

BLURRING THE BOUNDARIES – THE FUTURE OF COGNITIVE ENHANCERS

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The afternoon session began with a presentation by Professor Trevor Robbins, the third of the project's science advisers.

USING NEUROSCIENCE TO DEVELOP NEW DRUGS

He pointed out that neuroscience is now producing a wealth of new and interesting discoveries. These include our new awareness that new brain cells can develop in adults (neurogenesis) and that the brain can be altered by various new means, including growth factors, stem cells, and technologies such as deep brain stimulation and transcranial magnetic stimulation. Such developments, alongside drugs, offer possibilities for cognitive/performance enhancement, and thus may be subject to the same ethical and other considerations.

Numerous disorders represent possible targets for cognitive enhancement, from brain disease, such as stroke and dementia, through neuropsychiatric disorders, such as schizophrenia, and developmental disorders, such as attention-deficit/hyperactivity disorder (ADHD). Different approaches to improve symptoms in Alzheimer's disease are currently on the market or in clinical trials. Cholinergic agents such as nicotine have been shown to enhance sustained attention in patients with dementia and cholinergic inhibitors can be neuroprotective for those with an early diagnosis, but Prof Robbins suggested that these agents would not be considered as cognitive enhancers for the healthy population. However, increased understanding of the cellular and molecular processes that underlie learning and memory has led to interest in agents that modulate the glutamate receptor system, such as ampakines, that might improve consolidation of memory. Inhibition of the GABA inhibitory system is also showing promise.

MANIPULATING NEUROTRANSMITTER SYSTEMS TO IMPROVE PERFORMANCE

Another class of cognitive-enhancing drugs that are already in use includes Ritalin (methylphenidate), which is proven to reduce impulsivity in people with ADHD, and acts via dopamine and other classical neurotransmitters. Newly discovered neurotransmitter systems may prove fruitful targets for cognitive enhancement, such as

with the hypocretin agonist modafinil, which can act as a stimulant but also has beneficial effects on planning and working memory. Modafinil is also noted for its apparent lack of abuse potential.

The dopamine system, which is important in mediating reward and dependency, also has a role in various aspects of cognition and is affected in conditions such as Parkinson's disease and ADHD. Thus, agents that act via dopamine, such as L-Dopa and Ritalin, may also improve learning and working memory. Interestingly, neuroimaging has shown that cognitive enhancement with Ritalin is associated with reduced blood flow in the circuits that mediate working memory. Thus, it is possible that cognitive enhancement can occur by reducing the amount of effort required by the brain.

THE LIMITS ON COGNITION ENHANCEMENT

Also in these studies, the degree of cognitive enhancement was greater in those with a lower baseline ability. This suggests that such cognitive enhancement may be due to optimising performance, which would thus produce the greatest effects in subjects with the lowest levels at baseline. Further, such augmentation in individuals already at optimal performance levels might actually impair performance. Prof Robbins also noted that individual agents have differential effects on different aspects of cognition, so overall optimisation of cognitive function could be very hard. As seen with patients with Parkinson's disease, optimisation of one particular function could lead to impairments in others. Nevertheless, benefits to a particular cognitive function do not necessarily have a concomitant cognitive cost, as with modafinil. Individual drug effects can also differ according to dosage, individual genotype, situation and context.

Discussant Prof Barbara Sahakian pointed out that the potential benefits from cognitive enhancers are large from the point of view of people with cognitive impairment, such as dementia. However, it is important not to get complacent about harms, she said, noting that treatment for ADHD started as early as two years old in the USA and that many healthy people are already using cognitive enhancers.

BEYOND ENHANCEMENT

Increased interest is now being shown in drugs with the ability to help us forget. Such agents are being investigated for conditions like post-traumatic stress disorder. It has now been shown that during long-term memory retrieval, the associated biochemical processes become activated and so that memory becomes susceptible to modification. Manipulation of gene effects at this stage has been found to produce selective amnesia to a retrieved memory.

BRAVE NEW WORLD?

In considering the neuroethics of cognitive enhancers for use in healthy people, Prof Sahakian said that again it is a matter of how much society should have control over an individual versus individual freedoms. She noted that people are competitive and would want to benefit from the potential advantage offered by cognitive enhancers. Possible gains include better performance for people in critical roles such as air traffic control, or

for those under stress, such as when taking exams. Cognitive enhancers could potentially reduce disparity in schooling, for example. But while such drugs could provide some people with new opportunities, they will cost money and could increase inequality. They also may have long-term harms, including over-enhancement with excess memory storage. Widespread use might affect ideals of personal motivation or have the effect of homogenising society. There could be social pressure or coercion to use them, for example from employers or parents. She concluded that use of pharmacological methods to improve society should not preclude other means of improvement. Better cognitive enhancers used for brain disorders could provide great benefits for patients and for society, while pharmacogenomics could help with targeting drug use, but discussions on the emerging topic of neuroethics were important in order to explore the ethical and moral aspects of use in healthy people.

KEY POINTS

Mental impairments such as Alzheimer's disease have inspired research into cognitive enhancers, which may then be used by people without impairments.

Chemical cognitive enhancers have been shown to improve working memory in certain situations but may also cause impairments in other cognitive functions, and may only be truly effective in those starting from a low baseline.

There are increasing neuroethical considerations with the growth in use and availability of cognitive enhancers.