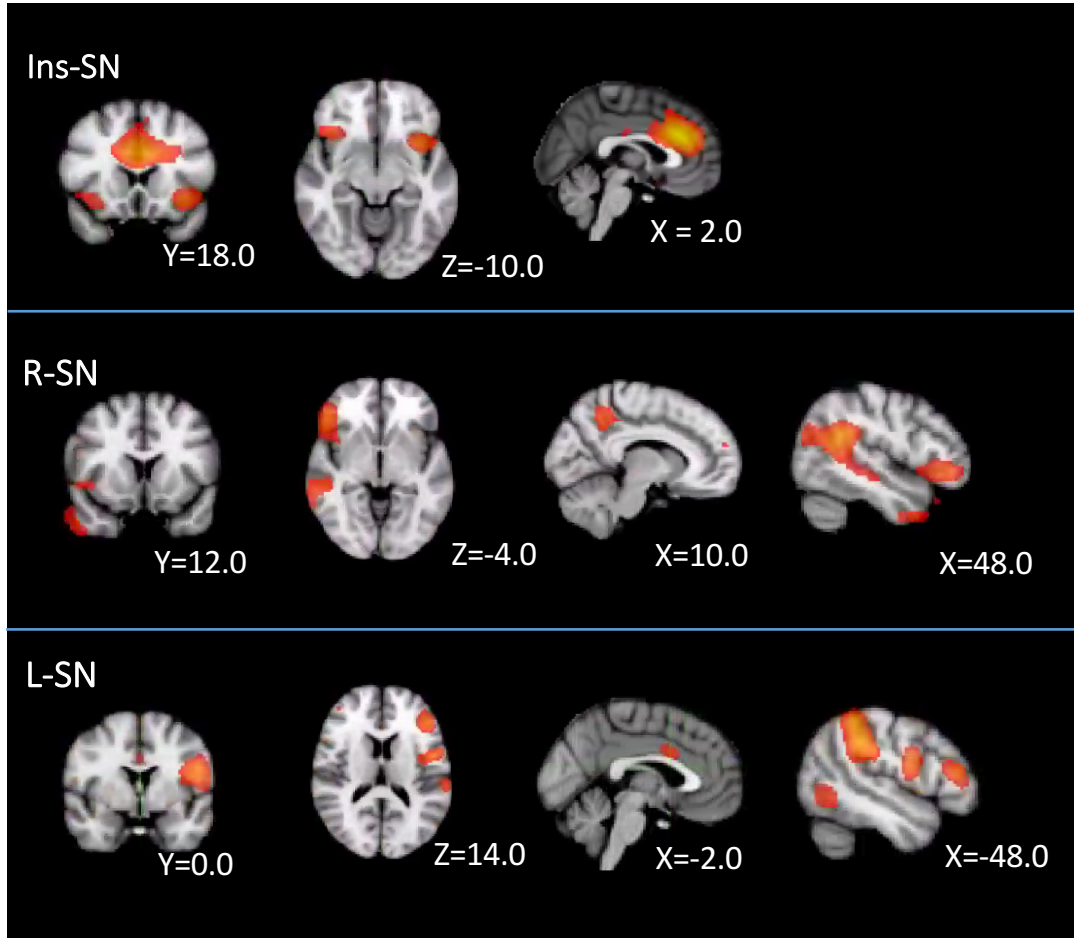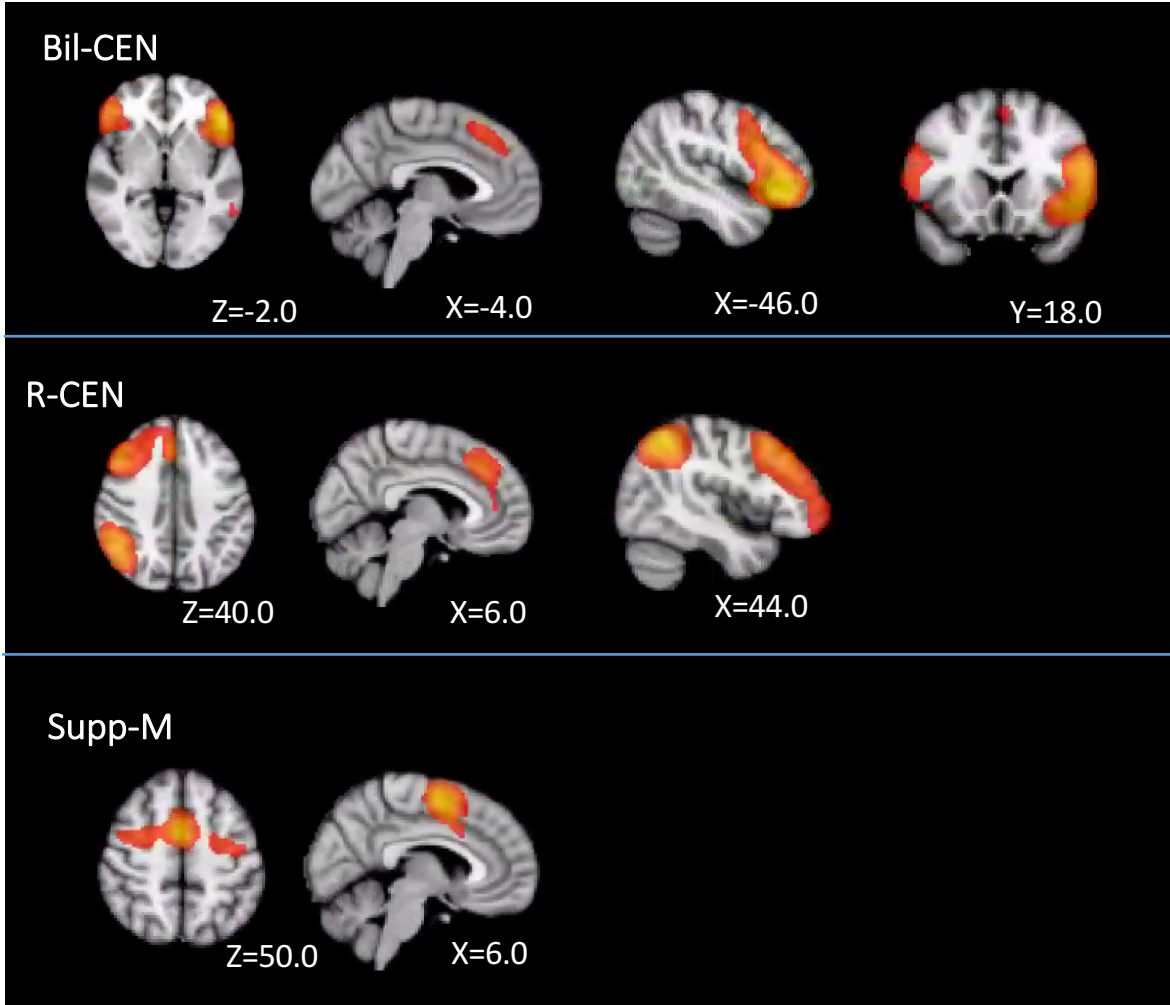

significant stim x group quadratic trend

significant stim x group linear trend

The Salience Network
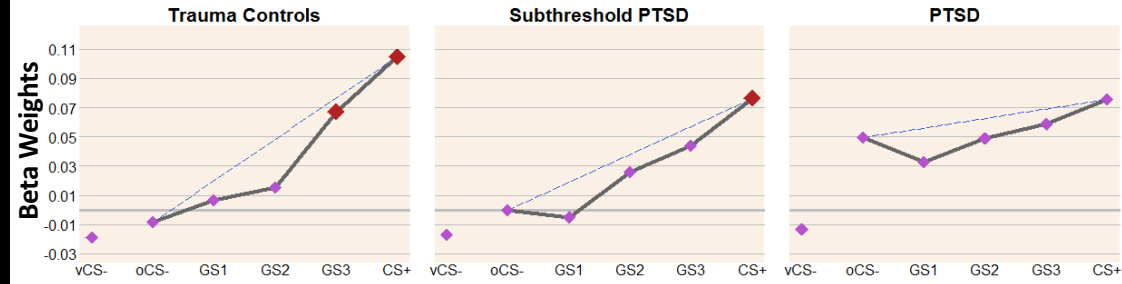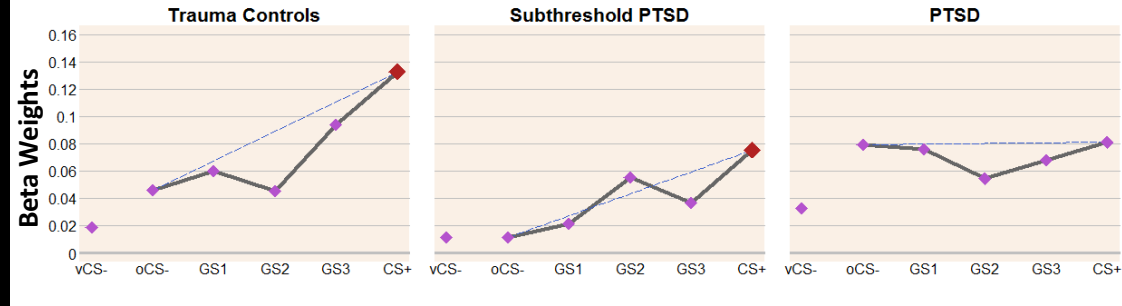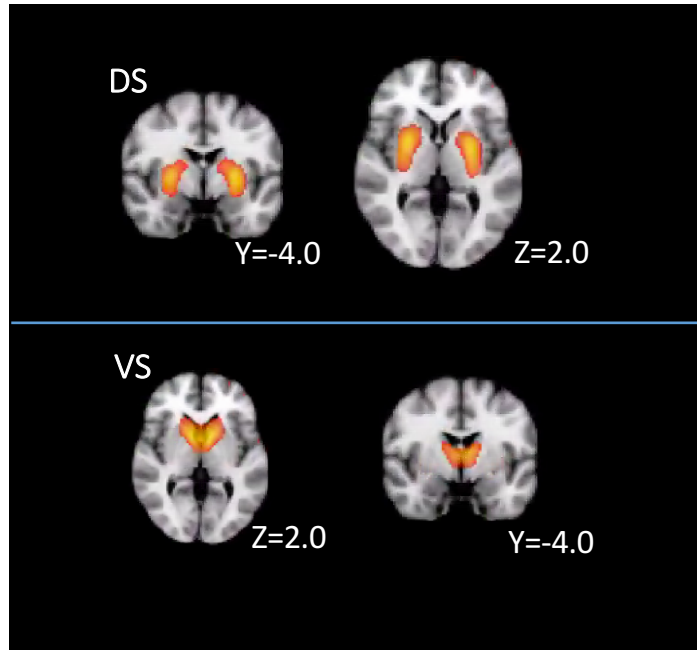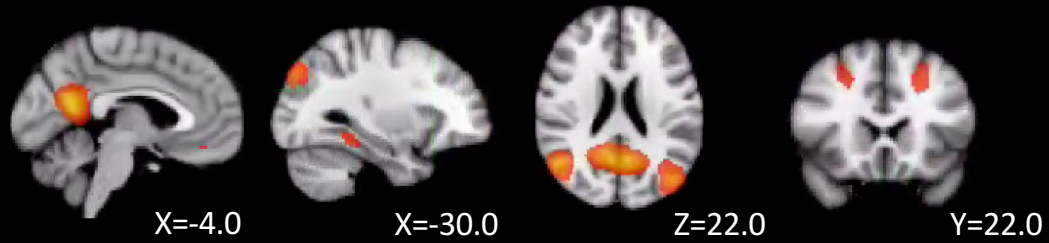

* significant stim x group linear trend
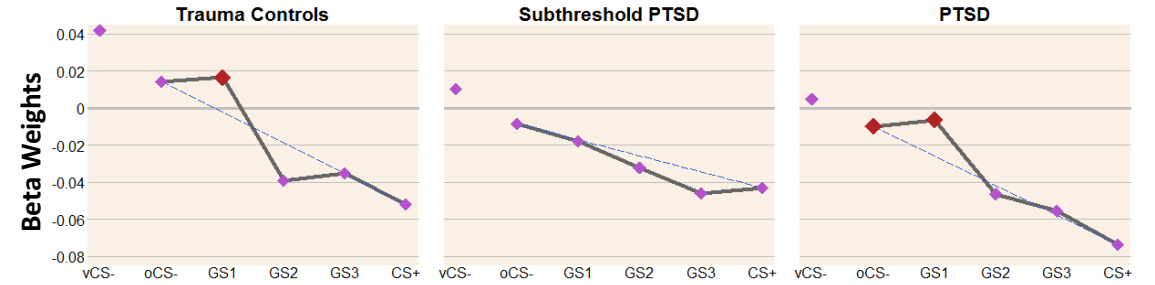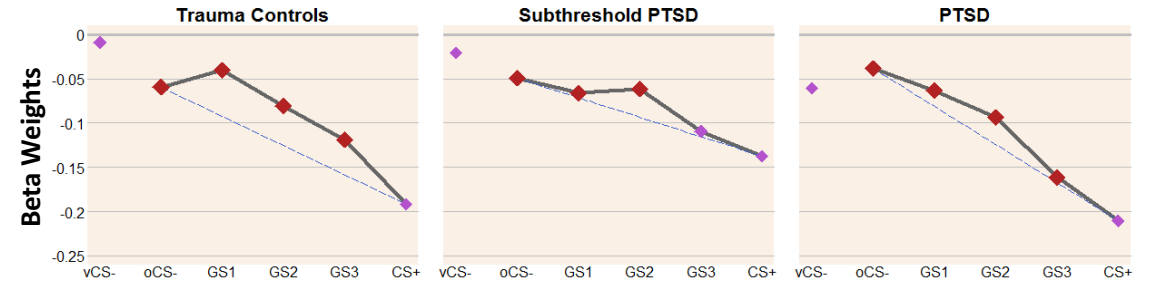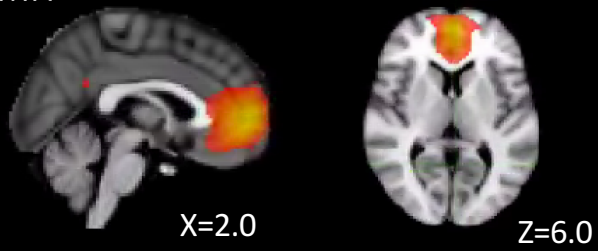
The Central Executive Network
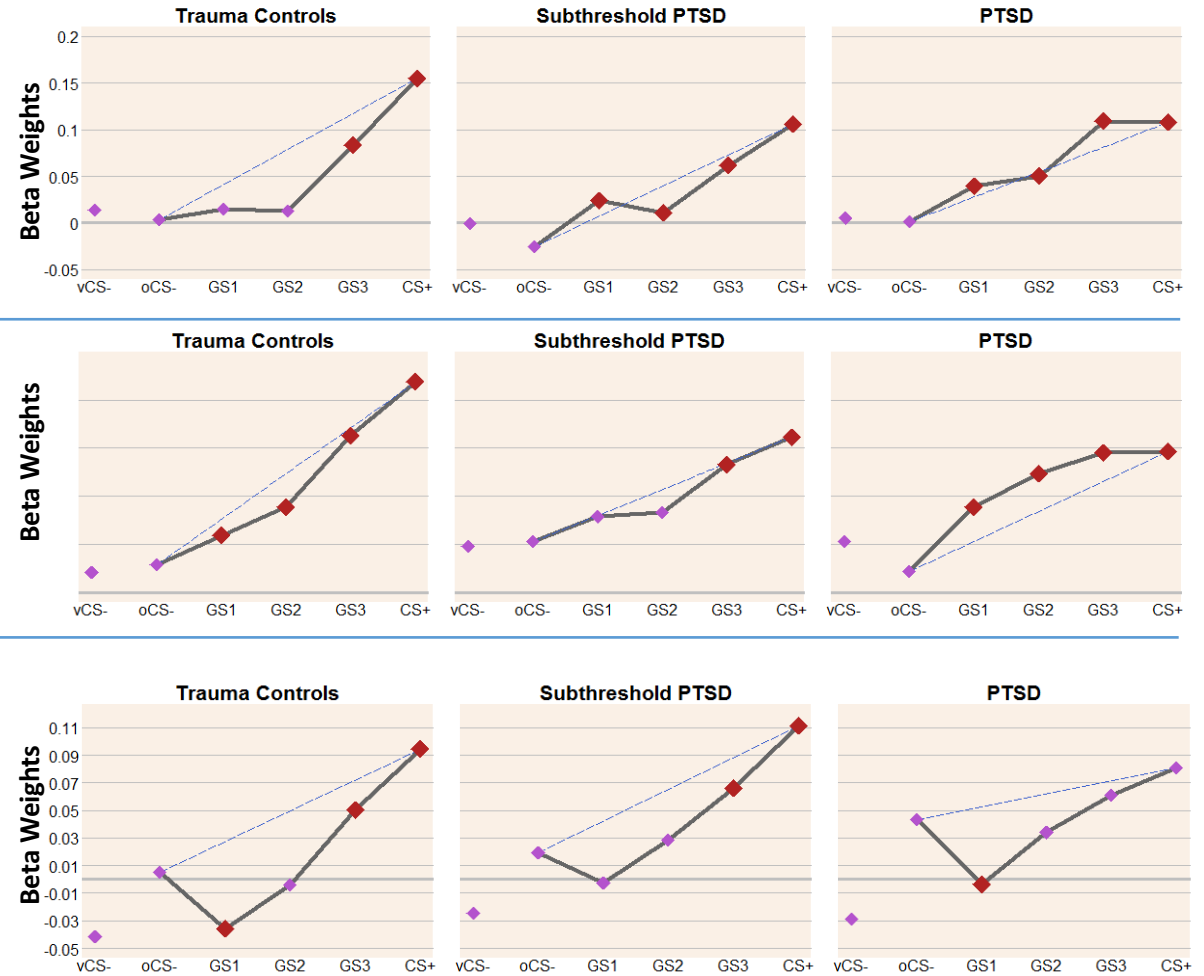
* significant stim x group quadratic trend
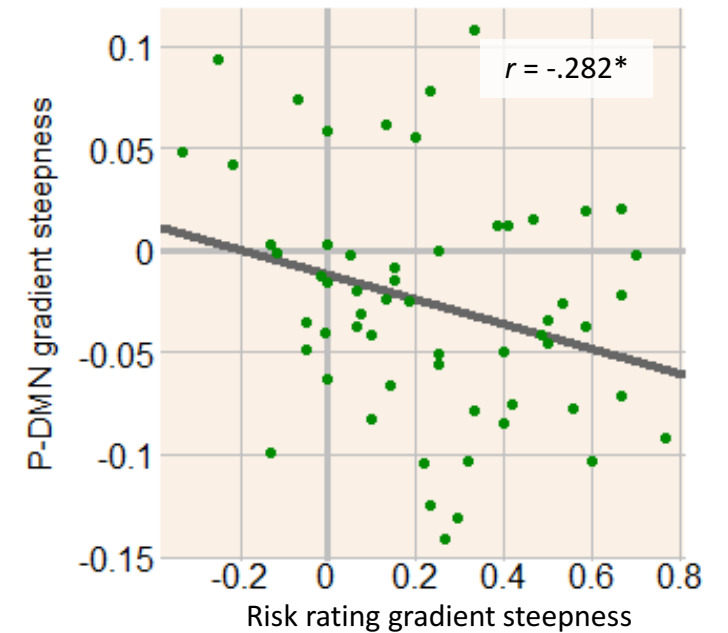
The Default Mode Network

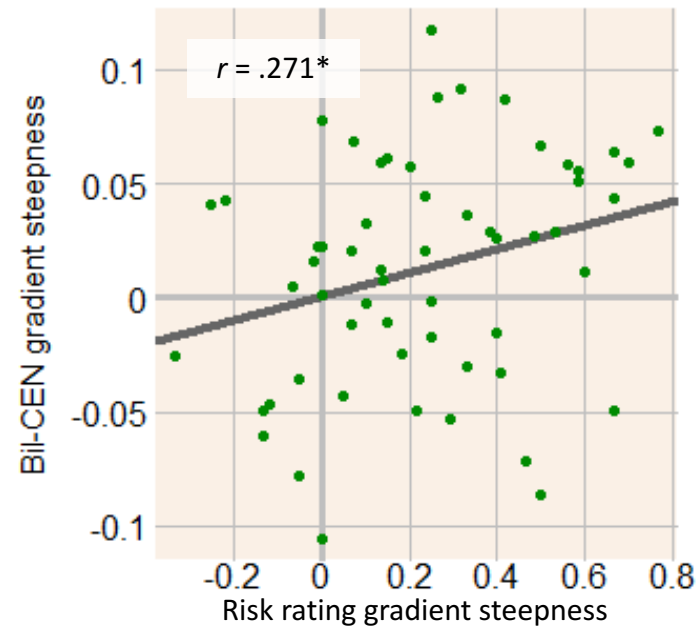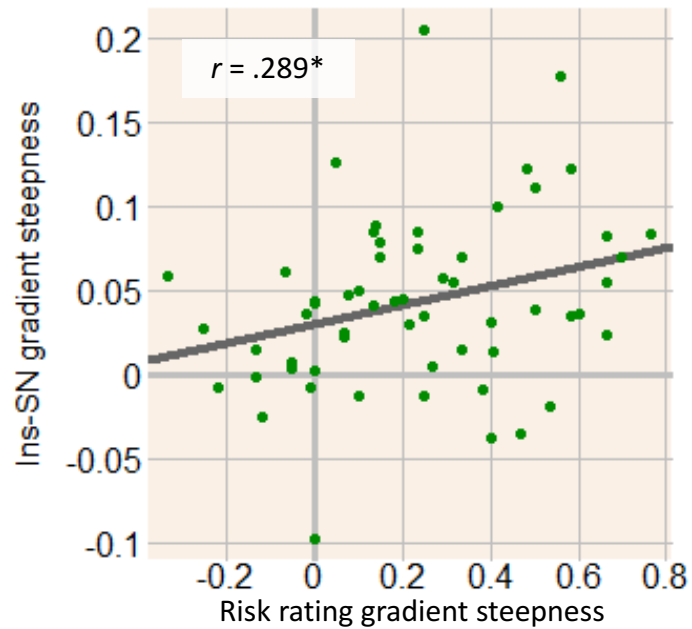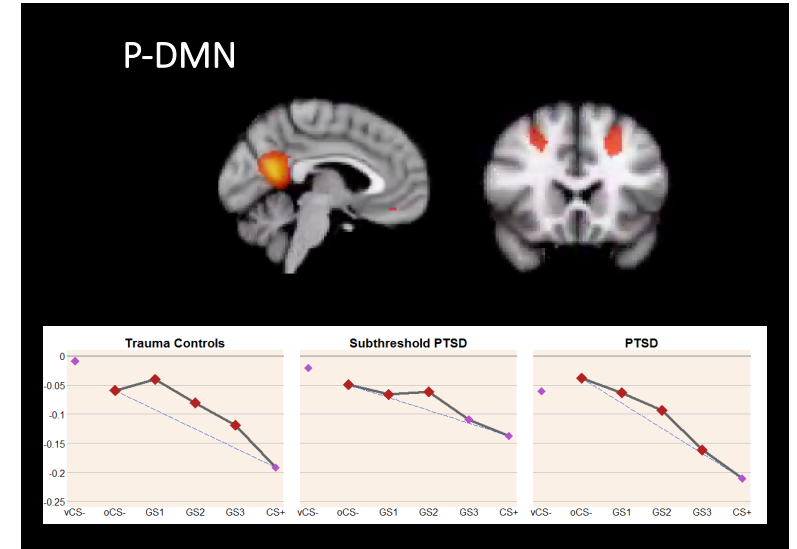# Tracking Perceived Risk
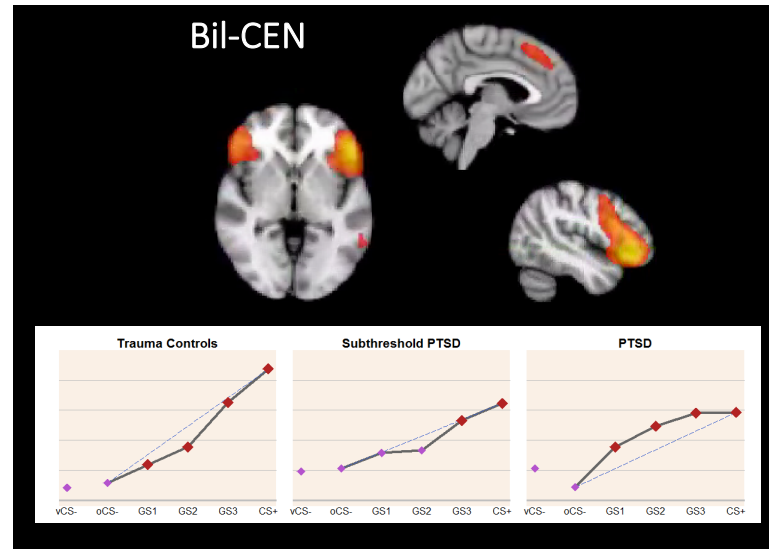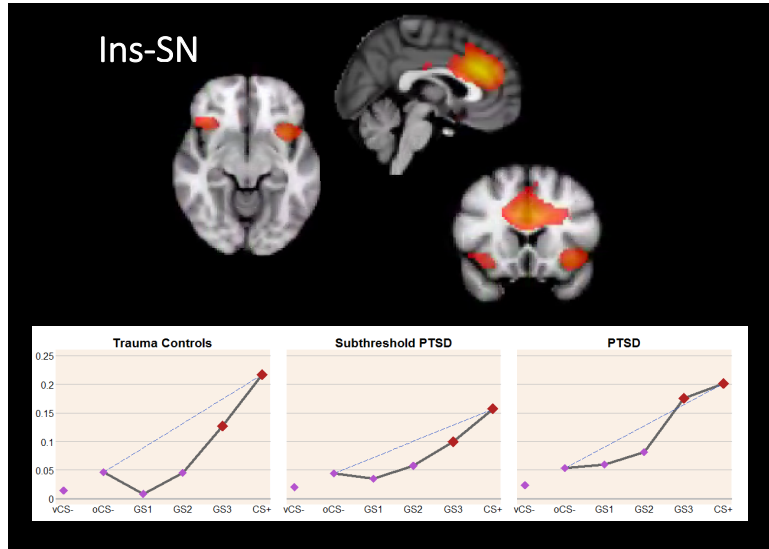
Tracking Symptom Severity
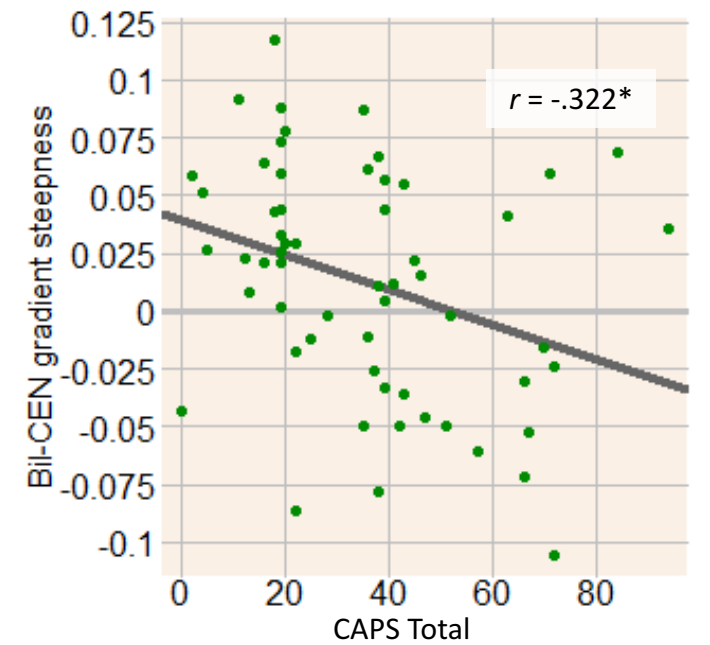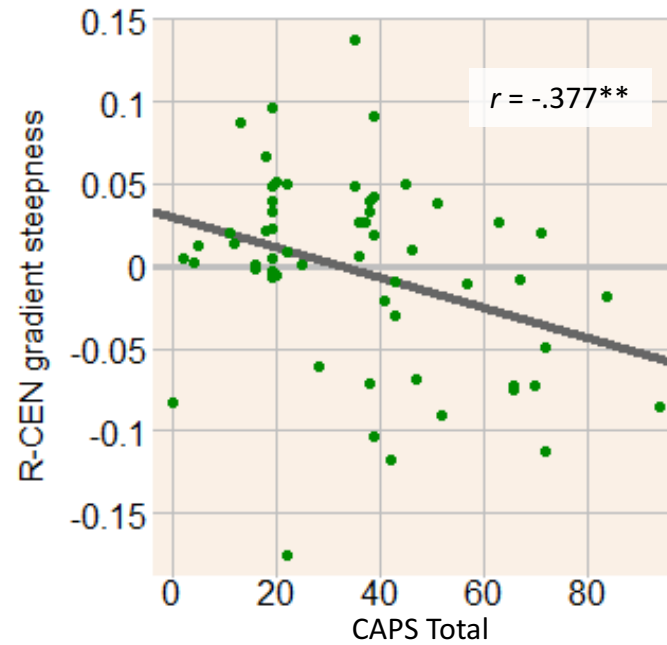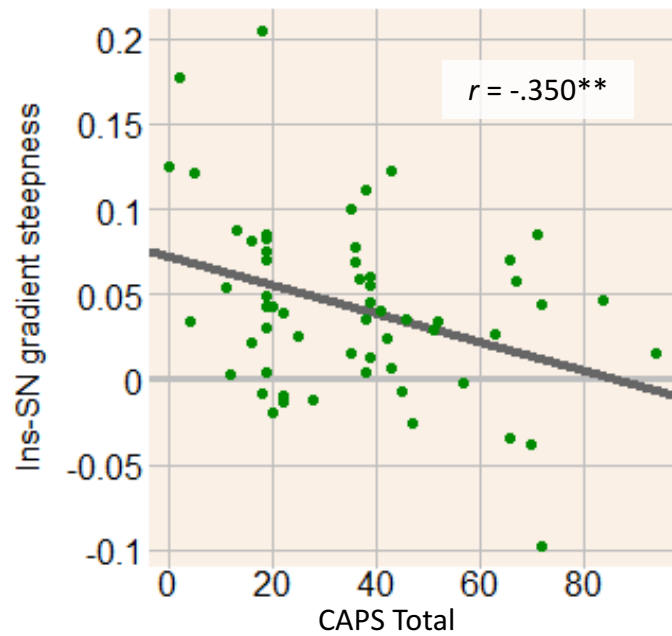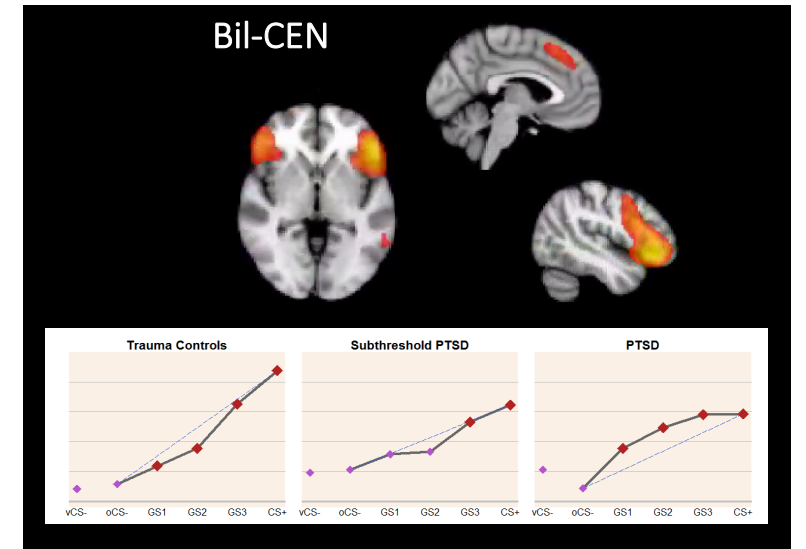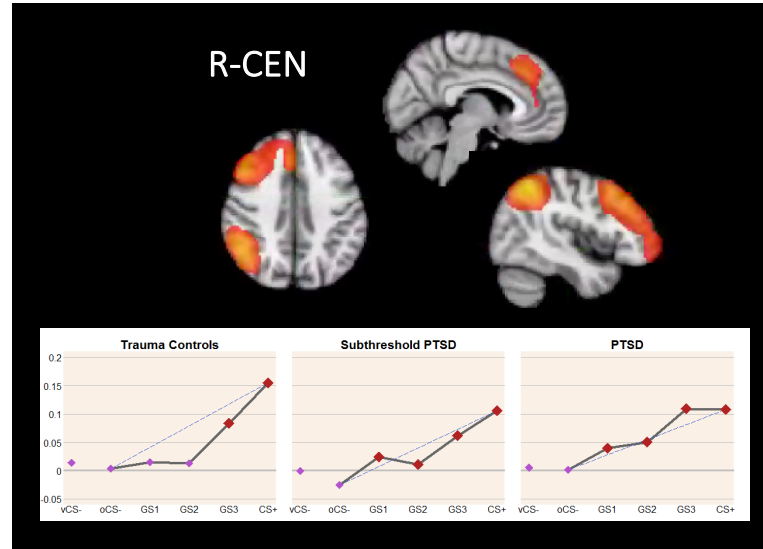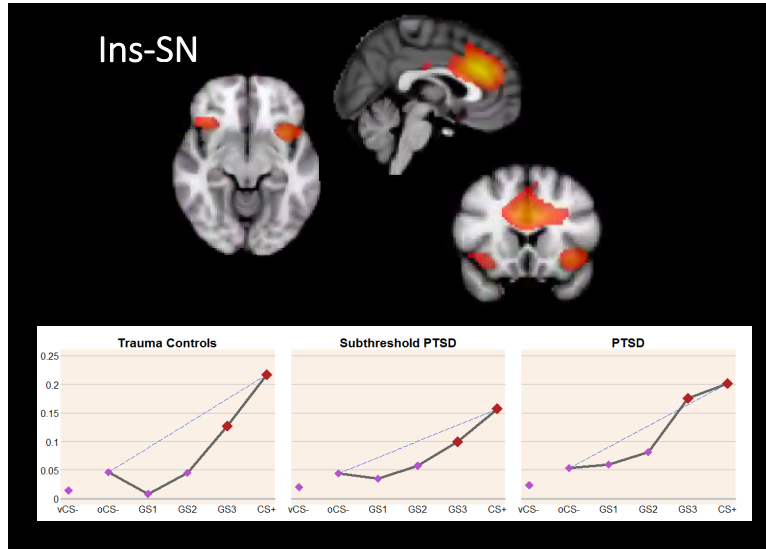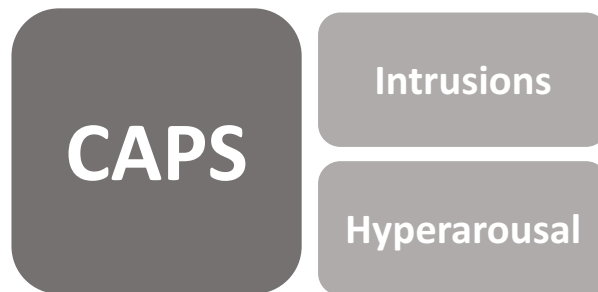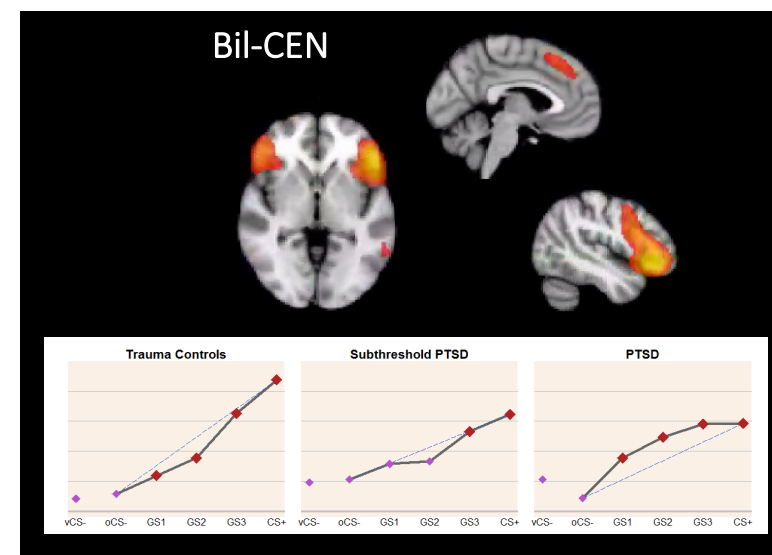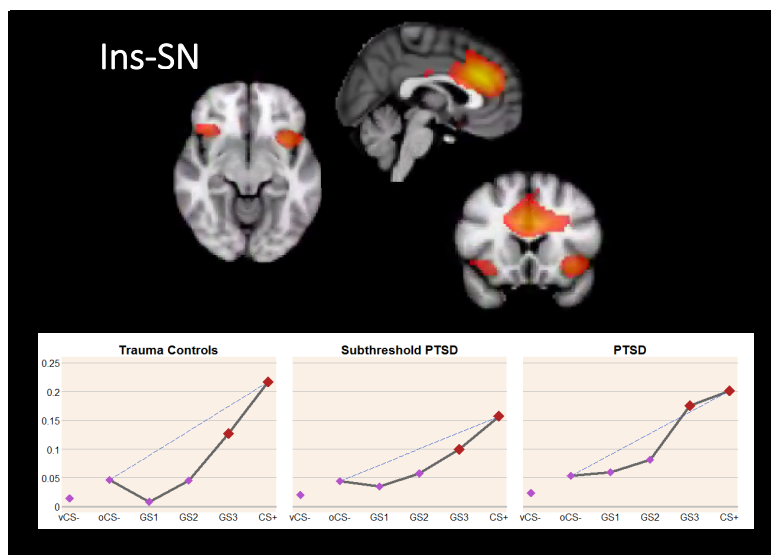
SN-CEN Connectivity

SN-CEN Connectivity
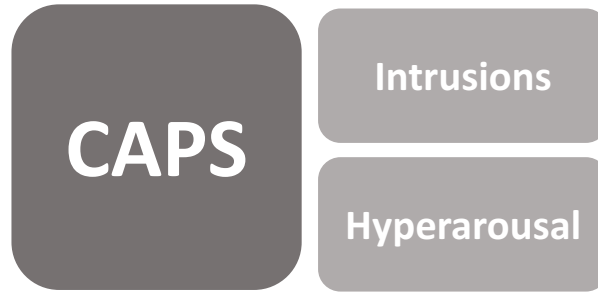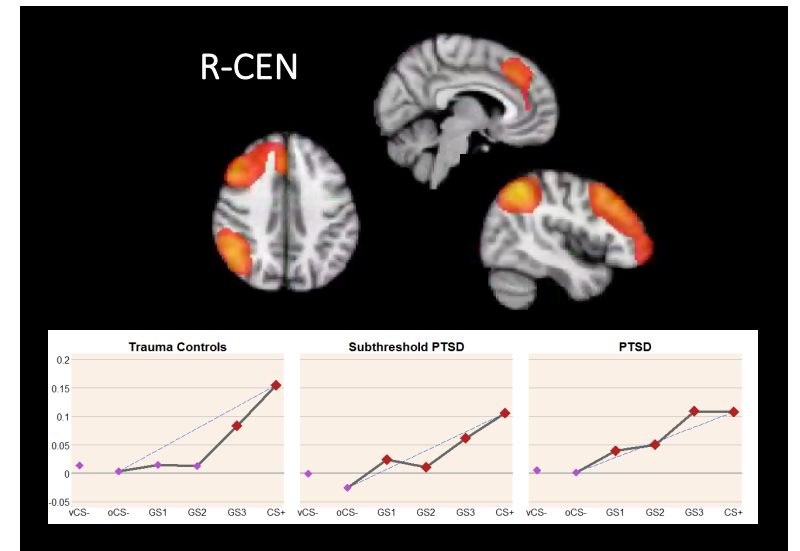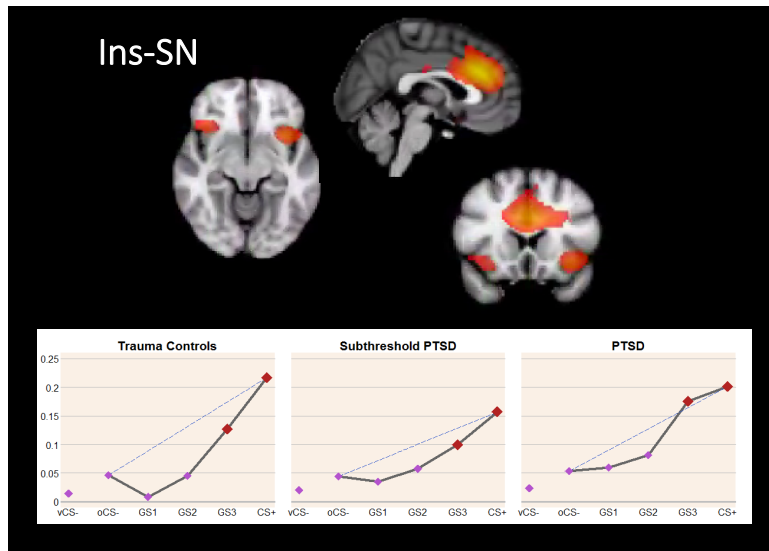
Return to the Triple-Network Theory

Salience Network

Codes for overgeneralization of perceived risk

Shows overgeneralization of threat response

Hyperconnectivity during generalization

Central Executive Network

Codes for overgeneralization of perceived risk

Shows overgeneralization of threat response

Default Mode Network

Codes for overgeneralization of perceived risk
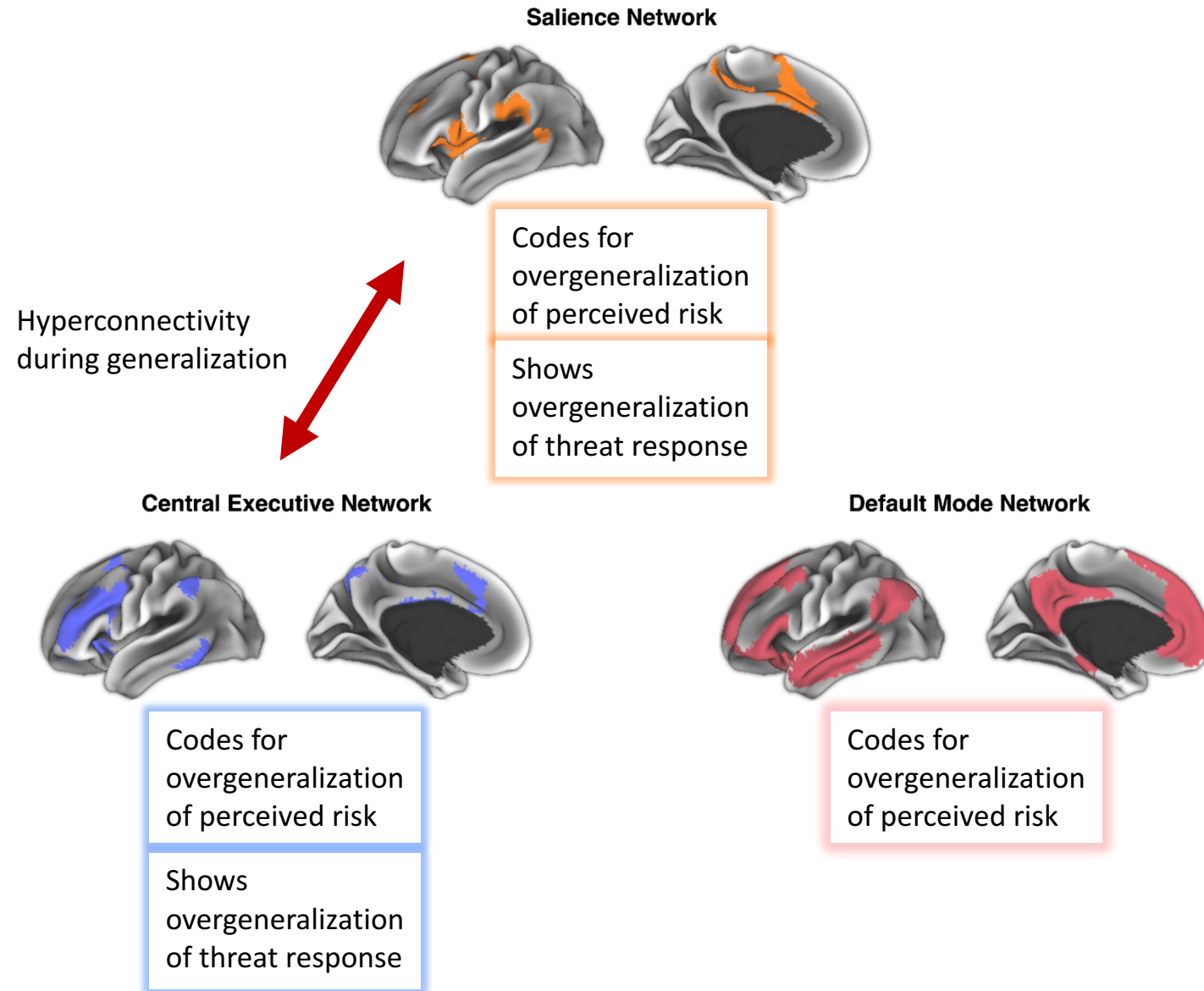
(adapted from Akiki et al. 2017, *Curr Psychiatry Rep*)

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