Proceedings of the International Conference on Modern Medicine and Global Health (ICMMGH 2023)
DOI: 10.54254/2753-8818/6/20230300

The influence of the nervous system on social behavior

Jinhao Peng

College of Life Sciences, Wuhan University, Wuhan, Hubei Province, P. R. China, 430072

2020302091022@whu.edu.cn

Abstract. Social behavior plays an essential role in our daily life, not only in humans but also in other species, contacting with others through sociability can help organisms to contact with comrades and distinguish surrounding environments to survive well in different situations. This paper will focus on some techniques that are used widely in detecting neurons and the role of the nervous system in conducting animals' social behavior through mouse models to provide new ideas for the treatment of social disorders.

Keywords: social activity, nervous system, social disorder.

1. Introduction

Social activity is an important physiological behavior in animals' daily life. No matter in the past or the future, changes in society and environments demonstrate the importance of making interaction with other animals. Only through constant communication and information interchange with similar species can animals meet the demand for food, enrich themselves, develop advantages, and expand their population. Sociability is a promising research direction in life science. Through the research of social activities, not only can scientists peer into the mental health of animals, but also the close connection between the nervous system and social interaction can be found directly. The social test which is commonly used by scientists to study the social cognition and social memory ability of rats and mice does help researchers find the relationship between the degree of deposition of amyloid β-protein in the brain and the frequency of interaction with other rats or mice [1]. Based on many social experiment models such as the three-chamber social test, it can be found that there is an obvious connection between the nervous system of animals and their social behavior. However, revealing how these neurons interact with each other and transmit plenty of information to regulate animals' social actions needs some new techniques to trace and control the activities of neurons to make the mechanism of the nervous system. Through previous experiments, Studies have shown that in patients with social disorders, abnormalities in the structure of neurons in different regions of the brain, such as the basal forebrain, can be found and these abnormal neurons lead to severe impairments in social cognition and interaction. Simultaneously, these dysfunctional neurons provide some new targets for social disorders. This paper will focus on some widely used biotechnology that can be used to detect specific neuron locations and record patterns of neurons firing. This paper will also concentrate on the neuronal excitability of experimental animals observed through different social experiments so as to explore the brain region governing social behavior, hoping to develop primary treatment strategies for patients with social disorders.

DOI: 10.54254/2753-8818/6/20230300

2. Preliminary

2.1. Neurons

Neurons are fundamental units in the nervous system to transmit information and conduct the behavior of animals, each neuron has only one axon and many dendrites. On the one hand, the axon is the primary signaling channel that can transmit the impulse from the soma to other neurons or effectors distributed in muscles or glands. On the other hand, dendrites distributed in soma can receive signals from other neurons.

2.2. Patch clamp recording technique

The patch clamp recording technique is a new electrophysiological technique developed in the late 1970s to regulate neuronal channel proteins. This technique is an essential and widely used tool to permit the observation of varied ion channel functions in different animal tissue by recording the status of channel proteins whose pores are selective to ions. The protein's activation is able to produce an ionic concentration gradient between the membrane, and the ion's diffusion can be recorded with high resolution in real time. This technique is frequently used in supervising neurons in brain slices because neurons can be preserved in the brain circuits which can provide a more physiologically suitable environment [2].

2.3. Calcium imaging technique

The technique of calcium imaging is widely used in measuring the calcium signals in cells. Calcium plays an important part in many physiological activities. For instance, the synapse has voltage-gated calcium channels on the cell membrane that will open when it receives stimulation and allow calcium floods into the cell to induce vesicles containing neurotransmitters to be released by the presynaptic membrane so that downstream neurons receive signals from upstream to complete the signal transmission. In vitro, many physiological signaling scenarios cannot be reproduced. However, calcium imaging can rely on calcium signals to record and analyze the intact cell in living tissue *in vivo* [3]. With the help of fluorescent indicators, it is possible to supervise action potentials and measure nerve activities *in vivo* [4].

2.4. Optogenetics

Optogenetics can detect activated neurons' behavior directly by using light. Optogenetic techniques provide a fresh perspective to research the function of different kinds of neurons and discover novel brain pathways that may become dysregulated and result in neuropsychiatric diseases [5]. Optogenetics also needs some activators such as channelrhodopsin (ChR), halorhodopsin, and archaerhodopsin (Arch) to regulate the activities and the response of neurons which can be recorded by some ions like calcium [6].

2.5. Virus Tracing

There are more than 860 billion neurons in our brain, these neurons transmit information to each other by synapses which form the intricate network in the brain. To discover the complex connection of neural circuits, neurotropic viruses provide new access to trace neural circuits. Neurotropic viruses are a series of viral vectors that can infect neurons and propagate along neural circuits and synapses [7]. Compared with traditional neural circuit-tracing methods, neurotropic viruses can not only transmit across synapses without any signal attenuation but also control the anterograde or retrograde direction of trans-synaptic transmission and also are compatible with many genetic markers [8]. These special characteristics let neurotropic viruses locate neurons and ascertain the direction of trans-synaptic transmission more precisely and stably.

DOI: 10.54254/2753-8818/6/20230300

3. The significance of BNSTpr^{Esr1} neurons in the regulation of social behavior

Mating and aggression are commonplace behavior in animals, they are both intuitive behaviors regulated by neurons in the hypothalamus and amygdala [9]. With the calcium imaging technique, it is clear to see that the BNSTpr^{Esr1} neurons make an impact on mice's social contact, especially for male mice. By using some indicators and inhibitors to weaken the BNSTpr^{Esr1} neurons' dynamic in male mice which have sex experience during the proximity or sniffing, it shows that the behavioral transition from proximity or sniffing to aggression is significantly reduced in male mice. In the same way, with the inhibition of BNSTpr^{Esr1} neurons, the consequence of the behavior shifting from approach or smelling to mating is reduced when facing female mice. What is more, if BNSTpr^{Esr1} neurons are inhibited during the attack of male mice, the aggressive behavior will be restricted significantly, but the inhibition of BNSTpr^{Esr1} neurons during the copulation has no effect on it [10]. It is possible that there is a positive regulation mechanism in this process.

4. The influence of SST neurons on social interaction

In the previous study, somatostatin can regulate the emotional state of mice during the process of social exploration activities. It is possible that somatostatin^{+} (SST) neurons can be activated strongly by social interaction. To find out the mechanism of SST neurons, by the way of optogenetics, when SST neurons are inhibited, the activity of social connection of mice is reduced distinctly, which indicates that SST neurons play an important role in mice maintaining good social behavior and meetin normal social needs. By using the virus tracing technique, it is clear that SST neurons have a close association with the ventral tegmental area (VTA) and the lateral habenula (LHb) [11]. However, only by einhibiting the pathway from SST neurons in the basal forebrain (BF SST neurons) to VTA can the sociality of mice be significantly reduced, while inhibition of the neural pathway from BF SST to LHb has no effect. Therefore, it is the pathway of BF SST neurons to VTA that regulate social behavior [12].

According to previous experiments, there is a positive correlation between social activity and the activity of dopamine neurons in the nucleus accumbens (NAc) of mice. Nevertheless, SST neurons are inhibitory neurons, it is possible that SST neurons act on neurons that use the neurotransmitter gamma-aminobutyric acid (GABA) in VTA to activate dopaminergic neurons [13]. With the evidence of the patch clamp recording technique, the neurons' activity of mice in the three-chamber interaction test can be recorded. It is obvious that SST neurons prefer to form synapses with GABAergic neurons rather than with dopaminergic neurons [14]. To evaluate the consequence of the inhibition of BF SST neurons, the competence and selectivity of halorhodopsin (NpHR)-EYFP expression in SST neurons have been proved by the immunohistochemical analysis and photostimulation efficiently hyperpolarizes SST neurons which are infected with this protein and completely inhibits their firing activities evoked by current injections, thus it is possible to use NpHR to suppress mice's neurons activity [15]. On the other hand, mice in the control group are injected with a Cre-dependent AAV which can synthesize and express a special fluorescent protein called enhanced yellow fluorescent protein (EYFP)-tagged eNpHR3.0 in BF SST neurons and plugged optical fibers into the BF and there are lots of fibers labeled thick and visible EYFP. In the three-chamber test, it is significant that compared to EYFP control mice, NpHR mice are reluctant to spend time in the social chamber. Moreover, regarding the index of BF SST to VTA which can demonstrate the frequency of social interaction, mice with NpHR are lower than mice with EYFP. Also, inhibition of the BF SST to VTA pathway does not alter entry times but dramatically decreases the average duration of individual explorations of the social chamber and social zone [15]. Together, the experiment shows that the pathway from BF SST to VTA is important to individual social behavior. Also, there are some pieces of evidence showing that when the pathway from SST neurons to VTA is blocked, the release of dopamine in NAc significantly decreased during social interaction in mice, which certifies the assumption of disinhibition. Above all, BF SST neurons can regulate neurons in VTA to stimulate social interaction.

DOI: 10.54254/2753-8818/6/20230300

5. The effect of dmPFC neurons on social behavior

When social interaction occurs, the excitability of the dorsomedial prefrontal cortex (dmPFC) increases incredibly. Through tracking and observing the social behavior mechanism of three rhesus monkeys and recording the neuronal activity, they sit at a turntable and each monkey can choose to offer food as a reward to either of the other two monkeys over continuous experiments. During each successive trails, one of three monkeys is acted as an "actor" who can decide to give food to one of the other two monkeys who act as recipients, and the actor is chosen from three monkeys in a pseudo-random fashion. Also, to distinguish the behaviors of the actor from another monkey who receives the reward, there is an apparatus that has a handle to ascertain that the actor can give the reward to the same monkey in different trials. However, there is a possibility that primates may use simply conditioned responses during the whole experiment, so it is essential to alternate the role of each agent. To prevent forming a link between the location and the role of receiving rewards, the three monkeys' physical locations are changed throughout the session. Through the research, it is apparent that animals tend to give positive feedback when they receive rewards from other animals. Some previous research has demonstrated that past behaviors or "assumptions" of particular individuals and their social dominance can dramatically change the way group members interact with them [16]. Besides, based on impressions from previous interactions, animals tend to change their choices and attitudes. Furthermore, all animals developed transient duopolies at probabilities that are significantly higher than expected from chance. Through the experiment, the same animal shows peculiar neuron activity in different situations such as they, any other agent, or specific other agents are rewarded, and neurons that control the response of a specific one's behavior show no difference when the reward is changed to a negative reward. It can be seen that different neurons in dmPFC are excited by different behaviors of other monkeys. Some neurons are irritated when receiving specific actions and reactions of specific individuals, some other neurons can record information about monkeys' behaviors. The information about past interactions with other members can induce monkeys to make the social decision of reward or revenge. In the contrast, destroying dmPFC neurons can reduce monkeys' response to reward, thus decreasing their ability to form a reciprocal group [17].

6. The role of amygdala circuits in social behavior

Amygdala can receive lots of information from other brain structures like the basolateral amygdala (BLA) and Anterior cingulate cortex (ACC) to adjust memory and social behavior. When using optogenetics to stimulate neurons in BLA, mice tend to display abnormal social exploration behaviors, whereas when these neurons are inhibited by optogenetics, related social behavior in mice will recover [18]. In the three-chamber test, the decrease in signal in the ACC-BLA pathway results in the decreased tendency of acting social avoidance behavior to strange mice [19]. Amygdala can also act as an output circuit to regulate social behavior. The medial prefrontal cortex (mPFC) has an effect on regulating sociability too. Through the three-chamber social test, it can be found that with the inhibition of the BLA-mPFC pathway, mice significantly increase the time that they spend on social exploration while mice activated this pathway spends less time exploring the surrounding environment. In general, with optogenetics, activating the pathway of BLA-mPFC will limit social interaction and shorten the time spent on social exploration, while the inhibition of the circuit will promote social interaction and social exploration behavior [20].

7. summary and conclusion

Social activity plays a crucial role in animals' evolution. To understand this complicated behavior, some advanced techniques such as optogenetics, patch clamp recording, and virus tracing play an important role in the research. By observing the activity level and excitability of different neurons, it is obvious that social activities are closely related to multiple brain regions. Neurons that participate in the regulation of social interaction can be marvel targets of treatment to prepare some drugs to remedy the social disorder. However, social behavior is complex and changeable, also there is a big difference

DOI: 10.54254/2753-8818/6/20230300

among different age groups, environments, and even personalities, there is still a long way to go to find out a treatment that can be in common use.

References

[1] Segev, A., Garcia-Oscos, F. and Kourrich, S., "Whole-cell Patch-clamp Recordings in Brain Slices." J Vis Exp. (112): 1-10 (2016).

[2] Robbins, M., Christensen, C. N., Kaminski, C. F., Zlatic, M. "Calcium imaging analysis - how far have we come?" F1000Res.10:1-26 (2021).

[3] Yang, W., Yuste, R. "In vivo imaging of neural activity." Nat Methods. 14(4): 349-359 (2017).

[4] Russell J.T. "Imaging calcium signals in vivo: a powerful tool in physiology and pharmacology." Br J Pharmacol. 163(8):1605-25 (2011).

[5] Sparta, D. R., Jennings, J. H., Ung, R. L., Stuber, G. D. "Optogenetic strategies to investigate neural circuitry engaged by stress." Behav Brain Res. 255:19-25 (2013).

[6] Duebel, J., Marazova, K., Sahel, J. A. "Optogenetics." Curr Opin Ophthalmol. 26(3):226-32 (2015).

[7] Rao, X., Wang, J. "Neuronal Network Dissection with Neurotropic Virus Tracing." Neurosci Bull. 36(3):199-201 (2020).

[8] Li, J., Liu, T., Dong, Y., Kondoh, K., Lu, Z. "Trans-synaptic neural circuit-tracing with neurotropic viruses." Neurosci Bull, 35:909–920 (2019).

[9] Yang, C. F. & Shah, N. M. "Representing Sex in the Brain, One Module at a Time." Neuron 82, 261–278 (2014).

[10] Yang, B., Karigo, T., Anderson, D. J. "Transformations of neural representations in a social behaviour network." Nature.608(7924):741-749 (2022).

[11] Do, J. P., et al., "Cell type-specific long-range connections of basal forebrain circuit." eLife 5, 1-18 (2016).

[12] Gunaydin, L. A., et al., "Natural neural projection dynamics underlying social behavior." Cell 157, 1535–1551 (2014).

[13] Hung, L. W., et al., "Gating of social reward by oxytocin in the ventral tegmental area." Science 357, 1406–1411 (2017).

[14] J. P. Do et al., "Cell type-specific long-range connections of basal forebrain circuit." eLife 5, 1-18 (2016).

[15] Wang, J., Li, J., Yang, Q., Xie, Y. K., Wen, Y. L., Xu, Z. Z., Li, Y., Xu, T., Wu, Z. Y., Duan, S., Xu, H. "Basal forebrain mediates prosocial behavior via disinhibition of midbrain dopamine neurons." Proc Natl Acad Sci U S A. 118(7):1-10 (2021).

[16] Ballesta, S., Duhamel, J. R. "Rudimentary empathy in macaques' social decision-making." Proc Natl Acad Sci U S A. 112(50):15516-21 (2015).

[17] Báez-Mendoza, R., Mastrobattista, E. P., Wang, A. J., Williams, Z. M. "Social agent identity cells in the prefrontal cortex of interacting groups of primates." Science. 374(6566):1-18 (2021).

[18] Xu, S., Jiang, M., Liu, X., Sun, Y., Yang, L., Yang, Q., Bai, Z. "Neural Circuits for Social Interactions: From Microcircuits to Input-Output Circuits." Front Neural Circuits. 15:1-9 (2021).

[19] Chang, S. W. C., Dal Monte, O. "Shining Light on Social Learning Circuits." Trends Cogn Sci. 22(8):673-675 (2018).

[20] Felix-Ortiz, A. C., Burgos-Robles, A., Bhagat, N. D., Leppla, C. A., Tye, K. M. "Bidirectional modulation of anxiety-related and social behaviors by amygdala projections to the medial prefrontal cortex." Neuroscience. 321:197-209 (2016).