

## COMMENTARY

# Neuropharmacology of addiction—setting the scene

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Addiction is a complex disorder, affecting not only the individual addict, but also their family and the community at large. While therapeutic strategies are available for the treatment of some forms of substance abuse/dependence, these are not without problems and are not universally efficacious. Moreover, in some instances (for example, cocaine addiction), there are still no medications specifically registered as treatment options. In this themed issue of the *British Journal of Pharmacology*, we highlight a number of addictions from a pharmacological perspective, with an emphasis on both mechanism and potential therapeutic approaches that are either under development or reflect preclinical work. As such, the authors endeavour to describe the latest thinking on the neural theory of addiction and corresponding novel pharmacotherapeutic targets, and in this way to set the stage for future advances in research and drug development. In addition, we have also attempted to draw attention to the clinicians' perspective in terms of the interface between basic science and care provision.

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Substance abuse and addiction are major public health issues of both the developed and the developing world. Importantly however, we should acknowledge that addiction is not a disease of the modern era. Indeed, mankind has been characterized throughout history as being a species that actively seeks to undergo 'mind-altering' experiences be it for cultural, religious or social reasons. Thus, while we should not blame the industrial and/or technological revolutions as contributors to the issue, we should actively seek to utilize their advancements to assist in seeking answers to the problem. Firstly, we need to understand the scale of the problem—sobering statistics may help to devise solutions for sobriety. The most recent published data (US Department of Health & Human Services) available suggest that the incidence of substance-use disorders among the general population is approximately 9.2% (see Aldworth *et al.*, 2007). The financial burden of drug addiction/dependence/abuse is rather difficult to determine; however, it has been suggested to cost up to 3.5% of the gross domestic product within Western society (Pouletty, 2002). Importantly, these figures only account for the economic burden, while addiction also carries an enormous and impossible-to-

underestimate social and emotional burden. Unfortunately, the cost of addiction to society is not mirrored by the funds invested for either basic or clinical research into this mind disorder.

Our intention is not to compare and contrast theories surrounding the transition from episodic to dependent or addictive drug use, as others have elegantly done so in recent times (see, for example, Everitt and Robbins, 2005; Kalivas and O'Brien, 2008; Koob and Le Moal, 2008). Rather, we will focus more squarely upon the therapeutic options available. It is cogent to note, however, that it is not the authors' belief that therapeutics will be simple, even with the development of medications that are efficacious. Inherent in the treatment of addictions are problems with co-morbidity, compliance and off-target effects of prescribed agents. Some of the articles within this issue may also assist clinicians in the identification of alternative treatment options to those currently in use, as compounds registered for one use may have other indications that do not necessarily become apparent to as wide an audience as they should.

As discussed in this issue by David Nutt and Anne Lingford-Hughes, a number of factors must be considered when treating addicts, including management of withdrawal symptoms, abstinence promotion strategies and craving as a therapeutic problem. In addition to these issues, one must also consider receptor dynamics and pharmacokinetics as serious factors. Furthermore, these authors also look to the future and discuss the potential for using drugs that

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influence learning and memory in the context of addiction medicine (Nutt and Lingford-Hughes, 2008). From the perspective of alcoholism, Rainer Spanagel and colleagues (Vengeliene *et al.*, 2008) provide a comprehensive review of the transmitter systems and receptors affected by chronic alcohol use and they put forward a number of possible candidates for development as therapeutic approaches. In parallel, Mayfield *et al.* (2008) provide a much-needed update on the genetics of alcohol dependence; indeed pharmacogenetic treatment strategies are also likely to be relevant in the treatment of not only alcoholism, but also other forms of addiction. At the molecular level, Thomas *et al.* (2008) identify brain-derived neurotrophic factor (BDNF) and extracellular signal-related kinases (ERK) as key molecules whose role in stimulant-induced plasticity demands further study. In relation to psychostimulants, McGregor *et al.* (2008) raise the intriguing possibility that oxytocin may not only be responsible for some of the immediate pro-social effects of drugs, but may also play a hitherto less recognized role in shaping some of the longer-term, adverse consequences of drug use. Further confirmation of this would clearly open the door to another path for therapeutic targeting of substance-abuse problems.

In summary, this themed issue should provide a useful resource for addiction researchers, both basic and clinical. Moreover, we also acknowledge that numerous clinical trials are currently underway for new medications or to identify wider applications for current medications. We do not intend to provide an exhaustive list of clinical trials underway, as some are still in the recruitment phase. Interested readers can follow such progress online (for example, see

<http://clinicaltrials.gov/search/?term=NIDA>). It is to be hoped that the list of newly developed compounds under trial expands and, more importantly, translates into prescribing options for healthcare professionals.

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