Review of: "Exploring the Microscopic Maze: The Structure and Function of the Hippocampal Arterial Supply"

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Potential competing interests: No potential competing interests to declare.

Dear Editor,

I have read the manuscript sent for review.. I think that the manuscript can be published after its content is corrected, except for a few grammatical corrections.

It is seen that they used a wide range of references, including anatomical variations.

Best regards

I am presenting below the places that need to be deleted and the expressions that need to be changed, marked.

Exploring the Microscopic Maze: The Structure and Function of the Hippocampal Arterial Supply

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Abstract

The Hippocampus is a critical organ for memory storage and processing. The Blood supply of the hippocampus is derived from the branches of the anterior choroidal artery and posterior cerebral arteries. Parts of the hippocampus are identified as a head, body and tail; (~~accordingly,~~) hippocampal arteries are named as anterior short, anterior long, posterior short and posterior long hippocampal arteries. Based on the origin of the hippocampal arteries, five (~~different~~) types of hippocampal blood supply have been identified. The hippocampal head has six microanatomical layers; that include the condensed pyramidal cell layer also. Hippocampal microvascular supply and perfusion depend on the lumen and structure of the arterioles. Hippocampal microvascular density is comparatively lower than the neocortical cerebral areas.

Introduction & Background

The hippocampus is a critical part of the limbic lobe involved in memory processing, learning, spatial navigation, and emotions [1]. The indusium griseum, gyrus fasciolaris, and longitudinal stria, along with the hippocampus proper, form the hippocampal formation [1][2][3]. The hippocampus can be divided into head, body and tail rostrocaudal[1][2][3]. Developmentally hippocampus is paleocerebrum, hence hippocampus has six histological layers including three cortical layers [1][2][3]. Hippocampal vascularization plays a significant role in various neurodegenerative pathologies, including dementia and Alzheimer's disease [3][4]. The microscopic vascular pattern and its density reduce as part of the ageing process, which may lead to cerebrovascular rarefaction [3][4][5]. This critical review will summarize the arterial supply of the hippocampus, including its branching pattern and density

Blood supply of the hippocampus

The hippocampus receives its blood from the posterior cerebral artery (PCA) and anterior choroidal artery (AchA)[5][6]. The hippocampal arteries can be classified into five (~~different~~)types based on the origin (Table 1) [7][8].

Type	Origin of the artery
Type A	Hippocampal arteries originate from both the AchA and PCA
Type B	Most of the hippocampal arteries originate from the PCA, specifically from all the inferior temporal arteries.
Type C	Hippocampal arteries originate exclusively from the PCA, specifically from all the inferior temporal arteries.
Type D	Hippocampal arteries originate directly from the PCA or a common trunk
Type E	Hippocampal arteries originate from the AchA

Table 1. Classification of the hippocampal arteries based on their origin

PCA = Posterior cerebral artery, AchA: Anterior choroidal artery

The cerebrum is supplied by the anterior cerebral artery, middle cerebral artery, and posterior cerebral artery, which are branches of the internal carotid artery and basilar artery. The basilar artery is formed by the union of two vertebral arteries [8][9]. Branches of the basilar artery (Posterior communication artery) join the branches of the internal carotid artery to form the arterial circle at the inferior surface of the brain. Cerebral branches divide to supply the cortical area (cortical branches) and the deep structure of the cerebrum (lenticulostriate /choroidal branches) [7][8][9].

The posterior cerebral artery (a terminal branch of the basilar artery) joins with the posterior communicating artery and completes the circle of Willis [1][9][10]. The posterior cerebral artery divides into three major branches: cortical branches, posterolateral striate branches, and the posterior choroidal artery [5][6][7][8][9][10][11][12]. The posterior cerebral artery can be divided into four segments: Pre-communicating segment (P1), Ambient segment (P2), Quadrigeminal segment (P3), and Calcarine segment (P4). The segments can be further classified as deep and superficial parts.

The part of the posterior cerebral artery from the posterior communicating artery to the posterior margin of the midbrain is considered the second part (P2). It gives the anterior inferior temporal artery and the anterior hippocampal para-hippocampal artery supplying the entorhinal area [5][6][7][8][9]. The posterior inferior temporal artery (a branch of the posterior cerebral artery) gives a branch known as the posterior para-hippocampal artery. The fourth part (P4) of the posterior cerebral artery gives a branch known as the parietooccipital arterial trunk supplying the para-hippocampal gyrus and hippocampus [10][11][12].

The anterior choroid artery (AChA) has a highly variable origin and distribution depending on the territory of the posterior cerebral artery [11]. It originates from the distal part of the internal choroid artery after the posterior communicating artery is given off [5][6][7][8]. The anterior choroid artery runs into the subarachnoid space, and the part of it up to the inferior horn of the lateral ventricle is called the cisternal segment [11][12].

The branches of the anterior choroid artery form the choroid plexus (located)in the inferior horn of the lateral ventricle [10][11][12]. It also supplies the optic tract, the globus pallidus, the uncus, the lateral geniculate body, and the internal capsule [8][9][10][11][12]. The amygdala and the hippocampus are supplied by the perforating branches of the anterior choroid artery [11][12][13][14]

Classification of Hippocampal arteries

The hippocampal arteries can be classified according to the territories (Head, body, and tail of the hippocampus) supplied by the arteries (Figure 1).

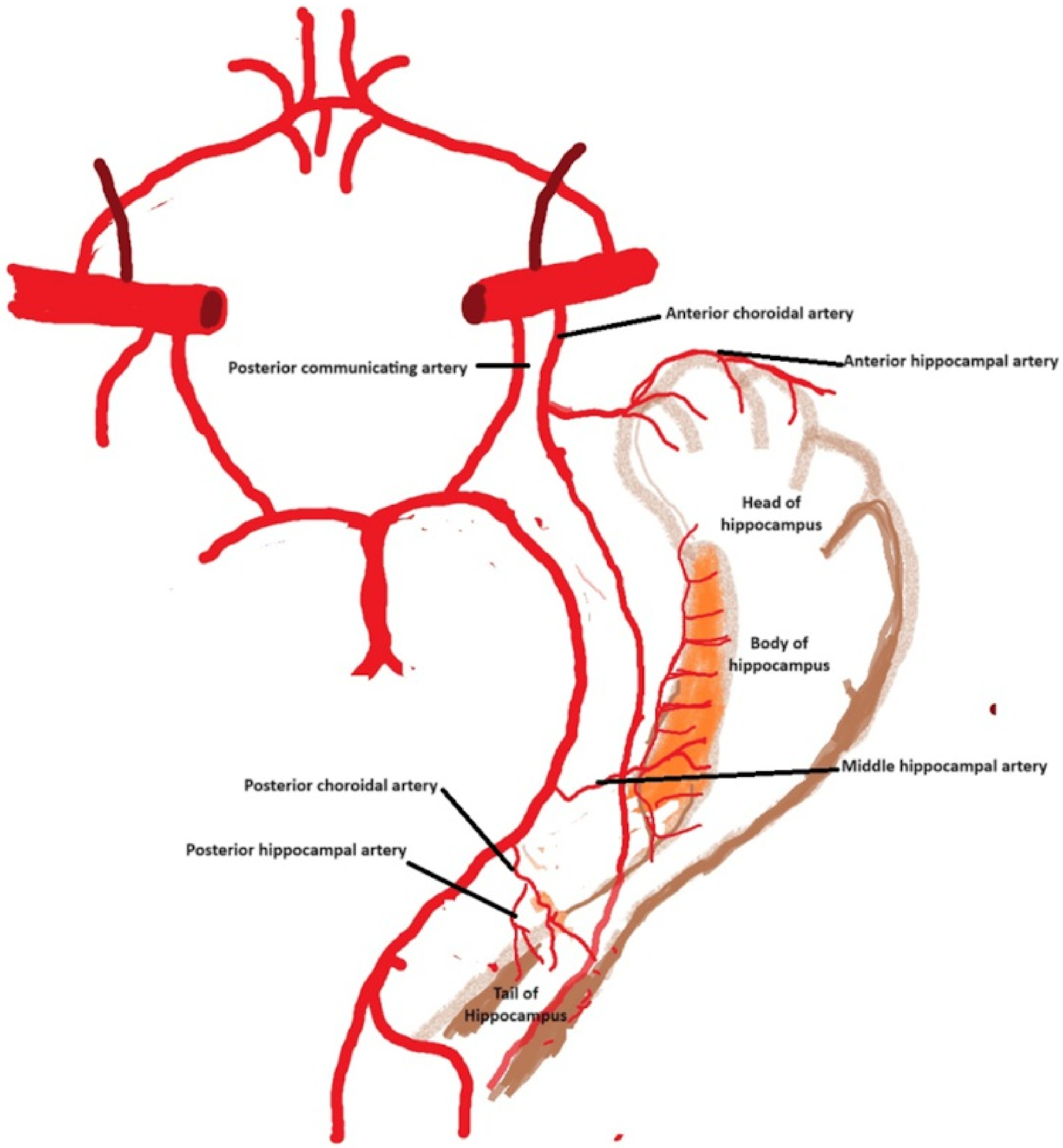

Figure 1. Hippocampal arteries and their origin

Anterior Hippocampal arteries (AHA): Artery supplying the uncus and head of the hippocampus is known as anterior hippocampal arteries [9][10][11][12][13][14]. The artery enters into the uncal sulcus to supply the head of the hippocampus and reach the surface of the pyriform lobe [10][11][12][13][14].

Posterior Hippocampal arteries (PHA): Arteries supplying the body and tail of the hippocampus are known as the posterior hippocampal arteries [12][13][14]. Posterior hippocampal arteries give large perforating branches, and small branches to supply the margo denticulatus and fimbria-dentate sulcus. A rich anastomosis is formed around the hippocampal sulcus by the large posterior hippocampal arteries [11][12][13][14].

Intrahippocampal arteries (deep branches): The intrahippocampal arteries are classified as small ventral, small dorsal, larger ventral, and large dorsal branches [11][12][13][14][15][16].

The proximal part of the dentate gyrus is supplied by small ventral arteries while the fimbria-dentate sulcus and adjacent areas are supplied by the small dorsal arteries [13][14][15][16]. The CA1, CA2 region, stratum lacunosum, molecular layer of the dentata gyrus, and stratum pyramidalis are supplied by the large ventral branches. The CA3, CA4 areas, and granular areas of the dentate gyrus are supplied by the large dorsal branches [11][12][13][14][15][16].

Anastomosis: Major extrahippocampal anastomosis between the AChA and PCA is present at the head of the hippocampus and transitional area between the mid and posterior part of the hippocampus [14][15][16]. Various postmortem and imaging studies have reported that deep arterial anastomosis and capillary anastomosis between hippocampal arteries are less frequent [15][16][17][18][19].

Hippocampal microvasculature: Microvasculature of cerebrum has been widely studied in both humans and animals, but any significant classification of the microvasculature has not been reported [14][15][16][17][18][19][20][21][22][23]. Resolution is the major limitation of the imaging method, because of which pre-capillary arterioles and post-capillary venules are missed in the studies [22].

In combination with post-mortem studies using histological methods (e.g. compound microscopy, confound 3-D microscopy, light sheet fluorescence microscopy) density of the intrahippocampal vasculature has been studied [20][21][22][23][24]. Hippocampal vascular density is less than the vascular density in the neocortical areas[25]. The hippocampal microvasculature is sparse and arterioles enter the hippocampus perpendicular to the coronal plane. Distance between vessels is comparatively higher than the other cortical areas [25][26][27].

The hippocampal microvasculature is arranged in alternative arcs of arterioles and venules creating a rake-like pattern. Hippocampal arteriolar lumen diameter is critical for maintaining the perfusion of the nervous tissue; which is determined by the vascular smooth muscles present in the wall [25][26][27][28]. In addition, the capillary endothelium lining also plays a pivotal role in hippocampal perfusion. Imaging studies using the Ferumoxytol-enhanced MRI reveal that the vascular density is low in the head (~~, as well as~~ and) in the CA1 (Cornu Ammonis 1) field of the hippocampus (~~in comparison to~~ compared to) the body and tail [24][25][26]. Similarly, hippocampal perfusion using high-resolution, multi-modal 7T MRI studies also shows the perfusion in the CA1 field is lower than the remaining fields of the hippocampus [26][27][28]. The reason behind the less perfusion is that the CA1 field is the farthest from the origin of vessels [26].

Conclusions

Microvascular density and diameter of the hippocampal blood vessels are important parameters in vascular-induced dementia and cerebrovascular pathology of the hippocampus. The head of the hippocampus and the CA1 field of the hippocampus are the least perfused areas because of their higher distance from an artery of origin.