Functional MRI Predictors of Posttrauma Psychiatric Symptom Trajectories

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EMORY

ATLANTA TRAUMA ALLIANCE

GRADY trauma PROJECT

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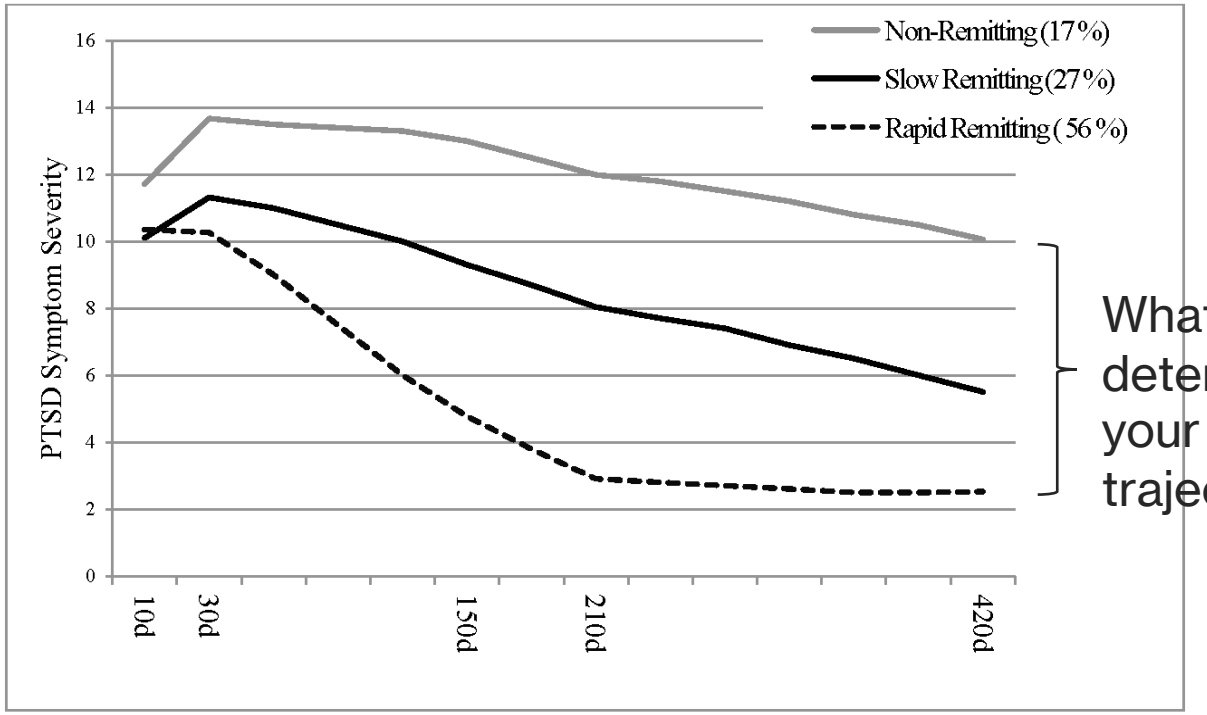
Trauma and mental health

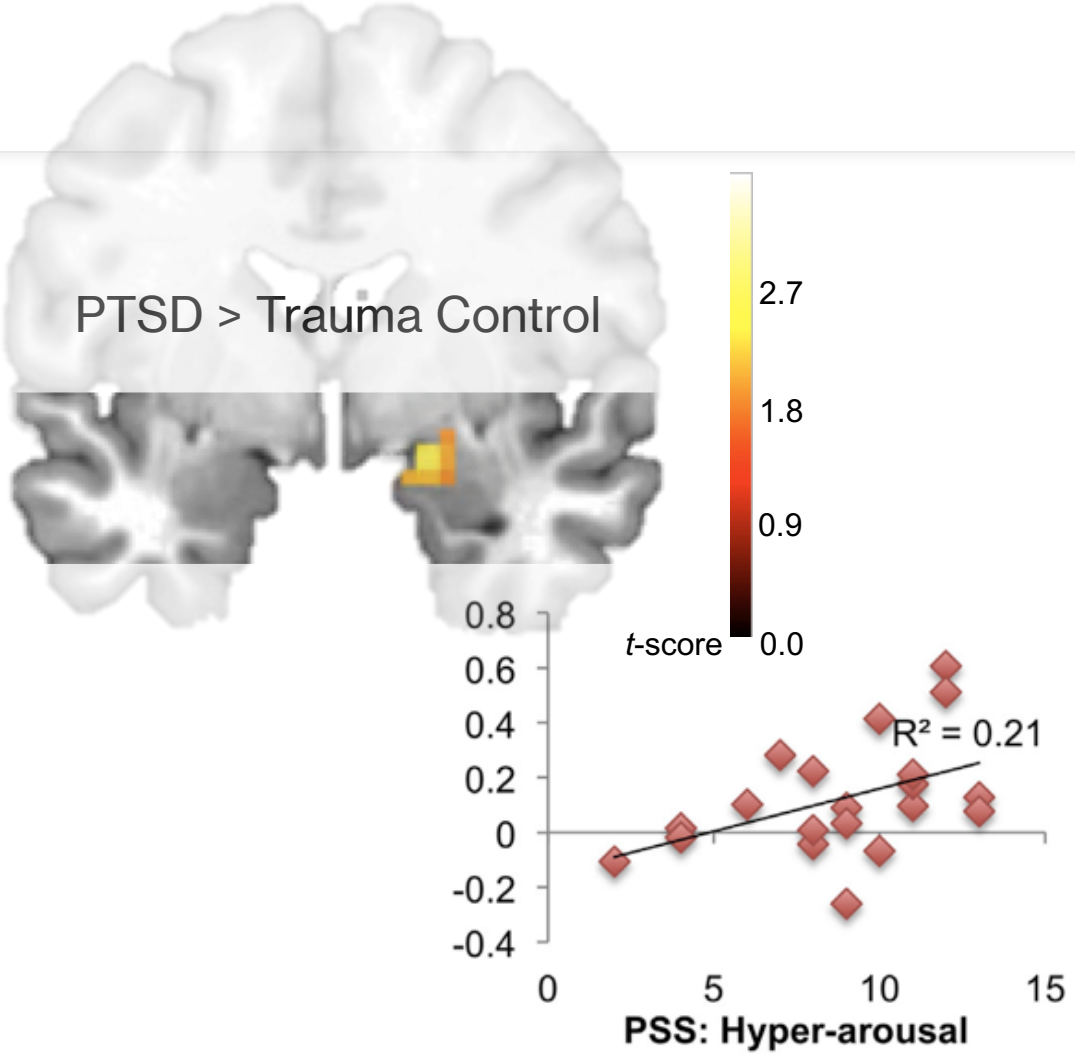


What factors determine your trajectory?

How do we change these factors to facilitate recovery?

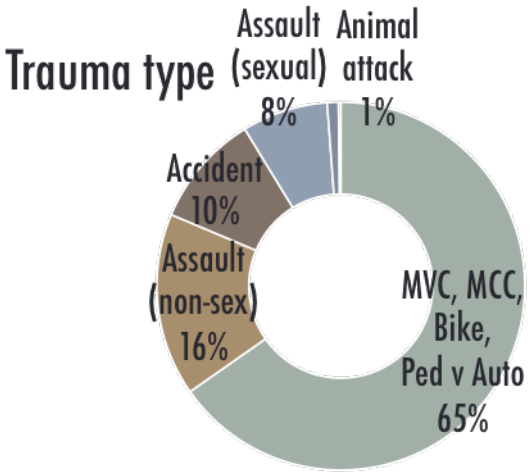
Galatzer-Levy et al. (2013) PONE

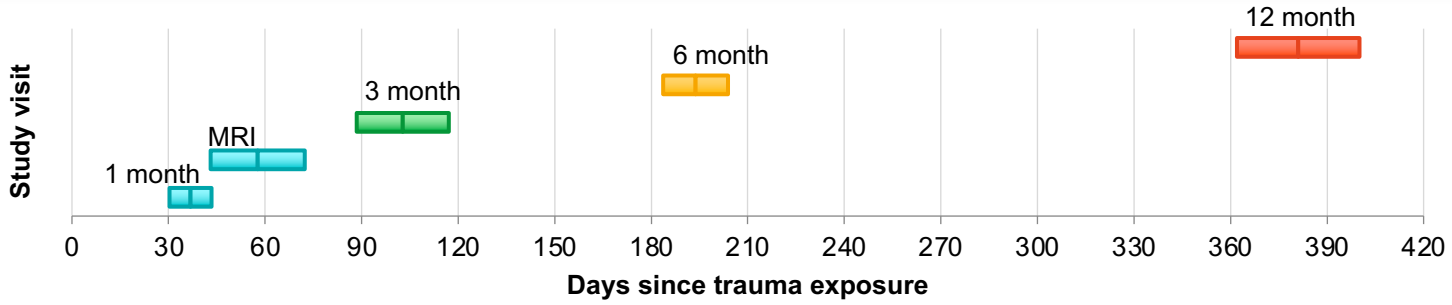
A simple example: The amygdala and heightened fear

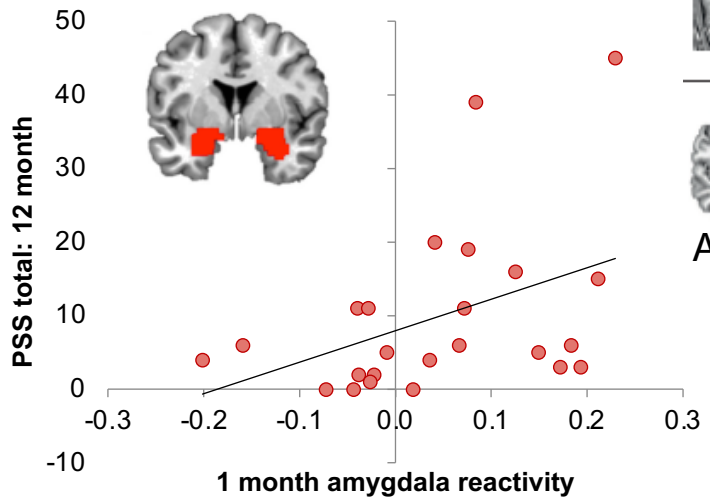


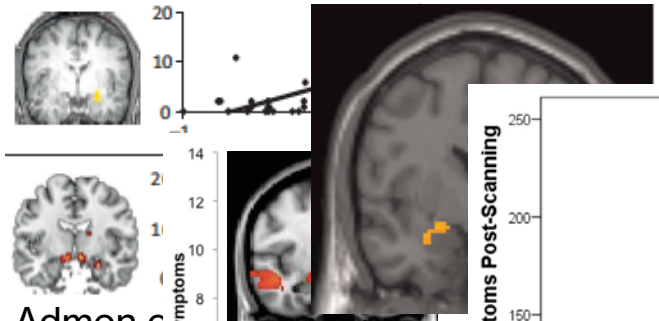
Stevens, Jovanovic... & Ressler (2013) *JPR*

Symptom of PTSD, or risk factor?



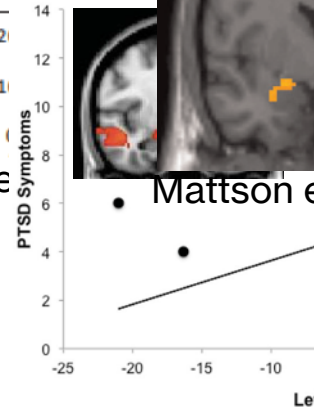




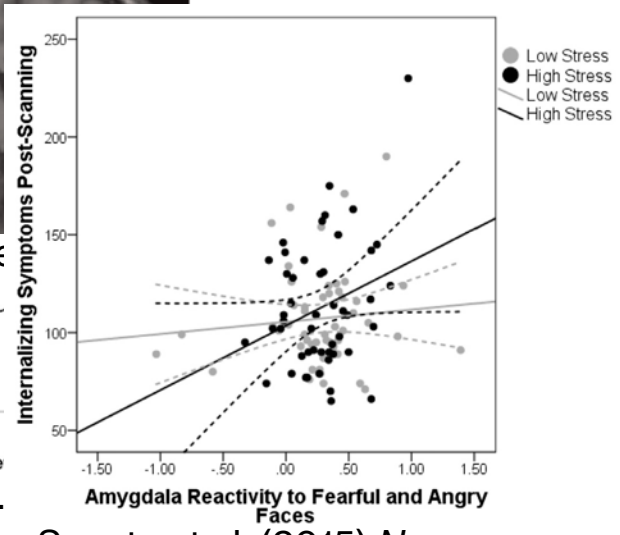


Admon e

Mattson e



McLaughlin et al.



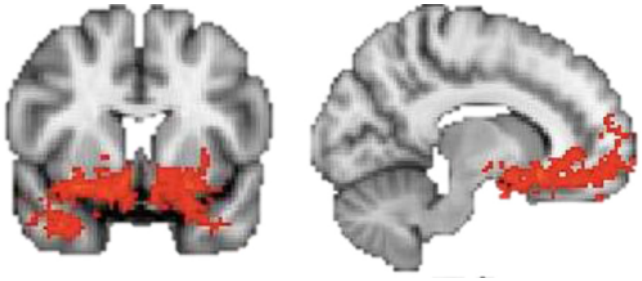
Swartz et al. (2015) *Neuron*

Stevens et al. (2017) *BPS*

Biological plausibility

What would convince us that this is real?

Structural pathway

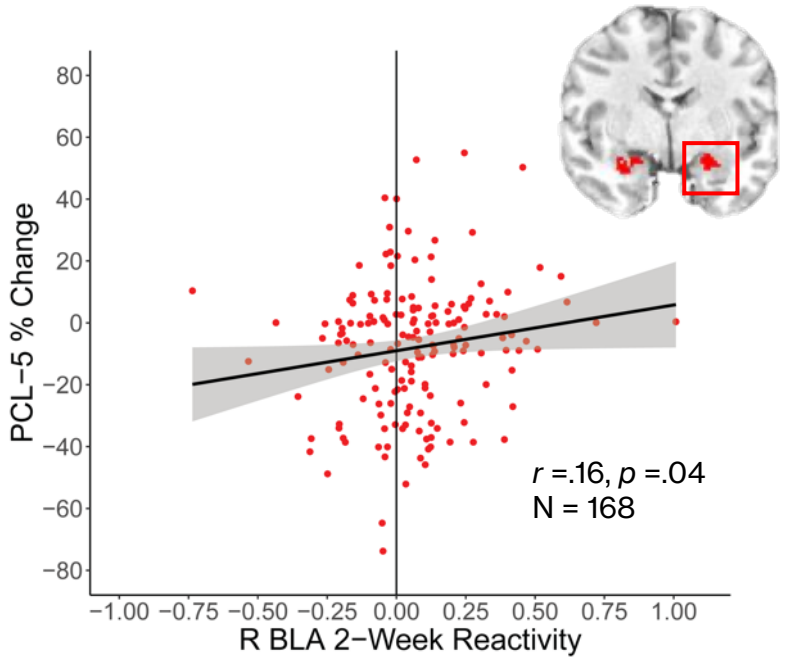


Fani... & Stevens (2019) *J Psyc Research*

Convergent peripheral biomarker

Hinrichs... & Jovanovic (2019) *Chronic Stress*

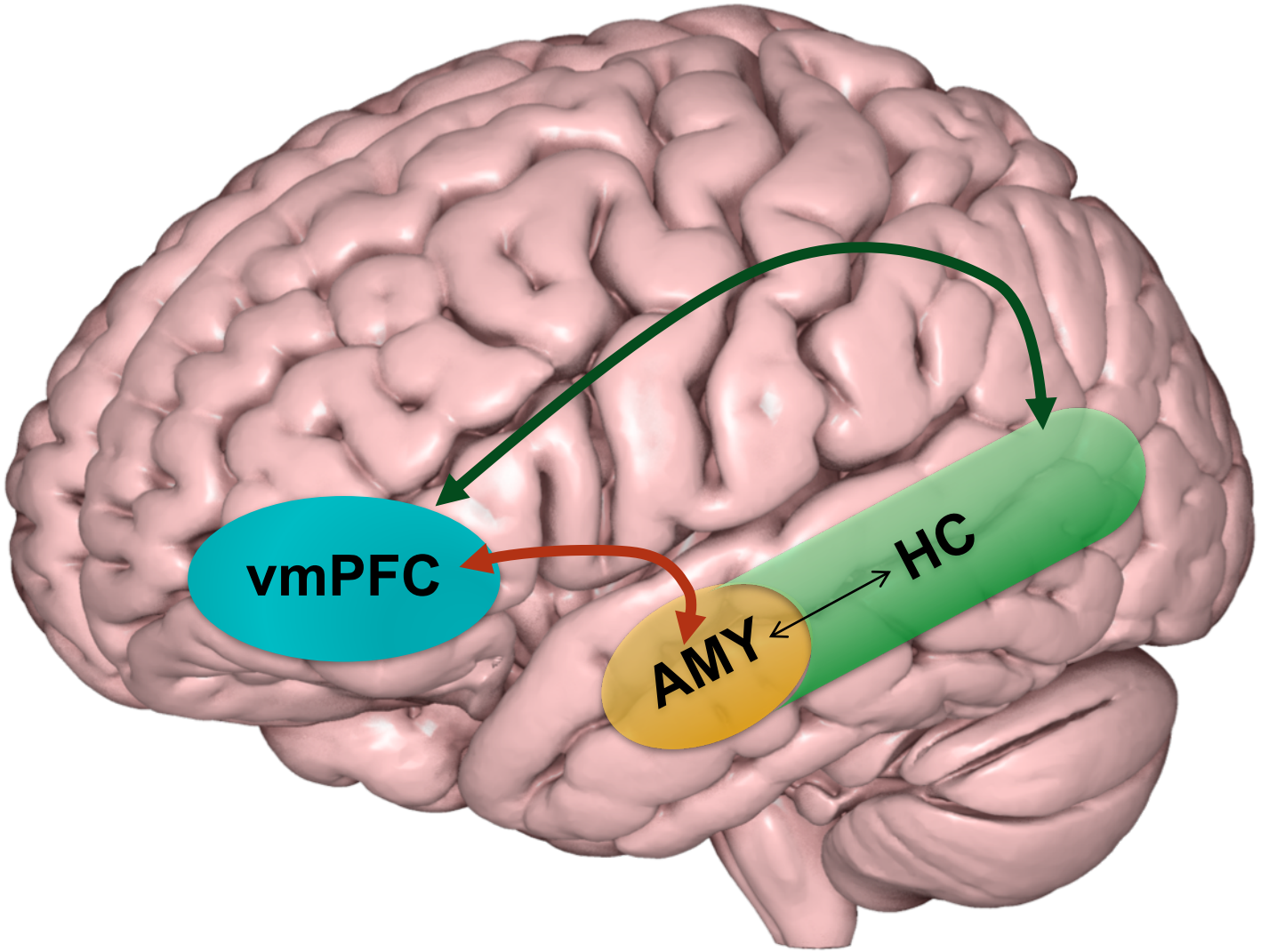
Nation-wide replication (22 EDs)



Roeckner... & Stevens (in prep)

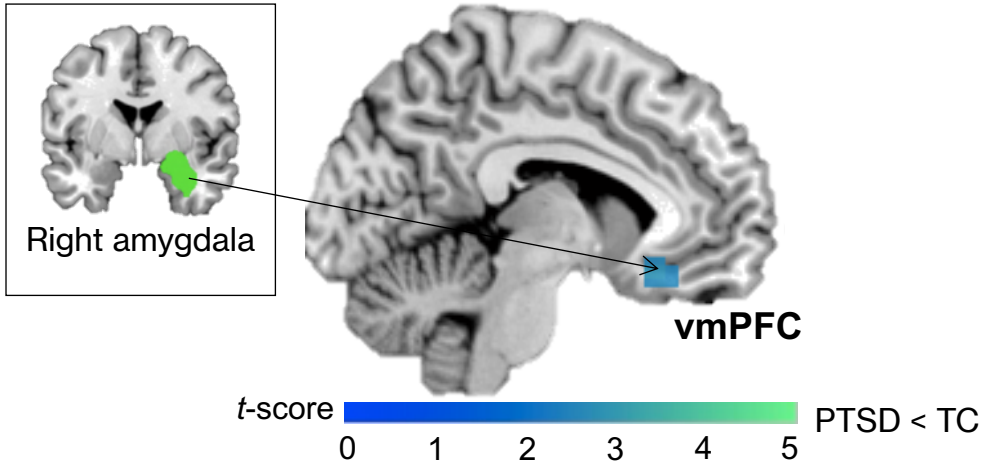
Fuller model of PTSD neurocircuitry

it’s not just about the amygdala...

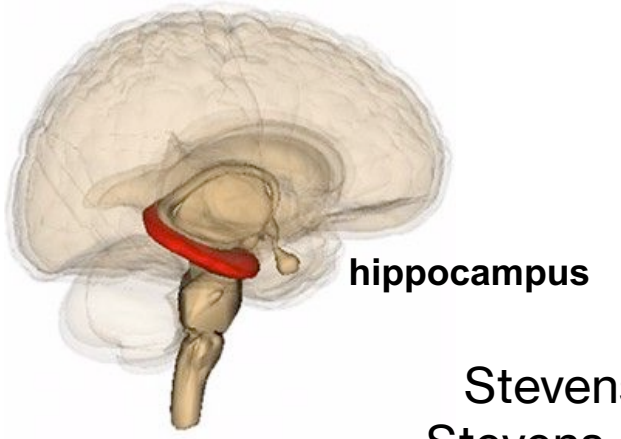


Hippocampus and vmPFC: Fear regulation

INHIBITION



CONTEXT



Stevens... & Ressler (2013) *JPR*
Stevens,,, & Ressler (2014) *PNAS*

Going beyond PTSD

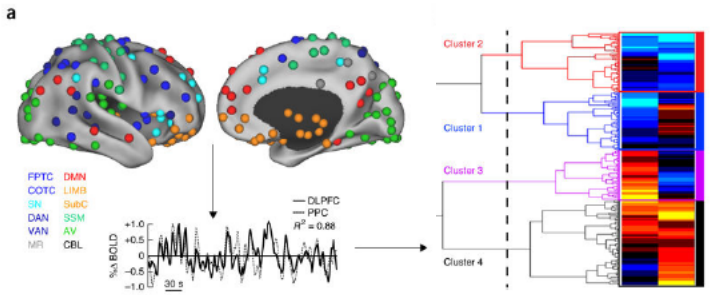
Fragmented syndromes: Most trauma survivors experience complex patterns of overlapping symptoms across traditional syndromes. Overlapping neurobiological substrate?

Brain-based model of outcomes following trauma

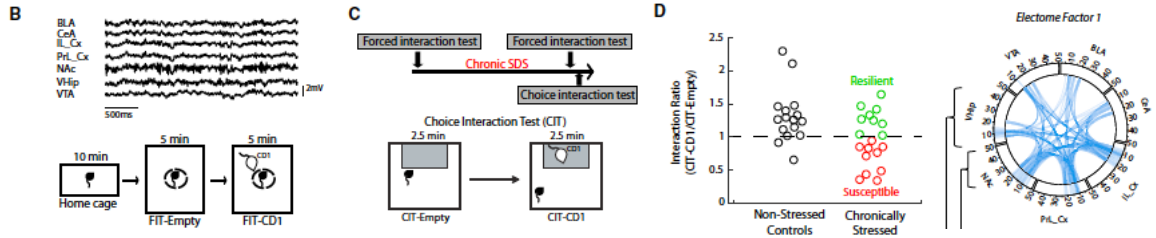
Ideal model would be bottom-up – identify what is there

- Use brain and peripheral data to find sub-populations
  - Immediately following / during trauma
  - Who maintain chronic disabling symptoms

Recent excellent examples



Drysdale et al. (2017) *Nat. Med.*

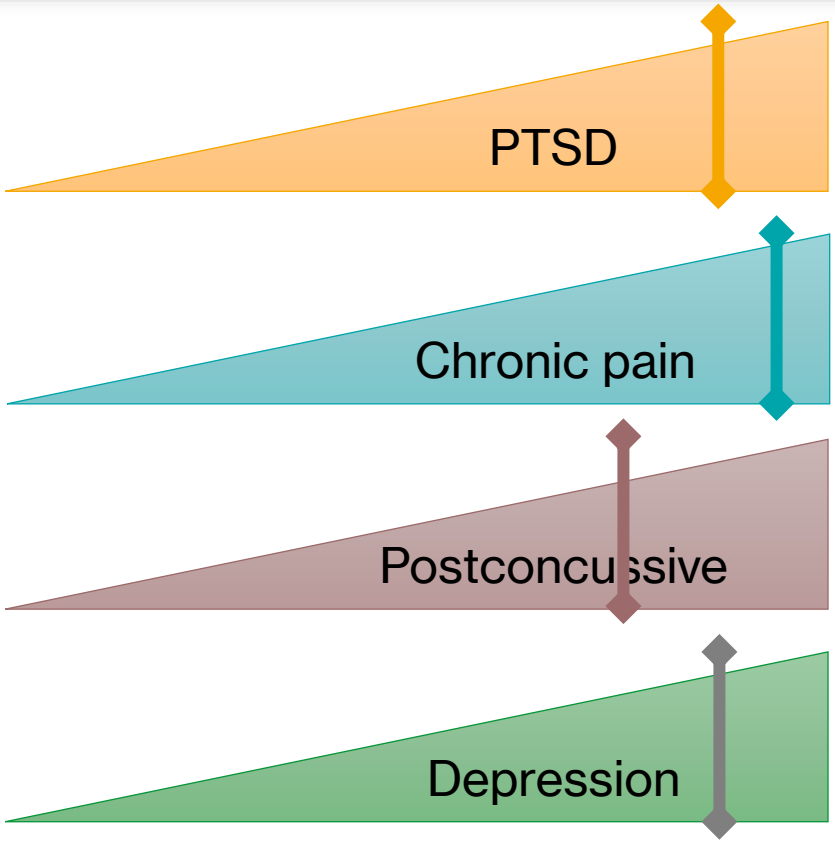


Hultman et al. (2018) *Cell*

The bottom-up model: Early post-trauma biotypes

Trauma & acute treatment

Peri-trauma (first few weeks)



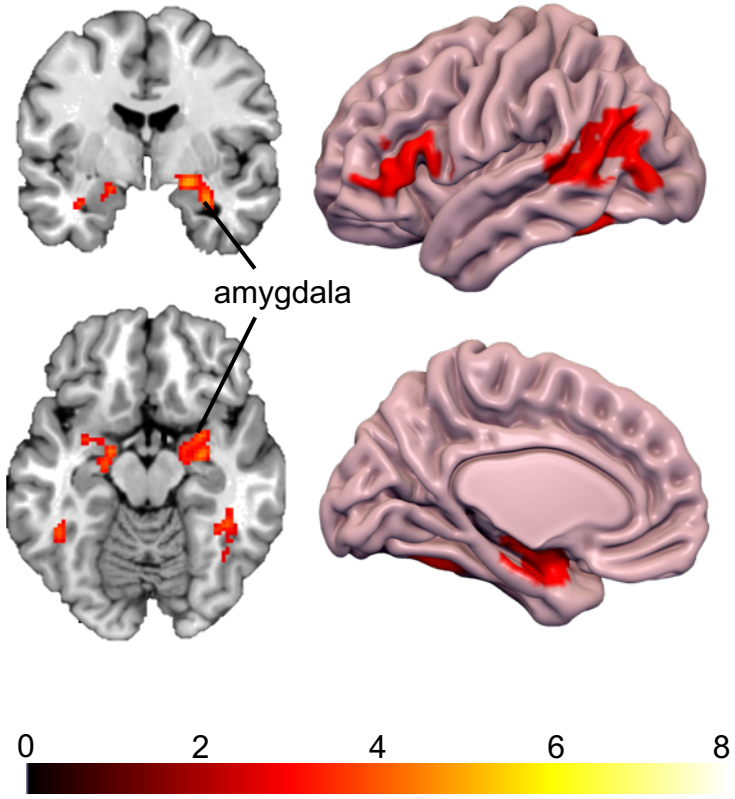
Differential risk / profiles, future mental health disorder

FMRI Approach

Threat

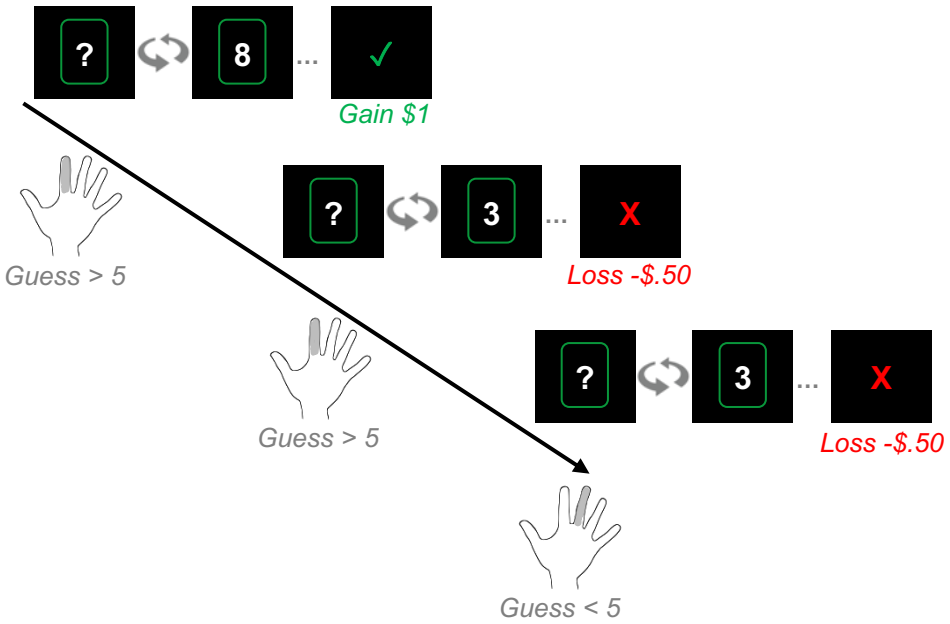
Fearful > Neutral Faces

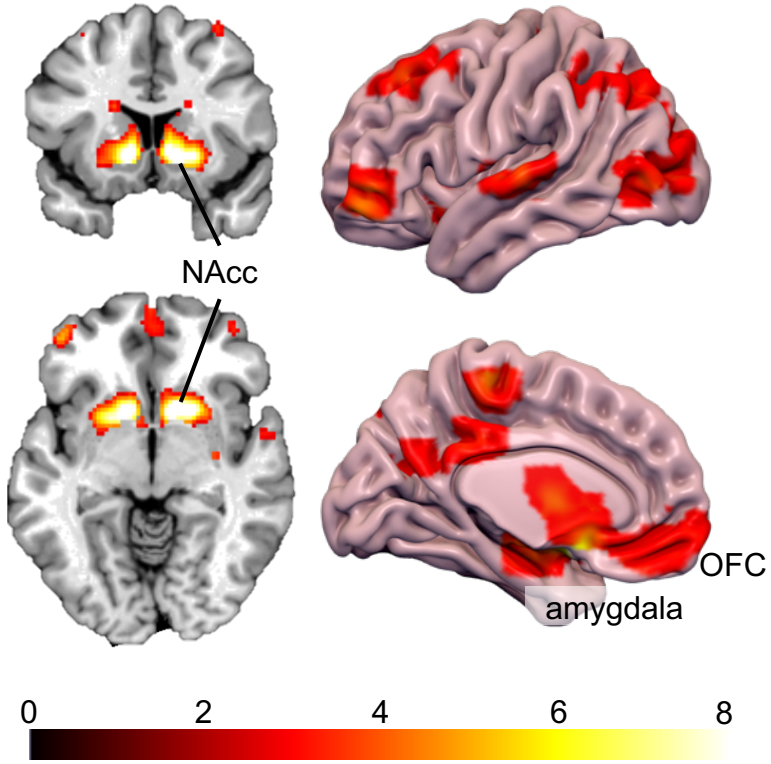
Passive viewing



Reward

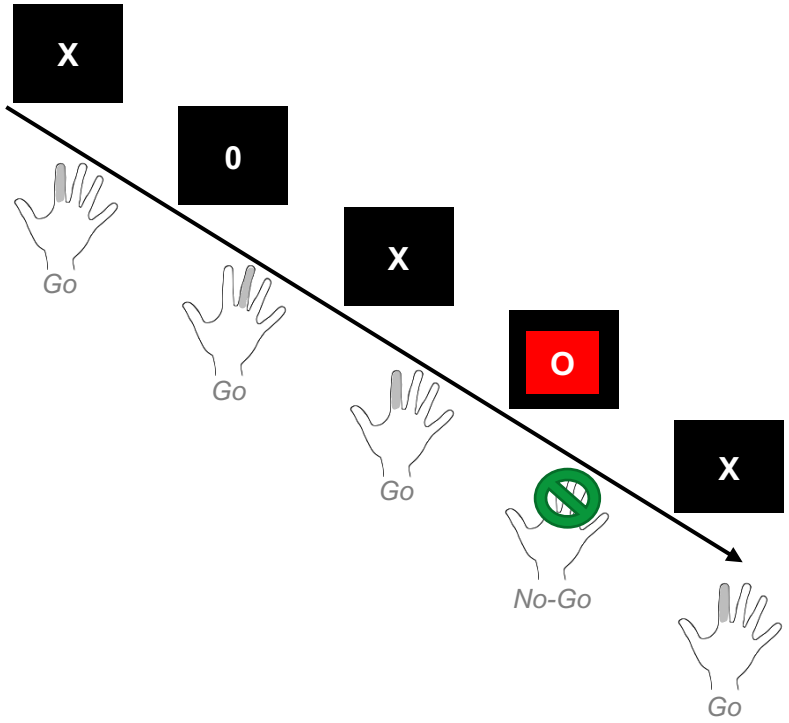
Monetary Gain > Loss

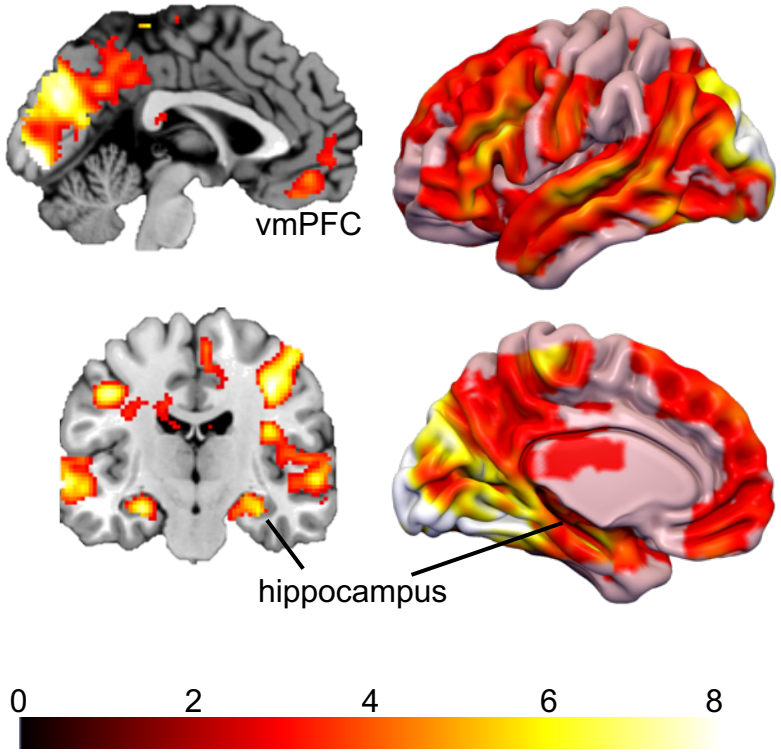




Inhibition

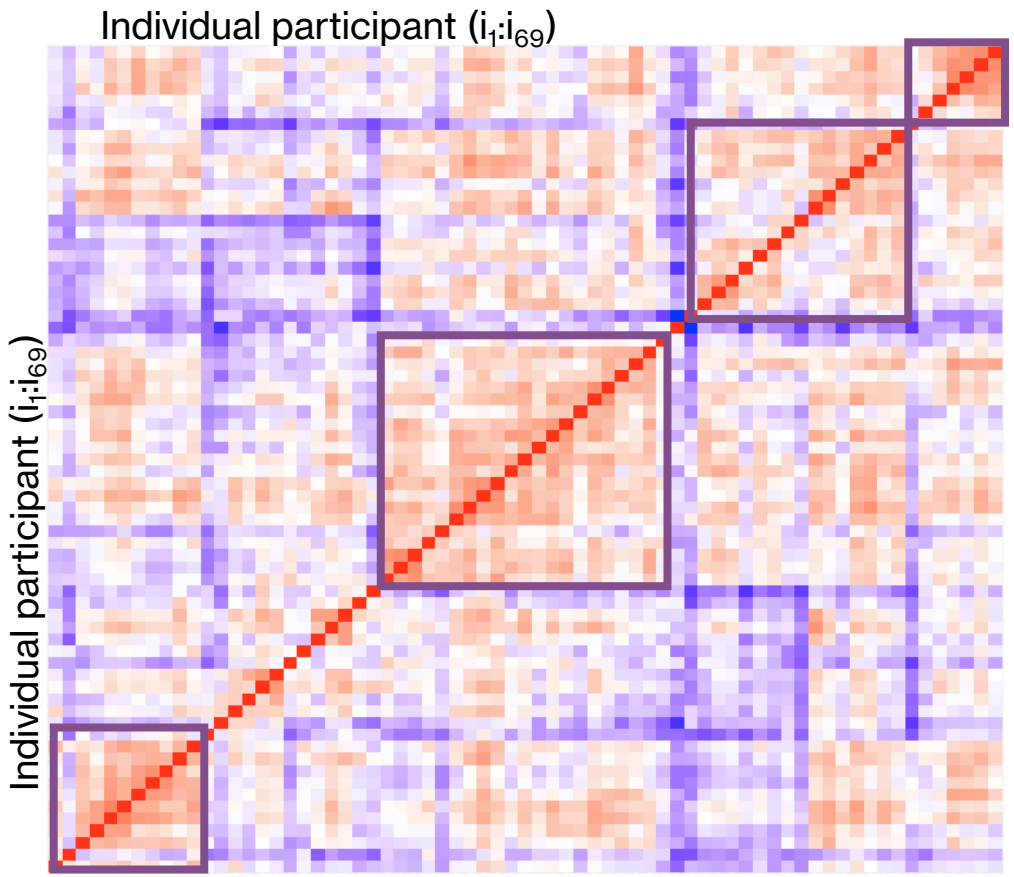
No-Go > Go (correct trials)



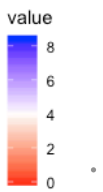


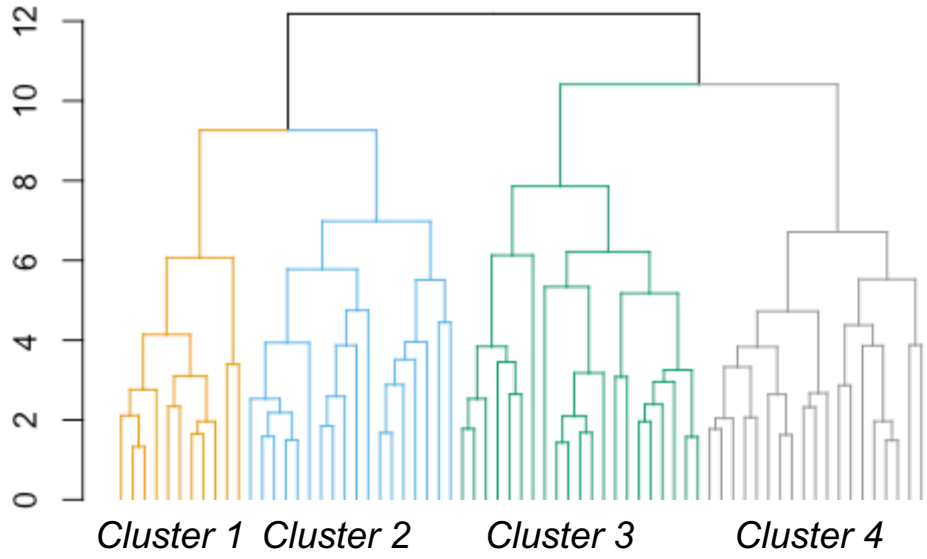
Clustering to identify “biotypes”

Data-driven clustering

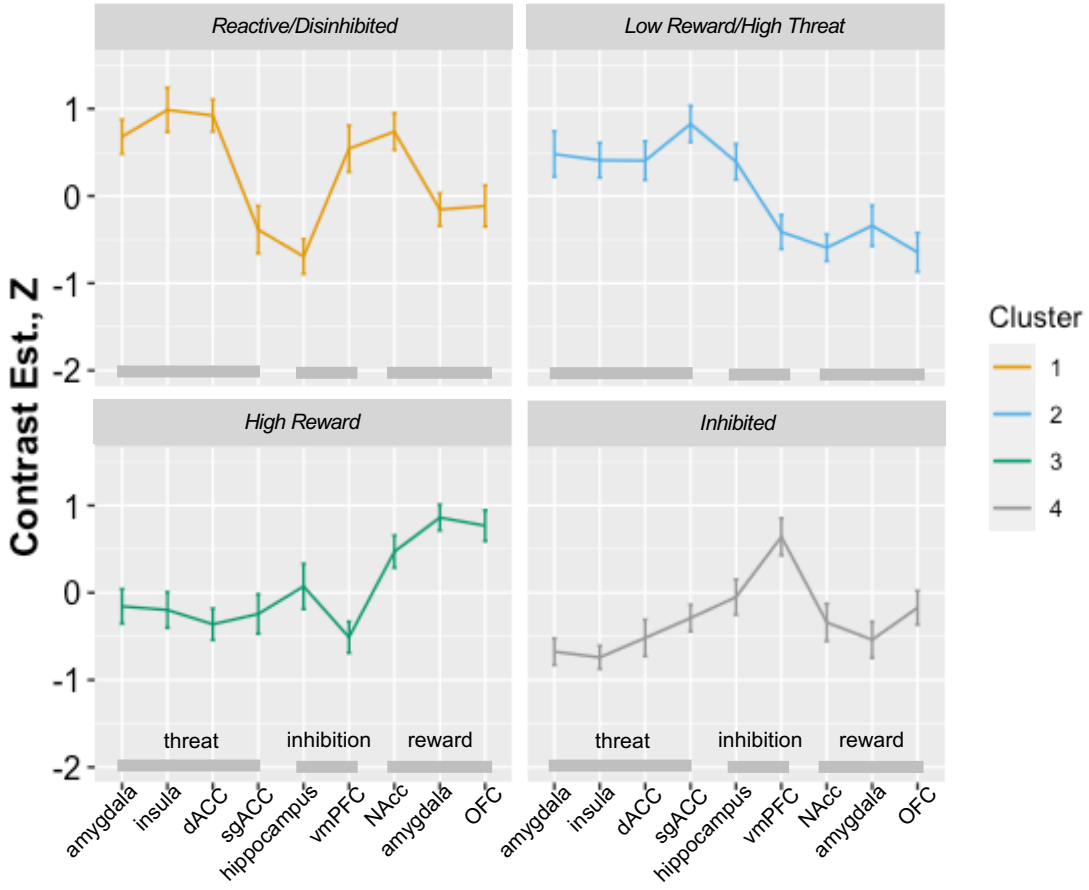


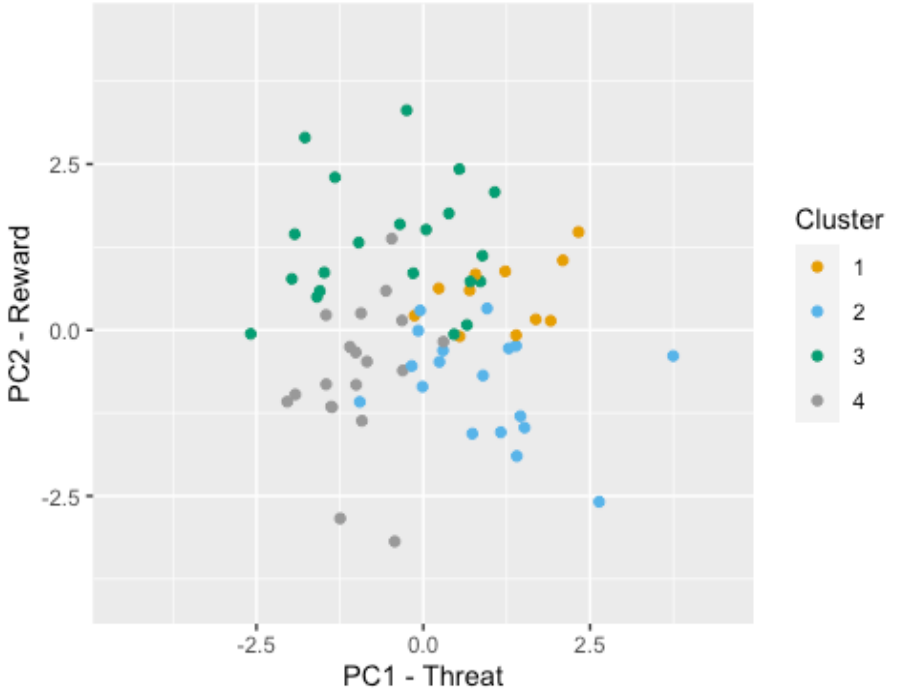
Blocks with less 'distance' between individuals represent potential clusters





Cluster profiles



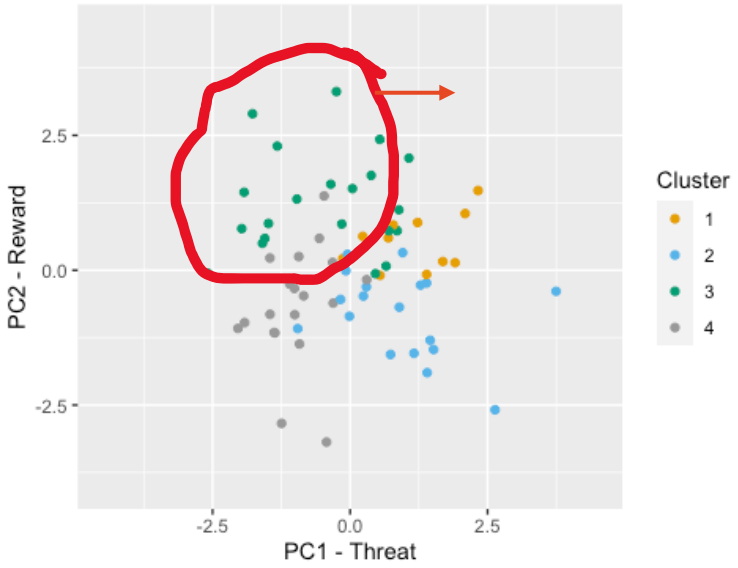


Is this just data sculpting?

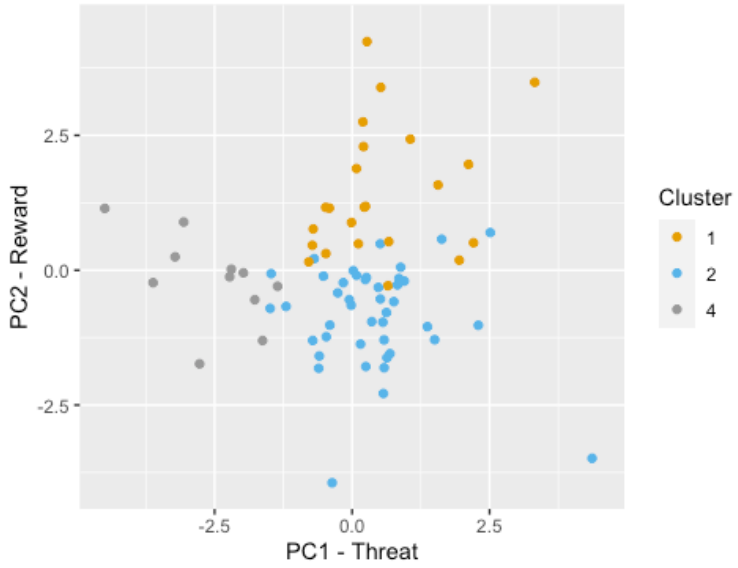
We need a replication!

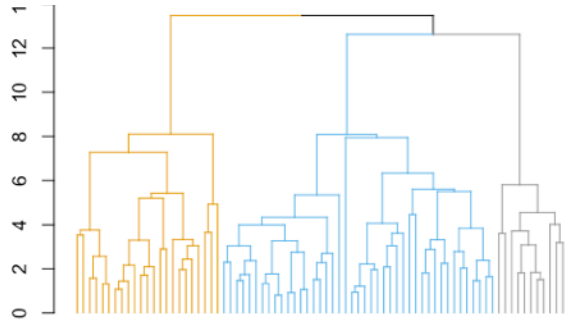
Replication

Discovery (n=69 MVCs)

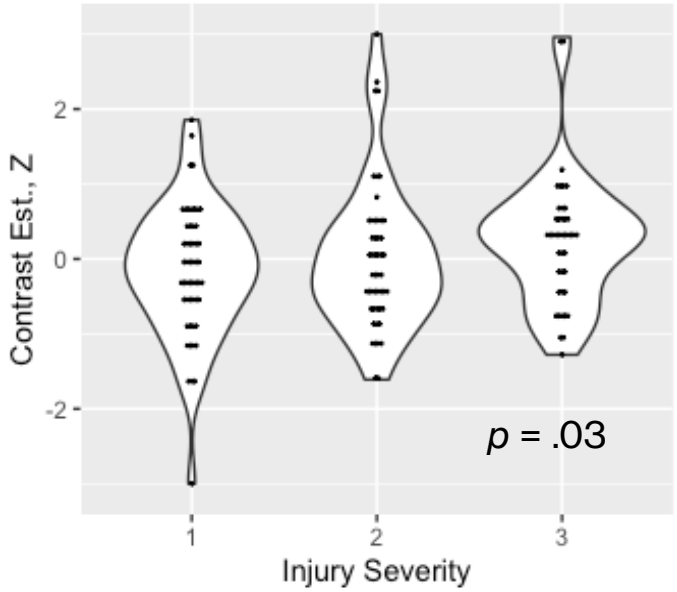


Replication (n=77 mixed traumas)



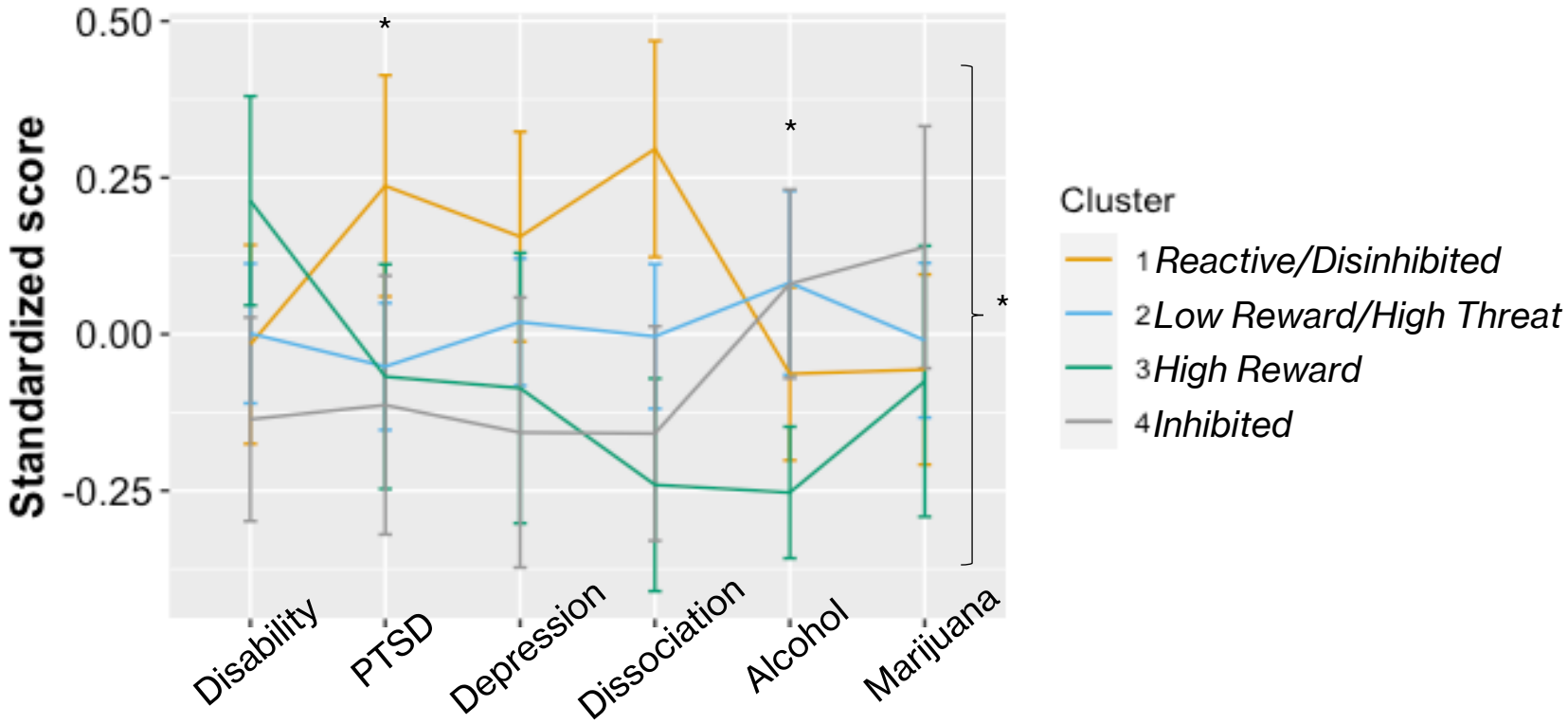


Threat reactivity: Amygdala



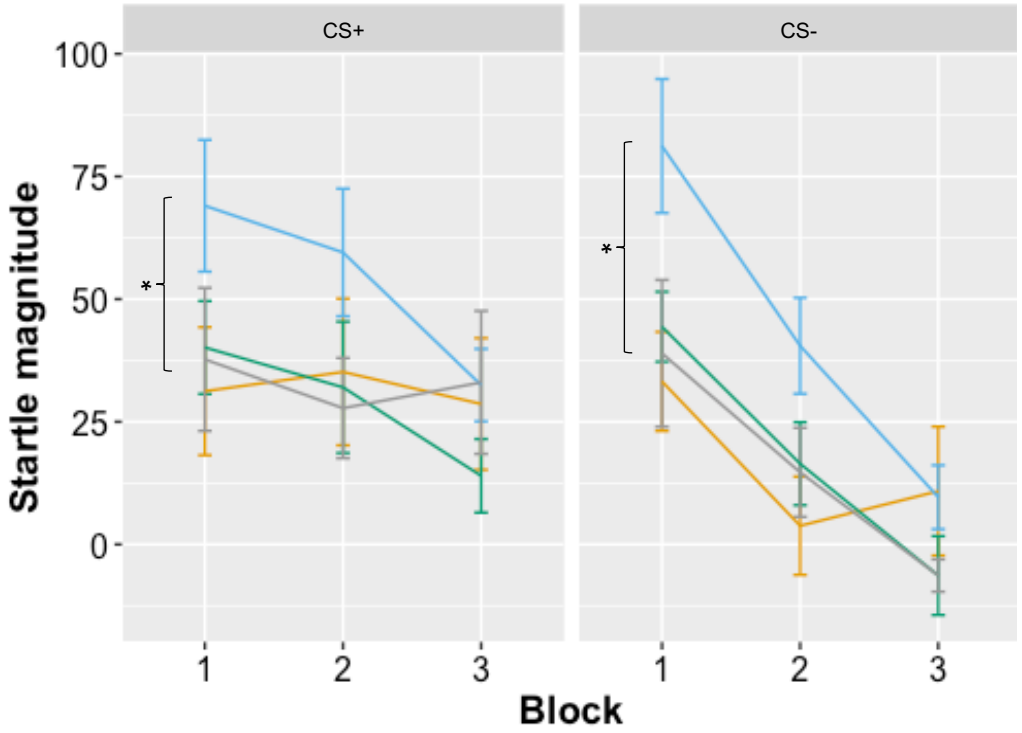
Mental health outcomes in the 4 “biotypes”

Future mental health in the 4 biotypes

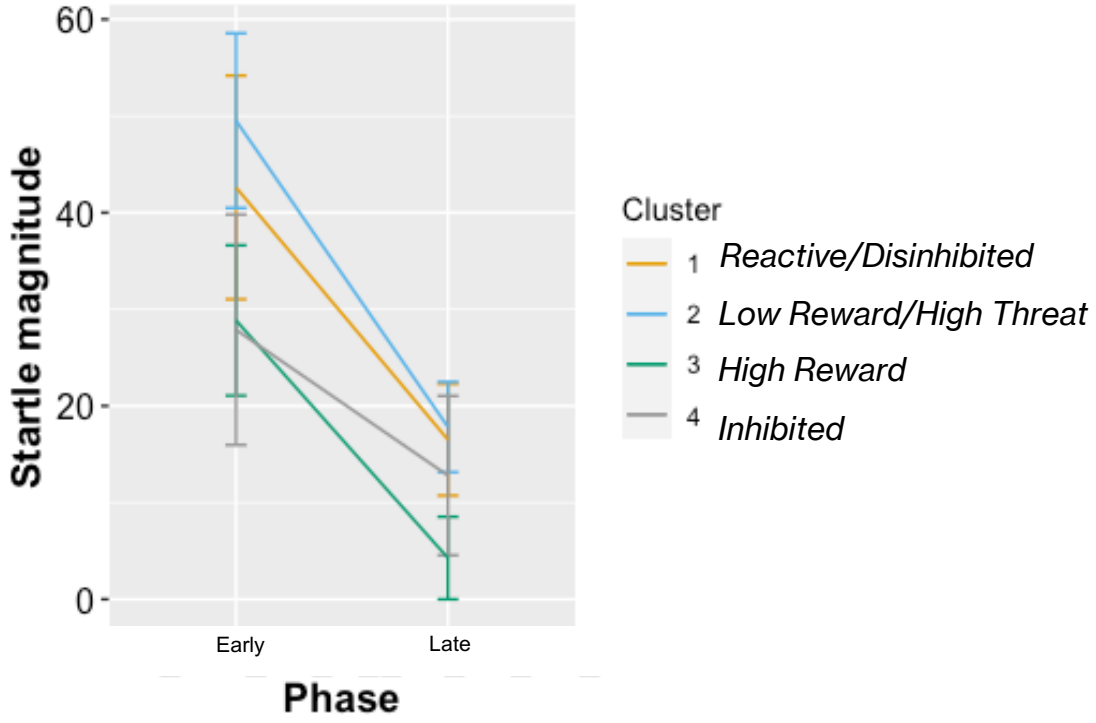


Convergent validity

Fear conditioning



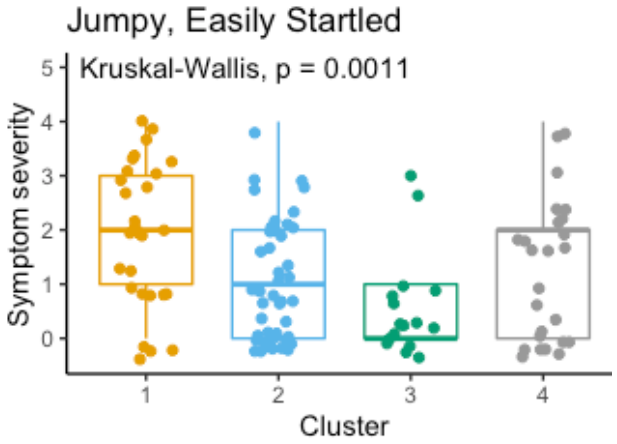
Fear extinction

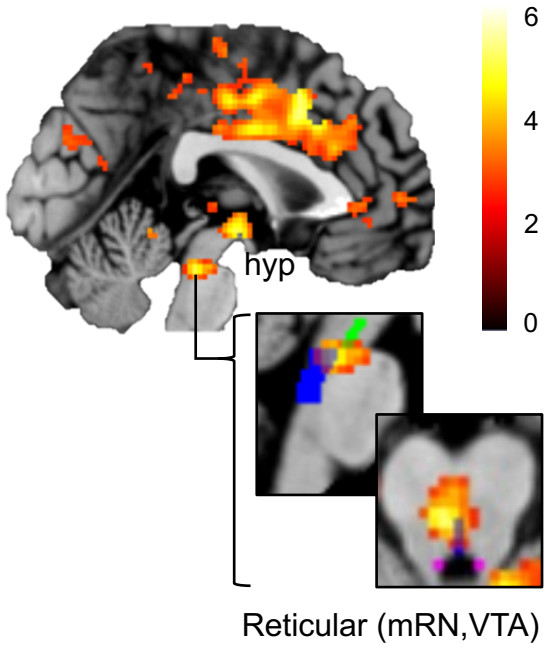


Two risk groups

Reactive/Disinhibited

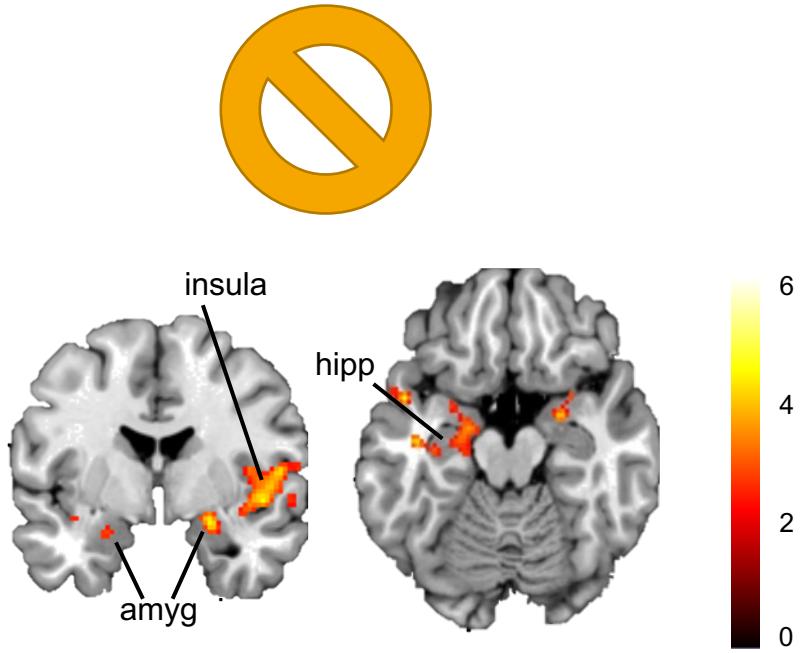
- Hyperarousal?





Low reward/High threat

- Anhedonia?



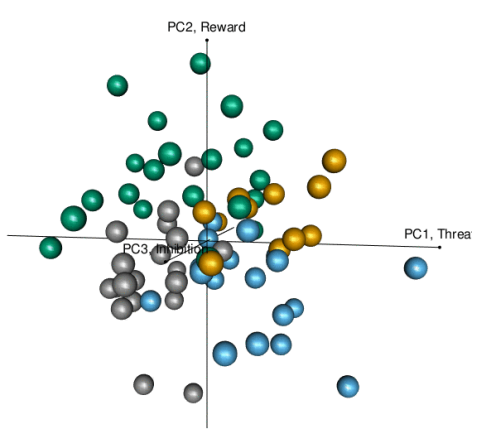
Cross-disorder genetics

Disorder	ASD	ADHD	SCZ	BD	MDD	AN	OCD	PTSD
ASD	0.24 (0.19-0.30) 0.74 (0.70-0.87)[c]	0.08 (-0.11-0.27)	0.21 (0.09-0.32)	0.10 (-0.03-0.23)	0.16 (0.04-0.27)	0.03 (-0.16-0.23)	0.00 (-0.21-0.21)	0.04 (-0.34-0.41)
ADHD	.87 (0.77-1.0)*	0.10 (0.08-0.12) 0.79 (0.61-0.88)*	0.22 (0.13-0.31)	0.26 (0.15-0.38)	0.52 (0.41-0.63)	-0.21 (-0.42- -0.00)	-0.07 (-0.25-0.12)	0.45 (0.11-0.78)
SCZ	N/A	N/A	0.26 (0.24-0.28) 0.77 (0.67-0.87)[¥]	0.68 (0.64-0.72)	0.34 (0.30-0.40)	0.22 (0.11-0.32)	0.33 (0.21-0.44)	0.15 (-0.03-0.32)
BD	0.24 (0.24-0.29)[&]	0.33 (0.32-0.39)[&]	0.68 (0.67-0.73)[!]	0.21 (0.19-0.22) 0.68 (0.64-0.72)[¥]	0.35 (0.28-0.41)	0.19 (0.08-0.30)	0.31 (0.18-0.44)	0.10 (-0.11-0.25)
MDD	N/A	N/A	N/A	0.65 (0.58-0.75)[$]	0.11 (0.10-0.12) 0.45 (035-0.55)¥	0.20 (0.03-0.30)	0.23 (0.11-0.35)	0.52 (0.23-0.81)
AN	N/A	N/A	N/A	N/A	N/A	0.17 (0.12-0.22) 0.57 (0.0-0.81)[¶]	0.52 (0.29-0.75)	-0.02 (-0.39-0.36)
OCD	N/A	0.63 (0.39-0.87)[%]	N/A	N/A	N/A	0.52 (0.26-0.81)[@]	0.26 (0.20-0.33) 0.45 (0.30-0.60)¥	0.28 (-0.08-0.64)
PTSD	N/A	N/A	N/A	N/A	1.0[§]	N/A	N/A	0.15 (0.03-0.30) 0.38 (0.25-0.52)[√]

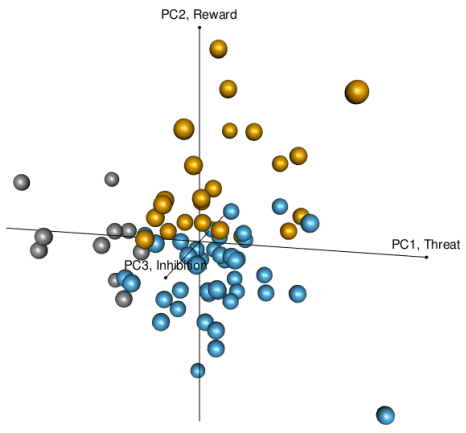
2 modes of susceptibility to trauma?

Smoller et al. (2018), *Mol Psy*

The 4 biotypes



Discovery

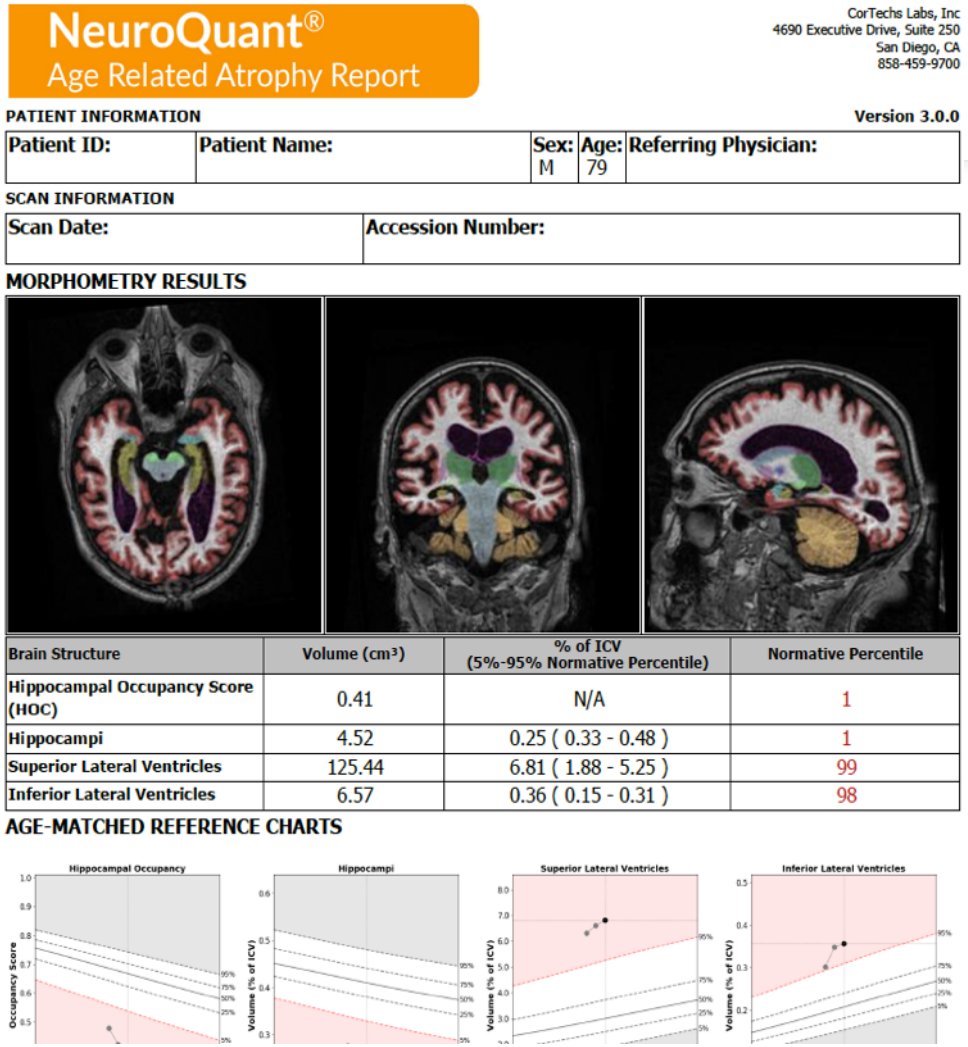


Replication

1. **Reactive/Disinhibited** High reactivity to all affective stimuli; brainstem-mediated? Greatest future PTSD symptoms.
2. **Low reward/High threat** Threat-reactive cortical emotion centers; low responsivity to reward. High over-general startle response. Greatest future alcohol use.
3. **High reward** Best mental health. Only apparent after low-acuity traumas.
4. **Inhibited** Candidate for stress resilience. Few participants.

What would we need next? *for single-subject ID*

1. Confirmatory model of subtypes
2. Solid reliability metrics + change expected with recovery



NeuroQuant®
Age Related Atrophy Report

CorTechs Labs, Inc
4690 Executive Drive, Suite 250
San Diego, CA
858-459-9700

PATIENT INFORMATION — Version 3.0.0

Patient ID:	Patient Name:	Sex:	Age:	Referring Physician:
		M	79	

SCAN INFORMATION

Scan Date:	Accession Number:

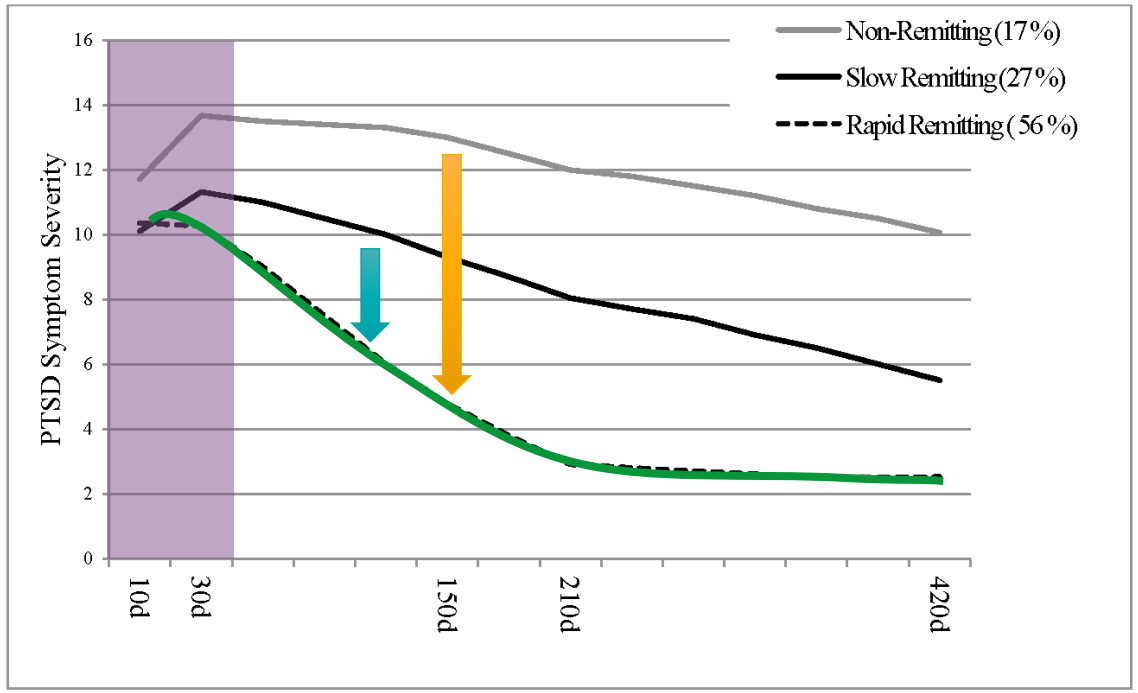
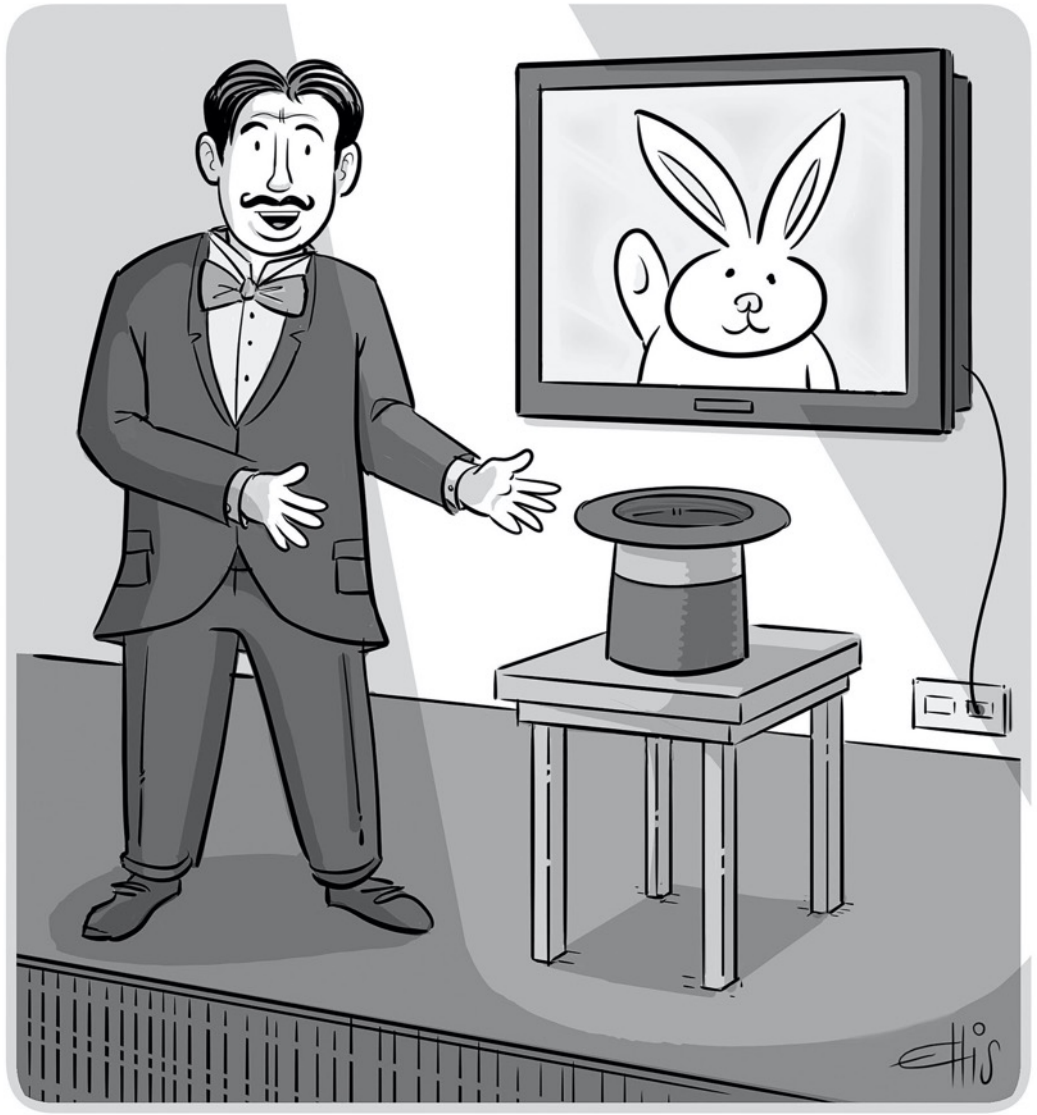
MORPHOMETRY RESULTS

Brain Structure	Volume (cm³)	% of ICV (5%-95% Normative Percentile)	Normative Percentile
Hippocampal Occupancy Score (HOC)	0.41	N/A	1
Hippocampi	4.52	0.25 (0.33 - 0.48)	1
Superior Lateral Ventricles	125.44	6.81 (1.88 - 5.25)	99
Inferior Lateral Ventricles	6.57	0.36 (0.15 - 0.31)	98

AGE-MATCHED REFERENCE CHARTS

Then what?

Early intervention



Thanks for listening!