Title

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Authors

Harhen, Nora
Baram, Tallie Z
Yassa, Michael A
et al.

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Research Method: Imaging: Mathematical Modeling

Formalizing the Relationship Between Early Life Adversity and Addiction Vulnerability: The Role of Memory Sampling

Nora Harhen[1], Tallie Z. Baram[2], Michael A. Yassa[1], and Aaron M. Bornstein[1]

[1]University of California, Irvine, [2]University of California, Irvine School of Medicine

Background: Over 60% of those treated for substance use disorder (SUD) treatment will relapse (McLellan, 2000). Relapse can occur after prolonged periods of abstinence, often prompted by drug-related cues and contexts. This suggests that episodic memory may play a distinct role in drug choice. Episodic memories carry rich spatial, temporal, and mental context that link experiences. A consequence of this structure is that incidental drug associations can reinstate webs of highly connected experiences that can strongly bias choice (Bornstein & Pickard, 2020). Memory structure may thus explain variability within SUD on its own, and also via interaction with Early Life Adversity (ELA). ELA is causally linked to both impaired context memory (Kosten, 2007) and relapse vulnerability (Levis, 2019).
Methods: We formalized the proposal that ELA affects relapse vulnerability via its effect on memory structure as a novel reinforcement learning model combining previous work on long-term memory's role in classical conditioning (Gershman, Niv, & Blei, 2010) and decisions (Bornstein & Norman, 2017).
Results: We simulated our model undergoing drug exposure, treatment, and re-exposure test. Our model showed relapse in the last stage, unlike a previous model (Redish, 2004) in which SUD affects reinforcement but not memory ($t(198) = 25.57$, $p < 0.0001$). Adding an effect of ELA on memory structure increased resistance to treatment ($t(198) = 64.99$, $p < 0.001$) and relapse likelihood ($t(198) = 5.22$, $p < 0.0001$).
Conclusions: Our results highlight the relevance of episodic memory in explaining heterogeneity in SUDs and supports the relation of ELA and SUD relapse.
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Keywords: Addiction, Episodic Memory, Early Life Adversity

Lifespan Normative Modeling of Internalizing & Psychotic Disorders

Saige Rutherford[1], Ivy F. Tso[2], Stephan Taylor[2], Elizabeth Duval[2], Christian Beckmann[3], Henricus Ruhe[4], and Andre Marquand[5]

[1]Radboud University Nijmegen, [2]University of Michigan, [3]Radboud University Medical Center, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, Centre for Functional MRI of the Brain, University of Oxford, [4]Radboudumc, Nijmegen, [5]Donders Institute for Brain, Cognition and Behaviour, Radboud University

Background: Case-control approaches have dominated the fields of clinical neuroimaging and computational psychiatry. These methods, which require disorder-related effects to overlap across individuals, have created an inconsistent set of patient-control group differences. Normative modeling has refocused objectives on individualized predictions that allow stratification of groups and careful separation of different sources of variation.
Methods: Using a large sample of (>15K) high-quality structural MRI-scans of subjects across 32 unique scanners, cortical thickness, and subcortical volume measures were derived using FreeSurfer (Destrieux atlas). A lifespan (ages 3-100) normative model was estimated using Bayesian linear regression. The training set contained healthy controls, and the test set included controls and patients. The patient test set groups included internalizing (unmedicated major depressive disorder, social anxiety disorder) and psychotic (early psychosis, schizophrenia) disorders. Deviation scores from the normative models were probed to learn which brain regions displayed the most extreme deviations.
Results: Compared to the control test set, all patient groups had increased variance in true and predicted values and greater (positive and negative) deviation scores. The internalizing disorder deviations were found in the subcortical volume measures (brainstem, amygdala, accumbens, pallidum, putamen, hippocampus), and the psychotic disorder deviations were across the cortex (inferior parietal sulcus, pericallosal sulcus, anterior transverse collateral sulcus, suborbital sulcus) and subcortical (accumbens, vessel, anterior corpus callosum).
Conclusions: Normative modeling is a robust framework for investigating individual biomarkers. These models reveal diverse patterns within/across clinical and healthy populations yet provide a methodology to address the challenge of heterogeneity that arises when mapping the neurobiology of psychiatric disorders.
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Keywords: Normative Modeling, Machine Learning, Big Data, Internalizing Disorders, Psychotic Disorders