Functional MRI Predictors of Posttrauma Psychiatric Symptom Trajectories

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I, Jennifer S. Stevens, have no commercial relationships to disclose.

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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 et al. (2009, 2013)

Stevens et al. (2017) BPS

McLaughlin et al. (2014)

Mattson et al. (2016)

Swartz et al. (2015) Neuron
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)

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AUC = .90
N = 95

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$r = .16, p = .04$
N = 168
Fuller model of PTSD neurocircuitry

it's not just about the amygdala...
Hippocampus and vmPFC: Fear regulation

INHIBITION

Right amygdala

vmPFC

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

- 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

- PTSD
- Chronic pain
- Postconcussive
- Depression
FMRI Approach
Threat
Fearful > Neutral Faces

Passive viewing
Reward
Monetary Gain > Loss

Gain $1

Loss -$0.50

Guess > 5

Guess < 5

Guess > 5

Guess < 5

NAcc

amygdala

OFC
Inhibition

No-Go > Go (correct trials)
Clustering to identify “biotypes”
Data-driven clustering

Individual participant \((i_{1:i_{69}})\)

Blocks with less 'distance' between individuals represent potential clusters

Cluster 1
Cluster 2
Cluster 3
Cluster 4
Cluster profiles

Cluster profiles for various brain regions under different conditions:
- **Reactive/Disinhibited**
- **Low Reward/High Threat**
- **High Reward**
- **Inhibited**

Graphs show the contrast estimates for each condition, with clusters colored differently:
- Cluster 1
- Cluster 2
- Cluster 3
- Cluster 4

The clusters are further analyzed with PC1 (Threat) and PC2 (Reward).
Is this just data sculpting?

We need a replication!
Replication

Discovery (n=69 MVCs)

Replication (n=77 mixed traumas)

Threat reactivity: Amygdala

$p = .03$
Mental health outcomes in the 4 "biotypes"
Future mental health in the 4 biotypes

Cluster
1 Reactive/Disinhibited
2 Low Reward/High Threat
3 High Reward
4 Inhibited
Convergent validity

Fear conditioning

Fear extinction

Cluster
1 Reactive/Disinhibited
2 Low Reward/High Threat
3 High Reward
4 Inhibited
Two risk groups

**Reactive/Disinhibited**
- Hyperarousal?

**Low reward/High threat**
- Anhedonia?

Jumpy, Easily Startled
Kruskal-Wallis, $p = 0.0011$
# Cross-disorder genetics

![Table](https://via.placeholder.com/150)

2 modes of susceptibility to trauma?

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Smoller et al. (2018), *Mol Psy*
The 4 biotypes

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
Then what?

Early intervention
Thanks for listening!