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Introduction to the special issue: “Role of corticostriatal circuits in addiction”

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Our knowledge of brain circuits involved in addiction has increased dramatically in the last few years. In particular, abundant evidence from new tools such as optogenetics and designer receptors have denied, confirmed and extended prior hypotheses about brain mechanisms in a host of behaviors, including addiction. Perhaps more than most behavioral disorders, animal models of addiction have great face and construct validity. This, combined with continuing support from the National Institute of Drug Abuse and the new tools available in neuroscience, have resulted in great advances in addiction research.

Corticostriatal circuits have long been associated with addiction behavior, from sensitization studies in the 1990s to reinstatement studies today. This special issue was inspired by the rapid advances in understanding these circuits in different aspects of addiction.

Several articles deal with changes at the molecular or genetic level that occur with drug administration and contribute to neuroplasticity that underlies persistence of addiction behaviors. These articles reveal roles for corticostriatal microRNAs in cocaine abuse (Heyer and Kenny), synaptic proteins (Marton et al., Smith et al.), glutamate receptors (Guo et al.), and epigenetic changes (Sadri-Vakili) in addiction to cocaine or opiates.

An additional theme of this issue is growth factors in corticostriatal circuits that contribute to the addiction process. Logrip et al. review evidence for a role of BDNF changes in alcohol abuse, and Barker et al., and McGinty et al., describe novel roles for BDNF in cocaine seeking and extinction. This set of studies represents another source of plasticity that is important in the addiction process.

Articles by Buchta and Riegel, and by Balleine et al., describe how cocaine exposure or self-administration alters physiological properties of corticostriatal circuits in a manner that interferes with normal plasticity and learning mechanisms. This interruption of normal learning processes may contribute to a nonplastic state that promotes persistent addiction behaviors. Similarly, Morein-Zamir and Robbins describe how interruption of normal response inhibition functions mediated by corticostriatal circuits may contribute to addiction behavior.

Other articles extend these molecular/cellular level studies to the circuit level, and detail how alterations in activity of neurons in corticostriatal circuits are involved in addiction. Moorman et al. describe unit recordings in prefrontal cortex that show changes in activity of prelimbic and infralimbic neurons that do not fit the classical model of ‘go’ vs ‘stop’ functions for drug seeking vs extinction processes in cocaine. Konova et al. show how stimulants interfere with normal connectivity in corticostriatal circuits, and how that may

contribute to addiction behaviors. Cruz et al. describe novel methods using the immediate early gene c-fos to identify and manipulate neurons in corticostriatal circuits that are involved in cocaine abuse. Finally, London et al. use neuroimaging in humans to identify abnormalities that arise in corticostriatal regions with methamphetamine abuse that may underlie a variety of cognitive and behavioral deficits.

Therapeutics for addiction have been lacking, and for stimulants there is no FDA-approved therapy to give patients to help achieve or maintain abstinence. Articles in this special issue review novel potential therapeutics that may be available in the future. Kravitz et al. review studies in animals using deep brain stimulation and transcranial magnetic stimulation (TMS) in patients to facilitate abstinence from cocaine; these approaches have promising potential applications in human addicts. Hanlon et al. describe a similar potential therapy from human experiments that involves theta burst stimulation of cortical regions with TMS. Other potential therapies are presented in papers by Limpens et al. who describe effects of inhibiting cortical area on cocaine seeking, and by Marchant et al. who show that manipulations of activity in corticostriatal circuits can attenuate context-induced reinstatement of cocaine seeking. Finally, Covey et al. review studies that show a potential benefit of manipulating cannabinoid signaling to interfere with addiction processes, with implications for legalization of marijuana.

Together, these articles offer a comprehensive update from the molecular through the circuit levels into alterations in brain that underlie addiction, and provide glimpses into potential future therapeutic approaches to treatment. This body of work supports the central role of corticostriatal circuits in addiction, and the way that knowledge about these circuits can lead to novel therapeutics to treat the persistent problem of addiction.