

Acute Posttrauma Resting-State Functional Connectivity of Periaqueductal Gray Prospectively Predicts Posttraumatic Stress Disorder Symptoms

Supplemental Information

Altered bilateral PAG connectivity prospectively predicted symptom clusters

After adjusting for MR scanner and two-week post-trauma physical pain ratings, acute post-trauma bilateral PAG RSFC predicted six-month post-trauma hyperarousal, intrusive, and avoidance scores. Results of multiple regression analyses examining PAG RSFC are reported in Table S1. Greater PAG RSFC with the PCC (-2, -52, 22; cluster size $k = 140$; $t(45) = 4.75$, $pFDR = .004$), frontal pole (0, 68, -0; cluster size $k = 102$; $t(45) = 4.46$, $pFDR = .009$), and lateral occipital cortex (-42, -78, 44; cluster size $k = 111$; $t(45) = 6.24$, $pFDR = .008$) predicted hyperarousal scores. However, decreased bilateral PAG RSFC with the supramarginal gyrus (-52, -36, 34; cluster size $k = 102$; $t(45) = 5.08$, $pFDR = .019$) and superior/inferior parietal lobule (-30, -42, 50; cluster size $k = 78$; $t(45) = 4.12$, $pFDR = .036$) also predicted hyperarousal symptoms.

Avoidance scores were also predicted by greater PAG connectivity with the PCC (-8, -58, 36; cluster size $k = 140$; $t(45) = 4.91$, $pFDR = .002$) and the frontal pole (0, 68, 0; cluster size $k = 99$; $t(45) = 5.49$, $pFDR = .007$). However, weaker connectivity with the superior parietal lobule predicted avoidance scores (-42, -50, 58; cluster size $k = 143$; $t(45) = 4.31$, $pFDR = .002$). Greater connectivity with the PCC (-2, -50, 34; cluster size $k = 215$; $t(45) = 4.31$, $pFDR < .001$), frontal pole/ventromedial prefrontal cortex (-2, 66, -2; cluster size $k = 78$; $t(45) = 5.12$, $pFDR = .020$), and the lateral occipital cortex (-42, -78, 44; cluster size $k = 138$; $t(45) = 6.58$, $pFDR = .001$) predicted intrusive symptoms.

Overall, similar PAG RSFC predicted total symptoms and all three symptom clusters. Considering the three subscales influence the total PTSD symptom score (and were highly intercorrelated), significant overlap between regions was expected. However, greater PAG-lateral occipital cortex connectivity predicted only hyperarousal symptoms and intrusive symptoms. Previous research indicates higher-order sensory areas (e.g., lateral occipital cortex) are increasingly recruited to process threatening information in PTSD (1, 2, 3, 4).

Table S1. Altered bilateral PAG functional connectivity associated with posttraumatic symptom clusters.

Contrast	Symptom(s)	Brain Region	No. of voxels	$t_{(45)}$	$p_{FDR-corrected}$	Peak Coordinates (MNI)		
						X	Y	Z
<i>Positive</i>	Hyperarousal	PCC	140	4.75	.004	-2	-52	22
		Frontal Pole	102	4.46	.009	0	68	-6
		LOC	111	6.24	.008	-42	-78	44
	Avoidance	Frontal Pole	99	5.49	.007	0	68	0
		PCC	140	4.91	.002	-8	-58	36
	Intrusive	PCC	215	4.31	<.001	-2	-50	34
		Frontal Pole	78	5.12	.020	-2	66	-2
		LOC	138	6.58	.001	-42	-78	44
	<i>Negative</i>	Hyperarousal	SMG	102	5.08	.019	-52	-36
SPL/IPL			78	4.12	.036	-30	-42	50
Avoidance		SPL	143	4.31	.002	-42	-50	58

Note. PCC, posterior cingulate cortex; LOC, lateral occipital cortex; SMG, supramarginal gyrus. SPL, superior parietal lobule; IPL, inferior parietal lobule.

Supplemental References

1. Schultz, D. H., Balderston, N. L., Geiger, J. A., & Helmstetter, F. J. (2013). Dissociation between implicit and explicit responses in postconditioning UCS revaluation after fear conditioning in humans. *Behavioral neuroscience*, *127*(3), 357.
2. Bingel, U., Rose, M., Gläscher, J., & Büchel, C. (2007). fMRI reveals how pain modulates visual object processing in the ventral visual stream. *Neuron*, *55*(1), 157-167.
3. Morey, R. A. et al. (2015). Fear learning circuitry is biased toward generalization of fear associations in posttraumatic stress disorder. *Translational psychiatry*, *5*(12), e700.
4. Sun, D., Phillips, R. D., Mulready, H. L., Zablonki, S. T., Turner, J. A., Turner, M. D., et al. (2019). Resting-state brain fluctuation and functional connectivity dissociate moral injury from posttraumatic stress disorder. *Depression and Anxiety*, *36*(5), 442-452.