DISSOCIATION IN ANIMALS

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Absract

Despite an overpowering empirical and theoretical focus on dissociation as a pathological process or an evolutionary defense mechanism associated with survival problems in nature, researchers are turning their awareness toward understanding the physiological and neural agencies that underlie these features. Research, observations, and debates on dissociation have suggested that disruptions in neurobiological mechanisms or natural defense mechanisms may be involved in the effects of stress and traumatic experiences on the brain in animal studies.

An accepted conception of the evolutionary view of dissociation is to assume that understanding of freezing mechanisms in mammalians may provide a basic approach to the human dissociative process. The findings, together with documentation of observation of wildlife and experimental studies in limited literature, may provide a rationale model for investigating the neurobiological implications of dissociative mechanisms. Additionally, early and recent studies with animals and humans demonstrated that various stressors and precisely-dosed administration of ketamine or phencyclidine can alter brain functions. There is considerable evidence that N-methyl-d-aspartate (NMDA) antagonists may transiently provoke glutamate release and create symptoms resembling dissociative states. Some authors have asserted that exposure to stress and traumatic process have created posttraumatic stress disorder (PTSD)-like symptoms in animals. They have also suggested that there is a parallelism between human experiences of traumatic experiences and psychological distress and those of animals founded on shared brain structures and physiological mechanisms. Although research investigating neurobiological action associated with dissociation-like symptoms and reaction to stress and traumatic experiences in animals is still limited, results from these examinations supply effective evidence that may assist in understanding dissociative reactivity to vital in nature challenges.

Key Words; dissociation, animals, evolution, freezing mechanisms, stress, traumatic experiences, defense mechanism

Dissociation in animals

Introduction

The title of “dissociation in animals” has to contain an evolutionary perspective. The evolutionary perspective ties all humans with animal species that had come before and relates us also to other animals that evolved in parallel with us. In the pathological dissociation approach, we work with a deficiency of the human mind and brain, such as deterioration of identity, memory, attention, and consciousness. But, experts in the field are often interested in evolutionary views about psychopathology, most of them do not consider understanding evolutionary aspects of the normal or adaptive process as a basis for pathology. Discussions in this concept may choose to focus on an animal-human continuity model of dissociation, evaluating whether certain stressors or other states lead to specific changes in the animal's brain, which lead to dissociative process.

Some authors have suggested that the behavior and physiology of the freeze response are routinely seen in the wild. Yet, as data provided evidence that freezing has a state of alert immobility, as in the mammalians that assumes an immobile state in the presence of a predator.

For an understanding of dissociation in the animal model, as some authors pointed out, must to also acknowledge the many similarities to behavior in animals in whom freezing has been elicited in a state of helplessness with later prevention of spontaneous recovery from immobility. Some animals manifest alert immobility has been considered to be primarily defense mechanism as "animal hypnosis". Similarly, dissociation also may be associated with the mainly parasympathetic tone, deformed cognition and learning behavior, and a propensity for conditioned perpetuation [1, 2]. An accepted conception of the evolutionary view of dissociation is to assume that understanding of freezing mechanisms in mammalians may provide a basic approach to the human dissociative process.

Evolution has been the driving power that has shaped humans, apes, and other animals' brains in the same way as it has developed body characteristics. Many adaptations about human identity, emotions, memory, consciousness, attention, and behavior emerged in habitual environments of evolutionary adaptedness, from which social living conditions deviate in one way or another. Such social living conditions and current environmental traits such as childhood traumatic experiences may cause the pathological process of the operation of these capacities. Yet, this is not to declare that any psychopathological symptoms of dissociation define an adaptation. Contrarily, signs and symptoms are really maladaptive in both the standard understanding of the term and its evolutionary meaning. Psychopathological symptoms may reflect the extremes of variation that may become dysfunctional due to their abnormal frequency, intensity, or inappropriateness in the current context.

Authors attempt to classification the dissociative symptoms with many and varied forms and expressions. These symptoms are characterized by large variety, particularity, and complexness such as emotional, perceptual, cognitive, or functional form. To describe that dissociative process-related phenomenons are an sign of some impaired mind functions are altered perception of time, space, sense of self, and reality. Altered sensory perceptions may produce the variable anesthesia, analgesia, and intolerable pain perception. Motor expressions consist of weakness, paralysis, and ataxia, but may also present as tremors, dysarthria, shaking, and convulsions. Cognitive fluctuation handles the confusion, dysphasia, dyscalculia, and severe deficits in attention. Memory alteration may include hypermnesia in the form of flashbacks, or as amnesia in the form of fugue states, or more selective traumatic amnesia [1].

Some interesting findings have emerged from the results of animals used in scientific experimentation. Ferdowsian et al. have reviewed the relationship between human and animal physiological and behavioral similarities. This literature on defining the used various terms used in trauma, pain, and stress research exists; there is a parallelism between human experiences of pain and psychological distress and those of animals founded on shared brain structures and physiological mechanisms [3].

Some findings have also emerged from the field of experimental mammalian brain studies indicating that the dissociative process, neurophysiological outcomes, some receptors, and neurotransmitters intertwined. Stress or some neurochemical stimuli-related alterations in the mammalian brain become important that they may serve as salient factors in the natural development or pathogenesis of dissociation. Besides to the recent debates focusing on identifying pathological manifestations of dissociation, some studies have examined neural mechanisms underlying dissociation. A study has demonstrated how some of the consequences of N-methyl-

d-aspartate (NMDA) antagonists in animals are blocked by drugs that attenuate glutamate release. Clinical investigations state that NMDA antagonists may transiently provoke glutamate release and create symptoms resembling dissociative states in humans [4]. Advanced imaging studies have been used extensively to examine cell-type-specific neural activity across the mammalian brain, potentially enabling the exploration of how brain-wide dynamical patterns give rise to complex behavioral states. In terms of the dissociation-like states, researchers have detected some important data from animal studies. A dissociation-like state has been precipitated by precisely-dosed administration of ketamine or phencyclidine in mice. From these results, it may be clear that molecular, cellular, and physiological properties of a conserved deep posteromedial cortical rhythm may underlie states of dissociation [5].

Since this area of the investigation remains in a relatively immature stage of inquiry, the chapter concludes with a discussion of limited data such as freezing mechanisms in mammalians and some experimental mammalian brain studies.

Freeze response in animals

Many findings of behavior and physiology of the freeze response have emerged from the field of animal studies and observations in the wild. Yet, as data provided evidence that freezing has a state of alert immobility, as in the mammalians that assumes an immobile state in the presence of a predator. If an animal is attacked by a predator, this state may proceed to sudden flight or, to a deeper state of freeze, that is associated with apparent unresponsiveness and with marked changes in basal autonomic state [1]. The answer to such situations may provide a conceptual framework that will clarify the common evolutionary mechanisms. This situation can be considered animal hypnosis and may point to the biological origins of the dissociation mechanism. Ultimately, this mechanism serves the survival of mammals. Debates in this area may choose to focus on an evolutionary model, evaluating whether certain stressors or psychiatric states lead to specific changes in the mind and body.

Hofer has attempted to correlate freezing reaction and parasympathetic system in laboratory animals. The limited literature on defining the terms in stress research exists a stressor is that stimulus situation that the animals perceive as a threat to its ability to cope. In the occurrence of an attack, when the animal is provoked helpless, a different state of freezing is stimulated, as cited. A study has evaluated the rodents that after exposed stress at a variety of predator-related stimuli in an open space with no means of flight. All rodents joined a deep phase of freeze, continuing for up to 30 min. The freezing response was likely to be manifestations of large bradycardia associated with cardiac arrhythmias, presenting a prominent state of vagal or parasympathetic tone [6].

Richter has demonstrated an association between freezing response and helplessness, or lack of control. In suffocation investigations, feral rats will swim for up to 60 h before dying from fatigue. If these rats experience inactivity in the researcher's hand and are then released into the water, they will drown within minutes. Some rats experience sudden death during induced immobility [7]. From these approaches, some important points emerge. While the freezing response is a survival strategy, it causes death in environmental changes. So it turns into an inappropriate reaction. Furthermore, as in this experiment, the intensity of a stressor should be a life-threatening feature. The stress response is the normal reaction to a stressor, and in the typical situation, once homeostasis is achieved the stress terminates.

A few studies have examined the relationship between intensive stress and inescapable shock. Some literature reviewed the representing the animals revealed to effective shock triggers in an escape-proof environment predictably freeze with next shock exposure. The following introduction of ways of escape in these animals does not evoke escape behavior—the animals stay frozen, and resume to show helplessness. They seem unable to learn from new experiences, even those that encourage escape or survival. But, animals exposed to escape route shock soon learn to use the escape route and do not freze [1]. Furthermore, to discuss the critical factor in trauma, It is necessary to emphasize the relationship of controllability of the development of the threat versus a condition of helplessness. The author has emphasized the great similarities between the human reaction to trauma and the animal response to the inescapable shock, author has also indicated that inescapable shock may be a biological prototype for posttraumatic stress disorder [8]. As stated in an article, the authors presented the new dissociation model in humans as an analogy to the change in defense and recovery behavior in animals exposed to inescapable shock [2]. Threat-related conditioned stimuli in this model will automatically elicit a thaw or freeze response rather than a more specific conditioned response to the stimulus. Thus, persistent dissociation will make the animal or human susceptible to a wide variety of stimuli that can be associated with the threat to continue freezing or dissociation [1].

This trend is an intermediate stage and is based on post-encounter defensive behavior: flight, freeze, and fight. In general, the freezing response noted has been in the direction of a defense mechanism in the survival chance. When a predator has been spotted, as mentioned earlier, the freezing response is the basic post-encounter mechanism in the some species. Thus, the freezing response is not likely to be merely manifestations of physical escape from threat and may have some aspects on the face of a potential escape route [2]. The effort to survive and reproduce is a fundamental evolutionary trend in living things. In this context, the freeze response serves this purpose.

This title has presented a brief review of the relevant areas of investigation and inferences that state that the freezing response and the dissociative mechanism are interconnected. Yet, it is an important shortcoming that the animals studies and literature are limited and old. New research and discussions are needed.

Biological aspects of dissociation in the mammalian brain

NMDA-type glutamate receptor antagonists provide the resemble effects of dissociation in healthy individuals. Glutamatergic systems are general biological entities of all brain structures but the cortex, hippocampus, thalamus, amygdala, and forebrain areas are especially sensitive. Under normal conditions, individuals who have received ketamine, have reported some dissociative symptoms and alterations in the sense of self. The identity changes may occur like depersonalization and derealization [4]. Ketamine has been introduced as a" anesthetic, hallucinogen, and dissociative agent". But, some researchers tend to suggest that ketamine is a new type of antidepressant and anti-posttraumatic stress disorder (PTSD) drug [9, 10].

Not only is the NMDA receptor's activity but their neurometabolic activity, when the effects on animals are studied, offer the possibility of improving knowledge of the neurobiology of dissociative disorders, an essential step towards the elucidation of their etiology. As a result of these scientific investigations of animals' brains, we can now better define the dissociative process. Therefore, so many judgments in this section are derived from animal studies. NMDA receptor is also localized in high concentrations throughout the cortex, hippocampus, and

amygdala, The activity of NMDA receptors affects neuronal action. NMDA activity plays a role in both neural plasticity and excitotoxicity. These two opposite activities are quite interesting. There is great interest in the development of clinically relevant NMDA receptor antagonists that block excitotoxic NMDA receptor activation without interfering with NMDA receptor function required for normal synaptic transmission and plasticity [4, 11].

Several studies have shown that a single dose of subanesthetic ketamine is associated with transitory psychotic-like symptoms in healthy individuals and aggravates psychotic symptoms in patients with schizophrenia [12, 13]. Although not surprising to researchers in human and animal studies, who have recognized the connections between the dose of subanesthetic ketamine and dissociative, psychotic-like symptoms, some findings have shown that the long-term frequent use of ketamine is associated with persistent neuropsychiatric symptoms, this situation is generally characterized as cognitive dysfunction and working memory deficits [12, 14]. Researchers have also evaluated the effect of chronic using ketamine on brain structures by neuroimaging techniques. Researchers have found that chronic ketamine using is associated with atrophy in the frontal, parietal and occipital cortices [10, 11], the disruption of white matter integrity [15], and reduced connectivity between thalamic nuclear groups and cortical regions [1]. Authors have emphasized that glutamatergic and dopaminergic dysfunction has been an important factor in the neurotoxic effects of ketamine [12]. The specific metabolic changes of repeated ketamine exposure that may be associated with some metabolites in the brain have not been adequately evaluated in animals and humans. For example, A study has shown that the many changed metabolites such as purine metabolism and glycerophospholipid metabolism have been identified in the prefrontal cortex, hippocampus, and striatum after repeated ketamine exposure in the rats. After one week of withdrawal intervention, most of the changed metabolites in the hippocampus and striatum were restored to control levels, while the metabolite changes in the prefrontal cortex were persistent. These results revealed that repeated ketamine exposure significantly altered purine metabolism and glycerophospholipid metabolism in the prefrontal cortex, hippocampus, and striatum, which may be involved in ketamine's neurotoxic effects [12].

The most consistent presence of mental abnormality found in extreme stress may have great value in neurobiological aspects. It may be that the reflection is seen in the induction of long-lasting forms of neural plasticity and neurotoxicity in some regions of the brain. Furthermore, several studies have emphasized the relation between neurophysiological response to environmental stress and increased glutamatergic activity in particular brain regions. As modeled with NMDA antagonists, the glutamatergic transmission may be related to dissociative symptoms as shown in animal and human studies [4, 16, 17].

Recently, several studies have suggested that high-speed recording and neuronal activity are associated with enabled biological and causal neural-circuit dynamics spanning the aniamal brain. Not surprising to researchers in this area, who have considered the connection between neural-circuit dynamics and dissociation, these findings have been generated from technological advancements as the cellular application of altered behavioral conditions. The normal integration of cognitive processing is disrupted in dissociation, which can occur for a variety of reasons, such as stress, epilepsy, dissociative drugs, or certain neuropsychiatric disorders. A selective detachment can be observed, where emotional or emotional responses are separated from sensory perceptions and the sense of self is separated from body position or action [5].

Vesuna et al. have evaluated the dissociative-like behavioral condition utilizing high-speed, brain-wide processes in both mice and humans, and recognized underlying deep posteromedial-cortex rhythmic dynamics along with molecular, cellular, and physiological agents. They have used ketamine or phencyclidine in mice for a dissociation-like state. They have found that these dissociative agents elicited a 1-3 Hz rhythm in layer 5 neurons of the retrosplenial cortex. They have also observed that electrophysiological recording with four simultaneously inserted high-density probes revealed rhythmic fusion of the retrosplenial cortex with anatomically connected components of the thalamus circuit, but separation from other brain regions – including a notable inverse correlation with anteriorly protruding thalamic nuclei. While testing for causal significance, they have found that rhythmic optogenetic activation of retrosplenial cortex layer 5 neurons recapitulated dissociation-like behavioral effects. Cyclic-nucleotide-gated potassium channel 1 pacemakers activated by local retrosplenial hyperpolarization have been required for systemic ketamine to induce this rhythm and elicit dissociation-like behavioral effects. From these results, it may be clear that molecular, cellular, and physiological properties of a conserved deep posteromedial cortical rhythm may underlie states of dissociation. Moreover, the authors have emphasized that in animals with these changes compared to human focal epilepsy, simultaneous intracranial stereo encephalography recordings from all over the brain have revealed a similarly localized rhythm in the homologous deep posteromedial cortex, which temporally correlated with pre-seizure self-reported dissociation, and local brief electrical stimulation of this region has elicited dissociative experiences [5].

This section has briefly reviewed the salient studies and debates regarding possible dissociative mechanisms in the mammalian and human brain. The study of the biological mechanism of dissociation in animals may provide an additional perspective.

The phenomena of trauma and distress in animals

Existing evidence shows the presence of various phenomenological dimensions of PTSD in chimpanzees and other animals [18, 19]. Further evidence comes from studies focusing on the fear and stress elicited in mice experiments. Mice show increases in hyperarousal, emotional blunting, persistent fear, and sensitive fear of social withdrawal, as seen in PTSD [20]. A study, on juvenile rats which have been designed for childhood trauma, has shown that exposing the rats to garbage washed in cat urine raised the likelihood that they would create long-term behavioral disturbances thought to describe PTSD symptom equals. Responses continued when rats were exposed a second time in adulthood [21]. Mice with juvenile trauma were also more likely to have been re-traumatized later in life. They may have more current PTSD like symptoms.

Automatic regrettable memories, distressing dreams, dissociative effect, intensive psychological distress, and physiological stress replies at exposure to internal or external cues that symbolize aspects of the traumatic event may occur, whereby affected individuals undertake efforts to avoid thoughts, memories, and feelings associated with the traumatic event. Distorted cognitions regarding the causality or results are frequently associated with acute stress disorder and PTSD, usually concerning self-blame and negative anticipations about oneself or others [22].

A single or repeated experience of severe traumatic, life-threatening events causes acute stress disorder and PTSD. Concerning the character of the trauma, events that threaten the

purpose of important biosocial plans are more likely to produce acute stress disorder and PTSD than events that do not interfere with biosocial goals. Behaviorally, PTSD can be viewed as a defensive strategy [23]. PTSD contains several defenses that seem to be arranged hierarchically. These include avoidance, mindful immobility, withdrawal, aggressive defense, appeasement, tonic immobility; vigilance, and risk check. All of these can be conceptualized as ancient survival instruments, some of which evolved millions of years ago in our vertebrate ancestors. Others more closely reflect our primate lineage and human aspects of memory formation [24]. Several reports are suggesting that PTSD may occur in captive non-human primates the following traumatization through the early detachment of infants from their mothers, solitary accommodation in small cages, and repetitive anesthesia for biomedical research [18, 22]. High attention levels help notice potential risks; thus, attention can serve above all the goal of preparing the organism for imminent danger [23]. From an ethological point of view, detailed observation of the environment may have evolved to avoid the predator threat. In species that live under stable predator threat, such vigilance is adaptive and chronic predator threat does not disrupt the stress response system [25]. It seems that species with a long life history are more likely to have chronic stress responses, while species with a short lifespan do not generate signs of chronic stress [22].

Animals of many species need early parental support for their development. This situation is a basic process that can directly be observed. Animals also commonly bond with their species for adequate social support and development. This view drive attachment as the primary biological development during early life. Interaction between the parent and offspring, especially the mother, becomes a very important biological factor. While noting the developmental effects of this interaction, if the mother is absent early in life, some authors claim that the offspring are likely to develop stereotypic behaviors. Mother-deprived animals develop several changes in neurotransmitter activity and anxiety and stress responses, including increases in stereotypical behavior [3, 26]. Researchers have reported that early separation from mothers also results in a range of negative behavioral and social effects in primate infants [3]. Early seperation from mother can be considered as a serious traumatic experience for animals as well. Evolution is an approach that cannot directly be observed. It has to be inferred from observation; nonetheless, there is no suspicion that evolutionary approaches have shaped humans and animals cognition, emotion, behavior, and traumatic experieences in the same way as neurobiology. Biological defense mechanisms developed against traumatic and stressful experiences may have a common origin in this context.

Conclusion

This chapter has presented a brief review of the relevant areas of investigation and debates that some neurobiological reactions in animals and the dissociation-like process are prominently interconnected. As for freeze response on possible neurobiological mechanisms of the brain, the trigger influence of stress on the brain has been described as well as the dissociation-like appearance of animals and the effects of neural reaction on the hypnotic phenomenon. The similarity between hypnotic phenomena and dissociative processes is obvious. The role of the freeze response-related hypnotic phenomenon and its neurobiological mechanisms in mediating this neural interaction should be investigated further. Common evolutionary influences on this activity included evidence that certain neural system products may have profound effects on the function of survival as a dissociative defense mechanism. The apparent interdigitations between the dissociation and evolutionary survival mechanisms

may provide the basis for investigations into the relationship between specific stressful, traumatic experiences and neurobiological mechanisms such as complex dissociative disorders in human beings.

It is suggested that mechanisms in the occurrence of PTSD and pathological dissociation similarity be evaluated in animals studies. Phenomena occurring in PTSD tend to have a high level of dissociative symptoms and similar formation mechanisms and thus may be more likely to have stress responses originating from basic evolutionary defense mechanisms. But, the studies evaluating dissociation and PTSD-like symptoms have not adequately addressed common evolutionary mechanisms in animals. Whether the basic evolutionary defense mechanisms associated with the dissociative process may be specific in animals and humans awaits clarification. Of equal importance, is a better understanding of the biological mechanisms underlying the PTSD-related alterations. Thus, by studying dissociation and PTSD in animal models, more about brain functioning in both processes (pathological or natural) may be learned.

This chapter has also reviewed the salient studies and debates regarding the consequences of NMDA antagonists in animals that are blocked by drugs that attenuate glutamate release. It is suggested that NMDA antagonists may transiently provoke glutamate release and create symptoms resembling dissociative states. Furthermore, it is hypothesized that the dissociation-like state can be induced by the administration of ketamine or phencyclidine in mice. Further evaluation of specific brain structures has shown that the dissociative process may be related to environmental stress and increased glutamatergic activity. In addition, this debate suggests that the level of NMDA receptors blockade may have therapeutic or aggravating effects on pathology. This is particularly relevant because recent studies have found a positive effect between the administration of ketamine and decreased symptoms of depression and PTSD. Further investigation of the molecules with similar effects in complex dissociative disorders should focus predominantly on specific neurobiological mechanisms. Bradley et al. have suggested that the possible contributions of hyperglutamatergic states to the acute and long-term consequences of exposure to traumatic stress, drugs that reduce glutamate release may have therapeutic and neuroprotective potential in traumatized individuals with dissociative symptoms [27].

The observations and studies in animals and humans that dissociation and related other mental states are associated with altered reactions to environmental factors that produce stress suggest that brain processes may influence the onset and course of complex disorders in which the basic evolutionary mechanisms play a prominent role. As a specific treatment approach should focus on these underlying neurological mechanisms, the role of interacting biological systems, stress response, NMDA receptors, and traumatic experiences, may also be further clarified.

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