Assessment of abuse potential of drugs: Translational perspectives

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Preclinical assessments of a drug’s abuse liability typically involve studies that assess the capacity of a drug to produce physiological dependence and those that assess the reinforcing effects of drugs with self-administration procedures. Most often, studies that examine physiological dependence do so by assessing whether a drug reverses the withdrawal signs that follow treatment with a standard drug. Withdrawal also occurs from drugs that are used therapeutically, but is typically referred to as rebound. Problems of abuse stem therefore, not from physiological dependence per se, but from the reinforcing effects of abused drugs, though dependence may influence reinforcing effects of drugs. Simple results from self-administration procedures are predictive of whether a drug will be abused in human populations. Nonetheless, there is documentation that the pharmacological history of a subject may predispose or counter predispose to reinforcing effects of other agents. Self-administration procedures are also used in searches for medications to treat drug abuse. This approach is the logical extension of abuse liability assessments, but has not been validated, the key concern of translation. Critical to assessments of the effects of potential drug-abuse medications is the shape of the self-administration dose-effect curve and how it is changed by treatment with the potential medication. Two types of effects of treatments have been discussed in the clinical literature – antagonism (e.g. naltrexone for opioid abuse) and substitution (e.g. methadone). How these types of treatments relate to the change in the self-administration dose-effect curve requires substantial focus to fully realize translational potential for laboratory studies.