Chapter 12
Cognitive-Enhancing Drugs, Behavioral Training and the Mechanism of Cognitive Enhancement

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Abstract In this chapter, I propose the mechanism of cognitive enhancement based on studies of cognitive-enhancing drugs and behavioral training. I argue that there are mechanistic differences between cognitive-enhancing drugs and behavioral training due to their different enhancing effects. I also suggest possible mechanisms for cognitive-enhancing drugs and behavioral training and for the synergistic effects of their simultaneous application.

Keywords Cognitive enhancement • Mechanism • Cognitive-enhancing drugs • Behavioral training • Synergistic effects

12.1 Finding the Mechanism of Cognitive Enhancement

Studies on cognitive enhancement aim to find effective ways to improve the cognitive functions of healthy subjects as well as unhealthy subjects. There are two main approaches to exploring effective cognitive-enhancing methods. The first one seeks to try different possible enhancers with different combinations of strengths and durations in order to find more effective ways from a variety of trials. The second approach is to find the underlying mechanisms of how enhancers modulate cognitive functions so that enhancers can be used more effectively. These two ways of finding effective cognitive enhancers are interdependent. On the one hand, data on how different cognitive enhancers work help to build and examine different proposals of the mechanism of cognitive enhancement. On the other hand, some ideas about the underlying mechanism of cognitive enhancement help to decide the types and the quantities of enhancers to experiment on without trying all variations

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of them. Both approaches of finding effective enhancing methods are necessary and worth pursuing. This chapter will contribute to the inquiry of finding effective enhancing methods by taking up the second direction.

In order to locate the mechanism of cognitive enhancement, I will start by reflecting on the synergistic effects of the simultaneous application of cognitive enhancing drugs and behavioral training, whose mechanism may play a crucial role in finding the general mechanism of cognitive enhancement, as suggested by Husain and Mehta in a review article (Husain and Mehta 2011). Several studies show that the resultant enhancing effects from the concurrent application of drugs and behavioral trainings are greater than the enhancing effects of applying either drugs alone or behavioral trainings alone (Knecht et al. 2004; Berthier et al. 2009). I suggest that the synergistic effects indicate that drugs and behavioral training modulate cognitive functions in different ways. I will justify this suggestion by discussing the difference of the enhancing effects and the mechanisms of cognitive-enhancing drugs and behavioral training. My argument regarding the difference between drugs and behavioral training is as follows: If cognitive-enhancing drugs and behavioral training enhance cognitive functions through the same mechanism, cognitive-enhancing drugs and behavioral training have the same enhancing effects. Cognitive-enhancing drugs and behavioral training do not have the same enhancing effects. Thus, cognitive-enhancing drugs and behavioral training enhance cognitive functions through different mechanisms. After arguing for the differences between the mechanism of cognitive-enhancing drugs and behavioral training, I will propose the mechanism for cognitive-enhancing drugs and for behavioral training and an explanation for the synergistic enhancing effects based on the conclusion of my argument. I suggest that this proposal could be a basis for the general mechanism of cognitive enhancement.

12.2 The First Premise: Thesis on the Mechanisms and the Effects of Cognitive Enhancement

My first premise is: if cognitive-enhancing drugs and behavioral training enhance cognitive functions through the same mechanism, cognitive-enhancing drugs and behavioral training have the same enhancing effects. Cognitive functions correlate with the excitation or inhibition of their corresponding neural networks. When drugs and/or behavioral training enhance a cognitive function, the corresponding neural network of this cognitive function is being modulated in a way that the cognitive function performs better. For instance, Ritalin enhances one's attention through its modulation of the corresponding neural network of attention (Husain and Mehta 2011). In addition, different dosages of enhancers may result in different strengths of enhancing effects; different types of enhancers may have different effects, such as the length of retention of the enhancing effects and the influence on brain activities after the end of enhancing treatment (Berthier et al. 2009;

Klingberg et al. 2005; Knecht et al. 2004; Maguire et al. 2003; Olesen et al. 2004). Because the effects of a cognitive enhancer are dependent on the way the enhancer modulates the corresponding neural network of the target cognitive function, we can then say that if two cognitive enhancers modulate the target neural network in the same way, (that is to say, if these two enhancers have same mechanisms,) then these two enhancers would have the same enhancing effects, such as achieving the same strength of enhancing effects, possessing the same duration of retention of the enhancing effects, and influencing brain activation patterns after the end of enhancing treatment in the same way.

12.3 The Second Premise: Different Enhancing Effects of Cognitive-Enhancing Drugs and Behavioral Training

The second premise of my argument states: cognitive-enhancing drugs and behavioral training do not have the same enhancing effects. There are four main differences between the enhancing effects of drugs and that of behavioral training.

First, the effects of behavioral training last longer than those of drugs after the end of enhancer usage. Berthier et al. (2009) show that even both memantine and constraint-induced aphasia therapy (CIAT) can achieve the same degree of improvement in patients with chronic poststroke aphasia after the same length of treatment; however, CIAT has retention effects of up to 3 weeks after the end of treatment, whereas memantine does not. In other studies on working memory, even though the retention of the enhancing effects of levodopa on working memory can last up to a month after the treatment (Knecht et al. 2004), behavioral training can last longer (up to 3 months) after the treatment (Klingberg et al. 2005).

Second, behavioral training changes brain activation patterns and neuronal growth. Studies on superior memorizers show that the strategy used by superior memorizers during their training change their brain activation patterns when performing tasks on memory (Maguire et al. 2003). Other studies on working memory training show that such training increases the density of dopamine receptors in the subjects' brains (McNab et al. 2009) and increased the activation of working memory-related brain activities (Olesen et al. 2004).

Third, drugs and behavioral training have different specificity on enhancing targets. For instance, levodopa treatment enhances subjects' ability to encode stimulus salience, while the repetition of behavioral training, which is required for the subjects to acquire the target cognitive skill, decreases salience (Knecht et al. 2004).

Fourth, studies show that only users with low performance are helped by the use of cognitive-enhancing drugs, while the same drugs may reduce the cognitive function of subjects who are already high-performing (Husain and Mehta 2011). On the other hand, even though behavioral training may not benefit the subjects with high performance, it does not seem to damage the subjects' cognitive performance as some cognitive-enhancing drugs do.

These differences between cognitive-enhancing drugs and behavioral training suggest that these two enhancing methods have different enhancing effects. Among the differences are: different retention rates, different influences on brain activation patterns and neuronal growth, different specificities, and different influences on subjects with varying cognitive abilities.

12.4 Conclusion: Different Mechanisms of Cognitive-Enhancing Drugs and Behavioral Training

I conclude that cognitive-enhancing drugs and behavioral training enhance cognitive functions through different mechanisms. Furthermore, I propose that drugs enhance cognitive functions by modulating only parts of the neural network that correspond to the cognitive functions, while behavioral training enhances cognitive functions by modulating a larger neural network within which the target neural network is only a part. The neural networks of cognitive functions usually involve more than one kind of neurochemical pathway. For instance, the neural network of working memory involves the neurochemical pathways of dopamine, noradrenaline acetylcholine, and serotonin, and the neural network of affective processes involves the neurochemical pathways of dopamine and serotonin (Cools et al. 2008; Harmer 2008; Luciana et al. 2001; Robbins and Arnsten 2009). When we use drugs to enhance cognitive functions, we usually use only one kind of drug. For instance, levodopa, which is the precursor of dopamine, is used to enhance working memory (Knecht et al. 2004). In this way, levodopa enhances working memory through modulating part of the neural network of working memory. On the other hand, behavioral training usually involves a neural network larger than the target neural network. For instance, working memory training involves not only working memory but also vision, attention, and, possibly, executive functions to complete the training.

The proposed mechanistic difference between cognitive-enhancing drugs and behavioral training provides an explanation for why there are synergistic effects when applying drugs and behavioral training at the same time. There are synergistic effects because drugs and behavioral training modulate different parts of neural networks independently. Thus, when drugs and behavioral training are employed at the same time, drugs and behavioral training can enhance the part that the other enhancer fails to enhance. Such a combination results in better enhancing results.

In addition, the proposed mechanistic difference between cognitive-enhancing drugs and behavioral training also suggests some explanations for the differences of the enhancing effects of these two enhancing methods. First, the enhancing effects of behavioral training last longer than those of drugs because behavioral training modulates not only the target neural network but also the interaction between the target neural network and other neural networks. I suggest that the enhancement of the interaction between neural networks helps to maintain the enhancing effects on the target neural network. Second, it is also possible that the interaction between

different neural networks that result from behavioral training makes it easier to change brain activation patterns and neuronal growth. Third, the fact that drugs and behavioral training have different specificity may be due to the range of neural networks that they influence. For instance, it is easier for levodopa to enhance the subjects' ability of encoding stimulus salience than behavioral training because levodopa acts on a more specific range of neural network, which may be what is required for the encoding of stimulus salience. Fourth, the negative effects of cognitive-enhancing drugs on subjects with high performance may result from the trade-off between different cognitive functions, as Husain and Mehta (2011) suggest. The reason why behavioral training does not have the same negative effects may be that the interaction between different neural networks resulting from behavioral training has already reduced the trade-off between different neural networks or different cognitive functions.

To conclude, given the interdependency between theories and empirical studies, the proposed mechanistic difference of cognitive-enhancing drugs and behavioral training proposed in this chapter provides a basis for finding more effective enhancing methods. This difference also needs to be examined by empirical studies. If empirical studies do agree with the proposed mechanistic difference, this proposal could then be a good start for developing the general mechanism of cognitive enhancement.

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