Formalizing the relationship between early life unpredictability and addiction vulnerability: the role of memory sampling

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Background

- Over 60% of those treated for substance use disorders will relapse (McLellan, 2000).

- Standard reinforcement learning models can account for addiction acquisition and response to treatment but not relapse (Redish, 2003)

- Even very distant experiences can trigger relapse suggesting long-term memories may be an additional addiction mechanism (Bornstein & Pickard, 2020).

- Early life unpredictability (ELU) is causally linked to memory deficits (Davis, 2017) and vulnerability to addiction acquisition and relapse and resistance to treatment (Sinha, 2008; Levis, 2019).

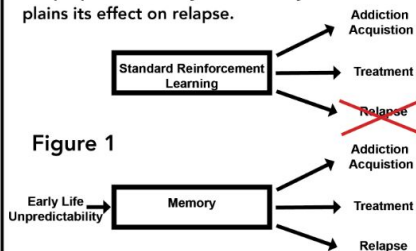**We propose that early life adversity's effect on memory explains its effect on relapse.**

Figure 1

Model

We formalize this proposal using an infinite capacity mixture model to describe how experiences are associated with one another in long-term memory (Gershman, Niv, & Blei, 2010) .

We provide some intutions for how the model works:

- Suprising events are particularly salient in memory. For example, the first high from a drug may provide a surprisingly intense, rewarding experience.

Model cont.

- Other experiences are organized around these surprising events, grouping based on shared features like location, time or goal. For instance, experiences that occured in the same physical context as the first high may be grouped together.

- Individuals may vary in what they consider to be surprising. This surprise threshold determines the number of clusters in memory. A high threshold produces fewer clusters.

-How experiences are clustered influences which memories are drawn on or sampled at decision time. Consequently, an individual's threshold for surprise shapes their decision-making.
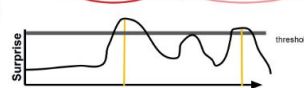

Figure 2

An unpredictable early life environment may tune memory to be less sensitive to suprsing events later in life. This is consistent with impaired reversal learning (Thomas, 2016) and worse context memory (Kosten, 2007). In our model this corresponds, to a higher threshold.

- We suggest that early life unpredictability produces a higher threshold for surprise that biases individuals towards sampling highly surprsing and rewarding early drug memories that makes them more likely to use even following treatment.

Early Life Unpredictability
Figure 3

Addiction	Treatment	Relapse
drug cue → reward	drug cue → reward	drug cue → reward ?
20 trials	50 trials	20 trials

Procedure
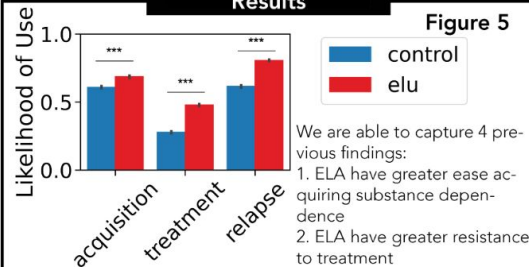**Figure 4**

Results

Figure 5

We are able to capture 4 previous findings:
1. ELA have greater ease acquiring substance dependence
2. ELA have greater resistance to treatment
3. ELA have greater likelihood of relapse.
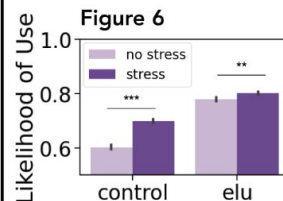4. Both groups have greater likelihood of relapse under stress.

Figure 6

Novel prediction: providing alternative rewards like social rewards may be particularly effective for preventing relapse in those who have faced early life adversity
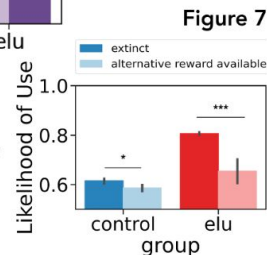

Figure 7

Conclusion

Our results highlight the relevance of episodic memory in explaining heterogeneity in SUDs and developing personalized treatment.

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