Neurochemical Regulation of Complex Behaviors: Conceptual Perspective

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The ultimate aim of psychopharmacology is to develop pharmacological tools that can modulate human behaviors. It is related to the concept that the abnormal human behaviors are the result of chemical derangements in the brain, representing somewhat deterministic viewpoint.

Animal behaviors are "determined" at various levels. There are some deterministic behaviors such as the responses of the autonomic nervous system and simple motor reflexes. These behaviors are thought to be hard-wired in the brain and can be predicted (controlled) somewhat "reliably."

However, many behaviors of the animals that have the central nervous system are by no means deterministic. Many behaviors are apparently random. The "free will" is a highly appreciated value in modern philosophy. However, some behavioral neuroscientists propose that the subjective perception of will is not the real "cause" of action. The real determinant of an instant behavior may be related to the stochastic release of neurotransmitters at synaptic terminals.

At most, we can predict with certain probability that an individual has tendency to choose a certain behavior among possible alternatives. This "tendency to act" in a certain way may be called the motivation. This implies that the motivation is a statistical concept. The motivational status of an animal can be altered by learning experiences, which are accompanied by the neurochemical changes. This also suggests that the motivation can be modulated by pharmacological tools.

The motivation may be modulated by the mood (affect) in higher animals. Mood is an enduring but variable behavioral parameter that may also be pharmacologically modulated. In human beings, there are more enduring behavioral parameters called the personality. Although the personality also has neurochemical substrates, its pharmacological modulation is limited.

These levels of behavioral determinism can be considered as a product of evolution, from deterministic behavior to stochastic behavior under individual-specific constraint.

I will show some examples of neurochemical regulation of behaviors of various levels of complexity.

1) Locomotor behavior

Locomotor activity is simple behavior, and somewhat reliably controlled (predicted) by the

neurotransmitter dopamine in the ventral striatum (Nucleus accumbens) of the brain. Novelty and psychostimulant drugs are representative stimuli that increase locomotor activity and both increase extracellular DA levels in the striatum. Repeated exposure to the former stimuli is related to the behavioral as well as neurochemical habituation, while repeated exposure to the latter results in the behavioral and neurochemical sensitization. So the behavioral status reliably reflects the chemical status.

2) Feeding behavior

The feeding behavior is also a kind of "hard-wired" behavior and anatomically centered on the lateral hypothalamus. But its neurochemical regulation is rather complex. There are multiple peptide neuromodulators that can either promote or inhibit feeding behaviors. Neurotransmitters such as dopamine and serotonin also affect the feeding behavior. Conversely, the function of these molecules is not restricted to the control of feeding. For example, orexogenic peptide orexin is also a regulator of vigilance. So, the neurochemical control of relatively simple behavior is by no means a simple one.

3) Drug addiction

Addiction is closely related to learning and motivation, and is a more complex behavior than above two. It is proposed that DA in the nucleus accumbens is related to the rewarding property of addictive stimuli. The general locomotor activity, which is a prerequisite for target-oriented behavior, is also regulated by DA as stated above. These components of circuit are hard-wired. However addictive behavior (drug self-administration) *per se* is a learned behavior and thus is a more plastic one. This type of motivational learning is affected by many neurotransmitters including DA itself. The neurochemical control of addictive behavior is complex and thus not fully understood. In human being, drug addiction is one of the hardest psychiatric diseases to treat.

4) Attachment

Attachment is basically an instinct and a hard-wired behavior as such. However, it is also a social behavior which is specific to a certain other individual in the environment. Although many component of attachment behavior is regulated by neuromodulators and neurohormones, the selection of specific object of attachment is related to learning.

Although we have discussed the neurochemical regulation of behavior, the neurochemical setup can be conversely regulated by the animal's behaviors. So the behavior and neurochemistry are mutually interactive ones.