International **J**ournal of **M**edical **R**eviews

Review Article

Reward System on Dopaminergic Pathway

Mohammad-Reza Zarrindast[1], Morteza Izadi[2], Mohammad Nasehi[1], Akram Paktinat[3], Mohammadjavad Hoseinpourfard[*1, 3]

Abstract

Nowadays some overused agents have influenced on cognitive neuroscience studies. Some of the brain structures that regulate and control our behaviors are from these aspects so one of these pathways has focused in this study. On the other hand, human behaviors such as perception, action, language, and emotion have been paid more attention in cognitive neural science. In this review study data has been gathered in a matrix that has been confirmed by these aspects. It tries to find the frequency of current researches in any of these branches of the research matrix. Some of these researches locate in at least situation in frequency. Nucleus Accumbens (NA) and Hippocampus have discussed in this way. This study try to classify recent studies in reward system and then suggest the approach for following studies.

Keywords: Reward System, Neural Pathway, Dopaminergic Pathway, Hippocampus, Ventral Tegmental Area, Amygdala, Nucleus Accumbens, Prefrontal Cortex

1. Institute for Cognitive Science Studies, Tehran, Iran
2. Health Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
3. Health Management Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran

* **Corresponding Author**
Mohammadjavad Hoseinpourfard, Health Management Research Center, Baqiyatallah University of Medical Sciences, Tehran, Iran
E-mail: hpf.javad@gmail.com

Submission Date: 2015/06/01
Accepted Date: 2015/08/21

Introduction

Reward has a powerful influence on cognitive studies. To reveal the reward and its effective factors what and where alter sensitivity and motor behavior, by focus on the principle of neural science studies, the four major subjects include: perception, action, emotion, and language have selected as functional aspects and anatomical aspects could be classified by five categories. These anatomical categories are Hippocampus, Ventral Tegmental Area (VTA), Nucleus Accumbens (NA) and Prefrontal Cortex. That's focused on dopaminergic pathway because it is one of the most sites in reward system.

James Olds and Peter Milner reported that rats preferred to return to the region of the test apparatus where they get electrical stimulation to the septal area of the brain by electric signals (1). 'It's a phenomenon that discovered the reward mechanisms in the brain involved in positive reinforcement and their experiments led to the conclusion that electrical stimulation could serve as an operant reinforcer' (1, 2). Their discovery emphasize to motivation that is an operational key in reward system (2).

Reward is one of the major topics in cognitive neuroscience studies. Many effective agents play roles in behavior. To reveal the mechanism of rewards by what, where, and when, we must firstly distinguish them. For focusing on the principles of neural science studies, four major subjects exist which are: perception, action, emotion, and language.

The reward anatomical map is one of the most important aspects in this review. In this regard we can find five major areas including: Hippocampus, Ventral Tegmental Area (VTA), Nucleus Accumbens (NA), Amygdala, and Pre-Frontal Cortex (PFC). Some of them have located in circulation like a pathway that is known as the dopaminergic pathway. Hence it is not easy to encapsulate these mechanisms in a simple pathway. Study about anatomical aspects of reward and many of the similarities between human and animals help us to reveal some attractive facts about this.

Certain neural structures whereas called the reward system are critically involved in mediating the effects of reinforcement. Reward can be like as an appetitive trigger that given to alter their own behavior. So it has typically called as a reinforcer. It does not necessarily imply that it is a reinforcer and a reward can be defined as reinforcer only if its delivery increases the probability of a behavior (3).

Reward is an objective way to describe positive values. It ascribes that to an object, behavior or a state. Rewards in 1st stage includes those that are necessary for human life such as food and sexual contact (4). Its 2nd stage derives their value from rewards in the 1st stage. Making money and its attraction is a good example for this matter. It can be produced experimentally by pairing a neutral stimulus with an object detection and attraction state about this. (Table 1)

Issues such as pleasurable touches and soft music are often said to be rewards in the 2nd stage but such claims are questionable. For example, there is a good deal of evidence that physical contact, as in cuddling and grooming, is an unlearned reward in the 1st stage (5).

Some studies in rewards pointed that the reward generally considered more desirable than that punishment in managing the behavior (6).

Structure and Function

The reward system is a collection of brain structures that attempts to regulate and control behavior by reinforcements for modulation which effects and activates pleasure state during behaviors performance. The circuit includes the dopamine-containing neurons of the ventral tegmental area, the nucleus accumbens, and part of the prefrontal cortex (7).

Table 1. Human Common Sense and Cognitive Object Detection

	Auditory	Vision	Touch	Smell	Gustatory
Sensation	αx	βy	γz	δt	θh
Perception	αx-βy		γz		δt-θh
Cognition		αx-βy-γz-δt-θh			
Cognitive Code		αxβyγzδtθh			

During behaviors performance. The circuit includes the dopamine-containing neurons of the ventral tegmental area, the nucleus accumbens, and part of the prefrontal cortex (7).

Reward System – Structure

Many pathways have major roles in the reward system. The ventral tegmental area (VTA) is one of the important sites for releasing the neurotransmitter dopamine. Dopamine acts on D1 or D2 receptors to either stimulate (D1) or inhibit (D2) the production of cAMP. Ascending dopamine fibers from the VTA to the nucleus accumbens (NA) makes a portion of dopaminergic pathway and one of the major sites in the reward system.

Hippocampus

Hippocampus is located under the cerebral cortex (8) in the medial temporal lobe, underneath the cortical surface. It contains two main interlocking parts: Ammon's horn [2] and the dentate gyrus (9). The hippocampus integrates the effects of emotion and monetary reward on episodic memory encoding (10). So, the behavioral performance of hippocampal functions have been shown to be affected by reward (10, 11).

Ventral Tegmental Area (VTA)

VTA is located on the floor of the mesencephalon. It is the origin of the dopaminergic cell bodies of the mesocorticolimbic (12). As the PFC provides excitatory input to VTA, this region was hypothesized to be a key mediator of rhythmic neural activation in reward system (13). Both the NA shell and the posterior VTA are in the reward system (14).

Amygdala

They are almond-shaped groups of nuclei located deep and medially within the temporal lobes of the brain (15). There is some differences between the right and left amygdala for example according to some studies the right amygdala play its roles on negative or unpleasant emotions such as fear, anxiety, and sadness (16), but Other evidences suggest that the left amygdala plays the both negative and positive roles however the amygdala is a well-known reward-related brain region and is critical for reward expectations (17).

Nucleus accumbens (NA)

The nucleus accumbens is a region of the human brain in the basal forebrain rostral to the pre-optic area (18). The olfactory tubercle collectively and nucleus accumbens form the ventral striatum. This sites forms one of the most important parts of the basal ganglia (19). Many researchers have indicated that the nucleus accumbens has an important role in pleasure including laughter, reward, and reinforcement learning, as well as fear, aggression, impulsivity, addiction, and the placebo effect (20-23). Both the posterior VTA and the NA shell are involved in the reward system (14).

Pre-Frontal Cortex (PFC)

The prefrontal cortex (PFC) is the thick outer layer (cerebral cortex) of the prefrontal lobe (the front portion of the frontal lobe) and contains Brodmann's areas 9, 10, 11(24). The prefrontal cortex (PFC) is a part of neuronal reward circuit involved in motivated and goal-directed behaviors (25). Some studies suggest that suppression of excitatory prefrontal cortex (PFC) networks via increased activity may enhance reward-related behavioral flexibilities (26).

Reward System – Function

Cognitive neural science structures develop from perception, action, language, and emotion (27-31).

Perception

Perception is considered to be the way you think about or understand someone or something, the ability to understand or notice something easily or the way that you notice or understand something using one of your senses (Miriam Webster's, 2015). It begins from receptor cells that are sensitive by hearing, vision, somatic, olfactory, and gustatory receptors in neural system (32, 33). Our cognition involves input which in turn results from environment triggers (34, 35). 'Perception involves "top-down" effects as well as the "bottom-up" process in neural system (36)'. 'The "bottom-up" processing transforms low-level information to higher-level information. The "top-down" processing refers to a person's concept, expectations, and selective mechanisms that influence perception. Perception depends on complex functions of the nervous system, but subjectively seems mostly effortless because this processing happens outside conscious awareness (34).

Action

Sensory-motor neural pathways represents brain functions in our behaviors. So it can be surveyed by some questions such as: "How does the brain determine behavioral goals?", or "How does the voluntary actions plan to achieve those goals?" (12). Dickinson and Balleine have pointed out that 'both animals and humans make an action quickly and preferentially if the action is expected to provide a valuable reward'. It's a key operational phrase in reward studies.

Table 2. Neural Science Studies in Functional Literature and Anatomical Site

Function / Site	Perception N#	Action N#	Emotion N#	Language N#
Hippocampus	7	49	15	2
VTA	12	43	26	2
Amygdala	18	78	52	5
NA	12	88	46	3
Prefrontal Cortex	14	72	43	4

Column (N#) shows the numbers of researches. Rows include anatomical sites. Columns include functional aspects.

Emotion

The word "emotion" dates back to 1579. It's pointed to a multidisciplinary neural system (38, 39). It can be briefed to both structural and functional aspects including: feeling, mood, and affecting (40).

Language

Language is a system of words or signs that people use to express thoughts and feelings to each other (Miriam Webster's, 2015). It communicates people by speaking, writing, or making signs (41, 42). It is also defined as the greatest skill and human beings highest achievement (43).

Study Matrix

According to this study, the reward system is in a dopaminergic pathway and has a component based complex structure including: Hippocampus, Ventral Tegmental Area (VTA), Nucleus Accumbens (NA), Amygdala, Prefrontal Cortex. The inclusion criteria included: English language sources from 2010 to 2014 in Google Scholar, and Highwire – stable accessible database in our context - by the search strings according to the both functional and anatomical site including: Reward AND Hippocampus, Ventral Tegmental Area, Nucleus Accumbens, and Prefr ontal Cortex; and 4 search string pertaining to the functional aspects include: Reward AND Perception, Action, Emotion, and Language. The screening of the gathered articles has been done according to the accessibility to their databases. The final check for the inclusion articles has been done under the supervision of experts.

Minimum studies have been done about NA and Hippocampus in Language (2 from 591) and Maximum studies have been done for NA-Action (88 from 591). In addition, according to functional categories, maximum studies had been done in Action (330 from 591) and minimum of them for Language (16 from 591) and according to anatomical category maximum of studies had been done in Amygdala (153 from 591) and minimum of them for Hippocampus (153 from 591). Table1 shows the frequency of studies and the references of them.

Future Approach

Because of wide variety pertaining to reward system both in functional aspect and anatomical site, this review classifies recent studies about reward systems in neuroscience literature by these axes and suggests an approach for future reward system researches. (Rational Unified Modeling) (44, 45).

References

1. Olds J., et al., "Reward and Drive Neurons." Brain Stimulation Reward. 1975; 1:1-30.
2. Milner P. "Brain Stimulation Reward: A Review." Canadian Journal of Psychology Outstanding contributions Series. 1991; 45(1):1-36.
3. Drugs B., et al., Behavior: The Science of Addiction". drugabuse.gov. Drugs, Brains, and Behavior: The Science of Addiction". drugabuse.gov.
4. Diamond R., Dopamine Involved In Aggression". Medical News Today. 2008-01-15.
5. Harlow, H. F., The nature of love. American Psychologist. 1958 (13), 679-685.
6. Scant B. Smacking children 'does not work'". BBC News. 1999-01-11. Retrieved 2010-05-22.
7. Health AB. Associated Behavioral Health.
8. Ribas GC., The cerebral sulci and gyri. Neurosurgical focus. 2010;28(2):E2. PMid:20121437
9. Wen HT, Rhoton ALJ, de Oliveira E, Cardoso ACC, Tedeschi H, Baccanelli M, et al. Microsurgical Anatomy of the Temporal Lobe: Part 1: Mesial Temporal Lobe Anatomy and Its Vascular Relationships as Applied to Amygdalohippocampectomy. Neurosurgery. 1999;45(3):549. PMid:10493377.
10. Shigemune Y, Abe N, Suzuki M, Ueno A, Mori E, Tashiro M, et al. Effects of emotion and reward motivation on neural correlates of episodic memory encoding: a PET study. Neurosci Res. 2010 May;67(1):72-9. PubMed PMID: 20079775.
11. Terada S, Takahashi S, Sakurai Y. Oscillatory interaction between amygdala and hippocampus coordinates behavioral modulation based on reward expectation. Frontiers in behavioral neuroscience. 2013;7.
12. Phillipson OT. Afferent projections to the ventral tegmental area of Tsai and interfascicular nucleus: A horseradish peroxidase study in the rat. The Journal of Comparative Neurology. 1979;187(1):117-43. PMid:489776.
13. Baltazar RM, Coolen LM, Webb IC. Diurnal rhythms in neural activation in the mesolimbic reward system: critical role of the medial prefrontal cortex. The European journal of neuroscience. 2013 Jul;38(2):2319-27. PubMed PMID: 23617901.
14. Brischoux F, Chakraborty S, Brierley DI, Ungless MA. Phasic excitation of dopamine neurons in ventral VTA by noxious stimuli. Proceedings of the National Academy of Sciences of the United States of America. 2009 Mar 24;106(12):4894-9. PubMed PMID: 19261850.
15. Barnea-Goraly N, Marzelli MJ. Introduction to Neuroimaging Research in Autism Spectrum Disorders. Comprehensive Guide to Autism. 2014:893-909.
16. Lanteaume L, Khalfa S, Regis J, Marquis P, Chauvel P, Bartolomei F. Emotion induction after direct intracerebral stimulations of human amygdala. Cerebral cortex (New York, NY : 1991). 2007 Jun;17(6):1307-13. PubMed PMID: 16880223.
17. Blundell P, Symonds M, Hall G, Killcross S, Bailey GK. Within-event learning in rats with lesions of the basolateral amygdala. Behavioural brain research. 2013;236:48-55.PMid:22944512
18. Carlson NR. Physiology of Behavior 11th Edition: Pearson; 2012.
19. Dautan D, Huerta-Ocampo I, Witten IB, Deisseroth K, Bolam JP, Gerdjikov T, et al. A Major External Source of Cholinergic Innervation of the Striatum and Nucleus Accumbens Originates in the Brainstem. The Journal of Neuroscience. 2014;34(13):4509-18. PMid:24671996.
20. Schwienbacher I, Fendt M, Richardson R, Schnitzler HU. Temporary inactivation of the nucleus accumbens disrupts acquisition and expression of fear-potentiated startle in rats. Brain Res. 2004 Nov 19;1027(1-2):87-93. PubMed PMID: 15494160.
21. Melanie M. Dopamine Involved In Aggression. Medical News Today [Internet]. 2008. Available from: http://www.medicalnewstoday.com/releases/94023.
22. Basar K, Sesia T, Groenewegen H, Steinbusch HW, Visser-Vandewalle V, Temel Y. Nucleus accumbens and impulsivity. Progress in neurobiology. 2010;92(4):533-57. PMid:20831892
23. "CELL-PRESS". Brain region central to placebo effect identified 2014.
24. Opris I, Casanova MF. Prefrontal cortical minicolumn: from executive control to disrupted cognitive processing. Brain. 2014:awt359. PMid:24531625
25. Katebi S-N, Razavi Y, Zeighamy Alamdary S, Khodagholi F, Haghparast A. Morphine could increase apoptotic factors in the nucleus accumbens and prefrontal cortex of rat brain's reward circuitry. Brain research. 2013;1540:1-8. PMid:24096212
26. Sparta DR, Hovelso N, Mason AO, Kantak PA, Ung RL, Decot

HK, et al. Activation of prefrontal cortical parvalbumin interneurons facilitates extinction of reward-seeking behavior. The Journal of neuroscience : the official journal of the Society for Neuroscience. 2014 Mar 5;34(10):3699-705. PubMed PMID: 24599468.
27. Vukovic N, Williams JN. Automatic perceptual simulation of first language meanings during second language sentence processing in bilinguals. Acta psychologica. 2014;145:98-103. PMid:24333464
28. Pessoa L, Engelmann JB. Embedding reward signals into perception and cognition. Frontiers in Neuroscience. 2010;4.
29. Ross D. Action-oriented predictive processing and the neuroeconomics of sub-cognitive reward. The Behavioral and brain sciences. 2013 Jun;36(3):225-6. PubMed PMID: 23663479.
30. Singh V. A potential role of reward and punishment in the facilitation of the emotion-cognition dichotomy in the Iowa Gambling Task. Front Psychol. 2013;4:944. PubMed PMID: 24381567.
31. Kandel ER, Schwartz JH, Jessell TM. Principles of neural science: McGraw-Hill New York; 2014.
32. Schacter D, Wagner A, Kandel E, Schwartz J, Jessell T. Perception. Principles of neural science (5th Ed). 2013.
33. Schacter D, Gilbert D, Wegner D. Sensation and Perception. Charles Linsmeiser Psychology Worth Publishers p 158. 2011;159.
34. Goldstein E. Sensation and perception: Cengage Learning; 2013.
35. Gregory RL, Zangwill OL. The Oxford companion to the mind: Oxford University Press; 1987.
36. Ekstrom AD, Watrous AJ. Multifaceted roles for low-frequency oscillations in bottom-up and top-down processing during navigation and memory. NeuroImage. 2014;85:667-77. PMID:23792985
37. Tachibana Y, Hikosaka O. The primate ventral pallidum encodes expected reward value and regulates motor action. Neuron. 2012 Nov 21;76(4):826-37. PubMed PMID:
38. Suchy Y. Clinical neuropsychology of emotion: Guilford Press; 2011.
39. Christensen W, Sutton J. Reflections on Emotions, Imagination, and Moral Reasoning Toward an Integrated, Multidisciplinary Approach to Moral Cognition. Emotions, imagination, and moral reasoning. 2012:257-78.
40. Schnall S. Affect, Mood and Emotions. Social and Emotional Aspects of Learning. 2011:59.
41. The Cambridge Encyclopedia of Language (Book). American Libraries.20(5):410. PMID: 10070545.
42. The Cambridge encyclopedia of the language sciences. Choice: Current Reviews for Academic Libraries. 2011;48(10):1872-4. PubMed PMID: 61288436.
43. Schacter D, Wagner A, Kandel E, Schwartz J, Jessell T. Perception. Language, Thought, Affect, and Learning. 2013.
44. Rafati H, Rashidi H, Hoseinpourfard M. Introduction of Planning Model for Research Priorities Determination. World Applied Sciences Journal. 2010;8(7):857-63.
45. Zarrindast MR, Nasehi M, Hoseinpourfard M. A Mini Review of Serotonin and Its Receptors. International Journal of Medical Reviews; (2014). 1(1).