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Hippocampal BDNF Expression From Early Development to Adulthood in Male Rats

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ABSTRACT: The hippocampus plays a crucial role in our memory. The manner in which we experience emotions and acquire knowledge. This research examined a substance known as BDNF, a specific type of stain, and its influence on the growth of the hippocampus in male albino rats at various ages. They divided twenty albino rats into four groups: one group was only one day old, another group was one month old, a third group was three months old, and the final group consisted of adult rats. Every one of these groups contained five rats. The BDNF expression in the CA1 region varied with age. At 1 day, observed minimal BDNF. At one month, there was an increased expression of BDNF. After 3 months, the BDNF decreased slightly. At 6 months, the CA1 area exhibited increased BDNF, notably in the stratum pyramidal. The CA3 subfield exhibited differences. At 1 day and 1 month, did not observe BDNF. At 3 months, the BDNF increased expression in the stratum oriens. At 6 months, there were increased neurons containing BDNF in the stratum oriens and stratum radiatum of the CA3 subfield. The dentate gyrus exhibited marked age-related variations, showing no observable staining at 1day, restricted expression in the polymorphic layer at 1 month, a slight rise at 3 months, and many BDNF-positive neurons at 6 months. The study shows the increase of BDNF expression related with age.

INTRODUCTION

Located in the medial area of the temporal lobe, the hippocampus is a part of the limbic lobe in humans **(Tatu and Vuillier,2014)**. A familiar curved formation of grey matter in the brain, the hippocampus spans the entire length of the inferior horn floor within the lateral ventricle.

It develops the pes hippocampus by prolonging its front end. Owing to its resemblance to a sea horse when viewed in a coronal section, the structure is referred to as the hippocampus **(Moser et al., 2014).**Numerous developmental brain disorders specifically impact the hippocampal formation, which is known to play a crucial role in memory and learning. Research on this brain region is essential for comprehending neurodevelopmental disorders **(Abdelrahim and Eltony,2011).**

The hippocampal formation is a multi-faceted structure within the medial temporal lobe that is involved in processing memory **(Lavenex et al.,2006).** The hippocampus transforms short-term memory into long-term memory, manages spatial memory, and retrieves past location experiences. It also has an essential role in emotions and behavior **(Chauhan et al .,2021).**

The development of the hippocampus (formation hippocampi) comprises the indusium griseum, longitudinal striae, gyrus fasciolaris, hippocampus proper (cornu ammonis, dentate gyrus, and subiculum), along with a part of the uncus **(Ten et al .,2018).** the development of the hippocampus has archipallial cortex and advances along the inferomedial aspect of the cerebral

hemisphere; during maturation, it follows the outer edge of the C-shaped choroidal fissure **(Dekeyzer et al.,2017).** The hippocampus is divided along its length based on the size and density of its principal pyramidal cells into four separate areas called Cornu Ammonis (CA1, CA2, CA3, and CA4) **(Mazher and Hassan, 2021).** the proper hippocampus, the polymorphic layer (OL), pyramidal layer (PL), and molecular layer (ML) **(Abdelrahim and Eltony, 2011).**

Behavioral research has suggested that developmental irregularities in hippocampal formation after birth might play a role in neurodevelopmental disorders like Down syndrome, autism, schizophrenia, and epilepsy. Grasping the functional maturation and structural evolution of the hippocampal formation is essential for obtaining insights into the particular developmental processes and information processing that may be influenced in neurodevelopmental disorders **(Lavenex et al .,2006).**

The Brain-Derived Neurotrophic Factor (BDNF) facilitates the growth and multiplication of cells in the hippocampus and plays a crucial role in long-term potentiation and the creation of memories **(Erickson et al., 2010).** It has garnered significant interest for its likely critical involvement in several neuropsychiatric disorders **(Autry and Monteggia, 2012; Castrén, 2014)**.

The aim of this study is to assess the progression in hippocampal tissues of male rats across different ages (one-day group, one-month group, three-month group, and adult group) by investigate the Brain-Derived Neurotrophic Factor (BDNF) with the postnatal development of the hippocampus in male rats.

MATERIALS AND METHODS

The twenty male albino rats were divided 4 groups: 1-day group, 1-month group,3-months group and adult group. Each of the experimental group contain 5 males rats.at the end of the study we examination immuonohistochemistry stain. Animals were anesthetized with chloroform, then decapitated, and their skulls opened via a longitudinal incision. After lifting the skull bones, the whole brain was extracted and placed in phosphate buffered saline on a cold dish.

The cerebellum and brainstem were separated, and the brain was divided into hemispheres. The hippocampus, located in the medial temporal lobe, was isolated after removing the cerebral cortex, appearing as an arched structure. The hippocampus was fixed in 10% formalin for immuonohistochemistry stain. examination in sterile containers.

RESULT

CA1 Region Immunohistochemical analysis of the CA1 region demonstrated age-dependent variations in BDNF expression. At 1 day (Figure 1A), only faint immunoreactivity was detected within the CA1 layers. In the 1-month group, a modest increase in staining intensity was observed relative to the 1-day specimens (Figure 1B). By 3 months, BDNF immunoreactivity showed a slight decline, as shown in figure(1C) . In contrast, the 6-month group exhibited a clear enhancement in BDNF expression, particularly within the stratum pyramidale.(Figure 1D).

CA3 Region In the CA3 subfield, BDNF immunoreactivity was limited in the 1-day and 1-month groups, with only a few positively stained neurons visible(Figure 2A and B), respectively. At 3 months (Figure C), the number of BDNF-immunoreactive neurons increased noticeably, particularly within the stratum oriens. By 6 months, BDNF-positive neurons became more numerous and were distributed across both the stratum oriens and stratum radiatum (Figure D).

Dentate Gyrus (DG) The dentate gyrus revealed distinct age-related differences in BDNF immunoreactivity. The 1-day group showed no detectable staining(Figure 3A). In the 1-month group, BDNF expression was primarily confined to the polymorphic layer(Figure 3B). At 3 months (Figure 3C), a mild increase in staining intensity was observed. By 6 months, numerous BDNF-positive neurons were present throughout the polymorphic layer (Figure 3D).

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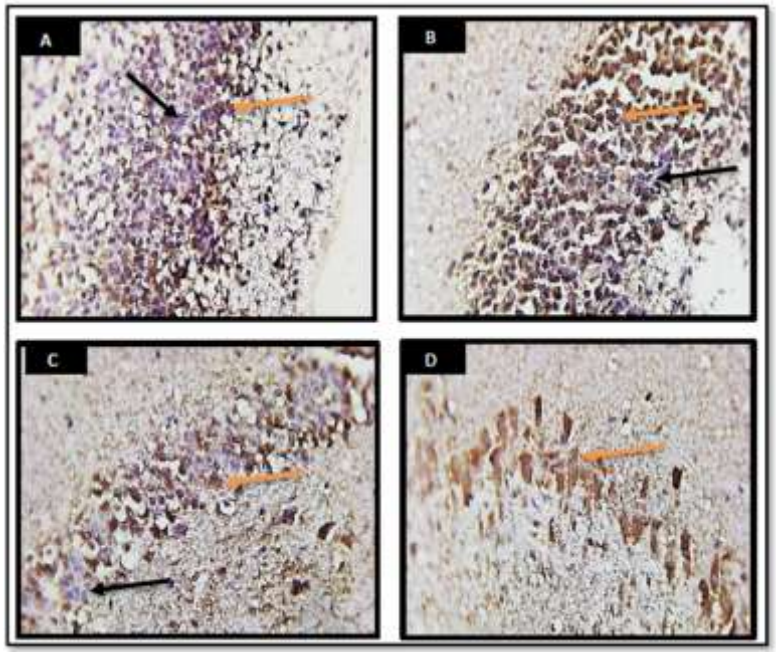


Figure:(1) immunohistochemical section in male rats showed Cornu Ammonis 1 (CA1) of hippocampus in different ages (A: 1 day, B: 1 month, C: 3 months, D: 6 months). Weak positive expression of BDNF immunoreactivity (orange arrow) is detected in the CA1 region in the 1-day (A) , 1-month (B) group and the 3-month. At 6 months, group (D), a marked strong positive expression of BDNF immunoreactivity becomes evident within the stratum pyramidal (SP) potive cell expression indicated by an orange arrow, while negative expression is indicated by a black arrow. immune reaction to BDNF(X40)

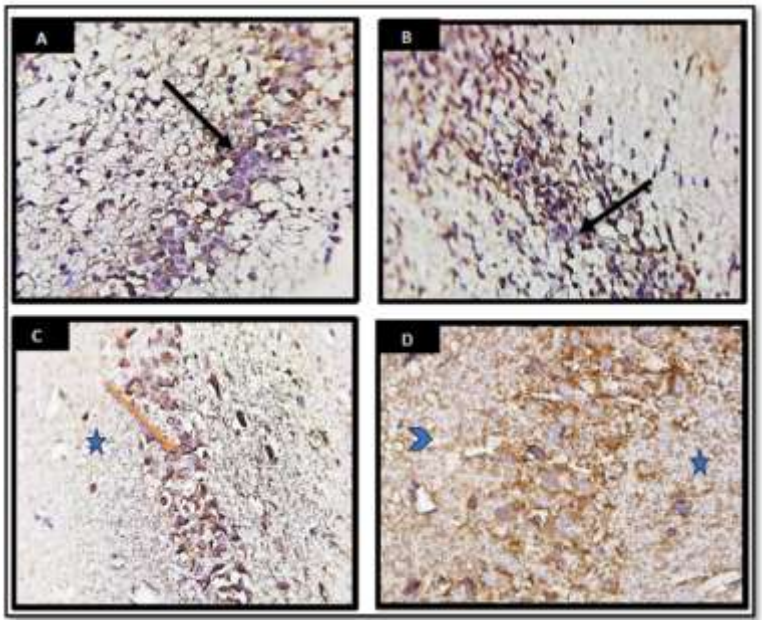


Figure: (2) immunohistochemical section in male rats showed Cornu Ammonis 3 (CA3) of hippocampus in different ages (A: 1 day, B: 1 month, C: 3 months, D: 6 months). (F). At 1-day and 1 month (A, B), a negative BDNF-immunoreactive observed in the CA3 region(black arrow) . At 3-months (C), BDNF-immunoreactive neurons are weakly positive in the stratum oriens(star) and moderately positive in the pyramidal cells (orange arrow). At 6-months (D), the number of BDNF-immunoreactive neurons increases in the stratum oriens(star)and stratum radiatum (arrowhead). BDNF (X40)

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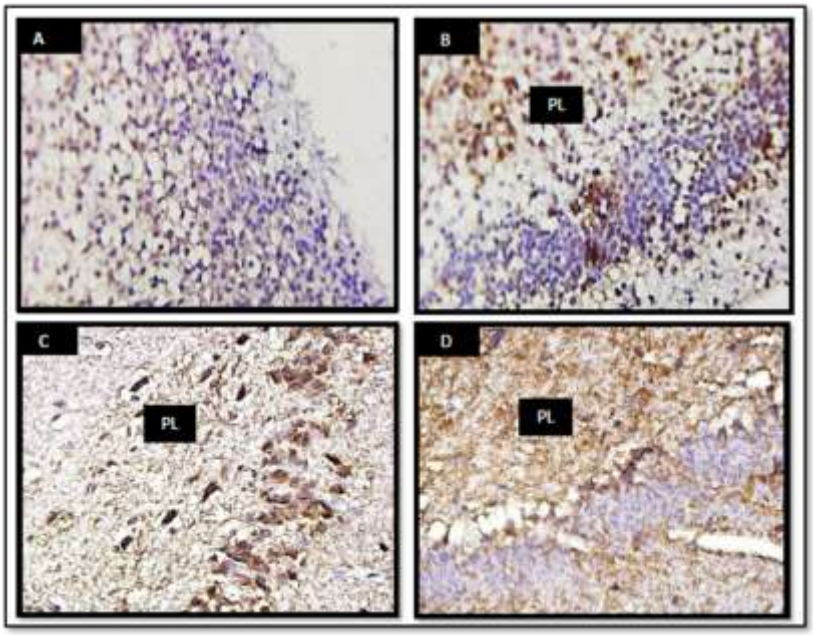


Figure:(3) immunohistochemical section in male rats showed the Dentate Gyrus (DG) of the hippocampus in different ages (A: 1 day, B: 1 month, C: 3 months, D: 6 months). At 1-day, there is a negative reaction(A) (black arrow), while in the 1-month group (B), positive BDNF immunoreactivity is predominantly localized within the polymorphic layer (OL) of the dentate gyrus. A moderate positive expression is noted in the polymorphic layer (OL) at 3-months (C). By 6 months of age (D), strong BDNF-positive neurons become evident throughout the polymorphic layer (OL) . BDNF (X40)

DISCUSSION

In the present study, found the number of BDNF-immunoreactive neurons increased significantly in the CA1 region of 6month specially in stratum pyramidal, that result also seen in result that reported by (**Hwang *et al.,* 2006)**. And in the CA3 region for 3months in the stratum oriens.in addition to a further increase in the CA3 region of 6months in both the stratum oriens and stratum radiatum, these results agree with result posted by **(Narisawa-Saito and Nawa 1996; Hattiangady *et al.,* 2005)**. also did not seen in the DG at 1 month staining of BDNF only in the polymorphic layer, and at 3 months a mild increase in staining immunoreactive neurons while in 6 months positive neurons were present throughout the polymorphic layer these results agreement with the result posted by (**Hwang *et al.,* 2006)**. However, in these regions (CA1, CA2 and DG) of others age groups (1day and 1 month) did not observe any noticeable changes.

(Erickson *et al.,* 2010), said that levels of BDNF were reduced related to both decline in hippocampal volume and elevated memory deficits. In rodents, BDNF moderates synaptic plasticity and neurogenesis in the dentate gyrus and has been directly related to learning rates in spatial memory paradigms **(Rex *et al.,* 2007; Silhol *et al.,* 2007).** By blocking either, the release of BDNF or the binding of BDNF to its receptor (TrkB), long-term potentiation is effectively eliminated in the hippocampus **(Pang *et al.,* 2004).** This abundance of BDNF and TrkB during early development may be required to facilitate normal development of the vestibular nucleus and its associated controls. High expression of TrkB during infancy most likely relates to its role in the proliferation of neural progenitor cells **(Cheng *et al.,* 2003)**. The high expression of BDNF would allow it to play its multiple roles in regulating the differentiation, survival and plasticity of different neuron populations **(Karpova, 2014).** Most other functional studies in memory/cognitive disorders found a correlation between declining expression or abnormal function of BDNF, rather than TrkB, including studies such as Alzheimer's disease **(Peng *et al.,* 2005)**

Furthermore, inducing BDNF production and secretion in the hippocampus can rescue long-term potentiation and relieve spatial memory deficits in aged mice **(Rex *et al.,* 2006, 2007; Simmons *et al.,* 2009).** shows age-related changes in BDNF mRNA levels in the hippocampus. In rat hippocampus**,** the level of BDNF mRNA expression remained almost constant from day 1–22 months of age **(Silhol *et al.,* 2005).** In a rodent model of successful aging in which the animals have longer lifespans

and preserved memory capacities, BDNF levels were higher than in animals that experience normal age-related patterns of decline **(Silhol *et al.,* 2008).** BDNF also moderates tau formation **(Elliott and Ginzburg, 2006),** beta amyloid neurotoxicity **(Arancibia *et al.,* 2008),** and hippocampal dependent memory performance in animal models of Alzheimer's disease **(Tapia-Arancibia *et al.,* 2008; Blurton-Jones *et al.,* 2009).** Previous reports have pointed to a role for BDNF in the control of hippocampal neurogenesis **(Larsson *et al.,* 2002; Lee *et al.,* 2002; Sairanen *et al.,* 2005).** For example, infusion of exogenous BDNF into the dentate gyrus leads to increased neurogenesis of granule cells **(Scharfman *et al.,* 2005).** However, BDNF administration suppresses hippocampal neurogenesis after an ischemic insult **(Larsson *et al.,* 2002)**. Thus, the actions of BDNF on sub granular progenitor cells differ between the intact and injured brain. Other studies have shown that an up-regulation of BDNF is critically required for the increase in survival of newborn granule cells following dietary restriction **(Lee *et al.,* 2002)** and antidepressant treatment **(Sairanen *et al.,* 2005).** A shortage of BDNF correlates with reduced granule neuron survival in immune-deficient mice **(Ziv *et al.,* 2006).**

Thus, BDNF appears to be a converging point for distinct signaling pathways impacting on hippocampal neurogenesis. In other cases, enhanced BDNF production affected proliferation in the sub granular zone with no net effect on neuronal survival **(Katoh-Semba *et al.,* 2002; Morcuende *et al.,* 2003).**

In summary, BDNF has been convincingly demonstrated to relate to memory formation, neurogenesis, and Alzheimer's disease pathology in aged animals.

CONCLUSION

The study shows The CA1 region's BDNF expression displayed age-related variations: weak at 1 day, modest at 1 month, a slight drop at 3 months, and increased at 6 months, especially in stratum pyramidale. CA3 showed limited BDNF at 1 day and 1 month, increased significantly at 3 months, and many positive neurons at 6 months. The dentate gyrus had no staining at 1 day, limited at 1 month, mild increase at 3 months, and numerous positive neurons at 6 months.

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