Impact of Dopamine on Reward Related Behavior of Animals and Therapeutic Role

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Abstract: Nowadays, some researchers proposed that human behavior are closely related to dopamine development. The effect of dopamine on esthesia of reward of humans and animals is very significant. This paper will use a literature review method to elaborate on the role of dopamine in experimental conditioning, animal reward circuitry, and what role dopamine plays in human behavior, such as reinforcement learning. This paper will also specifically illustrate the circuitry of dopamine secretion and the reinforcement process of the secretion process. As it is difficult to achieve human experiments, a large number of animal experiments will be used to demonstrate its effect on animals, then further apply some results on human. The paper found that the secretion of dopamine played a significant role in reward related behavior under experimental conditioning. This conclusion can also generalize to human behavior to a certain extent because of the genetic similarity between mice and other animals and humans. Therefore, this paper, via literature review, will show the role of dopamine in Parkinson's syndrome and the treatment and therapeutic effects of effective drugs on the syndrome.

1 INTRODUCTION

Neurotransmitter dopamine plays a significant role in human learning, motivation, and many other aspects. This paper will further strengthen the irreplaceable role of dopamine in reward circuitry by combining past literature, presenting the trajectory of dopamine in human brains and animal brains, and combine with experiments under Experimental conditioning, showing the degree that dopamine is practically involved in reward related behaviors in animals. In addition, dopamine is a neurotransmitter, and its system regulation disorder is the main cause of Parkinson's syndrome. Insufficient dopamine secretion leads to Parkinson's syndrome. Thus, it can be inferred that the secretion of dopamine is closely related to Parkinson's disease. Therefore, this paper, with a method of literature review, will also present the role of dopamine in Parkinson's syndrome and the treatment and therapeutic effects of effective drugs on the syndrome.

2 DEFINITIONS

2.1 Midbrain Dopamine

The Midbrain dopamine, also known as dopaminergic neurons in ventral mesodiencephalon (mdDA), is responsible for several functions as voluntary movements control, motivation behavior, maintaining working memories, adjusting emotions and more importantly, associations with rewarding stimuli (Bissonette & Roesch 2016).

Midbrain dopamine(mdDA) has a great influence on Reinforcement learning by adjusting strength of synaptic connection between neurons (Bromberg-Martin, Matsumoto & Hikosaka 2010). More specifically, this would permit a individual to learn the ideal choice of activities to pick up rewards, given adequate trial-and-error involvement. According to Montague et al (1996), such process could be described as a modified Hebbian rule. When a cell affect it's neibors which eventually result in a reward or punishment, brain would release dopamine in order to reinforce the connection between two cells, and eventually result in repeated behavior. Referring to(Figure 1.)

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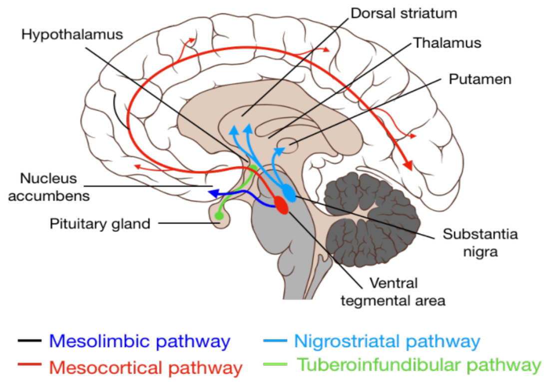

Figure 1: Nigrostriatal pathway and Mesocortical pathway displaying release of dopamine.

Furthermore, Mesolimbic, Mesocortical, as well as Nigrostriatal pathways are indispensable in the connective process of midbrain dopamine cells. The mesolimbic and nigrostriatal pathways are an integral part of the basal ganglia through its reciprocal connections to the ventral and dorsal striatum respectively (Ikemoto 2007). The nigrostriatal pathway is shown emitting mainly from SNc (Substantial Nigra pars compacta) neurons, which provide dopaminergic tone necessary for voluntary movements and also carrying salience and PE (predicted error) signal (Bissonette & Roesch 2016). Simultaneously, VTA (Ventral tegmental area) is also emanating from the Basal Ganglia through Mesocortical pathway to both the ventral striatum as well as Cortex. Corticostriatal input simultaneously travels to Dorsal Striatum and ultimately result in bodily movement, or behavior (Bissonette & Roesch 2016).

2.2 Reinforcement Learning

Reinforcement learning could be simply describe as learning from past experiences, or Law of Effect proposed by Edward Thorndike. Thorndike took observation of cats in a puzzle box possessing certain mechanism for cats to learn and ultimately, escape. This is a traditional Instrumental conditioning, or Operant conditioning experiment, a term used for experiments which reinforcement is contingent upon behavior (Sutton&Barto 2018). Furthermore, researchers placed food, as primary Reinforcement next to the confinement.

Qualitative data are taken during the observation. "The cat that is clawing all over the box in her impulsive struggle will probably claw the string or loop or button so as to open the door. And gradually all the other non-successful impulses will be stamped out and the particular impulse leading to the successful act will be stamped in by the resulting pleasure, until, after many trials, the cat will, when put in the box, immediately claw the button or loop in a definite way" (Burnham 1972).

3 CONNECTION BETWEEN REFINFORCEMENT LEARNING BEHAVIOR AND FUNCTION OF DOPAMINE

Instead of conduct in-depth research directly from human behavior, many experiments on reinforcement learning are initiated with animals, especially mice, due to similar brain structures and past knowledge on circuit when dopamine neurons are triggered and released. Two models of dopamine projection systems released from ventral midbrain to ventral stratum are responsible for reward related behavior (Haber 2014).

3.1 Dopamine Projection System from Ventral Midbrain

Recently, researchers have been utilizing Rats in order to refine our understanding localization within the ventral striatum and VTA that are responsible for the rewarding effects of drugs of abuse (Ikemoto & Wise 2004). Medial olfactory tubercle not only plays an important role in relevant to drug reward, but also shares a common function with the medial shell; they further suggest that the accumbens shell is functionally heterogeneous, as is the olfactory tubercle (Ikemoto 2007).

Rats could learn to lever-press for cocaine or amphetamine into the olfactory tubercle, although the medial portion of the tubercle is more responsive to the rewarding effects of these drugs than the lateral portion (Ikemoto 2003). A representation of dopamine signal circuitry has once been illustrated in "precisely timed dopamine signals establish distinct kinematic representations of skilled movements" (Leventhal & Bova 2020). The aim of this study was to determine the effects of precisely timed dopaminergic manipulations on a relatively unconstrained motor skill. This process effectively illustrated the circuitry movement in relevant to dopamine, with the use of experimental conditioning. Rats were utilized considering ethical guidelines in human is scarcely attainable. The procedure involves stimulating or inhibiting midbrain dopamine neurons in different time period of several groups while rats are performing a skilled reaching task, in which the coordinated forelimb and digit movements to reach for, grasp, and consume sugar pellets were involved. In detail, researchers had stimulated or inhibited substantia nigra pars compacta (SNc) dopamine neurons at specific moments during rat skilled reaching. Different Viruses as Tyrosine hydroxylase (TH)-Cre+ rats were injected bilaterally with a double-floxed channelrhodopsin (ChR2), archaerhodopsin (Arch), or control EYFP construct into SNc.

Explain further into the skilled reaching task, training and testing were carried out in custom-built skilled reaching chambers housed within soundproof, ventilated cabinets (Leventhal & Bova 2020). Trials were initiated with rats breaking a photobeam at the back of the chamber, which caused a pellet to be delivered in front of the reaching slot. Rats could make multiple reaches until the pellet delivery arm descended 2 s after the video trigger event. Following training, optical fibers were implanted over SNc contralateral to the rat's preferred reaching paw. Immunohistochemistry confirmed that opsin expression was restricted to TH-expressing neurons in SNc projecting to striatum (Leventhal & Bova 2020).

As a result, activity of SNc dopamine neuron which was altered gradually changes skilled reaching outcomes. Furthermore, dopamine neuron stimulation caused a trend of decline in performance. This shows that dopamine plays an indispensable role in reinforcement learning and similar skill acquisition.

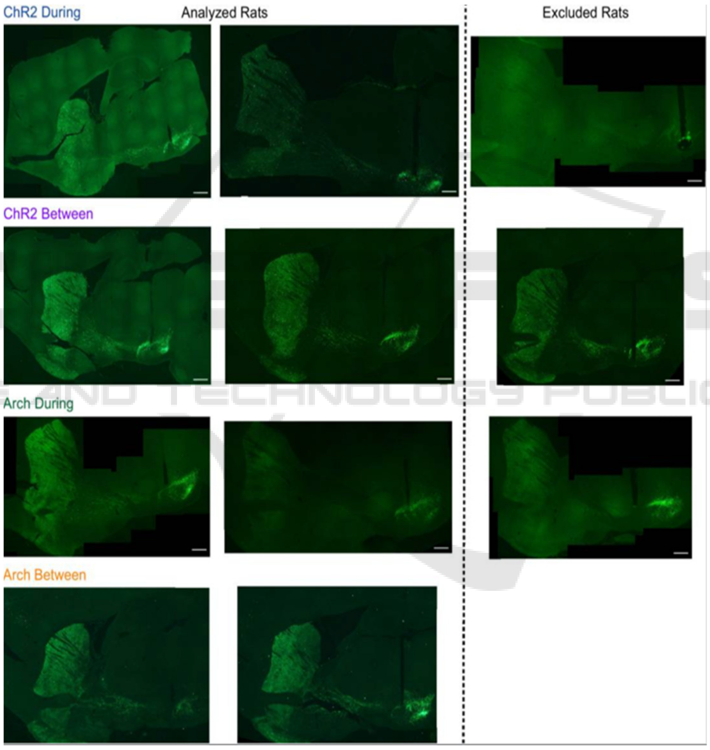

Figure 2: Examples of immunohistochemistry from rats for each group.

3.2 Dopamine Projection from Ventral Tegmental Area

Lichtenburg et al (2018) illustrated inner, dopaminergic circuitry, or movement while rats are encountering rewarding tasks or decision making (Lichtenberg, etc. Reward related behaviors are often signaled by DA system. Studies have shown that Dopamine neurons in the ventral tegmental area (VTA) and subsequent DA release into the NAc increases and decreases in response to events that are better or worse than expected. In the appetitive context, release of dopamine are usually determined by prediction of potential reward. In contrast, in aversive contexts, unavoidable aversive events as shocks or air puff, significantly reduce DA release, whereas unexpected omission of aversive events or the cues that predict avoidable shock reliably elicit phasic DA release (McCutcheon 2012).

In order to detect and obtain information on how Dopamine signals are modulated by appetitive and aversive events from conspecific (opponent), the research further recorded accumbal, dopamine release utilizing Fast-Scan Cyclic Voltammetry (FSCV), which is useful in detection of release of DA in response to different contexts.

Eight rats were observed during performance of Pavlovian Social Distress Paradigm. Each group involved two rats, with the recording rat and Conspecific, the opponent. They were separated by a guillotine door which is transparent, allowing visual, smelly, and vocal action permeate through. One of each directional light, food cup, and shock grid was placed in each room with a house light in the middle, placed right above the delineated line. To initiate each trial, the researcher first turn on the houselight; after 5 seconds, three different stimuli was randomly applied to each room correlated to reward, neutral or shock(punishment) outcomes., with no precursors to rats but display as which light would be on. Outcomes was eventually displayed while rats would then experience the FSCV session mentioned above.

False color plot from FSCV indicates that DA (dopamine) from rats merely released when outcome cue was displayed in contrast with little, or declined reaction after the directional cue. This indicates a correlation between DA release and reaction in response to a reward circuitry, or experimental conditioning. Some researchers also argue a depletion of DA neuron while individual encounter a reward-punishment process (Willard, etc. 2019, Bouchard 2015, Morita 2018, Lindahl & Hellgren 2017).

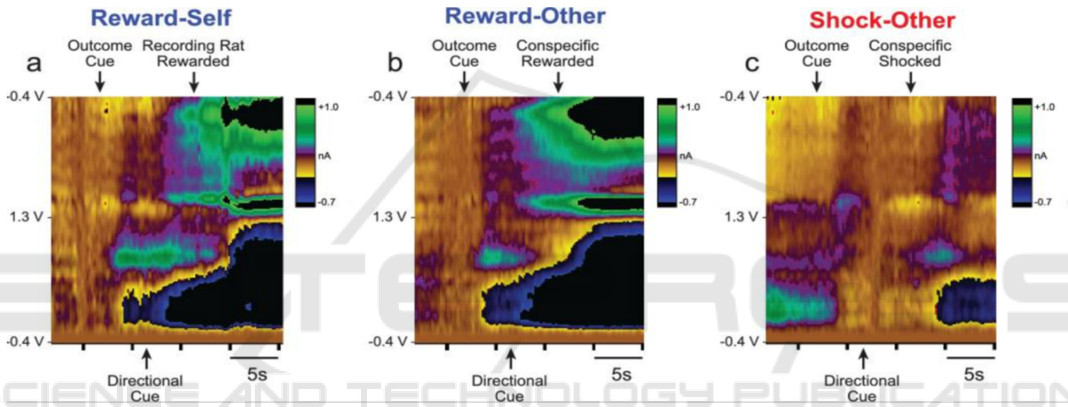

Figure 3: Fast-Scan Cyclic Voltammetry (FSCV) image presenting release of dopamine within rats.

4 FUNCTIONS OF DOPAMINE

4.1 Role in the Prefrontal Cortex of the Brain

Researchers believe that the role of dopamine is not only to use rewards to learn the value of past behaviors, but also that dopamine plays an indispensable role in the prefrontal cortex of the brain, enabling us to learn new tasks efficiently, quickly and flexibly (Wang, Kurth-Nelson, Kumaran 2018).

These researchers from London (deepmind organization) tested their theories by simulating six meta-learning experiments in the field of reconstructed neuroscience-each experiment requires an agent to perform tasks that use the same basic principles (or the same set of Skills), but different in some ways.

An experiment they replicated is called the Harlow experiment, which was a psychology experiment in the 1940s to explore the concept of meta-learning. In the original test, a group of monkeys were shown two unfamiliar objects, and only one of them would give them food rewards. The two objects were displayed 6 times in total, each time they were placed randomly, so the monkey must know which one will give them food rewards. Then, they were shown two other new objects again, and again, only one of them would give them food.

During this training process, the monkey develops a strategy to select objects that can be rewarded: it learns to choose randomly the first time, and then, the next time it chooses specific objects based on reward feedback, instead of from left to right. Right selection. This experiment shows that monkeys can internalize the basic principles of tasks and learn an abstract structure of rules—in fact, they learn how to learn.

In fact, researchers found that the meta-RL (reinforcement learning) agent can learn how to quickly adapt to various tasks with different rules and structures. Moreover, since the network has learned how to adapt to various tasks, it has also learned general principles on how to learn effectively (Wang, Kurth-Nelson, Kumaran 2018, Wang, Smith & Delgado 2016). They also found that most of the learning takes place in the recurrent network, which supports the view that the role of dopamine in the learning process is more important than previously thought. While traditionally, dopamine is thought to strengthen the synaptic connections of the prefrontal system, thereby strengthening specific behaviors.

4.2 Role in the Parkinson's Disease

Another function of dopamine is reflected in the concept of Parkinson's disease (Opara, Małecki & Socha 2017, Radhakrishnan & Goyal 2018, Seppi & Ray Chaudhuri 2019). With modern development, brain detection instruments like CT scan, MRI, and FMRI have been widely used in psychology, neuroscience and even medical fields (Tocchio, Kline-Fath, Kanal, Schmithorst & Panigrahy 2015, Villanueva-Meyer, Mabray & Cha 2017). Among them, FMRI has been heavily invested in the research on the reinforcement learning process and reward circuitry described in this article (Wang, Smith & Delgado 2016, Glover 2011). Parkinson's disease causes a characteristic combination of motor symptoms due to progressive neurodegeneration of dopaminergicneurons in the substantia nigra pars compacta (Glover 2011).

Currently, although there is no cure for Parkinson's disease with good results, we still cannot deny the existence of effective drugs (Seppi & Ray Chaudhuri 2019). In addition to being used for patients, these drugs can also test the change in dopamine and it's influence on parkinson's disease (Wang, Kurth-Nelson, Kumaran, et al 2018). Approaches in relevance to capturing dopamine variation in cerebral function, is to test patients in two conditions under FMRI scan; one is after dopamine withdrawal with relatively low levels of dopamine in a pragmatic OFF-medication state and once after dopamine intake with relatively high levels of dopamine in an ON-medication state. The differences in the patient's behaviour and neural activation between the ON- and OFF-medication state, considered together with the behaviour and activation patterns of healthy control participants, is then used to infer the functional effects of dopamine in the human brain. As shown in the figure, with the application of medicines, the overall performance of the patient has risen to a plateau, which is the top of the performance, and then decline. (figure 4)

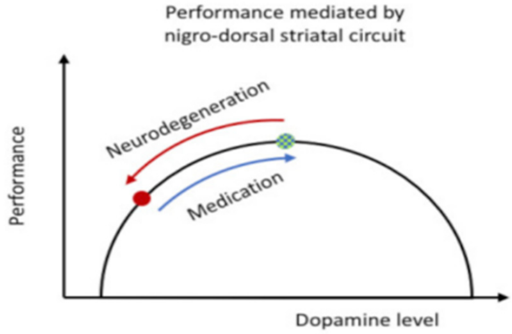

Figure 4: Performance mediated by nigro-dorsal stratal circuit.

5 CONCLUSIONS

From the analysis of theory and actual cases, when animals encounter certain tasks, the secretion of dopamine plays a significant role. When the hub tissues in animal brains encounter the same results or similar stimuli again and again, the secretion channels of dopamine are narrowed again and again until a fixed circuitry is formed. Furthermore, such discovery also further contributes to modern education or animal domestication. Human education is more from the perspective of students, similar to analogy, to promote students' learning. Unlike humans, although animals are far inferior to humans in their cognitive and observational abilities, animal trainers can also ensure that animals learn and understand certain tasks through such methods that have been used extensively, assimilated and similar to reinforcement learning. Simutaneously, one still need to be skeptical of dopamine effect on human. Although many experiments, including diseases as Parkinson's disease, have demonstrated the role of dopamine in human brain control and learning, too many experiments, especially those related to injection, violate the ethical guidelines of human experiments, and it is difficult for researchers to reach one solid conclusion stating a directly, causal effect between the two.

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