



Debate

Pharmacological cognitive enhancement in healthy people: Potential and concerns

Participants: Steve Hyman, Nora Volkow, David Nutt

Steve Hyman: This is a programme on pharmacological cognitive enhancement in healthy people, potential and concerns. I am your moderator Steven Hyman, Harvard University Distinguished Service Professor and Director of the Stanley Centre at the Broad Institute of MIT at Harvard. The two scientists who will be discussing the questions will be Nora Volkow MD who is Director of the US National Institute on Drug Abuse and is also a very accomplished researcher, most notably in brain imaging. She has previously been the director of various different departments including nuclear medicine at the Brookhaven National Laboratory in Upton, New York. Our other discussant is Dr. David Nutt who is the Edmund J. Safra Professor of Neuropsychopharmacology and Director of the Neuropsychopharmacology unit in the division of brain sciences at the Hammersmith Hospital, Imperial College London. He is currently President of the British Neuroscience Association and Chair of the Independent (UK) Scientific Committee on Drugs (ISCD) and among many other positions and honours he was previously the Chair of the Advisory Council on the misuse of drugs in Great Britain and President of the British Association of Psychopharmacology. Thus we have two highly qualified and important thinkers on the issue of cognitive enhancement.

Let me ask first Nora and then David about existing drugs, of which we have several, most notably caffeine, methylphenidate known by its brand name of Ritalin, amphetamines, and modafinil known by its brand name of Provigil that are used by healthy people to enhance alertness, make tasks more engaging, and generally to improve cognitive performance. Sometimes these are used illegally, for example without a doctor's prescription as "study drugs" in secondary school and University, among other settings. Do you think this represents a problem? Are there aspects that might not be problematic? Nora?

Nora Volkow: Certainly I can tell you that in the United States that abuse of stimulant drugs is a serious problem and in fact from surveys it is estimated that 8% of 12th graders have used amphetamine for non-medical purposes in the past year. If you look at the records of the reasons for admissions for prescription and over the counter (OTC) treatment, the number one reason among adolescents (12–17) has to do with stimulant drugs. So stimulant drugs are diverted, they are abused and they can produce quite severe addiction and in fact we know that in many countries addiction to amphetamine is very, very prevalent. So there is a serious problem with respect to the abuse and addiction liability of these drugs.

Steve Hyman: David, perhaps you want to continue in the same vein but consider whether for those people who are not at serious

risk of addiction, are there still serious problems and if not are there any advantages?

David Nutt: I think we need to see this issue in a historic perspective. The last war was fought with both sides taking stimulants, either amphetamine sulphate or methylamphetamine and it was then seen as a good thing and in fact still we know quite a lot of the military use modafinil to stay awake and keep optimal attention under times of prolonged sleep deprivation. Clearly there are also values in these drugs that have been established with the use of amphetamines and methylphenidate for 60 years now for the treatment of ADHD, so I don't think there's any major health issues around their use. I think the question of whether they lead to addiction or dependence in some people obviously is a concern. It's not an issue we are finding of particular concern in the UK at present. The ISCD has just done a survey of university students and we found about 8% have taken Provigil and about 3% have taken amphetamines to help with study, but there certainly is not a big problem with those people going on to seek help for dependence in the UK.

Nora Volkow: Can I interject here Steve to actually put a concept on David because yes, these stimulant drugs have been used by the military for more than 50 years but what's interesting is that the British stopped using them and it had to do with the fact that use of these stimulants can make a person paranoid and that in turn could have very adverse effects in a military situation. In the United States the use of stimulant drugs has indeed been associated with friendly fire, the cause of this resulted from friendly fire that led to distortions of perceptions as well as paranoid thinking, so there is clear apart from the issue of addiction the problem that some of these drugs more than others, particularly amphetamines can produce a full blown psychosis.

David Nutt: Certainly if they're taken for too long there's no question of possible harms, although our servicemen tend to look with envy at the fact the Americans can use Provigil because we don't even let them use that, so they feel they're a bit disadvantaged in periods of extreme sleep deprivation, but anyway, that's a side issue I think from what we're discussing tonight.

Steve Hyman: Right. I think the concerns with stimulants that leads to their being highly restricted are the side effects of the kind that Nora mentioned, and in addition, potentially cardiovascular side effects and addiction liability, but what I'd like to get to are the ethics and policy concerns raised by enhancing cognition in healthy people. So let's see if we can get away from the side effects of stimulants and imagine that scientists are finally successful in developing a drug to treat memory loss—in fact many are working on such drugs to treat symptoms of dementia. If we had

a drug that could enhance memory and did so by a neurobiological process that would also work in healthy people, how would you feel about such a drug? How would you feel for example if students were to use this as study drug? Would it raise the kinds of issues that we're seeing in sports when people use enhancers?

Nora Volkow: My perspective on this one is if you can develop medication that has no adverse effects and you can improve cognitive abilities either by enhancing your attention or your memory, my perspective is why not? I think the human brain has evolved in ways that allow us to do things that expand our capabilities as individuals, so I think it would be very, very exciting that there could be such medications, again I state without side effects because the current medications that are available do have side effects.

Steve Hyman: Yes, which we've already discussed for stimulants.

Nora Volkow: So when you're dealing with a sport you're actually trying to get people to have the same chances do you have a sportsman to see which wins, (a) or (b). When you have students and you want them to be able to say for example learn a new language or learn new mathematical skills, why not? Why not accelerate that process?

David Nutt: I wouldn't disagree with that. I would say that is another stepping stone in human evolution where rather than random selection of genes we now have some targeted medication to improve some mental functions. I wouldn't have a problem. We discussed this in the UK government's *Foresight* report of seven years ago now. The issue was then more one of equity, do the rich have it and the poor not, or do you give it to everyone in order to enhance the quality of a population or a country? We were actually seriously interested in whether these might be strategies that could be used by other countries which perhaps value achievement more than some countries in the West and that would put the West at an economic disadvantage. So there are very interesting political and moral issues of equity about this. But in principle I think if we were able to achieve that kind of drug we should fully endorse it and fully encourage its use.

Steve Hyman: I would certainly be interested in hearing Nora's view on these policy issues because regulators whether in the United States or Europe approve drugs to treat disease, to improve memory, for example, in dementia. For ethical, legal liability, and many other reasons companies don't perform clinical trials in healthy people, except for early studies of toxicity in healthy volunteers. It is also hard to imagine that health insurance would pay for these drugs for healthy people which goes directly David to the issue you raised. People who are well who wanted to obtain these drugs would probably have to pay for them out of pocket which creates an equity problem, the question of whether we would have chemical "haves" and "have nots" exacerbating current social inequities. Assuming we discover these drugs, what should we actually do?

David Nutt: I think this is why programmes like this are so important because the debate has to start now. These drugs could be discovered next year and we need to be ahead of the game. We've seen similar issues emerge for instance within in-vitro fertilisation etc, so as human technology is almost limitless, we definitely need to prepare the ethical and moral and intellectual groundwork, so I think we should be having this discussion. Maybe they should be pharmaceuticals in which case they will need licence authorisation, but people almost certainly will use them off label as they already are doing with the current stimulants which are licenced for ADHD for instance. But there's also another scenario, which is that they maybe invented simply as enhancers and not used in dementia. Maybe they will get to be more effective in brains that aren't demented and we've already some evidence for this from some of our own work with the alpha 5 inverse agonists of

the GABA-A system which is more obviously effective in impaired young people than it is in the elderly; so maybe people will just develop enhancers and they won't worry about diagnosis. They will simply sell them as foodstuffs or whatever, they will come by a different route.

Steve Hyman: Nora, any views on this?

Nora Volkow: I think David is completely correct, this is why we need to have these sorts of discussions because there are aspects related to equity and generating a greater gap between those that have it all and those that do not could actually be then amplified if you really have people that were much better prepared than others, but at the same time there's another area that I think would benefit us. Indeed we really have such type of medications which is we're seeing an increase in the lifespan of individuals and one of the very important aspects that needs to be addressed is have you increased the quality of life of the person as they go into their later years, so to be able to have medications for example on people that don't have any type of dementia but as part of the ageing process their memory is not as good as it was before or they cannot learn things will be extraordinarily valuable because you then would have this individual being able to learn new things and have a flexibility to shift their expertise on the basis of their needs, so the recognition that we are increasing the survival of the population and the importance of providing them with a very good quality of life really sets as one of the priorities that these individuals are functioning with their cognitive operations optimally.

Steve Hyman: Let me make this a little bit tougher because I agree with both of you, it's absolutely critical to be having these discussions. I think the first issue to be solved is that all societies are concerned about healthcare costs and probably would not be very excited about expenditures for new patented and presumably expensive drugs for people who have no illness—just as society doesn't pay for music lessons or sports training generally; then the second thing is unfortunately all drugs powerful enough to have the effect you want are also going to have some side effects. How are we going to understand what the risks and benefits are in healthy people as opposed to people who have an illness?

David Nutt: Shall I try that one?

Steve Hyman: Why not?

David Nutt: That's why I prefer a non-medical reason because that's new, that's different. We could then create our own rules about monitoring assessment, data collection etc about this new technology. It doesn't lend itself so easily to a medical model so maybe we should have a different sort of regulatory system for enhancers. You could throw things like creatinine and even steroids for muscle growth into that mix if you wanted. Maybe we should think of a different way of regulating these kinds of enhancing drugs?

Nora Volkow: My perspective on this one is that I think that we're going to have to re-think the way that we regulate things as there's more engagement and development targets, aspects that can improve the health of a person because you can improve and this for example we're seeing it very clearly in the case of obesity, so obesity we don't have hypertension diabetes, you could improve, right? But yet the pharmaceuticals are having a very hard time to get drugs approved for that condition. So I think that this is going to have to be resolved but I also want to put forward that it's not just medications that are likely to come across as helping in cognitive enhancers but it's obviously now methodologies such as transcranial magnetic stimulation or electrical stimulation that in the future may enable us to enhance sustainability of attention for example so that may have benefits also in cognitive enhancements, so it will not just be drugs. I predict that also there are going to be tools that will allow us to optimise the function of the brain.

Steve Hyman: One of the reasons of course that drug companies have had great trouble getting approval for obesity drugs is that

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