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PERSPECTIVE
Integrating Addiction into the Neuroscience Curriculum

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Addiction is a relevant and fascinating topic that can be readily taught within undergraduate neuroscience curricula. Modern research has afforded tremendous insights into the neuroscience of addictions, including substance use disorders, behavioral addictions, and disorders of impulse control and compulsivity. Building on the neuroscience of plasticity associated with learning and memory, we now understand a great deal about the temporal and spatial progression of these disorders in adult and developing brains. Addictions have considerable health and social consequences to modern society, particularly with legalization of marijuana, the increasing popularity of numerous gambling/gaming venues, and the surge of methamphetamine and opioid abuse. To guide healthy medical practices and help inform policy makers, there is an increasing need for neuroscientists informed on addiction topics. Undergraduate education for students with an interest in the neurosciences is an excellent venue to achieve this goal. Key to this education is what modern neuroscience informs us on addiction processes and making these concepts relevant to the undergraduate student. Toward that end, this editorial will illustrate how addiction neuroscience can be integrated into ongoing curricula at the undergraduate level.

Key words: addiction neuroscience, substance use disorders, behavioral addictions

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Addictions have long been a part of the human experience, and often considered to reflect character flaws or moral failings. Recent decades of neuroscience research have lead to the recognition that addictions reflect biological dysregulation of the brain that is akin to other organ diseases. This transformative concept should have high impact on how individuals struggling with addiction consider themselves, are understood by their family and friends, and are treated by society and the medical community. In spite of these neuroscientific advances, our culture still grapples with ethical issues related to addiction (e.g., brain disease vs. personal choice) and stigma associated with addiction. A better informed public would help cope with changing cultural norms and the need to make science-based policy decisions that have high impact on our society (e.g., legalization of marijuana; gambling).

Addiction-related topics are of great interest to students at all levels of neurobiological understanding. Addiction research provides a remarkably useful lens for focusing undergraduate neuroscience education - it integrates cutting edge knowledge and methodology from across the diverse levels of analysis within the neurosciences. Addiction-related topics also provide an interesting immersion into STEM education, especially for students targeting careers in biomedical fields. Pragmatically, this topic is particularly relevant to undergraduate-age individuals who are highly exposed to substance use disorders, eating disorders, internet and sports gaming/gambling, and pain management scenarios. Undergraduates are a receptive audience for understanding and appreciating scientific models of addiction. Thus, their education will significantly contribute to a better-informed public.

Addiction is a chronic, relapsing brain disease, in which the individual persists in using drugs even in the face of negative consequences. This definition relates to substance use disorders, behavioral addictions and disorders of impulse control and compulsivity. Addiction encompasses many topics central to the behavioral neurosciences, including decision-making, learning and memory, development, and nature *vs.* nurture. Addiction neurobiology involves all aspects of neurotransmission, including genetics, epigenetics, biochemistry, cellular physiology, circuits and human brain imaging. Accordingly, modern neuroscience is reshaping how we view addiction, and by inference, how we should teach topics related to addiction.

In this editorial, I overview concepts that are key to basic understanding of addiction neuroscience and provide examples of how these concepts can be incorporated into an ongoing curricula in undergraduate neuroscience. The emphasis is on teaching science-based, modern day concepts of the addiction process and relevant ramifications. The point is not to detail specific neurobiology *per se*, for these details should be customized to the level of the class (freshmen vs. seniors) and the background requirements for the course. There are numerous excellent reviews on addiction neurobiology that can guide this endeavor, and several are provided in the References (Dalley et al., 2011; Robbins and Clark, 2015; Volkow and Morales, 2015; Rash et al., 2016; Volkow et al., 2016; Gray and Squeglia, 2017; Sinha, 2018;). Here, I will provide examples of approaches that can be implemented into a given curriculum, including cluster topics – integrated or stand alone, case studies, non-fiction reading, and linking to community outreach.

In practical terms, addiction may be considered as a type of applied neuroscience, such that by understanding how addictions are a consequence of basic neurobiological principles, we may enhance understanding and empathy for those who suffer from this brain disease.

Key concepts that should be developed are that addiction is a *process,* which involves several distinct *phases*, many of which are *cyclic* in nature.

The idea that addiction is a process reflects modern understanding of brain substrates that underpin the differences in motivations to initially engage in the addiction behavior, and those that sustain the behavior following repeated exposure. The early motivators can be grouped into two categories: '*to feel good'* or '*to feel better*' (see the National Institute on Drug Abuse, (NIDA) https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drug-abuse-addiction).

'To feel good' refers to the desire to have positive feelings, sensations, and experiences. This often involves wanting to share these experiences with peers, and to receive peer approval for the experience. This behavioral profile is seen in risk-takers, sensation-seekers, and impulsive individuals. Several interesting topics can be considered with regard to the neurobiological underpinnings of "to feel good," e.g., *brain development*. The human frontal cortex is not fully matured until the early 20's for females, and mid 20's for males. As the frontal cortex is involved in several aspects of executive function, including inhibitory control, decision-making by teenagers and young adults reflect more emotionally-laden processes governed by subcortical limbic structures (e.g., the nucleus accumbens and the amygdala). In contrast to the frontal cortex, the brain's reward circuit, i.e., mesolimbic dopamine systems including the ventral tegmental area (VTA) to nucleus accumbens (NAc) pathway, is fully mature in teenagers and young adults. Mesolimbic systems are important in promoting behaviors that are needed for survival of the individual (e.g., eating, drinking) and the species (e.g., sex, nurturing of the young). Massive amounts of dopamine are released into the NAc by drugs that are abused by humans (with the exception of hallucinogens) and by engaging in behavioral addictions (e.g., gambling, compulsive shopping, binge eating). Thus, addictions are thought to occur when natural, healthy, reward-related processes are usurped or 'hijacked' by abused drugs and unhealthy habits.

Box 1: Additional Discussion
Related concepts that are relevant for discussion by the students:

- The differential development of cortical inhibitory control relative to reward motivation results in emotionally laden decision-making in youth. This may be beneficial to the species by ensuring the young are highly motivated in self and species survival, but it may also make the young much more vulnerable to exploring harmful drugs.
- As cortical development is ongoing, dramatic changes imposed on the function of the brain by, for example, psychoactive drugs has the greater potential to change the course of development, with long term consequences

'To feel better' refers to those circumstances where the individual is trying to lessen worries, fears, anxiety, feelings of hopelessness and/or depression. In other words, the individual is self-medicating for an underlying emotional problem, mental health disorder, and/or a stressful environment. This falls at the interphase of biology and environment interactions and provides for an excellent opportunity to engage in 'nature vs. nurture' discussions.

The motive for both 'to feel good' and 'to feel better' is that the individual takes a drug with the intent to change their emotional state, mood and/or perception - in other words, to change their brain. Thus, understanding *why* an individual takes a drug is neurobiologically (and clinically) relevant.

Box 2: Additional discussion
Topics may include genetic predisposition, the impact on freedom of choice, and stigma. The different motives for entrée into addiction may influence, for example, responding to treatment and outcome expectations in the criminal justice system.

The distinct phases of addiction are behaviorally indexed by exploration, recreational/controlled drug use, habits, binge/intoxication, compulsive drug use/addiction, withdrawal, abstinence, drug-seeking, and relapse (Everitt, 2014). The neural circuitry engaged during these phases is becoming understood (Koob and Volkow, 2010): Early phases of reward-motivated associative learning involve dopaminergic projections to the NAc. The development of habits depends on the dorsolateral striatum. The withdrawal phase involves the amygdala. Decision-making based on the subjective salience of the drug (e.g., craving and drug-seeking) involves the prefrontal cortex. Glutamate-driven synaptic plasticity is core to many of the circuit-related maladaptations associated with addiction, and this plasticity follows principles that underpin learning-related synaptic strengthening.

Box 3: Additional Discussion
Topics to be expanded upon are mechanisms that underlie synaptic strengthening. In the context of these key concepts, the neuroanatomical substrates of addiction, i.e., brain circuits and neurotransmitters and associated psychopharmacology can be considered. That is, each stage of the addiction process provides an opportunity for developing treatments that are particularly relevant to that stage. With advanced classes, modern theories of the addiction process can be considered.

The cyclic nature of the addiction process reflects the proclivity to relapse back to drug-taking even after protracted abstinence and by those who are motivated to quit. Relapse reflects the enduring maladapations in the brain that were induced and maintained during compulsive drug use. The triggers for relapse are fascinating topics of addiction neuroscience. The emotional components are thought to include the high importance attributed to the particular drug or behavior (e.g., gambling), the strength of the drug/behavior-associated stimulus to induce craving/ seeking, and the desire to avoid withdrawal-related suffering.

Box 4: Additional Discussion
Understanding the brain changes that occur during the addiction process allows students to challenge long-held concepts. For example, students may question the degree of voluntary control that one has over continued drug abuse. NIDA holds that "when drug abuse takes over, a person's ability to exert self-control can become seriously impaired" (https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drug-abuse-addiction). Key to this discussion is the brain imaging literature on those suffering from addiction. This literature documents physical changes in cortical regions that govern learning and memory, judgement, behavioral control and decision-making (Volkow et al., 2012).

Box 5: Additional Discussion
Understanding the pharmacology of abused drugs and what changes in the brain during the addiction process helps inform how addiction can be treated. Discussion could include, e.g., (a) The value of using pharmacotherapy (e.g., methadone) to treat drug abuse. (b) Behavioral addictions, impulse control disorders and compulsivity (e.g., problem gambling), including those that involve natural rewards (e.g., eating disorders, hyper-sexuality). There is a wealth of modern literature authored by experts that can be used to promote provocative discussions (e.g., Calorie intake and gambling: Is fat and sugar consumption "impulsive"? See Chamberlain et al. (2017).

Core Topics

As illustrated by the Key Concepts overview, an understanding of addiction processes requires knowledge of the neuroanatomical substrates of addiction, including those at the circuit level (VTA, NAc, frontal cortex) and the level of neurotransmission (dopamine, glutamate, serotonin, opioids, endocanabinoids, and the cognate receptors). The phases of addiction also involve particular behavioral/emotional features. Comparing and contrasting substance use disorders with behavioral addictions (e.g., compulsive eating, compulsive shopping, hypersexuality, gambling disorders) not only is culturally relevant, but also serves to underscore core features of addiction in general.

Understanding how various abused drugs work in the brain is key to understanding the neuroscience of addiction. Basic pharmacology for drugs for which the students would likely be most interested (Table 1) could include drug nomenclature and classification, and general pharmacodynamics (i.e., receptors, signaling proteins). These concepts can be augmented by comparing behavioral pharmacology/psychopharmacology of the different classes (e.g., cocaine vs. marijuana; alcohol vs. heroin). Overlaying the common circuits (mesocortico-limbic system) and transmitters (dopamine, glutamate) associated with all addictions, with the unique features of the different classes of drugs is a critical concept in understanding the core features of the addiction process with the unique behavioral and treatment challenges that are posed by different abused drugs.

Approaches for Supplementing Knowledge

Integrating addictions into a neuroscience curriculum provides an excellent venue to teach science-based, current concepts of the addiction process and relevant ramifications. The subject of neuroscience of addiction can be a standalone course, or the topics can be clustered and integrated into ongoing courses. Examples of approaches that are engaging to undergraduate students include the following:

Case Studies allow specific topics that are particularly relevant to the course or students to be highlighted. Case studies help personalize the neuroscience learned in the classroom and reinforce retention of information. Nagel and Nicholas (2017) provide an excellent discussion on this teaching approach.

Non-Fiction Reading is a powerful means to connect neuroscience to the effects of drugs on the human experience. Discussion focus can be on topics such as how different experiences are associated with the various drugs, why do different individuals take drugs, what is the human struggle to remain abstinent and avoid relapse, what is the impact on the abusing individual, their family and friends. Memoirs are an engaging means to enhance relevance of addiction neuroscience and may tool the students to develop more empathetic opinions regarding topics such as stigma and criminal policy. Pollack (2015) suggests several creative venues for implementing non-fiction reading in the classroom, including establishing a book club and utilizing role playing.

Drug	Class	Predominant Site of Action in the Brain
Amphetamines (e.g., meth)	Psychostimulant	presynaptic monoamine vesicular & cytosolic transporters
Cocaine	Psychostimulant	presynaptic monoamine cytosolic transporters
Nicotine	Psychostimulant	nicotinic receptors
LSD	Hallucinogen	5-HT1A receptors
Heroin, morphine, OxyContin®	Opioid	Mu opioid receptor
Marijuana	Cannabinoid	CB1 receptors
Alcohol	Sedative-hypnotic	GABA receptors
Barbiturates	Sedative-hypnotic	GABA receptors
Benzodiazepines	Sedative-hypnotic	GABA receptors

Table 1. Selected examples of abused drugs.

Link to Community Outreach is an excellent means to raise students' awareness about the neuroscience of addiction. Such enriching experiences supplement the content knowledge learned in the classroom, help develop professional skills, and promote citizenship.

CONCLUSION

Undergraduate education for students with an interest in the neurosciences is an excellent venue to teach addiction neuroscience. Key to this education is what modern neuroscience informs us about addiction processes and making these concepts relevant to the undergraduate student. Benefits of enhancing knowledge of this timely and highly relevant topic not only will be evident in the students' academic experience, but also in society as a whole.

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