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Hall W., Partridge B., Lucke J. Constraints on regulatory options for putatively cognitive enhancing drugs. *American Journal of Bioethics* 2013; **13**: 35-7

We welcome Velko Dubljevi´c's article (2013) as a useful step in moving neuroethical discussions about the regulation of putative cognitively enhancing drugs (CED) beyond armchair analyses from a priori ethical principles into the real world of drug regulation.

The adjective "putatively" CED should be understood as qualifying CED in the remainder of our commentary. As we have argued elsewhere, many ethical analyses of CEDs assume that there is evidence that stimulant drugs enhance cognition in individuals without a diagnosed cognitive impairment, when the evidence on their efficacy is equivocal (Lucke et al. 2011; Repantis et al. 2010).

Many analyses of the ethics of using CED start from a presumptively libertarian position that gives priority to the ethical principle of autonomy. Given this, it is unsurprising that these authors conclude that CEDs should be made available to any adult who wishes to use them (e.g., Harris 2009; Harris and Quigley 2008). Analysts who want to take account of possible harms to individuals from CED use often suggest a modified prescription system, with doctors as gatekeepers (Greely et al. 2008; Larriviere et al. 2009).One of us outlined the range of potential regulatory options nearly a decade ago (Hall 2004), but these suggestions have largely been ignored until Dubljevi´c's recent papers.

Dubljevi´c's article (2013) moves the debate about CED regulation in more productive directions by (1) arguing that we need to evaluate CEDs on a case-by-case basis that takes account of evidence on their safety and efficacy, and (2) pointing out that possible forms of regulation of CEDs are severely constrained by international drug control treaties of 1961 and 1971 to which the majority of developed countries are signatories. Many discussions in the neuroethics literature have failed to appreciate that these treaties effectively preclude the regulatory options bioethicists have suggested for CED using stimulant drugs.

We cannot, for example, use taxes to discourage the abuse of stimulant-based CEDs, in the same way as we can with alcohol and tobacco, because stimulant drugs cannot be sold as legal commodities under the 1971 United Nations Convention on Psychotropic Drugs. Adaptation of the coffee shop model for cannabis is also precluded, as Dubljevi´c points out, because cannabis is regulated under the 1961 United Nations Single Convention on Narcotic Drugs. There is debate about whether signatory states to the 1961 Single Convention must criminalize personal drug use, but this convention does prohibit the legal sale and distribution of cannabis. The Netherlands has argued that it retains the criminal prohibition on cannabis sales but under its expediency principle chooses not to enforce the law in the case of sales that occur in the restricted and tightly regulated circumstances of licensed coffee shops.

The 1971 Convention requires signatory states to criminalize
any use of stimulant drugs (and other psychotropic drugs that fall within its provisions) other than for medical or scientific purposes. As Dubljevi´c points out, the 1971 Convention on Psychotropic Substances specifically includes the amphetamine-type stimulants and methylphenidate within its provisions. This means that the regulatory proposals of Greeley and colleagues (2008) to allow sale and promotion of these drugs for enhancement purposes conflicts with the 1971 convention. Any newer stimulant drugs, or other pharmaceutical

drugs with putatively CE effects, are also likely to be included under the 1971 convention, if evidence emerges that they are being abused by young adults.

Dubljevi´c defends the prohibition on the nonmedical use of amphetamine salts. He argues that although these drugs are safe when used in recommended doses for medical purposes, allowing their enhancement use would likely harm a substantial proportion of users who may use these drugs in larger than therapeutic doses, over substantial periods of time, increasing the risks of dependence and psychosis. Historical experience with harms arising from recreational amphetamine use provides support for this argument (Bell, Lucke, and Hall 2012; Klee 1997; Rasmussen 2008).

Dubljevi´c argues that we should consider a different policy toward the enhancement use of sustained-release formulations of methylphenidate. Adults could be allowed to use this drug, he argues, under an appropriate licensing system for producers and users of the drug. Under his proposed system 1) there would be tight regulation of companies that produced and marketed this drug for enhancement purposes, 2) it would be heavily taxed to discourage abuse, and 3) potential users would be required to receive a license to use the drug by undertaking educational courses on the risks posed by its use.

This proposal sounds plausible but we see a number of major problems with it.

First, we should not assume that sustained-release forms of drugs will be safer than immediate-release forms when these drugs are widely used in the community. The epidemic abuse of sustained release forms of OxyContin in the United States and other developed countries provides a cautionary tale (Hall and Degenhardt 2007; Hall and Farrell 2011). These opioid formulations were claimed to have low abuse potential, but users quickly discovered how to extract the active ingredient. The result was an epidemic of opioid overdose deaths that exceeded the number of deaths caused by heroin (Okie 2010; Van Zee 2009). Opioids have a much greater risk of fatal overdose from respiratory depression than the amphetamine-type stimulants (Darke,Degenhardt, andMattick 2007), but the latter can cause premature deaths from myocardial infarction and stroke in healthy young adults (Darke et al. 2007; Singleton et al. 2009). The illicit production of methamphetamine from cold medicines containing pseudoephedrine in many countries indicates that this problem is not peculiar to opioids (McKetin et al. 2011).

Second, we have doubts about the feasibility and effectiveness of the proposed regulatory system. Tight regulations and high taxes would be major disincentives to the participation of the pharmaceutical system in the production and marketing of this drug for enhancement use. The high taxes and the inconvenience of obtaining a license to use may also mean that many stimulant users prefer to use diverted pharmaceutical or illicitly produced stimulants.

Third, the proposed system would also require a modification of the 1971 convention. As Dubljevi´c points out, the provisions of the international drug control treaties allow member states to renounce treaties and re-accede with specific reservations, as Bolivia has recently done with coca leaf. But these provisions have been rarely exercised and their use is likely to bring strong international disapproval on countries that propose such changes (Room 2012). There are a number of other points that we would make that are not central to Dubljevi´c's arguments but are nonetheless worth making about neuroethical discussions of the regulation of CEDs.

First, the libertarian views about the failures of drug prohibition that dominate the philosophical literature are not shared by drug policy analysts (Strang et al. 2012). Drug policy analysts certainly criticize the draconian enforcement of criminal penalties against drug users (e.g., Room and Reuter 2012), but their proposed reforms to existing drug laws fall well short of the complete repeal that is the logical implication of libertarian analyses. These critics do advocate more liberal regulatory policies toward cannabis (Room et al. 2010), but they favor less radical forms of regulation for other illicit drugs. These most often include a combination of policies, such as retaining the prohibition on nonmedical opioid use; increasing access to agonist maintenance treatment (e.g., methadone) for opioid addicts; and using prescription monitoring systems to minimize the diversion and abuse of pharmaceutical opioids (Strang et al. 2012).

Few drug policy analysts have advocated liberal regulation of stimulant drugs. One drug reform advocacy group in the United Kingdom has proposed a system of licensing users for stimulants and dance party drugs much like that suggested by Dubljevi´c (e.g. Transform Drug Policy Foundation). The reluctance of drug policy analysts to radically liberalize the regulation of stimulant drugs is for the reasons that Dubljevi´c summarizes in his article. We discuss these regulatory issues in a forthcoming chapter (see Lucke et al. 2013).

Finally, we think that the bioethical debate about enhancement use of stimulants should take account of a potential unintended adverse effect of the inflated estimates of the prevalence of CED use among young adults used to argue for liberalization. This is a reduction in the medical use of these drugs in the treatment of ADHD and other conditions. Critics of the medical use of these drugs to treat ADHD now cite the allegedly high prevalence of their enhancement use as an additional argument for severely restricting, if not banning, the medical use of these drugs (e.g., Whitely 2012).

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