Potential Problems in Pharmacologic Brain Enhancement in Healthy People

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Humankind is in the age of cognitive technology. New developments in neuroscience and pharmacology are increasing the knowledge about the structure of the mind. Accordingly, some of the studies are directed to psychopharmacologic enhancement of the brain. Researchers have discovered some drugs which support cognitive functions especially for some psychiatric disorders. However, non-medical uses of prescribed or non-prescribed enhancers are rising in recent years. Such drugs may augment one's memory, attention or mood, but they may also affect the one's mental health, autonomy and identity. So, uses of some psychopharmacologic drugs for improving the brain capacity may not be safe for healthy people. Moreover, they might damage their mental health and psychological status in a long-term period. Another point is those stimulant drugs might cause some social and cultural consequences such as inequitable competition between users and non-users, fairness of such actions and regulation of them. However, there are still unknown points in the area of cognitive science and efficacy or safety of enhancers might be different person to person, so they could not be generalized.

Cognitive enhancement is a technology which is based on many scientific disciplines to augment functions of the brain. Its aim is to restore or improve the memory, concentration or attention. Those developments include specially adapted gene therapy techniques for brain disorders, transcranial magnetic stimulation, augmented cognition devices, neurochips and pharmaceutical drugs (L.M. Solomon et al., 2009). Pharmaceutical drugs are most common and popular ones in the brain enhancement technology. In 2008, The Academy of Medical Sciences in England reported that more than six hundred compounds were used for neurodegenerative disorders' treatments (Horn, 2009). Some of enhancer drugs prescribed drugs on the market. For example, mixed amphetamine salts treat the Attention-Deficit Hyperactivity Disorder (ADHD), but healthy people use them for decreasing the need for sleep and increasing focus and concentration (L.M. Solomon et al., 2009). However, cognitive enhancers' molecular effects on brain cells are not well-known. There are three possible mechanisms while drugs are effecting the brain chemicals' normal regulation: they regulate the release of neurotransmitters (a neurotransmitter is a substance in the body that carries a signal from one nerve cell to another) that are involved in the processing of information, they modulate receptors and ion channels, or they affect neuronal gene expression (L.M. Solomon et al., 2009). In fact, exact knowledge about cognitive enhancer drugs' mechanisms at the molecular level could not be enough to predict such drugs' potential effects on the mental state because of the complex structure of the brain. An average normal human brain includes approximately 10 to 11 billion neurons (a neuron is a cell that carries messages between the brain and other parts of the body and that is the basic unit of the nervous system) which regulate very complex pathways (a pathway is a line of communication over interconnecting neurons extending from one organ or center to another) for fulfilling mental functions (L.M. Solomon et al., 2009). Therefore, safety of some cognitive-enhancing drugs is still not known and their potential side effects might be harmful for the brain.

Some popular drugs are frequently used as cognitive enhancers are *Methylphenidate (Ritalin®)*, *Amphetamine (Adderall®)*, *Caffeine*, *Nicotine*, *Modafinil (Provigil®)*, *Atomoxetine*, *Reboxetine*, Acetylcholinesterase (enzyme that breaks down acethylcholine at synapses) inhibitors (*AChEIs-Donepezil*, *Galantamine*, *Rivastigmine*) and *Memantine* (Husein and Mehta, 2010). *Caffeine* does not have a certain place in the medical use, but it has got a significant recreational use. It is not a controlled or prescribed substance and it can be also bought and sold legally (C.I. Ragan et al., 2013). *Methylphenidate*, *Amphetamine* and *Atomoxetine* are in widespread use for treatment of Attention Deficit Hyperactivity Disorder (ADHD) and they affect the response inhibition, working memory, attention and vigilance. *AChEIS* and *Memantine* are standard treatments for neurodegenerative disorders (Alzheimer's disease and Parkinson's disease) and they affect the episodic memory and attention (Husein and Mehta, 2010). *Adderall* and *Ritalin* have got some structural and mechanistic similarities and their legal status is the same. They are only available legally on prescription and shopping from on-line pharmacies is illegal (C.I. Ragan et al., 2013). Because, in normal clinical use they are taken orally and they do not have high risk ratios; if they are ingested nasally or injected, their risk ratios might increase significantly (Teter et al., 2008). In 2008, *Provigil* was a prescription-only drug in the US and its online purchase was legal but its sale was not legal (Arria et al., 2008). The common cognitive enhancers' pharmacologic mechanisms differ from the each other and their potential effects on cognition and side-effects which depend on non-medical use and abuse are different, too. If those drugs are abused they might cause severe psychological or physical damages. This means that different ways of

access to these drugs involve legal problems and a lot of risks which are based from users' aims and drugs' substances (C.I. Ragan et al., 2013). According to this, usage of those cognitive-enhancing drugs by healthy people needs to improve testing methods for their cognitive effects and their legal status should be evaluated carefully.

Adderall, *Ritalin* and *Provigil* are very popular drugs for students (for better grades), military personal (to awake for long missions), elderly individuals (to prevent from cognitive decline) and university academics (to maintain their performance) for non-medical uses (Husein and Mehta, 2010). "One example is the study conducted by Babcock and Byrne (2000), which included the question "Have you ever taken *Ritalin* for fun (non-medical purposes)?" to which 16.6% of respondents said "yes". While the question does not address CE (cognitive enhancer) use at all, in some highly prominent discussions (e.g. Farah et al., 2004) this figure is quoted as representing the proportion of students who use prescription stimulants without a medical indication to increase study performance" (C.I. Ragan et al., 2013). Students reach the drugs with different ways such as sharing prescribed drugs, showing fake symptoms to get a prescription or buying from on-line pharmacies (C.I. Ragan et al., 2013). According to this, there is a strong belief that usage of such drugs in healthy people is not fair, because they might have cognitive advantages more than non-users or unhealthy people. "One Ivy League student who had attention deficit disorder (ADD) expressed frustration on this issue: "It gives people an unfair academic advantage. For people with ADD, it just makes them normal, and for people without ADD, it makes them above average. If both me and someone without ADD were both on *Adderall*, I could never outdo them." (L.M. Solomon et al., 2009). Dr. Martha Farah who is a professor psychology at the University of Pennsylvania and director of the school's Center for Cognitive Neuroscience answers those concerns about unfair academic advantage that "the risk of cognitive enhancing drugs fostering inequality is remote, because there is a pretty clear trend across the studies that say neuroenhancers will be less helpful for people who score above average." (L.M. Solomon et al., 2009). However, cognitive enhancer drugs' safety and benefits in healthy people is still unclear, so it is not unclear that they should be permitted or not, too.

Biological factors might vary person to person, so effects of enhancers might vary, too. Therefore, it is important to understand how drugs' modulation on specific cognitive processes works: "How do drugs currently used as enhancers produce their beneficial effects? Is it through multiple effects on several different cognitive processes or do they enhance one cognitive mechanism – such as arousal or improved sustained attention – through which they lead to better performance across a battery of tests? For studies in clinical populations, the difficulty is that many standard cognitive test batteries used in clinical trials are very unlikely to be sensitive enough to answer questions on the specificity of cognitive modulation." (Husein and Mehta, 2010). For example, *Modafinil* is used for the treatment of Narcolepsy (it is a disorder associated with excessive daytime somnolence) as a wake-promoting agent. In healthy people that drug increases attention and memory, but this might be related with the drug's effect on the arousal (Repantis, D. et al., 2010). On the other hand, the drug might cause alterations in mood, anxiety, motivation or apathy (Husein and Mehta, 2010). Likewise, *Rivastigmine* improves learning on a motor task and making associations between symbols and digits, but it might impair verbal and visual episodic memory at the same time (Wezenberg, E. et al., 2005). Moreover, such cognitive-enhancing drugs may have side-effects to the some body systems such as gastro-intestinal system like all drugs. As an example, *Methylphenidate* frequently causes gastrointestinal upset or nausea (Husein and Mehta, 2010). Accordingly, there are concerns about the harmful impacts of cognitive enhancers, because all of those drugs have got extensive toxicological histories (C.I. Ragan et al., 2013). As mentioned, their side effects might not always be linked with nervous system. If *Modafinil* is handled again, it is advised that it should not be prescribed for obstructive sleep apnea, shift-work sleep disorder and idiopathic hypersomnia, because *Modafinil* has got serious risks such as skin reaction, suicidality, depression, psychosis and adverse cardiovascular events (C.I. Ragan et al., 2013). Even one of well-known substances *Caffeine* might have got serious side effects, too. Caffeine poisoning causes vomiting and affects gastrointestinal system negatively; this also causes some neurological problems such as anxiety tremor and hallucinations (C.I. Ragan et al., 2013).

One may argue that adults who are mentally competent should be free to use safe cognitive enhancers. However, in the medicine history there is no safe drug, there are drugs which have got benefits more than their harms. (C.I. Ragan et al., 2013). If there are usage of such drugs for non-medical purposes in healthy people, consequences would be more confusing and suspicious. Therefore, there should be done new studies to examine effects of enhancers in humans. There might be significant effects in experimental groups and some of them might be more significant in certain genotypes. On the other hand, new drugs for enhancing might change brain's modulator and response mechanisms; so humans might be more sensitive to some neurological and psychiatric diseases. Consequently, the neurobiologists have to focus how new drugs affect the human's central nervous system. They should make more pharmacological experiments and analyze their safety scales and risk groups. Enhancers might be useful for

treatment of some neurological disorders, so they need to be improved by the neurobiologists.

Safety, competition and changing the human condition subjects are important points in the cognitive enhancement. Central Nervous System is a very complex system and it might be affected with unanticipated consequences and long-term side effects (Fuchs, 2006). According to given examples, brain enhancement might finally impair memory retrieval, because external drugs might be disturbing the natural balance of remembering and forgetting. If cognitive enhancement is widespread, there would be a competition between healthy users, unhealthy users and non-users. Likewise, "cost barriers to enhancement would increase the disadvantages that are already faced by people of low socio-economic status in education and employment." (Glannon, 2006). Manipulating of human condition with changing personality traits and cognitive abilities is a debatable ethical issue in this century (Fuchs, 2006). Biotechnology companies target especially healthy people by offering overcome the limitations of their physical and mental conditions (Fuchs, 2006). However, cognitive enhancement threats the people's standard life to force them to be better. People might always be happy and reproductive; likewise, they might not accept negative feelings, average concentration or forgetting. Moreover, people might trust the cognitive enhancers too much, so without using them they might not face off the difficulties of life and failures. Consequently, cognitive enhancer drugs' positive effects would be reversible and when people stop to use them, their positive effects would stop, too. So, their coping skills might be decreased and they might want to take them, again. This causes abuse or addiction. On the other hand, cognitive enhancer's negative effects might be irreversible, so normal people might have be a mental disorder and permanent psychiatric problems. Unfortunately, some of them are easily accessible especially for students and their mechanisms and safeties are still not clear. Therefore, because of complexity of brain and inadequate experiments in long term uses those substances should be evaluated carefully, used by healthy people in control and enough research should be done.

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