Supplemental Methods and Results for

Mapping neural circuit biotypes to symptoms and behavioral dimensions of depression and anxiety

Authors: Andrea N Goldstein-Piekarski†[1, 2], Tali M Ball†[1], Zoe Samara‡[1], Brooke R Staveland‡[1], Arielle S. Keller‡[1,4], Scott L Fleming‡[1,3], Katherine A Grisanzio‡[1], Bailey Holt-Gosselin[1]‡, Patrick Stetz[1,2]‡, Jun Ma[5,6]‡ & Leanne M Williams*[1,2]

† These authors contributed equally to this work as first authors

‡ These authors contributed equally to this work

* Corresponding author

Leanne M. Williams
Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine Stanford, CA 94305, USA

Telephone: 650-723-3579

Email: leawilliams@stanford.edu

Affiliations:

[1] Psychiatry and Behavioral Sciences, Stanford University, Stanford, CA, USA

[2] Sierra-Pacific Mental Illness Research, Education, and Clinical Center (MIRECC) Veterans Affairs Palo Alto Health Care System, Palo Alto, CA, USA

[3] Biomedical Informatics, Stanford University, Stanford, CA, USA

[4] Graduate Program in Neurosciences, Stanford University, Stanford, CA, USA

[5] Department of Medicine, University of Illinois at Chicago

[6] Institute for Health Research and Policy, University of Illinois at Chicago

Table S3A. Circuit definitions, regions, z values, and coordinates for task-free circuits

Default Mode Circuit						
Circuit Type			**Condition**		**Task Contrast**	**Neurosynth Search criteria**
Intrinsic			Task-free		---	Term="default mode"; "resting state" Number of studies=516; 825 Search Date=6.4.17
Defines hypothesized dysfunction?	**Region label**	**Region anatomy: Full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Template coordinates and definitions**
Yes	D1	anterior medial PreFrontal Cortex	amPFC (BA 10)	M	22.0	-2, 50, -6
Yes	D2	Angular Gyrus	AG (BA 39)	L	26.1	-46, -70, 32
Yes	D3	Angular Gyrus	AG (BA 39)	R	20.6	50, -62, 26
Yes	D4	Posterior Cingulate	PCC	M	29.8	0, -50, 28
No	D5	dorsal Anterior Cingulate	dACC (BA 32)	M	12.1	2, 16, 44
No	D6	dorsomedial Prefrontal Cortex	dmPFC (BA 9)	M	12.8	-2, 54, 28
No	D7	Mid-Temporal Gyrus	MTG (BA 21)	L	15.0	-60, -14, -16
No	D8	Anterior Insula	AI	L	12.4	-34, 22, 2
No	D9	Anterior Insula	AI	R	12.8	34, 22, -2
No	D10	Hippocampus	HC	L	11.3	AAL
No	D11	Hippocampus	HC	R	10.6	AAL
No	D12	Thalamus	Thal	R	9.8	AAL
No	D13	Caudate nucleus	CdN	R	6.9	AAL
Salience Circuit						
Circuit Type			**Condition**		**Task Contrast**	**Neurosynth Search criteria**
Intrinsic			Task-free		---	Terms="salience network"; "salience" Number of studies=60; 269 Search Date=6.4.17
Defines hypothesized dysfunction?	**Region label**	**Region anatomy: Full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Template coordinates and definitions**
Yes	S1	Anterior Insula	AI	L	11.9	-38, 14, -6
Yes	S2	Anterior Insula	AI	R	14.8	38, 18, 2
Yes	S3	Amygdala	Amy	L	6.9	AAL
Yes	S4	Amygdala	Amy	R	14.7	AAL
No	S5	dorsal Anterior Cingulate	dACC (BA 24)	M	10.9	6, 26, 28
No	S6	Angular Gyrus	AG (BA 39)	L	10.9	-48, -64, 32
No	S7	Thalamus	Thal	L	6.9	AAL
Attention Circuit						
Circuit Type			**Condition**		**Task Contrast**	**Neurosynth Search criteria**
Intrinsic			Task-free		---	Terms="frontoparietal network"; "attention" Number of studies=1447; 79 Search Dat=6.4.17
Defines hypothesized dysfunction?	**Region label**	**Region anatomy: Full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Template coordinates and definitions**
Yes	A1	medial superior PreFrontal Cortex	msPFC (BA 6)	M	10.4	-2, 14, 52
Yes	A2	Lateral PreFrontal Cortex	LPFC (BA 9)	L	13.9	-44, 6, 32
Yes	A3	Lateral PreFrontal Cortex	LPFC (BA 9)	R	11.3	50, 10, 28
Yes	A4	anterior Inferior Parietal Lobule	aIPL (BA 40)	L	10.4	-30, -54, 40
Yes	A5	anterior Inferior Parietal Lobule	aIPL (BA 40)	R	10.4	38, -56, 48
Yes	A6	Precuneus	PCUN (BA 7)	L	13.0	-14, -66, 52
Yes	A7	Precuneus	PCUN (BA 7)	R	11.3	18, -68, 52
No	A8	Frontal Eye Fields	FEF	R	13.9	26, 0, 52
No	A9	Anterior Insula	AI	R	12.2	34, 22, -2

Notes: Z-scores and coordinates refer to peaks of meta-analytic Z values. Coordinates are in MNI atlas space and subcortical regions are defined by overlap with the AAL or FSL atlas.

Abbreviations: AAL = Automated Anatomical Labeling Atlas; FSL = FMRIB Software Library; MNI = Montreal Neurological Institute; BA = Brodmann Area; L = Left; R = Right; M = Medial

Table S3B. Circuit definitions, regions, z values, and coordinates for task-evoked circuits

Negative Affect Circuit: Sad						
Circuit Type		**Condition**			**Task Contrast**	**Neurosynth Search Criteria**
Task-evoked		Conscious Facial Emotion Viewing			Sad vs Neutral evoked by facial emotion stimuli	Term"threat" Number of studies=170 Search Date6.4.17
Defines hypothesized dysfunction?	**Region label**	**Regional anatomy: full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Coordinates**
Yes	N1	pregenual Anterior Cingulate	pgACC	M	6.3	6, 42, 4
Yes	N2	Anterior Insula	AI	L	17.4	-36, 20, -4
Yes	N3	Anterior Insula	AI	R	16.1	38, 22, -4
Yes	N4	Amygdala	Amy	L	28.4	AAL
Yes	N5	Amygdala	Amy	R	25.2	AAL
No	N6	dorsal Anterior Cingulate	dACC (BA32)	M	8.2	6, 22, 32
No	N7	dorsal Medial PreFrontal Cortex	dMPFC (BA6)	M	8.9	2, 2, 56
No	N8	Lateral PreFrontal Cortex/Inferior Frontal Gyrus	LPFC/IFG (BA44)	L	6.3	-46, 8, 28
No	N9	Lateral PreFrontal Cortex	LPFC (BA9)	R	6.3	34, 34, 24
No	N10	Precentral Gyrus	GPrC (BA4)	R	6.3	50, 6, 42
No	N11	Supramarginal Gyrus	SMG	R	6.3	54, -44, 34
No	N12	Fusiform Gyrus	FFG	L	7.6	-44, -54, -18
No	N13	Fusiform Gyrus	FFG	R	8.2	42, -48, -16
Negative Affect Circuit: Threat						
Circuit Type		**Condition**			**Task Contrast**	**Neurosynth Search Criteria**
Task-evoked		Conscious or Nonconscious Facial Emotion Viewing			Fear/Anger vs Neutral evoked by facial emotion stimuli	Term"threat" Number of studies=170 Search Date6.4.17
Defines hypothesized dysfunction?	**Region label**	**Regional anatomy: full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Coordinates**
Yes	T1	dorsal Anterior Cingulate	dACC	M	8.2	6, 22, 32
Yes	T2	Amygdala	Amy	L	28.4	AAL
Yes	T3	Amygdala	Amy	R	25.2	AAL
No	T4	dorsal Medial l PreFrontal Cortex	dMPFC	R	8.9	2, 2, 56
No	T5	Inferior Frontal Gyrus	IFG	L	6.3	-46, 8, 28
No	T6	Lateral PreFrontal Cortex	LPFC	R	6.3	34, 34, 24
No	T7	Precentral Gyrus	GPrC (BA6)	R	6.3	50, 6, 42
No	T8	Supramarginal Gyrus	SMG	R	6.3	54, -44, 34
No	T9	Anterior Insula	AI	L	17.4	-36, 20, -4
No	T10	Anterior Insula	AI	R	16.1	38, 22, -4
No	T11	Fusiform Gyrus	FFG	L	7.6	-44, -54, -18
No	T12	Fusiform Gyrus	FFG	R	8.2	42, -48, -16
*	T13	subgenual Anterior Cingulate	sgACC	M		4, 26, -10
Positive Affect Circuit: Happy						
Circuit Type		**Condition**			**Task Contrast**	**Neurosynth Search Criteria**
Task-evoked		Conscious Facial Emotion Viewing			Happy vs Neutral evoked by facial emotion stimuli	Terms="monetary reward"; "reward" Number of studies=84; 671 Search Date = 6.4.17
Defines hypothesized dysfunction?	**Region label**	**Regional anatomy: full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Coordinates**
Yes	P1	ventral Medial Prefrontal Cortex	vMPFC (BA10)	M	13.1	-2, 56, -8
Yes	P2	Ventral Striatum	VS	L	14.0	FSL
Yes	P3	Ventral Striatum	VS	R	7.9	FSL

No	P4	dorsal Medial PreFrontal Cortex	dMPFC	M	14.4	4, 22, 44
No	P5	dorsal Anterior Cingulate	dACC	M	11.1	6, 34, 18
No	P6	Mid Cingulate Cortex	MACC (BA23)	M	12.1	2, -26, 32
No	P7	Precuneus	PCUN	L	6.9	-10, -56, 16
No	P8	dorsal Lateral PreFrontal Cortex/Inferior Frontal Gyrus	dLPFC/GFi (BA44)	L	9.8	-44, 6, 32
No	P9	dorsal Lateral PreFrontal Cortex/ Inferior Frontal Gyrus	dLPFC/GFi (BA9/44)	R	10.5	46, 28, 32
No	P10	dorsal Lateral PreFrontal Cortex/ Inferior Frontal Gyrus	dLPFC/GFi (BA44)	R	6.9	46, 8, 28
No	P11	dorsal Lateral PreFrontal Cortex/ Inferior Frontal Gyrus	dLPFC/GFi (BA46)	L	6.3	-48, 34, 8
No	P12	Superior Parietal Lobule	SPL (BA7)	L	9.5	-28, -58, 46
No	P13	anterior Inferior Parietal Lobule	aIPL (BA40)	L	6.9	-44, -38, 44
No	P14	anterior Inferior Parietal Lobule	aIPL (BA40)	R	7.9	46, -44, 48
No	P15	Medial PreFrontal Gyrus	GfM (BA6)	L	6.9	-28, -2, 52
No	P16	Anterior Insula	AI	L	20.8	-32, 22, 0
No	P17	Anterior Insula	AI	R	27.0	34, 22, -4
No	P18	Posterior Insula	PI	L	8.2	-40, -6, 4
No	P19	Amygdala	Amy	L	21.2	AAL
No	P20	Putamen	Pu	R	6.9	AAL
No	P21	Hippocampus	HC	R	6.9	AAL

Cognitive Control Circuit

Circuit Type	**Condition**	**Task Contrast**	**Neurosynth Search Criteria**
Task-evoked	Go-NoGo task	No-Go vs. Go	Terms="cognitive control" Number of studies = 428 Search Date = 6.4.17

Defines hypothesized dysfunction?	**Region label**	**Regional anatomy: full name**	**Region anatomy: Abbreviation**	**Left, Right, or Medial**	**Z Value**	**Template coordinates and definitions**
Yes	C1	dorsal Anterior Cingulate	dACC	M	20.0	0, 18, 46
Yes	C2	dorsal Lateral PreFrontal Cortex/Inferior Frontal Gyrus	dLPFC/GFi (BA44)	L	20.4	-44, 6, 32
Yes	C3	dorsal Lateral PreFrontal Cortex/ Inferior Frontal Gyrus	dLPFC/GFi (BA44)	R	12.4	44, 34, 22
No	C4	dorsal Anterior Cingulate	dACC	M	9.6	6, 30, 28
No	C5	Mid Cingulate Cortex	MCC (BA23)	M	12.8	2, -26, 30
No	C6	Precuneus	PCUN	L	7.5	-10, -70, 52
No	C7	dorsal Lateral PreFrontal Cortex/Middle Frontal Gyrus	dLPFC/GFd (BA6)	L	10.4	-28, -2, 56
No	C8	dorsal Lateral PreFrontal Cortex Inferior Frontal Gyrus	dLPFC/GFi (BA6/44)	R	18.0	46, 10, 32
No	C9	dorsal Lateral PreFrontal Cortex /Middle Frontal Gyrus	dLPFC/GFd (BA44)	R	7.5	34, -2, 52
No	C10	Inferior Parietal Lobule	IPL (BA19/40)	L	15.6	-30, -58, 44
No	C11	Inferior Parietal Lobule	IPL (BA40)	R	12.8	48, -46, 44
No	C12	Inferior Parietal Lobule	IPL (BA40)	L	11.2	-46, -44, 48
No	C13	Superior Parietal Lobule	SPL (BA7)	R	10.4	30, -60, 50
No	C14	Lateral PreFrontal Cortex/Superior Frontal Gyrus	LPFC/GFs (BA10)	L	7.1	-34, 46, 24
No	C15	Lateral PreFrontal Cortex/Superior Frontal Gyrus	LPFC/GFs (BA10)	R	8.3	34, 52, 8
No	C16	Fusiform Gyrus	FFG	L	7.1	-44, -60, -12
No	C17	Angular Gyrus	AG	L	6.3	-54, -62, 28
No	C18	Anterior Insula	AI	L	23.6	-34, 22, 0
No	C19	Anterior Insula	AI	R	30.5	34, 22, 0

No	C20	Caudate nucleus	CdN	L	8.3	AAL
No	C21	Caudate nucleus	CdN	R	11.2	AAL
No	C22	Amygdala	Amy	L	7.1	AAL

Notes: Z-scores and coordinates refer to peaks of meta-analytic Z values. Coordinates are in MNI atlas space and subcortical regions are defined by overlap with the AAL or FSL atlas.

Coordinates represent peaks as defined by decreasing the minimum cluster distance in the 3dCluster algorithm and the clusters are visualized in Figure S2.

*Region T13 (subgenual anterior cingulate) was used instead of T1 (dorsal anterior cingulate) for the non-conscious threat vs neutral contrast only. Although the subgenual anterior cingulate region did not meet our quality control metrics for temporal signal-to-noise ratio, given both the difficulty of imaging this region and its importance of this region to defining the negative affect circuit elicited by implicit threat stimuli and to prior imaging findings in depression, we report supplementary analyses including this region.

Abbreviations: AAL = Automated Anatomical Labeling Atlas; FSL = FMRIB Software Library; MNI = Montreal Neurological Institute; BA = Brodmann Area; L = Left; R = Right; M = Medial