EDITORIAL

Toward an Improved Understanding of Anhedonia

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Anhedonia, the reduced ability to experience pleasure, has been critically implicated in a wide range of adolescent mental disorders and suicidal behaviors.[1,2] Presently, medication as well as most first-line psychotherapeutic approaches do not sufficiently address motivational and reward-processing deficits that characterize anhedonia, and thus, treatment failure is common. To overcome limitations of a categorical nosologic system and improve treatments for core dysfunction, the National Institute of Mental Health's Research Domain Criteria initiative provides a framework for research focusing on core domains of functioning, such as the Positive Valence Systems. Through this lens, research has sought to clarify the neural circuity underlying anhedonia and, in doing so, provide a framework to elucidate how and why anhedonia leads to adverse mental health outcomes across the lifespan.

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Toward addressing this gap, Pornpattananangkul et al[3] leveraged data from the Adolescent Brain and Cognitive Development Study to probe neural circuitry associated with anhedonia in children aged 9 to 10 years. The authors used the initial Adolescent Brain and Cognitive Development data release with reliable functional magnetic resonance imaging (MRI) data (n = 2878), which provides sufficient power for subgroup comparisons among children with anhedonia, low mood, anxiety, and attention-deficit/hyperactivity disorder (ADHD). Examining resting-state functional MRI, the authors found that relative to nonanhedonic children, anhedonic youths were characterized by hypoconnectivity among several large-scale networks, including between arousal-related and reward-related regions, which was not present in children with low mood, anxiety, or ADHD. Complementary task-evoked functional MRI data also demonstrated that anhedonic youths exhibited hypoactivation during reward anticipation in similar regions and networks; highlighting domain and context specificity, this blunted reward-related activation did not emerge in the low-mood, anxious, or ADHD youths, and anhedonic children showed blunted responses during reward anticipation but not a working memory task. Given the representativeness and sample size, advanced data analytic approach, and Research Domain Criteria–consistent framework, this study adds to a growing literature that has sought to clarify neural abnormalities linked to anhedonia. It also sheds light on key issues to be addressed moving forward.

Anhedonia: Beyond the Monolithic Identity

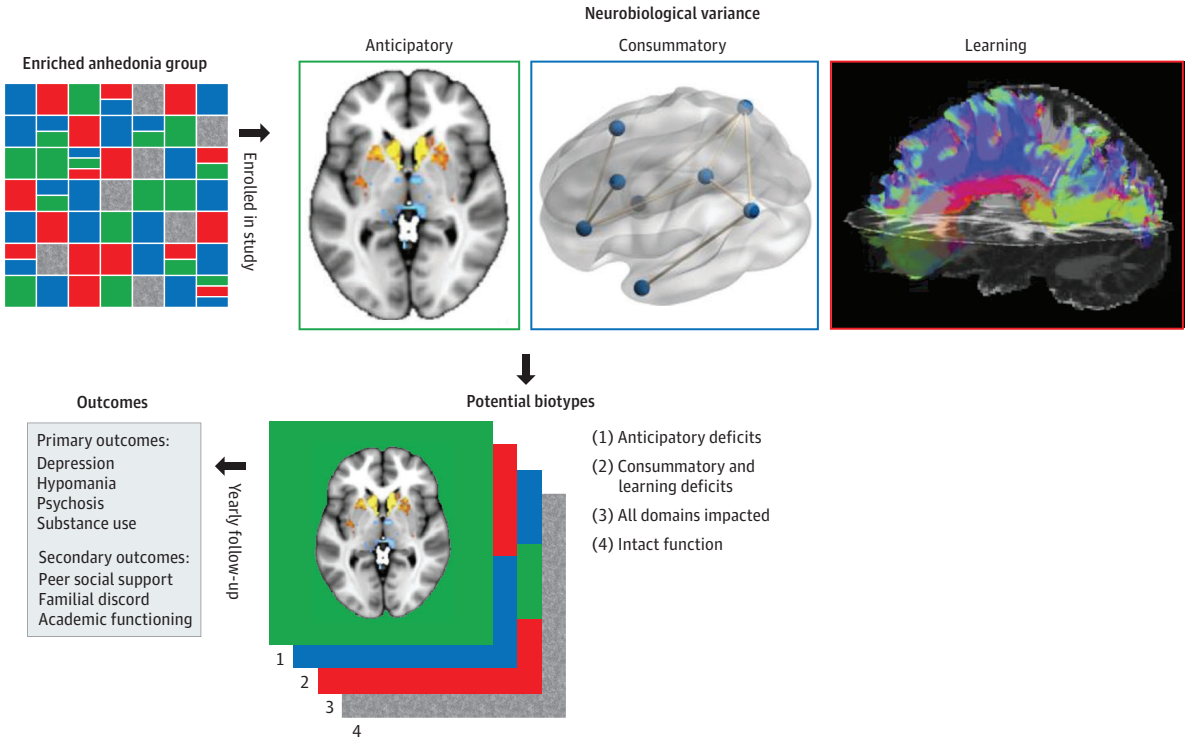
Prior research in youths[4] and adults[5] has shown that structural abnormalities within the dorsal striatum are associated with anhedonia severity, and together with the current resting and functional MRI connectivity findings, have consistently implicated dysfunction within the striatum (as well as associated networks).[3] These findings are promising and important, particularly as we pursue more nuanced ways to conceptualize neural risk factors of mental health outcomes (and origins). In this vein, Pornpattananangkul et al[3] provide an important framework, on the basis of phenotypes for conceptualizing risk. However, an equally meaningful consideration is that anhedonia is not a monolithic entity. Rather, animal and human research demonstrates that anhedonia can be separated into dissociable reward-related components, for example, anticipatory, consummatory, and reward learning processes, that rely on different underlying neurochemistry, neuroanatomy, and neurophysiology.[6,7] Further complicating this matter, each core component of anhedonia can be divided into substages (eg, anticipation: cue evaluation to determine what actions lead to reward, motor preparation, and feedback anticipation).[8] Thus, treating anhedonia as a unitary construct (comparing anhedonic vs nonanhedonic children) may have similar limitations to using *DSM-5* nosology (ie, presence vs absence of a mental disorder), particularly in characterizing neural circuitry and then mapping this onto the trajectory of long-term mental health outcomes.

In our view, Pornpattananangkul et al[3] help build a useful framework to identify risk that moves beyond diagnostic thresholds and boundaries. A potential next step is to elucidate meaningful biotypes that are sensitive to the heterogeneity of anhedonia, namely, clarifying the neural circuitry that maps onto core components that subserve anhedonia. An ideal study design would collect data from large patient and community samples, with a diverse panel of assessments probing core dimensions of anhedonia. Multivariate taxometric analyses could then clarify neurobiologically distinct biotypes that are not constrained by traditional diagnostic boundaries. Such an approach has begun to be used; for example, Clementz et al[9] used biomarker panels to develop biotypes to clarify neural boundaries between schizophrenia, schizoaffective disorder, and bipolar disorder. The investigators found that 3 biotypes, as assessed through the biomarker panel, outperformed traditional diagnoses in sorting individuals by brain abnormalities.[9] Although promising, this approach has not been used to parse a construct such as anhedonia. That said, prior research has shown that anhedonia is composed of dissociable factors, and if certain facets of anhedonia cohere more strongly, it would likely have a profound effect on understanding the course of mental health outcomes.

Conclusions

Pornpattananangkul et al[3] have clearly demonstrated the value in clinical screening for the presence of anhedonia as a sub-

Figure. Anhedonia Biotypes Differentially Associated With Long-term Clinical Outcomes



A number of complementary methods can be used to probe distinct dimensions of anhedonia, including multimodal neuroimaging, electrophysiology, behavioral and cognitive experiments, experience sampling, and self-report. For example, in this model study, participants endorsing elevated scores on an anhedonia self-report instrument (ie, the enriched group) would be assessed with multimodal neuroimaging approaches that probe neural circuitry associated with core domains of anhedonia (exemplar images functional magnetic resonance imaging [anticipatory], resting state functional magnetic resonance imaging [consummatory], and diffusion magnetic resonance imaging [learning]). Multivariate taxometric analyses would use these aggregate data to form anhedonia biotypes and determine whether these separable biotypes lead to distinct psychiatric outcomes over time.

type (relative to diagnoses) to characterize neural circuitry associated this debilitating phenotype. Although these findings provide important information about the pathophysiology of anhedonia in youths, as highlighted by the authors, the assessment of anhedonia within the Adolescent Brain and Cognitive Development sample is rather limited and relied on a categorical operationalization derived from a clinical interview. In addition to a more granular conceptualization of anhedonia, future studies would greatly benefit from assessment of anhedonic behavior in daily life (eg, ecological momentary assessments). Accordingly, a natural extension of this work would be to provide a finer grained neural and phenotypic assessment of the processes that subserve anhedonia, particularly in an enriched sample of adolescents with elevated levels of anhedonia (irrespective of diagnosis). Further, it will be essential to follow up adolescents longitudinally through adolescence into early adulthood, during a peak period of onset for mental disorders.[10] This would allow us to determine whether distinct anhedonia biotypes, which may reflect disparate alteration of core anhedonia components, differentially effect the trajectory of psychiatric symptoms (**Figure**). If successful, this approach would address 2 key goals that have mired progress in the field. First, if anhedonia biotypes can be linked to long-term symptom outcomes, there is real promise in providing more targeted preventative intervention at earlier ages. For example, if a specific biotype characterized by neural dysfunction in anticipatory and reward learning deficits is longitudinally linked to substance-related problems, it may shape the type of services afforded to youths following the initial assessment. Second, clarifying anhedonia biotypes associated with different long-term outcomes may provide novel targets for psychotherapeutic and pharmacologic interventions, and perhaps provide different paths forward for treatment that has often been frustrated with stagnated progress. Overall, targeting phenotypes as opposed to disorders offers new promise, and yet, as we forge forward with this new approach, ensuring attention to heterogeneity of specific subprocesses may provide a more promising means of generating reliable and reproducible clinical breakthroughs that meaningfully effect early detection and treatment.

ARTICLE INFORMATION

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