Pharmacology and learning

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Introduction

This chapter will discuss the impact of pharmacology on learning. That is, how pharmacological agents – drugs – may positively impact learning. It will not venture (much) into the neuroscience of learning, as that is more expertly discussed elsewhere in this book. I will situate the discussion of pharmacologic action on learning within the model of learning proposed by Peter Jarvis in numerous texts, including Adult and Continuing Education: Theory and Practice (2004), Adult Education and Lifelong Learning: Theory and Practice (2010), and this Handbook. My goal is that this unique approach to the discussion of the pharmacologic action on learning will add a different perspective to the body of knowledge in the current literature.

This discussion of pharmacology and learning will be limited to adult learners. Neuroscientists and social scientists agree that the learning process is very different in children than in adults.

Further, this chapter will discuss the enhancement of learning in “normal” or healthy individuals through pharmacological agents. However, the action of natural health products (e.g., ginkgo biloba), vitamins, minerals, and foods are beyond the scope of this discussion.

The learning process

One could devote this entire book to a discussion of the learning process, and many have. That is not the purpose of this chapter. But it is important to our discussion of pharmacology and learning to start with a common understanding of “learning”.

Most simply, Illeris tell us that “all learning implies the integration of two very different processes, namely an external interaction process between the learner and his or her social, cultural or material environment, and an internal psychological process of acquisition and elaboration” [italics added] (2005: 89).

Jarvis takes this basic explanation further and proposes his own more complex and complete model. For more information regarding Jarvis’s model, the reader is referred to the Introduction to this volume. In order to discuss the impact of pharmacology on learning we must define “learning”. The reader is referred to Jarvis’s discussion of ten types of learning (2010: 87–90).

Some scientific researchers have proposed that memory, attention and creativity represent three different cognitive domains, which are interconnected and contribute to the “mental performance” of an individual
But social science researchers and teachers know that “learning” is composed of more than memory, attention, and creativity. For example, this explanation does not include aspects such as reasoning, judgment, executive functioning, and problem-solving. Therefore this chapter includes discussion of the impact of pharmacological agents on many different aspects of “learning”, but we will not try to classify each pharmacological agent by its action on a particular aspect of learning.

The learner

Unlike many scientists, Jarvis describes a learner as more than the mind or brain. Jarvis’s model of learning portrays the whole person: body/mind/self/life history within the life world in his descriptions of the learning process.

The learner and his body

Jarvis describes the learner’s body as being made up of genetic, physical and biological components (2010: 81).

We know from psychological and physiological research that our body—our “biology”—influences learning. In fact, learning depends on biology. Neuroscience research has proven that all brain processes are chemical. Learning is a neurochemical process; it is mediated by neurotransmitters, including, but not limited to, norepinephrine, acetylcholine, dopamine, GABA, glutamate, serotonin, histamine, adenosine, and cholecystokinin. Manipulation of these neurotransmitters by pharmacologic agents has been shown to affect learning, both positively and negatively.

But our body is more than its biology. Science has now proven that learning is also impacted by genetics—both our genetic make-up and the genetic processes of transcription. In just one example from the literature, Vecsey et al. demonstrated that pharmacologic agents that impact the genetic process of transcription affect memory: “our results suggest that HDAC inhibitors enhance memory processes by the activation of key genes regulated by the CREB:CBP transcriptional complex” (2007: 6128). Further, the work of researchers such as Mattay suggests “a future role for pharmacogenetics to determine which individuals could benefit from certain types of cognition enhancers” (as cited in de Jongh, Bolt, Schermer, and Olivier, 2008: 763).

Learning is also affected by our physical body. Lojovich reports:

Aerobic exercise not only has been found to impact cardiovascular systems but has also shown benefits to brain function itself and specifically in the domain of memory and learning. Recent evidence is shedding light on the mechanisms possibly impacting cognitive performance following the participation in exercise. Literature has demonstrated increased hemodynamics within the brain, changes in neurotransmitters, and increasing levels of brain-derived neurotrophic factor that stimulates neurogenesis.

(2010: 184)

And finally, our physical body enables our learning. Kinesthetic learners learn best by moving their bodies, but all learners learn by doing. As an example, one would never learn to drive a car just by reading about it or watching another do it.

The learner and his mind

In Jarvis’s model of the learning process, the learner’s mind is described as “knowledge, skills, attitudes, values, emotions, meaning, beliefs and senses” (2010: 81). Since emotions and senses are especially susceptible to effects of pharmacologic agents, we will examine these two components of the mind more closely.
Emotions

Dirkx submits “personally significant and meaningful learning is fundamentally grounded in and is derived from the adult’s emotional, imaginative connection with the self and with the broader social world” (2001: 64).

Most learners would acknowledge that their emotions impact their learning. They will recognize that some of their most memorable learning experiences were accompanied by emotions, sometimes pleasure and sometimes fear or stress. Mackeracher tells us “learning is much affected by emotions from three sources: those we bring to the learning process, those that are generated during the learning process, and those we feel when we receive feedback” (2006: 15).

Further, Merriam and Caffarella (1996) and Taylor (1996) postulate that “emotion and feelings are deeply interrelated with perceiving and processing information from our external environments, storing and retrieving information in memory, reasoning, and the embodiment of learning” (cited in Dirkx, 2001: 68).

Scientifically speaking, since emotional responses release neurotransmitters, it follows that emotions influence learning in a physiological manner. For example, McGaugh (2006: 345) reported the following:

the adrenal stress hormones, adrenaline and corticosterone (cortisol in humans), normally released by emotional arousal enhance long-term memory when administered to rats or mice shortly after a training experience. These stress hormones influence noradrenergic activation within the amygdala, and amygdala activity in turn modulates memory processing in other brain regions, including (but not restricted to) the hippocampus. Human studies have also reported that memory is enhanced by administering adrenaline shortly after learning or by inducing stressful conditions that release adrenaline.

Therefore our discussion of the impact of drugs on learning must include those drugs that affect the neurotransmitters impacted by our emotions. But the discussion must also include drugs that affect our emotions. For example, what might be the impact of antidepressants on learning, through their actions on our mood, including their actions on the neurotransmitters of mood such as serotonin and dopamine? What might be the impact of anxiolytics, such as the benzodiazepines lorazepam, diazepam and alprazolam, on learning through their effect on anxiety and stress?

Senses

Obviously, our senses contribute to our learning. We know that learning relies on input from the senses (hearing, seeing, touching, tasting, feeling, smelling). But this is not the only way our senses influence learning. Mackeracher cites Hart (1975): “both sensory overstimulation (information overload) and understimulation (boredom) can produce physical stress responses that interfere with learning. Adults who are getting too much or too little information for their current learning task may not be learning” (2006: 92).

Mackeracher also points out that our senses can negatively impact information-processing and thus learning. She states: “in the presence of excessive amounts of information from the environment (sensory overload, overstimulation) the adult processes information in ways that delete, distort, oversimplify, and overgeneralize” (2006: 127).

Thus, we can extrapolate that, in some cases and depending on the learner and the situation, drugs that influence the awareness of the senses, either increasing or decreasing, may positively impact learning. It may be that enhancing our senses could lead to enhanced learning. For example, cocaine and methamphetamine enhance sensations by increasing levels of dopamine in the brain. Unfortunately, their side effects limit their usefulness. In another example, Liang, Poytress, Weinberger, and Metherate propose that
“nicotinic acetylcholine receptors (nAChRs) contribute to sensory-cognitive function, as demonstrated by evidence that nAChR activation enhances, and nAChR blockade impairs, neural processing of sensory stimuli and sensory-cognitive behavior” (2008: 138).

The learner and his life history

Knowles proposed that “learners bring their lifetime experience to the learning situation” (as cited in Jarvis, 2006: p. 78). Mackeracher (2006) describes the dichotomy of our biography: “past experience is an essential component in learning, both as a base for new learning and as an unavoidable potential obstacle” (p. 35).

It is easy to envision that drugs could positively impact learning by affecting our memories of past experiences. Likewise, improving our ability to remember experiences as they occur will impact our learning. A great deal of research focuses on how our experiences result in “learning”, by laying down short-term and long-term memory. In an interesting contrast, Frank, O’Reilly, and Curran showed that “the benzodiazepine midazolam, which inactivates the hippocampus, causes profound explicit memory deficits in healthy participants, but enhances their ability in making implicit transitive inferences” (2006: p. 700).

Another approach to memory and learning might be to reduce the obstacles of our past experiences by modulating or suppressing our memories. de Jongh et al. reported on the work of Cahill, Pham and Setlow (2000), Debiec and Ledoux (2004) and McGaugh (2004): “propranolol was able to block the enhancing effect of arousal on memory” (2008: 767). If we go back to our understanding of the effect of emotions on learning, we can see that the beta-blocker propranolol could block the action of epinephrine and nor-epinephrine that are released in response to stress, and thus “block the enhancing effect of arousal on memory” that Cahill et al. found (ibid).

Some researchers have proposed that amnesiac agents such as propranolol may even interfere with our established memories (de Jongh et al., 2008: 767). However, more recently Muravieva and Alberini reported the following:

we found that systemic administration of propranolol disrupts the reconsolidation of Pavlovian FC [fear conditioning] and that its injection following a retrieval elicited by cue exposure also interferes with the reconsolidation of contextual FC. Hence, propranolol disrupts the reconsolidation of Pavlovian FC, but has no effect on the reconsolidation of IA [inhibitory avoidance]. The results indicate that the efficacy of systemic administration of propranolol in disrupting the reconsolidation of fear memories is limited.

(2010: 306)

Regardless of Muravieva and Alberini’s latest findings, it may be that future research will find other agents that do affect our established memories.

Pharmacological enhancement of learning

“Pharmacological neuroenhancement is an attempt to increase cognitive performance in healthy humans” (Normann, Boldt, Maio, and Berger, 2010: 66). Pharmacological neuroenhancement is one aspect of cognition enhancement, defined by Ingole, Rajput, and Sharma as “the amplification or extension of core capacities of the mind through improvement or augmentation of internal or external information processing systems” (2008: 42). The literature refers to agents used for pharmacological neuroenhancement as nootropics, “smart drugs”, memory enhancers, cognitive enhancers, and neuroenhancers. There are some differences in the exact meaning of these terms (for example, “nootropics” usually includes supplements, nutraceuticals, functional foods, and natural health products, as well as drugs) but these are all useful key words when searching the literature.
There is great interest, on several fronts, in developing the perfect “smart drug”—a drug that would make us smarter, without side-effects, and counteract the effects of aging or the limitations of our biology. The pharmaceutical industry recognizes the financial benefit: there is even greater profit to be made from a drug that can be used in millions of healthy individuals than in the limited market of patients with pathologies such as Alzheimer’s disease. Those of us who are aging (and who isn’t?) yearn for a drug that will keep us sharp. Students desire a drug that will help them garner a high Grade Point Average and thus admittance to competitive schools or desirable jobs. Workers are looking for a competitive edge in the workplace. The journal *Nature* reported that, in its poll of 1,400 readers, “one in five respondents said they had used drugs for non-medical reasons to stimulate their focus, concentration or memory” (Maher, 2008: 674).

Our increasing understanding of the “biology of learning” opens the door to the possibility of enhancing the learning process through manipulation of the neurochemical processes. Our knowledge and understanding of the action of drugs on learning is informed by our research of their effects in pathology, such as Attention Deficit Hyperactivity Disorder (ADHD), Parkinson’s disease, Alzheimer’s disease, schizophrenia, and depression. Thousands of studies over the years have researched the effects of drugs in these diseases and conditions; however, relatively little research, particularly scientifically rigorous research, has been done on the impact of drugs on learning in healthy individuals. Therefore our understanding of these effects is poorly informed by science. We cannot assume that the effects of drugs used in pathology are the same or even similar in healthy individuals. To further complicate the issue, as discussed earlier in this chapter, our understanding of the learning process opens the door to enhancement of learning through principles other than neurotransmission.

A thorough discussion of all possible neuroenhancers is not possible in this short chapter. Today more than 100 drugs are currently being developed, tested or used for cognitive enhancement (Förstl, 2009). However, we will look at some of the more commonly used classes of drugs and examine how they work, what their effects on learning might be, and what scientific research has proven, or not proven, so far. Discussion of agents that are still only in animal trials is not included, as the list is long and those agents may never make it to human trials or use in humans.

**Acetylcholinesterase inhibitors**

The drugs donepezil (Aricept™), galantamine (Reminyl™), and rivastigmine (Exelon™) belong to a class of drugs called “acetylcholinesterase inhibitors” (AChEIs), or more simply, “cholinesterase inhibitors”. They were developed as treatments for mild-to-moderate Alzheimer’s disease. It is important to note that these drugs slow the progression of Alzheimer’s disease in some individuals; they do not cure Alzheimer’s disease.

These drugs act by inhibiting the metabolism of acetylcholine, which increases the amount of acetylcholine in the synaptic cleft and thus enhances the activity of acetylcholine at both muscarinic and nicotinic receptors in the hippocampus and cortex.

While Lanni *et al.* and Narahashit *et al.* claim that “all of these compounds have also been proved efficacious in healthy aged people to enhance learning and memory” (as cited by Ingole, Rajput, and Sharma, 2008: 44), other researchers do not necessarily agree.

Repantis, Laisney, and Heuser’s systematic review of the literature concluded the following:

In six small trials lasting 14–42 days, the following results emerged: donepezil improved the retention of training on complex aviation tasks and verbal memory for semantically processed words. In one study episodic memory was improved, whereas in others it remained unaffected by donepezil. In a sleep deprivation trial, donepezil reduced the memory and attention deficits resulting from 24 h of sleep deprivation. Two studies reported even transient negative effects.

(2010: 473)
On the other hand, Zaninotto et al. reported “positive cognitive effects of acute donepezil can be observed in various cognitive domains including mood, but its full nootropic potential is more clearly found close to theoretical peak-plasma concentration” (2009: 453). Zaninotto et al. (2009) found that:

donepezil improved long-term recall of prose, objects recall, recall of spatial locations, and integration of objects with their locations, some effects having been related to self-reported mood enhancement. However, improvement of performance in the central executive measure (backward digit span) occurred only at Tmax.

Of some concern are the findings of Beglinger et al. (2005):

Conversely a recent trial with donepezil in healthy elderly subjects, reported that the donepezil group showed an impairment on speed, attention and short-term memory compared to the placebo group; in addition an improvement in performance was not observed on any test performed during donepezil treatment. In this last study, the authors question whether the impairment observed could be consequence of a misbalance when AChEIs are introduced in healthy people.

(as cited in Lanni et al., 2008: 199)

**Ampakines**

Ampakines are activators of alpha-amino-3-hydroxy-5-methyl-4-isoxazole propionic acid (AMPA) receptors. Researchers Lynch and Gall explain that:

ampakines bind to a site on the AMPA receptor but have no agonist or antagonist effects; instead, they stabilize the receptor in its channel-open state following the binding of released transmitter (glutamate). This prolongs current flow through the receptor and thus enhances synaptic responses.

(2006: 554)

Lynch and Gall postulate that there are three different ways in which ampakines may modify and enhance cognition: increasing transmission within the cortex; facilitating long-term potentiation (LTP) by lowering the induction threshold and increasing the magnitude to accelerate learning; and upregulating brain-derived neurotrophic factor (BDNF) to improve memory consolidation (ibid.).

At this time there are no ampakine drugs approved for use in humans, although a few pharmaceutical companies are currently conducting animal and human studies.

**NMDA receptor antagonists**

**Memantine**

Memantine is an NMDA (N-methyl-D-aspartate) receptor antagonist and is registered for the treatment of moderate-to-severe Alzheimer’s disease. It is sold under the trade name Ebixa™.

Memantine’s mechanism of action in Alzheimer’s disease is not fully understood, particularly since it works very differently from other drugs in this pharmacologic class, such as ketamine. We know that memantine, as an NMDA receptor antagonist, blocks glutamate from interacting with these receptors, thereby reducing the toxicity of excess glutamate. The title of Parsons, Stöffer, and Danysz’s article sums up the mechanism of action of memantine nicely: “Memantine: A NMDA receptor antagonist that improves memory by restoration of homeostasis in the glutamatergic system—Too little activation is bad, too much is even worse” (2007).

Rogawski and Wenk (2003) found “at lower, clinically relevant concentrations memantine can under some circumstances promote synaptic plasticity and preserve or enhance memory in animal models of AD.
In addition, memantine can protect against the excitotoxic destruction of cholinergic neurons (p. 273). If their findings are borne out in other research, memantine may have a role in neuroprotection as well as memory enhancement.

Repanis, Laisney, and Heuser’s review of the literature found only seven small studies about the effects of a single dose of memantine, insufficient to answer their research question (2010: 473). They were unable to find any studies with repeated doses of memantine.

In the seven studies that Repantis et al. reviewed, no significant positive effects on cognition by memantine were found.

**Stimulants**

This group includes the drugs most commonly associated with the concept of “cognition enhancement”—drugs such as methylphenidate (Ritalin™), amphetamines (including dextroamphetamine [Dexedrine™] and mixed salts amphetamine [Adderall™]) and modafinil (Alertec™ in Canada, Provigil™ in USA). It is believed that the stimulant drugs work through multiple pathways to exert their positive effects.

**Amphetamines**

Amphetamines were the first prescription drugs used to enhance cognition, going as far back as the Spanish Civil War, whenamphetamine was used by the military to promote alertness (Sulzer, Sonders, Poulsen, and Galli, 2005: 410).

Benzedrine was the first commercially available amphetamine, and “Bennies” became well known for their use by soldiers, truck drivers, musicians, and even housewives. Today amphetamines are approved for use in sustained release formulations to treat ADHD (e.g., mixed salts amphetamine [Adderall™]) and narcolepsy (e.g., dextroamphetamine [Dexedrine™]) (Canadian Pharmacists’ Association [CPhA], 2009). Illicit use and abuse of stimulants is rampant, either as amphetamine or its derivatives methylphenidate, MDMA, and methamphetamine.

Amphetamines are thought to increase the release of norepinephrine and dopamine into the extraneuronal space and block the reuptake of these neurotransmitters into the presynaptic neuron, resulting in overall increased activity of norepinephrine and dopamine. Sulzer, Sonders, Poulsen, and Galli proposed that amphetamines act by two primary mechanisms:

- the redistribution of catecholamines from synaptic vesicles to the cytosol, and induction of reverse transport of transmitter through plasma membrane uptake carriers, (as well as) additional drug effects that affect extracellular catecholamine levels, including uptake inhibition, effects on exocytosis, neurotransmitter synthesis, and metabolism.

(2005: 406)

Breitenstein et al. (2004) reported on several researchers’ findings on the effects of amphetamines on cognition measures in healthy volunteers, including response speed (Kumari et al., 1997), retention and recall of verbal memory (Soetens et al., 1995; Soetens et al., 1993; Soetens, Carter, Bruno and Cohen, 1995), attention and working memory performance (Mattay et al., 2000; Servan-Schreiber et al., 1998), reasoning (Mattay et al., 1996), response times during the Wisconsin Card Sorting Test (Mattay et al., 2003), procedural learning (Kumari et al., 1997), and language acquisition (Breitenstein et al., 2004).

The therapeutic use of amphetamines is limited by their potential to produce neurodegeneration, addiction and psychosis. However, these side effects can be attenuated by using sustained release formulations.
Methylphenidate

Methylphenidate is chemically related to amphetamine. It has been used for many years to treat ADHD in children and adults.

Scahill, Carroll, and Burke summarized the mechanism of action of methylphenidate thus:

The mechanisms of action for amphetamines and methylphenidate differ slightly (Solanto, Arnsten, and Castellanos, 2001). Methylphenidate (MPH) promotes release of stored dopamine from presynaptic vesicles and blocks the return of dopamine into presynaptic nerve endings. Amphetamines also block dopamine reuptake, but appear to promote the release of newly synthesized dopamine more selectively. The combined action of promoting release and blocking reuptake results in a net increase in extracellular dopamine in basal ganglia, cortex, and other brain regions to a lesser extent (Volkow et al., 2001).

(2004: 86)

There is substantive evidence that methylphenidate does improve cognitive functioning of individuals with ADHD, as evidenced by the fact that both the Food and Drug Administration (FDA) in the US and Health Canada in Canada have approved its use for this indication based on submissions proving both safety and efficacy.

Various researchers have reported positive effects of methylphenidate in healthy adults, as cited by Agay, Yechiam, Carmel, and Levkovitz (2010): higher average digit-span test scores but not decision-making tasks (Agay, Yechiam, Carmel and Levkovitz, 2010); enhanced spatial working-memory performance (Mehta et al., 2000); and enhanced executive function on novel tasks, but impairment of previously established performance (Elliott et al., 1997).

However, Repantis, Schlattmann, Laisney, and Heurser’s review of the literature (46 studies) found that “for methylphenidate an improvement of memory was found, but no consistent evidence for other enhancing effects was uncovered” (2010: 187).

Turner et al. (2003b) concur: “in healthy elderly volunteers (61 years old), methylphenidate (20 and 40 mg) was without effects on working memory, response inhibition and sustained attention, suggesting that it is not a useful countermeasure for age-related cognitive decline” (as cited in de Jongh et al., 2008: 764).

Modafinil

In Canada and the USA, modafinil is approved for the symptomatic treatment of excessive sleepiness in adult patients with narcolepsy, obstructive sleep apnea/hypopnea syndrome (OSAHS) and shift work sleep disorder (SWSD) (CPhA, 2009).

Based on a review of the literature, Minzenberg and Carter concluded that “modafinil exhibits robust effects on catecholamines, serotonin, glutamate, gamma amino–butyric acid, orexin, and histamine systems in the brain. Many of these effects may be secondary to catecholamine effects” (2008: 1477).

While approved for symptomatic treatment of excessive sleepiness in pathology, modafinil has been used off-label and studied for its effects on cognition. It has been used in work settings, such as for pilots and physicians, to improve performance in sleep-deprived individuals (e.g., Gill, Haerich, Westcott, Godenick, and Tucker, 2006).

Turner et al. demonstrated that modafinil improved subjective attention and alertness, as well as objective performance on digit span, visual recognition memory, spatial planning, and stop–signal reaction time (2003a). They suggested that “modafinil improves accuracy by causing an increased tendency to evaluate a problem before initiating a response” (as cited in de Jongh et al., 2008: 763).
However, based on the research of Randall, Shneerson, and File (2005) and Müller et al. (2004), de Jongh et al. concluded that modafinil “appears to be most effective during suboptimal performance, due to either sleep deprivation, or ‘lower natural abilities’” (2008: 763). Repantis, Schlattmann, Laisney, and Heuser’s review of the literature (45 studies) concluded that:

Modafinil … was found to improve attention for well-rested individuals, while maintaining wakefulness, memory and executive functions to a significantly higher degree in sleep deprived individuals than did a placebo. However, repeated doses of modafinil were unable to prevent deterioration of cognitive performance over a longer period of sleep deprivation though maintaining wakefulness and possibly even inducing overconfidence in a person’s own cognitive performance.

(2010: 187)

Do they work?

So, after all this discussion of learning and neuroenhancers we come to the crux of the matter—do they work? At this point, Normann and Berger probably sum it up best: “So far, all clinical trials of neuroenhancing drugs have either failed or demonstrated only very limited efficacy” (2008: 110).

Questions

At this point in this area of science there are more questions than answers. One of the problems with applying rigorous scientific standards to the research in this field is the difficulty in quantifying “learning”. When one reads the research, one is struck by the different aspects of learning that are tested—short-term memory or episodic memory, long-term memory, response inhibition, sustained attention, wakefulness, information processing, executive function, coordination, and concentration. Applying scientific standards for literature evaluation, one cannot extrapolate results from one type of test to other aspects of learning (i.e., apples to oranges), and so it is often difficult to compare different studies on the same pharmacologic agent, never mind compare different pharmacologic agents. Repantis, Schlattmann, Laisney, and Heuser caution us that “a common limitation in neuropsychological research is that performance in most tests is influenced by more than one cognitive process” (2010: 196). Dosing is also an important variable—dose used, number of days dosed, timing between dosing and testing. One example of the effect of dose cited earlier in this chapter is the research by Zaninotto et al. (2009) on donepezil.

In addition, there are difficulties in interpreting the results of studies on neuroenhancers. As one example, de Jongh et al. examined the studies of Yesavage et al. and Gron et al. on the effect of donepezil. There seems to be disagreement on whether the effects of donepezil that Yesavage et al. observed in licensed pilots were due to the drug’s effects on the subjects’ memory or the drug’s effects on performance during testing (de Jongh et al., 2008: 762).

Further, one can never discount the placebo effect, although one could argue that an effect is still an effect. The scientific research into pharmacologic neuroenhancers has posed the following questions:

- Do neuroenhancers work the same in ‘normal’ or healthy individuals as in those affected by some pathology, e.g., Alzheimer’s disease or ADHD?
- Do neuroenhancers work the same in the middle-aged or elderly as in the young? For example, Turner et al. found the following when they researched methylphenidate:

The results of this study demonstrate that, in elderly subjects, the cognitive effects of methylphenidate are grossly attenuated and distinct from the profile previously described in younger volunteers. It is suggested that methylphenidate may not be appropriate as a pharmacological intervention in elderly patient groups, such as those reporting age-related cognitive decline.

(2003b: 455)
Do neuroenhancers work as well in highly intelligent individuals? Several researchers have reported that the effects of various cognitive enhancers seem to depend on the subjects’ baseline capabilities. One example cited earlier in this chapter is Randall, Shneerson, and Filé’s paper “Cognitive Effects of Modafinil in Student Volunteers May Depend on IQ” (2005).

Do neuroenhancers actually impair learning at sub-optimal or super-optimal doses? de Jongh et al. describe “the inverted U-shape”, in respect of the dose-response curve of select pharmacologic neuroenhancers. That is, “performance is optimal at intermediate (prefrontal) catecholamine levels and impaired at levels that are either too low or too high” (2008: 768).

What is the impact of multiple agents? This is particularly intriguing if we consider using drugs that impact different neurotransmitters or different factors involved in learning.

Might neuroenhancers enhance some aspects of learning, but at the expense of other aspects, such as creativity?

Likewise, might neuroenhancers enhance learning, but at the expense of other components of the learner, such as his “mind” (e.g., mood or emotion) or his “self”?

And concerns

The use of drugs in the absence of pathology is fraught with concerns, both ethical and scientific. Much has been written about the ethical concerns of cognition enhancement. After reviewing the international literature, de Jongh et al. suggest that there are six important ethical questions: safety (including the risks of abuse and addiction as well as the inevitability of side-effects); societal pressure to use enhancers; fairness and equality (i.e., “haves” versus “have not’s”); enhancement versus therapy; authenticity and personal identity; and happiness and human flourishing (2008: 772).

Förstl suggests the following:

Beyond more general neuro-ethical reservations regarding neuro-enhancement, future research will need to address the following neuropsychiatric issues:

1. Will the benefits of longer term neuro-enhancement outweigh potential disadvantages such as rebound effects and other neurobiological and psychosocial trade-offs?
2. What will be the neuropsychiatric sequelae of a soft coercion towards drug usage at work and for recreational purposes?
3. Will there be new and specific neuropsychiatric diseases due to long-term usage of neuro-enhancers in a larger population?

(2009: 841)

A thorough discussion of ethical concerns of pharmacologic neuroenhancement is beyond the scope of this chapter. The topic is raised, though, because it is of enormous consequence as pharmaceutical companies race to market a proven cognitive enhancer and as people are already experimenting with off-label use of prescription drugs. Scientists of all genres are called upon to thoroughly investigate the ethical and scientific issues before taking the lid off this Pandora’s box. Or perhaps it is already too late?

Conclusion

The field of cognition enhancement is intriguing, fraught with ethical and scientific questions, extremely complex, and evolving incredibly quickly. The scientific research is difficult to comprehend without extensive training in fields such as neuroscience, medicinal chemistry, pharmacology, psychology, and statistics. The whole question of measuring enhancement of cognition is limited by the difficulties in
quantifying “learning”. One is reminded of the adage, “However, not everything that can be counted counts, and not everything that counts can be counted”. Perhaps enhancement of learning is actually occurring and researchers cannot or do not measure it?

The discussion of cognition enhancers in this chapter has focused on drugs that are currently being used for this purpose, albeit off-label. The research has revealed multiple mechanisms of action for enhancement of learning, when a mechanism of action can be elucidated. A great deal of research is occurring in this field; more mechanisms of action will be determined, new pharmacologic agents will be developed, and new uses for old drugs will be discovered in the very near future. One only has to search the medical databases for “cognition enhancement” to see the overwhelming amount of literature on the topic and how it grows weekly. But I submit that it’s time to add a new direction for this research.

Our consideration of the factors that may influence learning, situated in the model of the learning process as proposed by Jarvis, has revealed many opportunities for intervention in the learning process. Imagine the possibilities if educators and social scientists helped guide scientists’ research or pointed them in directions previously not contemplated. Some of these possible directions are suggested in our earlier discussion of the learning process, but there must be many more if we are open to exploring them.

This is not to say that the neuropsychopharmacologists, pharmacologists, medicinal scientists, and so on have not contemplated interventions at different points of the learning process. But, think how much educators could open their minds to areas they may not have thought of, like the learner’s concept of “self”. Let us approach the topic of cognition enhancement with a more holistic approach, rather than chopping the learner up into his neurotransmitters, his genes, his receptors. Let us situate our research in Jarvis’s model, and introduce interventions at the level of the whole person, his life-world, his emotions, his experiences, and his thoughts. Of course it will be difficult, if not impossible, to measure. The studies may never be scientifically rigorous enough to get a new nootropic approved by the FDA or Health Canada. But consider this: “Far away there in the sunshine are my highest aspirations. I may not reach them, but I can look up and see their beauty, believe in them, and try to follow where they lead” (Louisa May Alcott, as cited by Hubbard, 1923: 62).

References


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### Additional Reading


