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Advances in Emotional Cognition and Reward Mechanisms after Craniocerebral Injury

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Abstract: After craniocerebral injury, there are various sequelae such as motor disorder, sensory disorder, and cognitive impairment, and it has been found that there is a strong link between the treat mechanism and emotional and cognitive disorders after craniocerebral injury. Reward mechanisms include incentives and stimulation in various ways, and the results of related studies on reward mechanisms show their importance in neurorehabilitation and foretell a broad prospect for future research. In this paper, the correlation between affective and cognitive disorders after craniocerebral injury and the reward mechanism, as well as the main modes of action of the reward mechanism, are described, aiming to provide a theoretical basis for the rehabilitation treatment after craniocerebral injury.

In recent years, with the continuous progress of medical technology, the mortality rate of patients with traumatic brain injury (TBI) has decreased significantly. However, with the decrease of mortality rate, there is a significant trend of increasing disability rate, and some patients are left with motor, sensory and language disorders, and emotional and cognitive disorders are also important factors affecting patients' quality of life [1], which have also attracted the attention of a large number of scholars. In modern rehabilitation research, the role of the reward mechanism has received more and more attention in recent years. The mode of action of the reward mechanism mainly affects the perceptual and cognitive functions of the organism by stimulating the nucleus ambiguus, amygdala, ventral striatum, thalamus and hippocampus, as well as dopaminergic neurons, γ-aminobutyric acid (GABA)-ergic neurons, and glutamatergic neurons, etc[2]. Therefore, this review reviews the correlation between affective cognition and the treat mechanism during recovery from craniocerebral injury and the mode of action of the treat mechanism, with a view to providing a corresponding theoretical basis for promoting the development of neurological rehabilitation.

1. Craniocerebral Injury

Traumatic brain injury (TBI) is a kind of brain injury disease that often occurs clinically due to mechanical forces such as head impact, sudden acceleration or sudden deceleration, and is one of the main causes of death and disability. TBI not only leads to nerve cell damage and death in the

cranium, but more importantly, the interaction of inflammatory response, oxidative stress, energy metabolism disorders, and release of apoptotic factors induced by brain injury greatly increases the difficulty of neurological recovery after craniocerebral injury, and may lead to long-term neurological deficits[3]. At the same time, a series of pathological changes such as astrocytosis, myelin axonal lesions, microvascular injury, and perivascular neuroinflammation are also often accompanied after TBI, which can affect mood, cognition, behavior, and even sleep disorders, and also cause a variety of sequelae such as post-traumatic stress [4].

2. Symptoms Associated with Treat Mechanisms After TBI

After TBI patients usually experience a variety of sequelae such as mood disorders, cognitive disorders, behavioral disorders, sleep disorders, post-traumatic stress and decreased physical mobility. In imaging and molecular biology, the symptoms of TBI patients are clearly manifested. In terms of pathophysiologic mechanisms, problems such as abnormal protein accumulation, blood-brain barrier damage, and cerebral metabolic abnormalities may lead to altered neurologic and psychiatric conditions in patients [5]. However, it is worth noting that the reward mechanism is associated with the brainstem and the limbic system of the midbrain, such as the striatum, the nucleus ambiguus, and the prefrontal cortex, and influences the activities of the body such as emotions and behaviors by modulating the neuronal activities in these regions and neurotransmitters such as dopamine, serotonin, and endorphins [6], which suggests that the reward mechanism plays an important role in the neurological and psychiatric alterations after TBI.

Mood disorders are one of the common complications after TBI, mainly including anxiety, depression and irritability, whose mechanism of action is related to the dysregulation of neurotransmitters, neuroinflammatory responses, neurological abnormalities, and neuronal and neural circuit damage [7]. In addition, studies have shown that about 50% of TBI patients develop cognitive deficits, which are mainly characterized by attention deficit, memory loss, decision-making impairment, and executive impairment [8]. There is no single explanation for the mechanism of these cognitive deficits. Relevant studies suggest that it may be related to brain damage in cognitively functional regions such as the living hippocampus of the cerebral cortex, while neuronal death, impairment of pre-existing neural networks and information transmission, as well as inflammatory responses, glial cell activation, salience dysfunction and reduced neuroplasticity may be associated with the emergence of cognitive deficits [9].

2.1 Mood Disorders and Reward Mechanisms

Patients after TBI often experience a range of mood changes such as impulsivity, irritability, anxiety, depression and communication disorders. The reward mechanism has an important role in ameliorating these mood disorders through a positive stimulus. Specifically, the link between mood disorders and reward mechanisms involves the mesocortical limbic reward circuitry including the nucleus accumbens, ventral pallidum, ventral pallidum, amygdala, hippocampus, anterior cingulate gyrus, orbital frontal cortex, and other prefrontal cortical regions, and is closely related to a variety of neurotransmitters such as dopamine and serotonin. This suggests that reward mechanisms play a multifaceted role in the regulation of mood disorders[10]. Several studies have pointed out that positive mood therapy enhances reward responsiveness and thus effectively improves clinical symptoms in depressed and anxious patients [11]. In addition, the reward mechanism also improves mood by reducing the release of inflammatory factors such as tumor necrosis factor-alpha (TNF-alpha) and interleukin 1 (IL-1), the underlying synaptic mechanisms that contribute to depression [12]. This suggests that reward mechanisms may play an important role in the synaptic mechanisms of depression. Imbalances in neurotransmitters such as serotonin, dopamine, and

norepinephrine may contribute to anxiety and dysphoria in depressed patients [13], which can be regulated by modulating neurotransmitter homeostasis and thereby improving mood. However, it is not clear whether these mood disorders can be effectively prevented by enhancing patients' cognitive control. In addition, endogenous cannabinoids play a fine-tuned role in regulating neurotransmitter release from different neuronal populations, which in turn affects mood and stress responses, as well as in brain reward mechanisms[14]. It has been found that signaling pathways associated with depression and dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis may also be affected[15], and the reward mechanism, through the modulation of hormones, may also affect the regulation of the HPA axis.

In summary, treat mechanisms play an important role in regulating mood disorders after TBI by modulating processes such as neurotransmitters, inflammatory factors, and neural signaling pathways. Therefore, subsequent studies need to focus on these pathways to further understand the relationship between mood disorders and reward mechanisms.

2.2 Cognitive Impairment and Reward Mechanisms

TBI leads to cognitive decline involving reduced memory, reflexes, executive abilities, and attention, severely affecting the quality of life of patients. Notably, the development of cognitive impairment is closely related to the regulation of reward mechanisms, which mainly involves the cerebral cortex, basal ganglia, neurotransmitters, and inflammatory responses [16]. Oveis et al[17] showed that opioid receptors and GABA receptors play important roles in regulating the activity of dopaminergic neurons in the ventral tegmental area, and since dopaminergic neurons play an play an important role in the brain reward mechanism, the interaction of transmitters released by stimulated neurons is important for the improvement of cognitive impairment. Specifically, opioid receptors play a role in cognitive function by modulating GABAergic transmission and inducing neural plasticity. Further studies have shown that methamphetamine ameliorates cognitive deficits and altered decision-making in rats, an effect largely attributed to the importance of the balance between excitatory and inhibitory properties in the frontal cortex, and that methamphetamine enhances extracellular levels of dopamine in the brain by reversing the dopamine transporter protein [18]. This suggests that cognitive impairment can be effectively improved by modulating the dopamine system. In addition, microglia show a potential role in attenuating cognitive impairment associated with TBI. Microglia are able to reduce inflammatory responses, cell signaling disturbances, and neuropathological alterations associated with TBI, particularly in dopamine signaling, cellular long-term potentiation, calcium signaling, and gene function related to synapse formation [19]. However, microglia and endothelial cells may also exacerbate symptoms of cognitive impairment by triggering inflammatory vesicle mediators and apoptosis in melanoma 2 (AIM2) [20]. Therefore, inhibiting the growth and proliferation of AIM2 may provide novel therapeutic strategies to ameliorate cognitive impairment. Therefore, modulating the activity of dopaminergic neurons and their related transmitter interactions is important for improving cognitive impairment. Future studies need to focus on how to effectively modulate these transmitter systems through pharmacological or other interventions with the aim of achieving better therapeutic outcomes.

3. Treat Mechanisms

The reward mechanism is a process of benign stimulation of the brain that involves a variety of neurons, neurotransmitters, neural circuits, and brain regions that interact with each other to influence an individual's behavioral response to reward. This mechanism is primarily associated with brain sites such as the nucleus ambiguus, amygdala, ventral striatum, thalamus, and hippocampus, as well as the dopamine system, the glutamate and GABA systems, and neural

synapses. This suggests that the reward mechanism has a multifaceted impact in regulating brain function. The reward mechanism works in various ways and principles, one of the basic principles is that the glutamatergic neurons in the prefrontal cortex, hippocampus and amygdala and the dopaminergic neurons in the ventral tegmental area co-stimulate the neurons in the nucleus ambiguus, and this interaction realizes the neuromodulation through the activation of excitatory synaptic transmission and the formation of new synapses[21]. When the brain is stimulated, it produces a range of key neurotransmitters including acetylcholine, serotonin, glutamine, enkephalins, dopamine and opioid receptors [22]. These chemicals interact with each other and are critical for regulating motivation, cognition, pleasure, stress response, decision-making processes, memory, and well-being. In particular, activation of opioid receptors and kappa opioid receptors can affect brain regions such as the prefrontal cortex, amygdala, hippocampus, insula, and ventral tegmental area, which, in turn, promotes the release of more dopamine from these regions, further stimulating the brain. Opioid receptors also play a key role in regulating stress and reward processing, with corticotropin-releasing factor (CRF) being particularly important for enhancing rewarding stimuli and stimulating the amygdala to help regulate mood. In addition, research has identified a variety of neuroendocrine systems, such as the oxytocin, dopamine, and opioid systems, that regulate cellular homeostasis, signaling, changes in physiological function, protein transcription, ion channel activation, neuronal excitability, and hormone release through the activation of G-coupled protein receptors.

4. Ways to Treat Mechanisms

The mode of action of reward mechanisms is implemented in a variety of ways through a variety of pathways, such as auditory stimulation, visual stimulation, meditation, neuromodulation, non-invasive brain stimulation, medication, and social support. Social support, including the interaction of family, friends, and social networks, can also produce positive reward effects and enhance an individual's sense of well-being and social fulfillment. This paper focuses on auditory stimulation, visual stimulation, non-invasive brain stimulation and rehabilitative exercise.

4.1 Auditory stimulation

The auditory network is a complex process in which sounds travel through the ears to the brain, where they are analyzed, processed, and decoded, allowing us to understand the meaning of those sounds, a process that involves the influence of several factors such as memory, attention, and emotion, and is primarily associated with the frontal lobes, the limbic system, the temporal lobes, and the auditory cortex. Among the many forms of auditory stimulation, music is particularly prominent, as listening to music activates the dopamine system in the brain, which in turn promotes the formation of memories through musical reward mechanisms [23]. Several studies have shown that music with different rhythms stimulates activity in the basal ganglia regions of the brain (including the nucleus ambiguus, caudate nucleus, and nucleus accumbens), as well as in prefrontal and parietal regions associated with reward, resulting in feelings of pleasure. In addition, music-induced pleasure enhances the excitability of the prefrontal striatal pathway by activating cortical striatal circuits. Musical stimulation also has significant effects on striatal structures, for example, frequent music listeners form an auditory channel in the brain that enhances functional connectivity between auditory areas and the medial prefrontal cortex, potentially supporting healthy aging. Music training has also been found to stimulate functional neuroplasticity in the orbitofrontal cortex network, which can help improve daily behavioral regulation and cognitive deficits in patients with traumatic brain injury (TBI).

In summary, music, as an auditory stimulus, has a significant effect on enhancing memory,

increasing pleasure and improving cognitive disorders by activating the dopamine system, frontal lobe, temporal lobe and auditory cortex regions in the brain. Subsequently, we can delve deeper into the specific mechanisms of music's effects on brain function and the potential of music training in treating cognitive impairment and promoting brain health. In addition, the study can be extended to how music affects other brain regions and cognitive functions, as well as the effects of music in different populations (e.g., older adults and TBI patients).

4.2 Visual Stimulation

Visual information is transmitted and processed in the brain primarily through direct pathways from the retina to the cerebral cortex and indirect pathways from the retina through the thalamus to the cerebral cortex, and these pathways and their connecting regions in the brain collectively form the visual information processing network, which are the structures and networks that allow for the rapid reception, processing, and comprehension of visual information, with important implications for perception, cognition, and behavior. Related experiments affecting performance in the primary visual cortex of mice by exposing them to visual stimuli have shown that reward-related responses enhance stimulus performance in a subpopulation of the visual cortex of these mice [24]. This suggests that visual stimuli are closely related to reward mechanisms. However, some experiments suggest that high-reward signals may even lead to the opposite effect of executive power, keeping attention longer, implying that the reward mechanism may conflict between automatic and targeted attentional processing. The findings suggest that striatal and dopamine activation is associated with reward and that there is a positive correlation between this activation and changes in spontaneous eye opening rate and pupil dilation. Specifically, the higher the striatal and dopamine activity, the greater the spontaneous eye opening rate and pupil dilation. This reveals that visual information processing not only relies on complex neural networks, but is also closely related to cognition, attention, and reward mechanisms.

4.3 Non-invasive Brain Stimulation

In the current field of medical science and technology, non-invasive brain stimulation technology has gradually become the focus of research due to its unique advantages. Covering various forms such as transcranial magnetic stimulation, focused ultrasound stimulation and electrical stimulation, this technology shows a wide range of application prospects by regulating the activity of neurons in the cerebral cortex and affecting the functional connectivity and neuroplasticity of the brain. Research results show that non-invasive brain stimulation techniques play an important role in regulating bodily functions, such as acting directly on the dopamine system to effectively alleviate addictive behaviors caused by drugs such as cocaine and methamphetamine. In addition, non-invasive brain stimulation has shown great potential in improving quality of life, e.g., deep brain stimulation can improve the quality of life by reducing alcohol craving through effects on the nucleus ambiguus. This suggests that individual behavioral patterns and emotional states can be remodeled to some extent by precise brain area stimulation. However, it is not clear that this type of stimulation is equally effective for all people, and therefore, subsequent studies need to focus on its mechanism of action and the definition of the applicable population. Applied studies of transcranial magnetic stimulation have further broadened researchers' understanding of the potential of non-invasive brain stimulation, especially through transcranial magnetic stimulation of the prefrontal-striatal pathway, which not only arouses emotions such as feelings of pleasure, but also significantly increases feedback to music. This finding highlights the importance of prefrontal striatal function in music-induced emotional responses and motivation. Meanwhile, a single high-frequency transcranial magnetic stimulation treatment was effective in inducing an acute

increase in beta-endorphin levels in obese subjects, suggesting that the activation of the reward pathway may have a positive effect on the control of binge eating behavior. It is noteworthy that the ventral medial prefrontal cortex plays a key role in reward prediction and processing. Experiments have shown that activation of prefrontal functional areas by transcranial direct current stimulation not only increases prefrontal activation, but also elicits pupil dilation and optimism in reward prediction. This suggests that stimulation of specific regions can make adjustments to a person's mood and expected outcomes. Although non-invasive brain stimulation techniques have shown promise in the treatment of problems such as drug addiction or binge eating, their effects and mechanisms still require further research and validation. In particular, the effects on the dorsolateral prefrontal cortex, whose reduced neuromodulatory excitability is important for alleviating cravings for addictive behaviors. In addition, non-invasive transcutaneous auricular vagus nerve stimulation studies have revealed that transmission and feedback through the vagus nerve can have an impact on a variety of aspects such as food reward and enhance reward motivation. This series of findings not only enriches researchers' understanding of non-invasive brain stimulation techniques, but also provides new research ideas and directions for future clinical applications. Therefore, in-depth exploration of the mechanisms and effects of noninvasive brain stimulation techniques, especially the potential for application in different fields, focuses on how to precisely stimulate specific brain regions to adjust mood and anticipation, as well as how to treat behavioral problems such as drug addiction and binge drinking through noninvasive brain stimulation techniques. With further research, non-invasive brain stimulation techniques are expected to play a greater role in clinical treatment.

5. Summary and Outlook

This review provides an extensive discussion of performance and reward mechanisms during recovery from TBI. Rehabilitation after TBI is a complex and challenging process involving a variety of sequelae such as motor deficits, sensory deficits, and cognitive impairment. Reward mechanisms play an important role in emotion and cognition. Applications of reward mechanisms include visual stimulation, auditory stimulation, and non-invasive stimulation, which aim to regulate the body's emotion and cognition by stimulating nerves and modulating neurotransmitters and synapses.

The application of treat mechanism in the field of TBI rehabilitation is promising. Through in-depth study of the mechanism of treat mechanism in the brain, we can more accurately regulate and optimize the rehabilitation treatment plan. In addition, combining the advantages of modern technology, such as artificial intelligence and machine learning in data analysis and pattern recognition, can further improve the effectiveness and personalization of rehabilitation strategies. Therefore, continuous exploration and innovation of the application methods of treat mechanisms will help to provide more efficient and comprehensive rehabilitation support for TBI patients.

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