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A neuropsychological approach to the treatment of substance use disorders

**Neuropsychology and psychoactive substance use**

Neuropsychology intends to understand how cognitive deficits arise from various damages to the brain, including injury and neurodegenerative illness. Although there is significant research on the neuropsychological effects of psychoactive substance use, findings could be better implemented in clinical settings to improve rehabilitation efforts. Research has investigated the specific deficits associated with different psychoactive substances, an approach that assumes the various addiction disorders are heterogeneous (Cadet & Bisagno, 2016). While different substances clearly bear varied neural consequences, certain cognitive dimensions, such as risk-based decision-making, can reliably predict aspects of recovery across various types of substance use disorders (Vadejo-Garcia et al., 2019).

Addiction research also improves our general understanding of the relationship between brain and mind. Aside from substance use disorder (SUD) rehabilitation efforts, the impacts of psychoactive substances can affect treatment outcomes for other neuropsychological conditions, like traumatic brain injuries (TBI). There is a growing literature on interaction effects between substance use and brain injury, though the current research tends to focus on the effects of chronic alcohol misuse (Christensen et al., 2020). Such research is hindered by the limits of correlational studies and current animal models, but offers a path to understanding the unique challenges that face populations with high incidence of both TBI and substance use disorders, like combat veterans.

**Cognition and chronic substance use**

It is well established that substance use disorders of sufficiently severe magnitude or duration result in cognitive deficits. A review by Verdejo-Garcia et al. discussed the difficulties in developing appropriate tests to measure the nature and severity of such deficits, given that SUD appears to influence higher-order processes like executive functioning. Although certain drugs of abuse give rise to relatively worse deficits in specific functions (for example, stimulant users demonstrate particular difficulty with inhibition and shifting between tasks), some deficits are common between users of most substances. The researchers highlight selective attention, episodic memory, executive functioning, and reward-based decision-making as areas of particular concern (2019).

Given that each substance use disorder causes a particular set of cognitive changes, perhaps our methodology should focus on describing differential prognoses, rather than attempting to unify an entire class of disorders under a single theoretical framework (Cadet & Bisagno 2016). Neuropsychology should seek to better document neural changes in current users and abstinent former users in order to estimate which cognitive functions can be improved through treatment, and to what extent. The present review identifies avenues for further understanding that will improve prognosis and help neuropsychologists create better treatment plans for those with SUDs.

**A representation model of addiction**

Although such review studies are important for understanding the unique challenges that people face while seeking rehabilitation, they do not provide a clear theoretical framework for understanding substance addiction. In another review, Verdejo-Garcia et al. posit that three psychological processes are crucial to the maintenance of an addicted state: self-awareness, denial, and lying (2013). Verdejo-Garcia’s team defined self-awareness as “a human tribute [sic] that allows not only awareness of the self but also awareness of one’s position in his/her social environment.” Such a view is supported by evidence that the prefrontal cortex (PFC) is crucial for such social awareness and reasoning, and that repeated psychoactive drug use alters the structure and function of this brain region. Chronic substance use alters lower-order processes, like selective attention, that are necessary to collect and encode the requisite social information for self-awareness (Stuss & Alexander, 2000). Lesions in the prefrontal cortex can cause behavioral changes even in the absence of cognitive symptoms, which provides tentative support for the hypothesis that self-awareness is diminished in chronic substance users.

The researchers argue that the second dimension, denial, allows those with SUD to continue destructive drug-seeking behavior in the face of negative consequences. Denial is distinct from a lack of self-awareness because it is based on a lack of affective response to repercussions, whereas deficits in self-awareness arise from issues in obtaining and integrating information about negative consequences. Both processes together give rise to lying, the phenomenon by which patients deceive themselves and others to avoid negative consequences. The researchers cite hemispheric lateralization as a potential mechanism for lying. By this view, information is held in the right, silent hemisphere of the brain while the left, language-producing hemisphere experiences and espouses contradictory information. Lying can often frustrate clinicians and infringe on rehabilitation efforts, but this view positions lying as the locus for treatment rather than a willful gesture that hinders treatment (Verdejo-Garcia et al., 2013).

**A state-based model of addiction**

Aside from mitigating social difficulties, neuropsychology can better assist with rehabilitation by researching and treating the mechanisms that give rise to craving. An alternative framework proposed by Kwako et al. posits diminished executive function, altered incentive salience, and increased negative emotionality as the primary causes of addiction (2016). The different frameworks propound distinct constructs, but are nevertheless compatible with one another. For example, the dimension of incentive salience describes alterations in the perceived benefit of a reward and magnitude of risk and is very similar to the proposed shift in PFC activity for integrating social information, which is a possible mechanism underlying the lack of self-awareness theorized in the representational model.

Unfortunately, it seems that substance-specific methods will be most effective at reducing cravings. Negative emotionality regarding cognitive deficits can produce significant distress in individuals undergoing treatment. However, given that drugs induce changes in the cognition of rewards, it is also important to ensure that patients understand the magnitude of the problem and the extent of their progress. In this way, the two models coexist, one informing the other, together explaining the individual causes of repeated substance use, and the higher order cognitive changes that allow those with SUDs to continue use in the face of negative consequence (Verdejo-Garcia et al., 2019).

**Neural features of addiction**

Although there is a diversity of potential theoretical frameworks, reactivity to stimuli associated with the substance of choice is a common dimension of analysis. Chronic drug use not only impairs motivation, it sensitizes addicted individuals to conditioned cues that elicit craving and maintain the drug-seeking behaviors that distinguish addiction from recreational drug use (Kalivas & Volko, 2005). Cue reactivity is associated with a network of brain regions composed of the following: the (1) ventral tegmental area (VTA), (2) ventral striatum, (3) amygdala, (4) lateral hypothalamus, (5) hippocampus, and (6) ventromedial prefrontal cortex (VPFC). One’s particular level of cue reactivity may predict the likelihood of relapse for nicotine, alcohol, cocaine, and opioids (Courtney et al., 2015).

Verdejo-Garcia et al. reviewed a number of new therapeutic methods intended to reduce cue reactivity for different substance users (2019). They note a recent trend toward combining bottom-up cognitive training for working memory and motivation with existing training exercises for top-down skills, like executive functions. Therapies that combined both types of training reduced the salience of reward cues in cocaine users and chronic alcohol users. The researchers suggest that cognitive phenotyping will be crucial to creating better biological and social interventions to mitigate various deficits in motivation, impulsivity, and decision-making that together lead to repeated substance use. Computational models have also proven valuable tools in predicting reward behaviors.

A study of a polymorphism on the gene for L-type Ca2+ channels yielded support for the phenotypic model as well. The design attempted to isolate endophenotypes for social behavior and reward behavior. Researchers discovered that polymorphisms on the genes that code for calcium channels can cause increased activation for brain regions crucial to facial processing and a vulnerability for anxiety and depression. Knockout studies have reinforced the role of this gene in regulating social behavior and mood. Interestingly, the amygdala is associated with both social behavior and addictive behavior and is a potential mechanism for the link between social awareness and addiction. The studied polymorphisms also affected the ventral tegmental area, amygdala, and hippocampus, which are implicated in cue reactivity. Conditioned responses are thought to account for some of the changes to the brain (Kabir et al., 2016), but there is no clear consensus on the precise causal relationship between substance use, social, and reward behaviors. Studies on the mPFC show that drug consumption causes a number of changes in activation that persist even in abstinence, further obfuscating the causal directionality between chronic substance use and diminished cognition (Porter & Sepulveda-Oregano, 2019).

**Neuropsychological assessment and existing treatments**

Treatments for SUDs usually attempt to alleviate the cognitive distress associated with cravings and encourage self-regulation. In order to track progress and adequately treat addiction, it is important that neuropsychologists have effective measures. Existing tests can predict certain aspects of treatment outcome but a comprehensive battery is still in the early stages. For example, the MicroCog test, which is a measure designed to assess cognitive functioning, was shown to predict treatment retention. Tests of executive functioning, which is thought to be impaired in individuals with SUDs, are not as predictive, though there are concerns about construct validity (Verdejo-Garcia et al., 2019). Preliminary tests show correlations between denial and executive function impairments, though this might change as tests improve (Verdejo-Garcia et al., 2013). A self-awareness scale has been developed and measured for validity using informants to corroborate self-reported data (Verdejo-Garcia & Perez-Garcia, 2008). When measured with the scale, an abstinent population that had formerly abused drugs showed significant lack of awareness of their own apathy and executive dysregulation. Gambling tasks are another popular paradigm, and are intended to measure decision-making ability and risk reactivity (Verdejo-Garcia et al., 2019 & Verdejo-Garcia et al., 2013).

Kwako et al. have proposed an Addictions Neuroclinical Assessment (ANA) framework that offers a more comprehensive battery of the various processes that could possibly be impaired or interrupted in those with SUDs (2016). The measure consists of a number of tests chosen to assess the three proposed domains of executive functioning, negative emotionality, and incentive salience. Most of the tasks are behavioral, but a few include self reports, designed to test depression, anxiety, etc., in order to identify possible comorbidities that may obstruct treatment. The battery also incorporates neuroimaging measures including a cue reactivity task. The team hopes to collect more comprehensive data about the range of vulnerabilities that lead to substance use disorders, and create therapies that more precisely target the problem. The ANA framework has the potential to better inform clinical decisions and help individual patients achieve and maintain abstinence. By creating a unified dataset, it allows us to compare the relative effectiveness of common treatment paradigms like the Alcoholics and Narcotics Anonymous’ twelve-step program.

Computer-assisted cognitive behavioral therapy (CBT) is one treatment approach that attempts to restore performance on cognitive measures that predict relapse. One such therapy yielded improvements in executive functioning, namely impulse control and reward evaluation (Cadet & Bisagno, 2016). Diminished cravings are associated with activity in regions of the brain that are usually implicated in emotional control, namely the prefrontal-striatal pathway (Kober et al., 2010). CBT is effective for helping patients to regulate their own behavior and has been shown to diminish the intensity of cravings. Another computer therapy called cognitive bias modification (CBM) reinforces alternatives to established drug cues, which could potentially trigger relapse. CBM is implemented in conjunction with other therapies designed to interrupt drug cues using mindfulness, with the intent of supporting both top-down and bottom-up improvements (Verdejo-Garcia et al., 2019). There have also been studies on psychosocial interventions, though the effect on cue reactivity is not as clear (Courtney et al., 2015). The ANA framework seems a promising tool for neuropsychologists interested in treating addiction. The test has been criticized because it requires 10 hours to administer, but it also contributes to a large comparable data set because it constitutes a set of standardized measures (Ghitza, 2017).

**Conclusion**

As researchers begin to uncover more and more of the underlying cognitive and neural factors that lead to compulsive substance use, the need for a robust addictions battery becomes increasingly obvious. Although the current ANA framework represents a crucial first step, further study and development is required to produce a scale sensitive to the various dimensions that impact the severity and longevity of addiction and predict the success of treatment. An ideal assessment battery would reliably measure the strength of craving, level of self-awareness and denial, and mood in patients seeking treatment for SUDs. Developing an addictions scale should be a priority for those interested in treating SUD in order to objectively measure the relative effectiveness of the various rehabilitation strategies and programs available. As more precise biological models of addiction continue to be developed, having an addiction scale at the ready would allow for more rapid testing and approval of potential future pharmaceutical interventions.

Addiction is a peculiar condition and has not traditionally been included in the range of disorders that neuropsychology is equipped to treat. Nonetheless, the literature suggests that addiction rises from various changes and damages to the brain that result in cognitive modifications, and reveals addiction research as fertile ground for neuropsychological investigation. Addiction research will undoubtedly improve scientific knowledge about the psychological processes that we use to assess risk and make decisions, which will transfer to the understanding and treatment of other disorders and illnesses. Most importantly, however, the neuropsychologist armed with sufficient understanding and psychometry could offer a more fruitful path to rehabilitation for those struggling with substance use disorders.

One study of postgraduate psychiatry students undergoing their first experience with addiction treatment shows how attitude can impact diagnosis and treatment outcomes. One participant reflected on their own biases and the commonly held misconception that those living with SUD are simply not sufficiently motivated to abstain:

I found myself amazed at the fact; despite his burning desire to quit he was unable to make progress. The impression I had before was that if someone really had the will to quit and the intelligence to make a good plan then they would have little difficulty in abstaining, but clearly I was wrong. (Ballon & Skinner, 2008, p. 221)

Education and research impact the quality of care that patients receive and the quality of life that treatments may offer them. Perhaps the first step toward adequate treatment is recognizing substance use disorder as a neuropsychological problem.

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