

実験心理学を基盤とした行動分析法である行動薬理学に関する 米国心理学会における最近の見解

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Introduction of Recent Opinion of the American Psychological Association Regarding Behavioral Pharmacology, One of the Methodologies of Behavior Analysis based on Experimental Psychology

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要旨

【目的】実験心理学を基盤とする行動薬理学を学ぶために2012年10月から3ヶ月間、米国ミシガン大学医学部薬理学講座のJames H. Woods教授の研究室に滞在して、いくつかの知見を得た。【方法】滞在中、米国心理学会から発行された「行動分析」にWoods教授が執筆した「行動薬理学」を基に米国における行動分析を学んだ。また、Woods教授ならびに薬理学講座の研究者と直接あるいはセミナーやミーティングなどで議論することで理解を深めた。【結果ならびに考察】実験心理学を基盤とする行動薬理学とは、従来私が理解していた主に分子機構に基づいた神経科学的なものではなく、行動の変容から薬物の作用機序を考察するものであった。古典的な考え方もいえるが、薬物の持つ薬理作用の本質をついているとも言え、私にとって新しい発見となった。【結論】実験心理学を基盤とする米国流行動薬理学の基本的な考え方を修得できた。

キーワード：行動薬理学；行動分析；強化；オペラント条件付け；古典的条件付け

Abstract

I have studied abroad to learn about "Behavioral Pharmacology" at Department of Pharmacology, School of Medicine, the University of Michigan, from October to December in 2012. During staying at the University of Michigan, I could learn about "Behavior Analysis", especially "Behavioral Pharmacology" in Prof. James H. Woods's laboratory. During my visiting Prof. Woods's laboratory, I tried to organize my thoughts about "Behavioral Pharmacology" with reading Chapter 23 written by Prof. Woods and his collaborator. I also learn about it by attending some lectures, seminars, and meetings, in addition to discussions with Prof. Woods or his colleagues. I have learned some new concepts or ideas of "Behavioral Pharmacology". Especially, I could learn about some idea how I consider the mechanism of behavioral changes induced by drugs or diseases. In addition, I could learn about the importance of the stimulus effects of drugs, as I didn't know much about the stimulus effects of drugs without considering about the molecular basis of drugs-induced behaviors.

Key words : Behavioral Pharmacology; Behavior Analysis; Reinforcement; Operant conditioning; Pavlovian-conditioning

Introduction

I have studied abroad to learn about "Behavioral Pharmacology" at Department of Pharmacology, School of Medicine, the University of Michigan, from October to December in 2012. During staying at the University of Michigan, I could learn about "Behavior Analysis", especially "Behavioral Pharmacology" in Prof. James H.

Woods's laboratory. "Behavior Analysis" emerged from the non-human laboratories of pioneered experimental preparations designed in order to find orderly relations between environment and behavior. "Behavior Analysis" begins with the replicable behavioral processes and products of individuals, even if it ends with the behavioral processes and products of populations. This emphasis on the behavioral processes has its roots in the basic research laboratories of Ivan Pavlov (1849–1936) and Burrhus F. Skinner (1904–1990). Their research proved formative in the founding and evolution of behavior analysis as it, and the research that it inspired, demonstrated lawful, orderly relations among behavior and its antecedents and consequences. Especially, I suppose that Skinner was one of the most important researchers in the field of "Behavior Analysis including with Behavioral Pharmacology" because the field of behavior analysis did not exist when he began to do his pioneering work which was called operant behavior by Skinner. Skinner invented the operant conditioning chamber, also known as the Skinner box. Skinner was a firm believer of the idea that human free will was actually an illusion and any human action was the result of the consequences of that same action. If the consequences were bad, there was a high chance that the action would not be repeated; however if the consequences were good, the actions that lead to it would be reinforced. Skinner called this the principle of reinforcement. Prof. Woods provides an overview of how a wide variety of commonly prescribed drugs, abused drugs, or both affect specific aspects of operant and Pavlovian behavior. In addition to providing an approachable summary of Pharmacokinetics, these authors discuss drugs as antecedent and consequent stimuli – the latter providing a widely used model of human drug seeking, drug taking, and drug abuse.

This paper is something that has organized my learning about "Behavioral Pharmacology" throughout staying in the University of Michigan.

Methods

During my visiting Prof. Woods's laboratory, I tried to organize my thoughts about "Behavioral Pharmacology" with reading Chapter 23¹⁾ written by Prof. Woods and his collaborator. I also learn about it by attending some lectures, seminars, and meetings, in addition to discussions with Prof. Woods or his colleagues.

Results and Discussion

Drug-receptor interactions

I have considered again what the receptor theory in the Pharmacology is after I was reading about section of "Drug-receptor interactions". And then, I was interested in the three mechanisms by which apparent behavioral responses can be produced by established antagonists in particular. As Prof. Woods mentioned, I also considered important that an antagonist with no efficacy itself could produce the opposite effect as the agonist or endogenous ligand if it is likely as an inverse agonist. Moreover, antagonist will produce parallel rightward shift if the behavioral response induced by an agonist is true response. After reading this section, I remember one my own paper entitled, "Relationship between cholinergic dysfunction and discrimination learning disabilities in Wistar rats following chronic cerebral hypoperfusion". Although this paper was finally accepted, I was troubled to clarify the relationship between cholinergic dysfunction, especially reduction of total muscarinic acetylcholine receptor binding and discrimination learning disability. Of course, I think that this case is more complicated than drug-receptor interaction because this model is produced by permanent bilateral common carotid arteries in rats.

However, I thought that it might be possible to have more accurate results if I would have checked the effect of muscarinic agonist and / or muscarinic antagonist on this model, after reading their chapters.

Text-system sensitivity

I read with interest in Prof. Woods's suggestion regarding "A very sensitive test system may reveal that one drug is more effective than another; whereas a less sensitive system may suggest that both drugs have full efficacy". I agree with his suggestion. And, he presented specific (individual, concrete) cases in the addition to explanation of the concept of receptor reserve, about his important question as "What might sensitivity mean mechanistically?". I think that his suggestions are not only natural but also important to evaluate the effect of drugs on the behavioral changes. I could recognize the importance of sensitivity when we evaluate the efficacy or potency of drugs according to this section.

Drug effects on classically-conditioned behavior

Although I have ever known a little about "classically (Pavlovian)-conditioned behavior", I could learn about the effect of drugs on classically-conditioned behavior with reading this section. Although I knew drugs become conditioned stimulus (CS) instead of foods, throughout studying this section, I also learned we can evaluate the ability of the drugs to modify learning of the CS-unconditioned stimulus (US) associations. According to my understanding, we can evaluate whether or not unknown compounds have potency, at least efficacy, for the special receptor as the target of drug's action to analyze the effect of drugs on the acquisition of the CS. Moreover, we can also clarify the pharmacological characterization as agonist, inverse agonist, and antagonist using a well-established behavioral preparation.

Drug effects on operant behavior

Prof. Woods suggested the importance of accurately recognition for behavioral mechanisms induced by drugs to explain the effect of drugs on avoidance behavior such as the difference between escape and avoidance. For example, we can understand the characteristics of the effects of various classes of drugs with considering that drugs increase rates of punished responding whether drugs are as a negative reinforcer or a punisher. Similarly, we need apply the effect of drugs on behavior maintained by a positive reinforcer such as food. Thus we have to understand carefully and exactly when we interpret the meaning of drug-induced behavioral changes whether a positive reinforcer or a negative reinforcer.

Drugs as discriminative stimuli

As Prof. Woods suggested some example of drugs as discriminative stimuli such as opiates or benzodiazepines, I thought that it is important that to understand the drug-discrimination procedure can prove useful in the pharmacological classification of drugs. Namely, we can understand the pharmacological classification of drugs whether or not the drug discrimination curve of behaviorally-active drugs is produced rightward shifts by receptor-selective competitive antagonists. In the end of this section, he suggested several lessons. Especially, like L-838417, we have to pay attention to the possibility of important differences in efficacy at different subtypes.

Drugs as reinforcing stimuli

The reinforcing stimulus effects of drugs have been widely and usefully studied as models of human drug taking and abuse. And, Prof. Woods pointed out several merits of self-administration studies. Although I didn't know much about self-administration studies, I could learn it a little bit. I was interested in the difference between discriminative stimulus effect and reinforcing effect. In particular, self-administration studies usually have only one of two outcomes, such as either a reinforcer or not. On the other hand, it was also interesting to me that drug self-administration procedures have proven useful in evaluating agonist-antagonist interactions. I knew that analysis of behavioral changes by evaluating agonist-antagonist interactions only are behavioral

pharmacological concept. In addition, he suggested that it was no problem not to know clearly if it was hard to explain about all agonist-antagonist interactions completely, with introducing the interaction between cocaine and dopamine antagonists. I also strongly think so if we can explain sufficiently and consistently about it.

Other stimulus effects of drugs

Frankly speaking, it wasn't until I read this section that I might have been able to understand essentially the meaning of behavioral pharmacology. On the behavioral pharmacology, I have learned we need think that it is important which drugs have what kind of stimulus effects. I had supposed until now that it is important which drugs have what kind of molecular mechanisms. Of course, in the view point of behavioral pharmacology, I have to pay attention to the importance of the stimulus effects of drugs, although it may be important to think about the molecular basis of drugs. Prof. Woods suggested five other stimulus effects as a typical example. I'm interested in all these five stimulus effects. Although I knew the first two stimulus effects, "stimuli that elicit specific behavior patterns or punishing stimuli to reduce behavior", I didn't know much the last three stimulus effects. As it was difficult to understand the concept of "context" for me, I have tried to learn about various stimulus effects of drugs. And, I understood that the research of Prof. Woods's lab would be based on these concepts, according to my understanding by attending lab meeting and by reading this chapter or their papers.

Discussion regarding "Distinguishing Behavioral Pharmacology from Neuroscience"

I was the most interested in this matter throughout reading this chapter because I was troubled how I understand the mechanism of behavioral changes when I have thought the meaning of behavioral changes which is induced by drugs or disease. As Prof. Woods pointed out, I also think that neuroscientists are usually searching for an underlying brain mechanism that is related to a drug's action. As I'm rather a neuroscientist, I have usually examined not only behavioral changes but also molecular changes in the brain. I think the point at issue is whether or not we can confirm relationship between behavioral changes and molecular changes. However, I have always thought that it was unexpectedly difficult to prove whether it's true or not. According to his suggestion, behavioral pharmacologists seem to focus on how the drug alters ongoing behavior and find sufficient explanatory value in the behavioral changes. I might be able to understand a little how I consider the mechanism of behavioral changes induced by drugs or diseases by having read their chapters. Namely, if we would avoid our misunderstanding the meaning of behavioral changes induced by drugs or diseases, we need consider carefully the results of the molecular changes when we correlate these two results. On the other hand, I suppose we cannot avoid using neuroscience, as recent neuroscience is making markedly advances. That is why I believe we have to consider again about the importance of typical theory of behavioral pharmacology. Moreover, we have to consider how we would better utilize for interpretation of behavioral changes in addition to how we adopt these results from neuroscience. With regard to thinking about the correlation of both results of behavioral pharmacology and neuroscience, in future, I would like to consider these interpretations carefully and comprehensively, but not shortsightedly.

Conclusions

Until now, I have examined to clarify the effect of diseases or drugs on behavioral changes due to behavioral investigations²⁻⁵⁾. However, I was troubled how I understand the mechanism of behavioral changes when I have thought the meaning of behavioral changes which is induced by drugs or disease. Throughout these experiences I could have in the University of Michigan, I have learned some new concepts or ideas of "Behavioral Pharmacology". Especially, I could learn about some ideas how I consider the mechanism of behavioral changes induced by drugs or diseases. In addition, I could learn about the importance of the

stimulus effects of drugs, as I didn't know much about the stimulus effects of drugs without considering about the molecular basis of drugs-induced behaviors. I come to think of it once again, Pavlov and Skinner did not possess expertise about the viewpoint of Pharmacology or Neuroscience nor pay attention to the molecular mechanism such as genetics or biological systems. Namely, I could understand that drugs have at least not only the characteristics as a pharmacological stimulus but also that as a behavioral stimulus. In future, when I'll examine the behavioral changes induced by drugs, I would like to pay attention to, for example, whether it is true that molecular changes induced by drugs will be the cause of the behavioral changes induced by drugs or not.

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