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Anatomy of the hippocampus and its emerging roles in modulating emotion-dependent autonomic activities

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Abstract

The hippocampus is popularly known to be involved in learning and memory. However, emerging evidence indicates that the hippocampus also mediates emotions in a process that involves modulating motor and autonomic outflow. The parts of the hippocampus involved in modulating autonomic activities are distinct and thus support the argument of inherent structural and functional segregation. It is suggested that the ability to modulate emotion-dependent autonomic rhythm results from descending synaptic interactions with nuclei in the hypothalamus and brainstem where the rhythm of motor and autonomic activities is generated and maintained. However, there is little knowledge of the anatomical pathways and circuit physiology that support the modulation of such autonomic activities. Also, in coordinating physiologic responses, forebrain structures operate through functional networks, but the neural pathways and mechanisms involved in such complex interactions are not clear. Thus, the current review aims at elucidating the anatomy of the hippocampus with emphasis on the intra and inter structural circuits responsible for modulating emotion-dependent autonomic activities.

Keywords

Hippocampus, anatomy, emotion processing, autonomic nervous system, descending pathways.

Introduction

Emotional behaviours are processed, formed and expressed by a complex network of brain structures known as the limbic system, which relies upon sensory perception of the external environment. During the expression of emotions, autonomic responses are responsible for maintaining homeostasis and meeting metabolic demands. Early studies also suggested that autonomic activities can be used to distinguish between emotions (Ekman et al., 1983). However, there is limited understanding of the forebrain areas that modulate autonomic activities, and the mechanisms/neural pathways involved.

Studies have identified the hippocampus as a potential mediator in the processing of emotions (Kjelstrup et al., 2002; Maren and Holt, 2004; Ballesteros et al., 2014). More recent studies have examined certain autonomic concepts that are relevant to the expression of emotions and identified significant roles played by the ventral hippocampus (Ajayi and Mills, 2017; Ajayi et al., 2018). For instance, stimulation of the

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ventral hippocampus completely suppressed the motor expression of augmented breaths (Ajayi and Mills, 2017). The same region of the ventral hippocampus was implicated in regulating the expression of fear and anxiety (Kjelstrup et al., 2002; Maren and Holt, 2004; Ballesteros et al., 2014). Juxtaposing these two findings suggests that during the emotional processing of fear and anxiety, the motor expression of augmented breaths is modulated. Empirical studies in rats have buttressed this inference by showing that the expectation of the termination of an aversive stimulus increases the incidence of augmented breaths by about 20 times (Soltysik and Jelen, 2005). Similarly, the physiological changes demonstrated in anesthetized animals during a neurochemical mapping study (Ajayi et al., 2018) are consistent with those that accompany the behavioural expressions of emotions thought to be regulated by the ventral hippocampus. These pieces of evidence indicate a need for further research into the hippocampus in the light of descending autonomic control.

Against the backdrop of the emerging evidence about the roles of the hippocampus in processing emotions, the current review aims at elucidating the anatomy of the hippocampus with emphasis on the intra and inter structural substrates responsible for modulating emotion-dependent autonomic activities.

Anatomy of the hippocampus

The hippocampus is a paired forebrain structure that is relatively conserved both functionally and phenotypically across the animal kingdom. In the rat, the structure extends from the septum all the way to the medial portion of the temporal lobe (Bregma; -1.72 to -6.84 mm). As it extends caudally, it assumes different shapes, with specific portions appearing in different sections (Figure 1). Hence, in a midsagittal brain section, the hippocampus is only partially visible in an area immediately ventral to the posterior half of the corpus callosum and lying at an oblique angle (septal area, Figure 1A). The hippocampus in approximately full extent is only visible in serial coronal sections between 4.36 - 5.88 mm caudal to Bregma, where the ventral hippocampus lies adjacent to the amygdaloid complex. In this region, the outline of the hippocampus assumes a C-shape (Figure 1) (Tombol et al., 2000; Cappaert et al., 2015; Striedter, 2016).

Histologically, based on the presence of three cortical layers and distinct unidirectional connections, the hippocampal region is composed of two sets of cortical structures: 1) the hippocampal formation and 2) the parahippocampal region. The hippocampal formation is divided into three distinct regions: a dentate gyrus, Ammon's horn also known as *Cornu Ammonis* and a subiculum. The parahippocampal region consists of areas that surround the ventral and caudal portions of the hippocampal formation. These areas include the entorhinal, perirhinal and postrhinal cortices, presubiculum and parasubiculum, all of which possess more than three lamina layers and reciprocally connects with the hippocampus (Witter and Amaral, 2004). However, the two sets of structures, hippocampal and parahippocampal, are interconnected and function together in a unidirectional circuit to produce physiological changes.

On the basis of cell types and laminar organization, the Ammon's horn is further divided into subfields: CA1, CA2 and CA3 according to the terminology of Lorente de Nó from 1934 (El-Falougy and Benuska, 2006). Each subfield is identified based

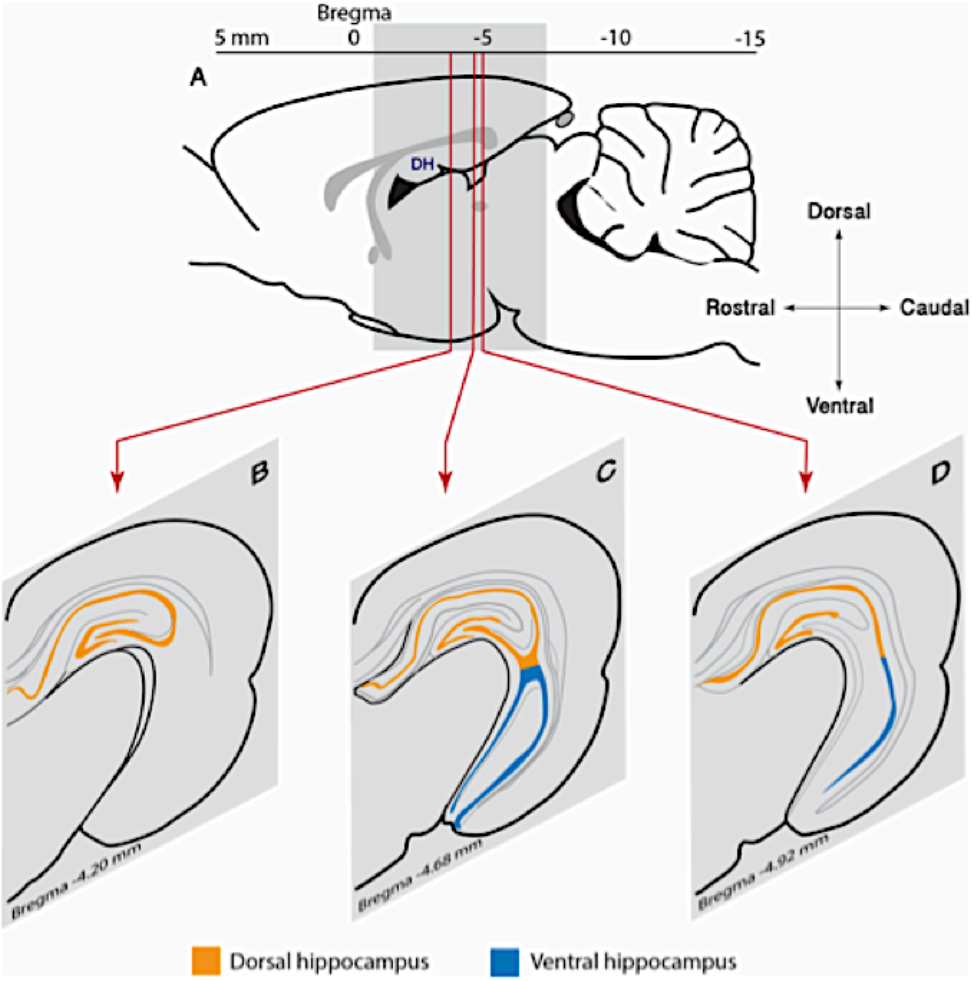

Figure 1. Schematic representations showing the organization of the dorsal and ventral hippocampal region in the rat brain. A) A midsagittal section of the whole rat brain. The shaded portion represents the area of the brain that contains the hippocampus. Only the dorsal hippocampus (DH) is visible in this plane. B - D) Illustrations showing the progressive change and organization in shape of the hippocampus rostrocaudally.

on the features of individual neuron structure and cytoarchitectural organization of neuron clusters (Ishizuka et al., 1995; Altemus et al., 2005). These subtle variations in structure also suggest possible differences in function and information processing.

Each subfield of cells is further organized into distinct layers. *Stratum pyramidale* (also known as the Pyramidal layer or Cell body layer) is the main cellular layer containing approximately 300,000 – 400,000 cells in the rat (Miettinen et al., 2012). Neurons from the pyramidal layer project to different cortical and subcortical structures except in a few instances where one neuron simultaneously projects to two differ-

ent regions (Ishikawa and Nakamura, 2006). However, the implication of the diverse projections are still subjects of debate. A recent study that perturbed the ventral hippocampus, physiologically and anatomically, suggested that anatomic projections from the ventral hippocampus to the medial nucleus of the amygdala were responsible for modulating bulbar cardiorespiratory control circuits (Ajayi et al., 2018). Other studies have also indicated the presence of multisynaptic connections originating from the ventral hippocampus, and with a capacity to modulate the sympathetic nervous system (Westerhaus and Loewy, 2001). Although the study by Westerhaus and Loewy (2001) did not show the structures that constitute the descending pathway, Ajayi et al. (2018) identified the medial nucleus of the aamydala as one relay structure. Further studies would be required to highlight details of the structures that complete the pathway for descending autonomic modulation.

Other cell layers include the following. The *Stratum oriens* is relatively cell-free and deep to the pyramidal layer. The *Stratum lucidum,* is a layer found only in the CA3 field. The layer is also cell-free and located above the pyramidal layer. In CA1 and CA2 subfields, the *stratum lucidum* is immediately superficial to the pyramidal cell layer and contains the apical dendrites of the cells in the pyramidal cell layer. Also, mossy fibres that project from the dentate gyrus to the CA3 subfield predominantly occupy this layer. *Stratum radiatum* is located superficial to the *stratum lucidium*. The *stratum radiatum* contains intrinsic fiber connections such as CA3 to CA3 connections and CA3 to CA1 connections. Finally, there is a *Stratum lacunosum-moleculare,* which is the most superficial layer of the hippocampal region. It is the area that receives terminal projections from the entorhinal cortex, thalamus and other cortical areas (Cappaert et al., 2015). Since the CA1 plays a significant role as an output relay for the hippocampus, emphasis will be placed on this region as literature is reviewed.

Differences between the CA1 and other CA subfields

The CA1 field has been distinguished from CA2 and CA3 fields based on morphological (Figure 2) and electrophysiological properties. The morphological differences include soma size of pyramidal cells: CA1 pyramidal cells are significantly smaller than those of CA2 and CA3 (Altemus et al., 2005; Mercer et al., 2007; Luszczewska-Sierakowska et al., 2015). Furthermore, the pyramidal cells of CA1 subfield give off apical dendrites that enter the *stratum lacunosum-moleculare*. This feature has been observed with both Golgi-Cox and intracellular labelling techniques in monkeys (Altemus et al., 2005). Electrophysiologically, the average spiking rate of CA1 cells is significantly higher than CA2 neurons but less than CA3 neurons (Mizuseki et al., 2012; San Antonio, 2014). These distinguishing features indicate differences in function and direct synaptic connections with nerve terminals from extrinsic sources.

Neuronal connections of the hippocampus

The hippocampus possesses unique intrinsic and extrinsic connectivity patterns recruited to regulate other regions, including autonomic functions (Ajayi et al., 2018; Ajayi and Mills, 2017). Nevertheless, understanding the functions of the hippocampus can be enhanced by analyzing the neuronal projections to and from this region.

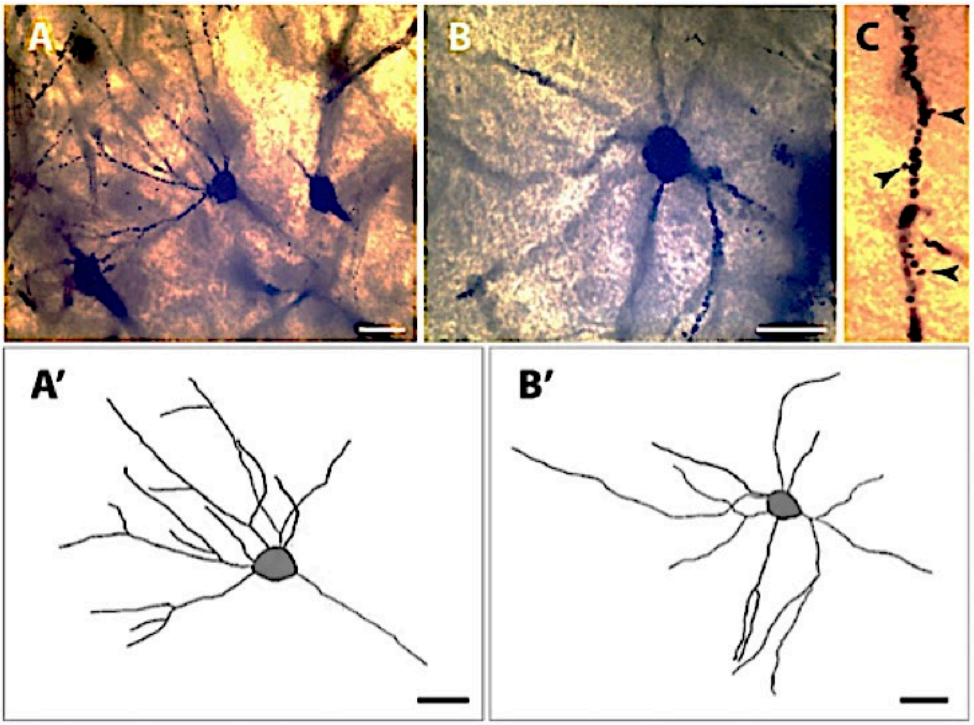

Figure 2. Neurons in the ventral hippocampus with the ability to modulate the autonomic nervous system are typically pyramidal. Light photomicrograph showing two distinct geometries of pyramidal cells, including the distribution of their dendritic trees, in the stimulated areas of the dorsal (A) and ventral (B) hippocampus as reported by Ajayi (2016). A modified Golgi-Cox technique was used to stain the neurons. The black arrows in (C) point at dendritic spines. Note: The neuron of the ventral hippocampus was selected from the CA1 field because the region was by far the most responsive area of the ventral hippocampus. Within the dorsal hippocampus, the representative neuron was also selected from the CA1 region. A′ and B′ are camera lucida reconstructions of the micrographs in A and B, respectively. Scale bar: 20 μm. Adapted from Ajayi (2016).

Intrinsic circuits of the hippocampus

The intrinsic connections of the hippocampus have a unique glutaminergic unidirectional organization (Andersen et al., 1971), although some studies have reported a colocalization of both glutamate and GABA within the same terminals (Munster-Wandowski et al., 2013). The intrinsic circuit is thought to begin in the entorhinal cortex, which is a region believed to link projections from other cortical areas with the hippocampus proper. The entorhinal cortex then sends excitatory signals to the dentate gyrus through a fiber bundle called the perforant pathway. Neurons of the dentate gyrus project to the hilus of CA3 field through mossy fibers. The CA3 neurons, in turn, project to the CA1 area through the Schaffer collaterals. The CA1 neurons project to the subiculum, which sends projections back to the entorhinal cortex and other cortical structures (Witter et al., 2000). A simplified illustration of the unidirectional circuit within the hippocampus is presented in Figure 3. Although details of

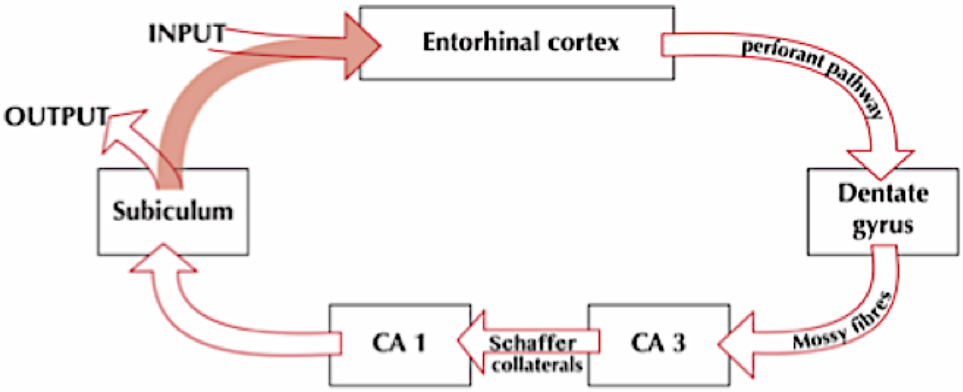

Figure 3. Diagram of the unique unidirectional intrinsic circuit of the hippocampus. The figure is a representation of the parahippocampal-hippocampal neuronal circuitry, illustrating the unique unidirectional connectivity loop within the hippocampus. Note that while the subiculum is the major output structure in the loop, it also projects back to the entorhinal cortex. This projection is represented by the red shaded arrow from the subiculum to the entorhinal cortex. It is also important to note that recent advancements in science have reported output projections from the CA1 region to other limbic structures involved in emotion processing.

the contribution of each area in this circuit is still being investigated, signals reaching the hippocampus are processed through this intrinsic loop before being transmitted downstream.

Output pathway of the hippocampus to cortical/subcortical structures

The subiculum, which is located in both dorsal and ventral hippocampal fields, has been reported as the principal output structure of the hippocampus. The subiculum receives major projections from the CA1 region and, in turn, targets various cortical and subcortical structures such as the infralimbic, entorhinal and perirhinal cortices, *nucleus accumbens*, thalamus and amygdala (Witter and Groenewegen, 1990; Witter et al., 1990). Subicular fibers that target these regions are thought to travel through three principal routes: the fornix, angular bundle and amygdalohippocampal area (Agster and Burwell, 2013). While the dorsal subiculum utilizes the first two routes, the ventral subiculum utilizes the amygdalohippocampal area. It is through the amygdalohippocampal area that ventral subicular projections connect to structures such as the ventral hypothalamus and amygdala (Witter, 1986).

However, there is evidence that the subiculum is not the only output structure of the hippocampus. Classical anatomical studies show that the ventral CA1 region also sends direct projections to cortical and subcortical structures (Cenquizca and Swanson, 2006, 2007; Ishikawa and Nakamura, 2006; Kishi et al., 2006; Ajayi et al., 2018). Perhaps there are different synaptic mechanisms in the connections between the subiculum and the ventral CA1, which have not been tested. It is also unknown if each pathway serves a different behavioral function.

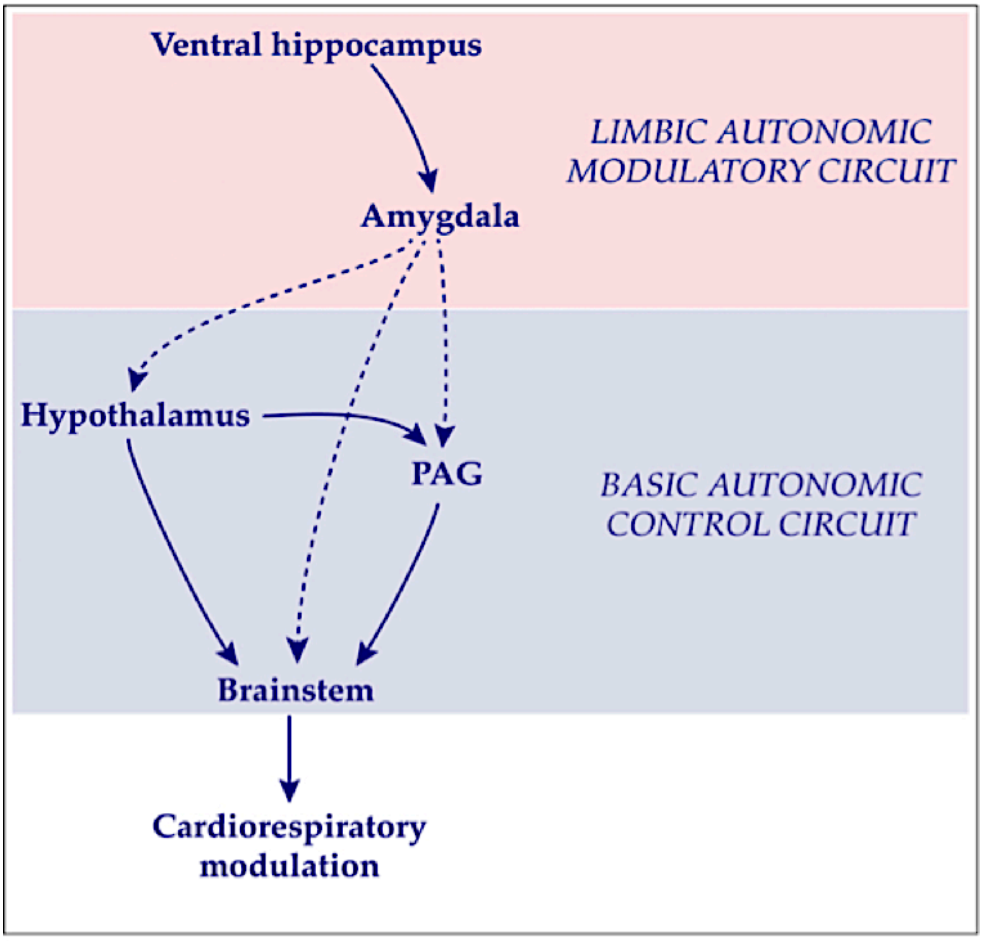

Figure 4. Proposed descending circuit diagram of the pathways for ventral hippocampus modulation of autonomic functions. The solid lines represent circuits that have been established using anatomic tract tracing techniques and confirmed by physiological manipulations. The broken lines represent identified anatomical projections but without confirmatory physiological evidence. The current thesis represents both anatomical and physiological evidence of pathways for autonomic modulation between the ventral hippocampus and the amygdala. PAG: periaqueductal gray.

Extrinsic connections with the potential to influence autonomic activities (Figure 4) include connections with the medial prefrontal cortex, specifically the infralimbic (Swanson, 1981; Cenquizca and Swanson, 2007) and prelimbic areas (Verwer et al., 1997; Cenquizca and Swanson, 2007), hypothalamus (Cenquizca and Swanson, 2006) and amygdala (Kishi et al., 2006; Ajayi et al., 2018). These projections are reported to be GABAergic following *in vivo* electrophysiological cell recording, labeling and neuron tracing (Jinno et al., 2007; Miyashita and Rockland, 2007), but most of the studies were limited to the dorsal hippocampus with the exception of ventral hippocampal

projections to the amygdala (Kishi et al., 2006; Ajayi et al., 2018). Thus, the functions and synaptic mechanisms of cells in the ventral hippocampus, particularly regarding emotional behavior, are uncertain.

Structural and functional segregation of the hippocampus

In the past decade, evidence argued in favor of anatomical and functional differences between the dorsal and ventral hippocampal fields (Bannerman et al., 2004a; Trivedi and Coover, 2004; Strange et al., 2014). The dorsal field of the hippocampus is the area adjacent to the septum and corresponds with the posterior hippocampus in humans while the ventral field is the distal half of the hippocampus located medial to the amygdala in the temporal lobe, and it corresponds with the anterior hippocampus in humans (Witter and Amaral, 2004). Although both fields possess similar cytoarchitectural configuration, less attention was given to the ventral hippocampus. This may be due to focus on elucidating and expanding on the breakthroughs that emerged from the dorsal field of the hippocampus, i.e. the discovery of place cells (O'Keefe and Dostrovsky, 1971; O'Keefe, 1976). However, today, the differentiation into dorsal and ventral fields is becoming significant as physiological, lesion and molecular studies uncover major differences (Bannerman et al., 2004b,c; Trivedi and Coover, 2004).

While the dorsal hippocampus is implicated in spatial navigation, episodic memory and associative learning, the ventral hippocampus is implicated in modulating stress responses and emotional behaviors such as fear and anxiety (Strange et al., 2014). This functional difference has been studied using a range of approaches among which include behavioral assays and separate lesioning (McHugh et al., 2004; Pentkowski et al., 2006), chemical stimulating and inhibition of various neuron populations within the ventral and dorsal hippocampus (Bertoglio et al., 2006; McHugh et al., 2008a; Zhang et al., 2014). The studies implicate the ventral hippocampus in anxiogenesis without much emotional effect from the dorsal hippocampus. On the other hand, lesioning and inactivation of the dorsal hippocampus have resulted in spatial memory impairment (Morris et al., 1982) and learning deficits in rats (Moser et al., 1995; McHugh et al., 2008a,b).

Interestingly, using a combined approach of optogenetics and electrophysiology, Ciocchi et al. (2015) demonstrated that the ventral hippocampus is capable of sending information of emotional content to specific neuron populations in the amygdala, *nucleus accumbens* and medial prefrontal cortex. In a combined experimental approach of multi-site neural recording and optogenetics, Padilla-Coreano et al. (2016) showed that inhibition of ventral hippocampus projections to the medial prefrontal cortex disrupted the behavioral expression of anxiety. However, studies of this association have given less attention to the involvement of the ventral hippocampus in modulating basic physiological parameters such as respiratory and cardiovascular function. Rather more attention has been given to holistic behaviors.

Motor and autonomic functions are amenable to modulation by the ventral hippocampus through direct and multisynaptic connections to the hypothalamus (Herman et al., 2005) and perhaps the periaqueductal gray (PAG). Such modulations are less likely influenced by the dorsal hippocampus (Ajayi and Mills, 2017; Ajayi et al.,

2018). Ballesteros et al. (2014) demonstrated that lesions in the ventral hippocampus affected the ability of the periaqueductal gray to produce the defensive freezing posture normal observed upon stimulating the dorsal region (Carrive and Morgan, 2012). Their study reported that neither the dorsal nor ventral hippocampal lesion completely disrupted periaqueductal gray activity. However, ventral hippocampal lesions significantly reduced defensive freezing behavior (Ballesteros et al., 2014). A similar report by Rogers et al. (2006) emphasized a greater involvement of the ventral hippocampus in fear conditioning. Thus, in addition to ventral hippocampal connections to the hypothalamus, these findings suggest possible connections of the ventral hippocampus to the periaqueductal gray.

Functions of the hippocampus

The hippocampus plays a crucial role in the limbic network because of its involvement in memory and cognition. These functions were first identified and described in 1953 following bilateral removal of the medial temporal lobe structures to ameliorate refractory epilepsy (Scoville and Milner, 1957). The frequency of seizures decreased, but the patient suffered from amnesia, suggesting that the hippocampus played crucial roles in storing memory (Scoville and Milner, 1957). The role of the hippocampus in memory and learning was further established by the discovery of the so-called "place cells", which fire bursts of action potentials in specific places ('place fields') as an animal worked through a maze (O'Keefe, 1976).

The seminal discovery of place cells over four decades ago (O'Keefe and Dostrovsky, 1971) has significantly shaped the functional knowledge of cells in the hippocampus. The correlation of neuron firing activities with particular locations of an animal in a defined space suggested that hippocampal cells could provide an accurate representation of the animal's location. This discovery was termed "the biological global positioning system", and it lead to a Nobel Prize in Medicine and Physiology in 2014. Since the discovery of place cells, several studies have attempted to further characterize the morphological features and physiological properties of the cells as well as define their precise distribution in the hippocampus. To this end, studies have suggested that there is a high density of place cells in the dorsal parts of the CA1 region (Henriksen et al., 2010). This observation implies that cells in the ventral hippocampus serve other functions.

Researchers have reported that the ventral hippocampus plays crucial roles in the expression of emotions, such as anxiety and stress (Bannerman et al., 2004c; Trivedi and Coover, 2004; Bertoglio et al., 2006; Fanselow and Dong, 2010; Femenia et al., 2012; Ballesteros et al., 2014; Padilla-Coreano et al., 2016), as well as the development of associated disorders, including post-traumatic stress disorder and major depressive disorder (Bonne et al., 2008; Femenia et al., 2012). A common feature in the expression of these emotions is an alteration of basic physiological parameters and it is becoming clear that the hippocampus is involved in autonomic regulation by modulating various aspects of cardiorespiratory rhythm, including the motor expression of augmented breaths (Ajayi and Mills, 2017; Ajayi et al., 2018). However, the mechanisms through which these behaviors are expressed are yet to be clarified.

Emotion processing and the hippocampus

Emotions are physical behaviors that reflect the mental state of an individual. These behaviors, which are expressed as joy, sadness, pleasure, fear, etc., are subjective, and in experimental conditions, mostly non-reproducible. Thus, most of the studies that attempt to describe the mechanisms of emotions are questionable. However, the Pavlovian fear-conditioning paradigm has been very useful in defining objective principles for the study of emotions. The Pavlovian paradigm involves the pairing of two stimuli: a conditioned stimulus (non-aversive) usually a light or a sound, and an unconditioned stimulus (aversive) often a foot shock. Following repeated pairing, the conditioned stimulus can produce the effect of the unconditioned stimulus (fear reaction). The paradigm has been used to objectively reproduce fear, a primary emotion that is conserved across species. Based on this paradigm, the amygdala is identified and extensively researched as a crucial structure in expressing the objective emotion of fear (LeDoux, 2003, 2007, 2012). However, the amygdala does not function as an entity in producing a fear reaction. Rather it is part of a circuit. Evolving evidence suggests that either by direct modulation of sensory inputs of an environmental challenge or by modifying neural mechanisms in the amygdala through synaptic transmission, other brain areas play crucial roles in forming and expressing emotions. One of such brain areas is the ventral hippocampus. Studies have demonstrated that lesion pf the hippocampus completely abolishes the Pavlovian reflex (Anagnostaras et al., 2002) but it is uncertain if this effect results from loss of the memory component of the conditioning stimulus or direct involvement in expressing the behavior. Studies also showed that the limbic system recruits the medial nucleus of the amygdala to produce autonomic changes (Ajayi et al., 2018). These studies are indications that emotional behaviors are processed through functional networks rather than individual brain regions.

In expressing an emotional behavior, changes in underlying physiologic parameters are expected as a homeostatic mechanism of adaptation to altered metabolic demands. Studies have shown that lesions to the ventral hippocampus create a fundamental homeostatic imbalance that could result in gastric ulcers (Henke, 1990a,b) although other autonomic parameters were not measured. Owing to established anatomical projections of the ventral hippocampus to the amygdala (Kishi et al., 2006; Ajayi et al., 2018), and the involvement of the amygdala in stress (Ressler, 2010), there is an interaction between the ventral hippocampus and amygdala that supports the physiological changes during emotional behaviors. Moreover, Henke (1990b) showed that high-frequency stimulation of the ventral CA1 region evoked potentials in the amygdala, and animals that received such stimulations were less vulnerable to stress-induced gastric ulcers.

In a more behavior-focused research in rats, Bannerman et al. (2003) demonstrated deficits in the expression of fear following lesions that encompassed 50 % of the ventral hippocampus. The lesions led to significant reduction in freezing following a foot shock stimulus. Furthermore, there were clear indications of increased anxiety demonstrated by observing various physical indices. All these effects were restricted to the ventral hippocampus (Bannerman et al., 2003).

Various physiological investigations (Ballesteros et al., 2014; Zhang et al., 2014) have also provided evidence underpinning the ventral hippocampus in emotions

using the principles of chemical inhibition and fear conditioning, respectively. Inhibition of the ventral hippocampus using optogenetics has also been shown to alter aspects of contextual fear (Goshen et al., 2011). All the reports mentioned above are in addition to human data where significant changes have been observed in people with post-traumatic stress disorder (Bonne et al., 2008) and bipolar disorders (Frey et al., 2007). However, the specific role(s) of the ventral hippocampus regarding inter-structural neuronal interactions require more investigations as only a few studies (Ajayi and Mills, 2017; Ajayi et al., 2018) have provided insight in the context of motor and autonomic functions underlying these behavioral changes.

The mechanisms involved in expressing emotions and stress include a collection of smaller motor and autonomic processes. For example, during the expression of an emotion such as anxiety, depression or fear, an organized and simultaneous recruitment of multiple motor and autonomic components is expected: the phrenic nerve and vago-sympathetic systems would be recruited as final motor tracts to modulate the respiratory and cardiovascular systems, respectively, so that homeostasis is maintained while adapting to the situation. At the same time, nerve supplies to specific skeletal muscles associated with emotional expression will be recruited to relax or tense such muscles. The simultaneous occurrence of these events suggests that circumscribed higher brain areas, known to control emotional behaviors, exert their effects by modulating, resetting and recruiting motor and autonomic drivers in the brainstem.

However, it is important to note that there are no known direct projections of the ventral hippocampus to brainstem autonomic centers but indirect connections could exist. Studies have shown that one relay structure between the ventral hippocampus and the brainstem is the amygdala (Ajayi et al., 2018). The role of the amygdala does not rule out the involvement of other critical relays such as the hypothalamus and periaqueductal gray. In fact, it is possible that the amygdala, in turn, recruits both hypothalamus and periaqueductal gray for motor and autonomic control.

Concluding remarks

The hippocampus and amygdala are principal components of the limbic system due to their roles in expressing emotions and processing memory. However, in appropriating emotional behaviors, the hippocampus and amygdala rely on complex linkages, known as functional networks, between other brain regions to process information and express distinct behaviors. For example, the hippocampus is known to be involved in memory, learning (Bannerman et al., 2014) and limbic modulation autonomic activities (Ajayi and Mills, 2017; Ajayi et al., 2018) while fear is principally regulated by the amygdala (LeDoux, 2003, 2007; Phelps and LeDoux, 2005). However, these regions must interact with other structures that directly control autonomic and endocrine functions to produce homeostatic changes, necessitating that the limbic structures provide a modulatory hierarchical level in autonomic control. It is through such interactions that integrated respiratory and autonomic changes accompany emotional behaviors (Ajayi et al., 2018). However, the interactions are complex and involve mechanisms and pathways many of which have not been fully elucidated. The studies to date have focused on the medial prefrontal cortex because of its established roles in processing emotions. However, more recently, other parts of the limbic system such as the ventral hippocampus

have been shown to affect emotion processing, and also modulate motor and autonomic function (Ajayi and Mills, 2017; Ajayi et al., 2018). A likely pathway maybe through the periaqueductal gray. The periaqueductal gray directly regulates autonomic function and it is believed to be essential to the integration of various autonomic responses, such as respiration, vocalization, cardiovascular function and micturition for the expression of emotions during a survival challenge (Bandler et al., 1991; Zhang et al., 1994). Investigations into the anatomic organization of inputs into the periaqueductal gray, the synaptic mechanisms driving such inputs and the manner in which the inputs shape the output of the periaqueductal gray would be relevant in broadening current knowledge of descending modulation of emotion-dependent autonomic activities.

Conflict of interest

The author declares no competing financial interests.

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