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Case Report

Reduced Right Hippocampal Volume on MRI and Correlation with Major Depressive Disorder

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Abstract

Introductions: Many studies have shown in the field of psychiatry results in specific changes in brain anatomy and function associated with measurable clinical outcomes. One of the biggest difficulties in diagnosing and treating psychiatric disorders is that human behavior involves complex mechanisms when compared to experimental animals. **Case:** 25-year-old female, diagnosed with Major Depressive Disorder (MDD) 6 months ago at a General Hospital in Malang, Indonesia. The patient felt depressed, had trouble sleeping, and had attempted suicide. MRI of the hippocampus was performed at the power of 3 Tesla magnetic strength (PHILIPS INGENIA 3.0T). MRI data processing and hippocampal volumetric analysis were performed using the volBrain HIPS software. **Discussion:** The left hippocampus volume was larger than the right volume, with a history of the patient never doing exercise or exercising regularly. In general, the hippocampus can be asymmetrical on both sides and larger on the right side. Although asymmetry in the hippocampus is normal, but there are no studies that say the volume of the left hippocampus is larger than the volume of the right hippocampus in a normal people. **Conclusions:** a person with depression should be screened and planned for early treatment. In the field of radiology, psychoradiology plays an important role in the main clinical situation in guiding decisions, especially treatment planning, as well as monitoring the results of care carried out in patients with psychiatric disorders.

Keywords: Hippocampus, MRI, Depression.

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Introductions

The hippocampus is a bilaminar gray matter structure located in the medial temporal lobe of the lateral ventricles and occupies the medial area. In the axial plane, the hippocampus resembles a seahorse shape and curves around the mesencephalon in the axial and sagittal planes [1,2]. Several mechanisms have been implicated in changes in hippocampal structure, including trophic factors such as Brain-Derived Neurotrophic Factor (BDNF), angiogenesis, and neurogenesis [3]. BDNF is a neurotrophin and plays an important role during neurodevelopment. BDNF continues to be expressed at high levels in the adult mammalian brain, particularly in the prefrontal cortex (PFC), hippocampus, amygdala, and hypothalamus, which are involved in the regulation of mood-related behaviors [3,4].

Mature BDNF and ProBDNF trigger opposite pathways. Tropomyosin kinase type B (TrkB), a receptor-coupled tyrosine kinase receptor, acts as a regulator of the mechanism of action of neurotrophins in BDNF signaling. ProBDNF increases apoptosis, induces long-term depression (LTD), reduces dendritic spines, and causes growth crone retraction. Meanwhile, mature BDNF promotes cell survival, neurogenesis, and spinogenesis and increases long-term potentiation (LTP) and neural plasticity (NP) [4]. In an animal model of stress, mice with loss of BDNF expression in specific areas of the forebrain exhibit stress-like behavior, and deletion of BDNF enhances depression-like behavior. TrkB interactions with glucocorticoid receptors were found in signaling pathways in the cytoplasm; glucocorticoids, under certain conditions, can act as TrkB activators; and BDNF increases serine phosphorylation of glucocorticoid receptor [5].

In previous studies, it was shown that HPA axis hyperactivity will trigger the formation of glucocorticoids, which will cause negative feedback, reducing glucocorticoid receptor signaling in the hippocampus [6]. This process will decrease glucocorticoid signaling by the TrkB activator. When the TrkB activator is down, the proBDNF regulator increases and triggers apoptosis, which MRI imaging visualizes as a shrinkage of the hippocampus. In this case report, we obtained an inverted imaging picture based on the neurotrophic depression theory. We found an enlargement of the left hippocampus, which is generally found in normal people but rarely or may never be found. The left hippocampus structure is larger than the right structure. Asymmetrical volume in the hippocampus is normal for normal people, but few studies say the left hippocampus is larger than the right hippocampus.

Case

A 25-year-old female was diagnosed with major depressive disorder six months ago at a general hospital in Malang, Indonesia. The patient felt depressed, had trouble sleeping, and had attempted suicide with a cutting on her hand. A suicide attempt was first made in 2016 but was not taken to psychiatry because she felt she did not need help.

Major Problem

The main complaint of the patient now feels like committing suicide again and depressive mood disorder.

Medical History

The patient has a history of attempted suicide in 2016.

Family History

The patient's sister was diagnosed with depression about 4 months ago, and the patient's family history, her uncle was diagnosed with schizophrenia.

Present Illness and assessment

According to the DSM-V, the patient met the criteria for MDD disorder; there were symptoms of depressed mood (MD) and anhedonia (loss of interest), weight changes, difficulty sleeping (insomnia or hypersomnia), feeling guilty and useless, and attempting to commit suicide [7]. The patient has a total Hamilton Depression Rating Scale (HDRS) with a score of 23. The HDRS has

17 points with a score range of 0-52, with the highest score representing very severe depression. In this study, 17 points had cutoff points as is generally standard: >24 = very severe, 17-23 = moderate, 8-16 = mild, and 0-7 do not have depression [7].

Treatment History

History of treatment with fluoxetine 1x10 mg/day in the first two weeks after being diagnosed 6 months ago, two weeks later after diagnosis, the dose of fluoxetine was increased to 1x20 mg/day due to not improving the treatment and added aripiprazole 1mg/day, with vitamin B1 and trihexyphenidyl. The patient dropped out of medication 4 months ago because the patient said she was feeling well.

Diagnosis

The patient was diagnosed with Major Depressive Disorder (MDD) by a psychiatrist at General Hospital, Malang, Indonesia, 6 months ago.

MRI Protocol and Segmentation Method

MRI of the hippocampus was performed at the power of 3 Tesla magnetic strength (PHILIPS INGENIA 3.0T) with a 32-channel head coil. The volumetric assessment of the patient's hippocampus was processed on sagittal T1-weighted images.

MRI data processing and hippocampal volumetric analysis were performed using the volBrain HIPS software, which provides hippocampus subfield segmentation (v.1.0, http://volbrain.upv.es), a free-access software for analyzing volumes in the hippocampus. VolBrain is an algorithmic automated segmentation technique based on patch-based multiatlas fusion label segmentation technology, with the results shown in Figure 1 [8,9]. In the MRIcroGL software application, where the DICOM file format was changed to NIfTI to clarify the volume of the hippocampus, two asymmetrical images of the hippocampus were seen, where the volume of the left hippocampus was larger than the volume of the right [10,11].

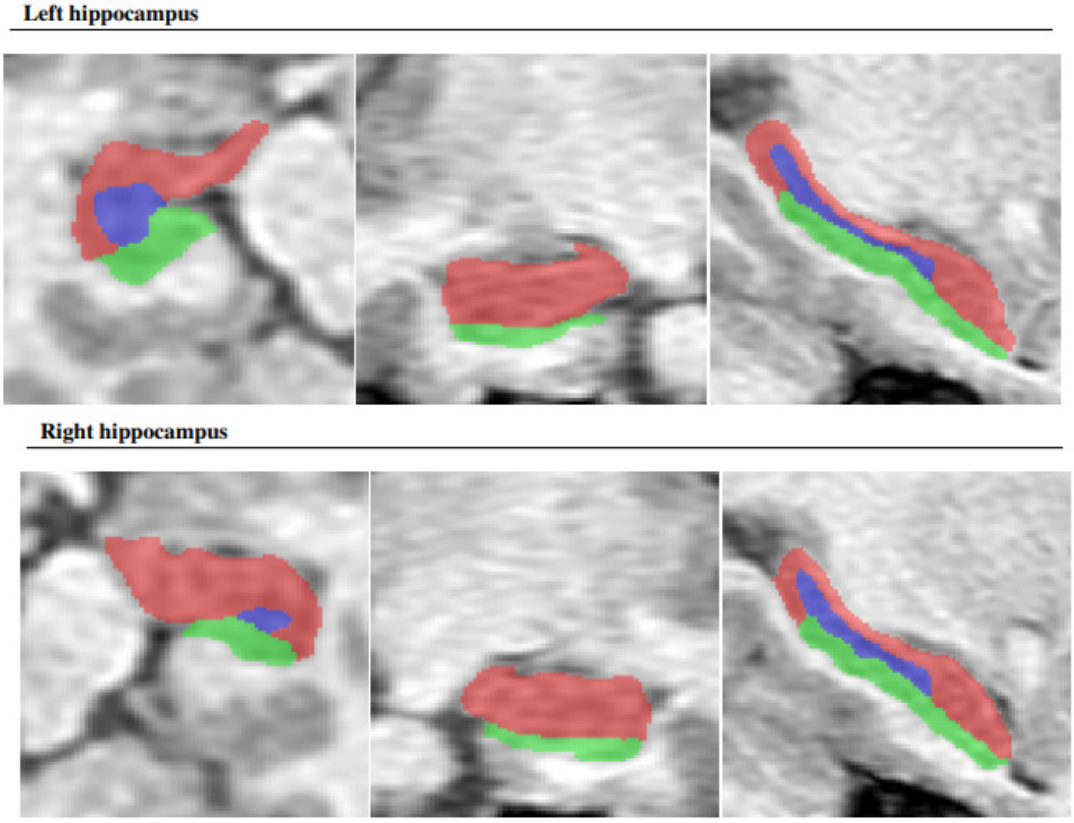


Figure 1. Sequentially left and right hippocampus: (Red), Cornu Ammonis (CA) 1-3, (Blue) CA4-Dentate Gyrus (DG), (Green) Subiculum.

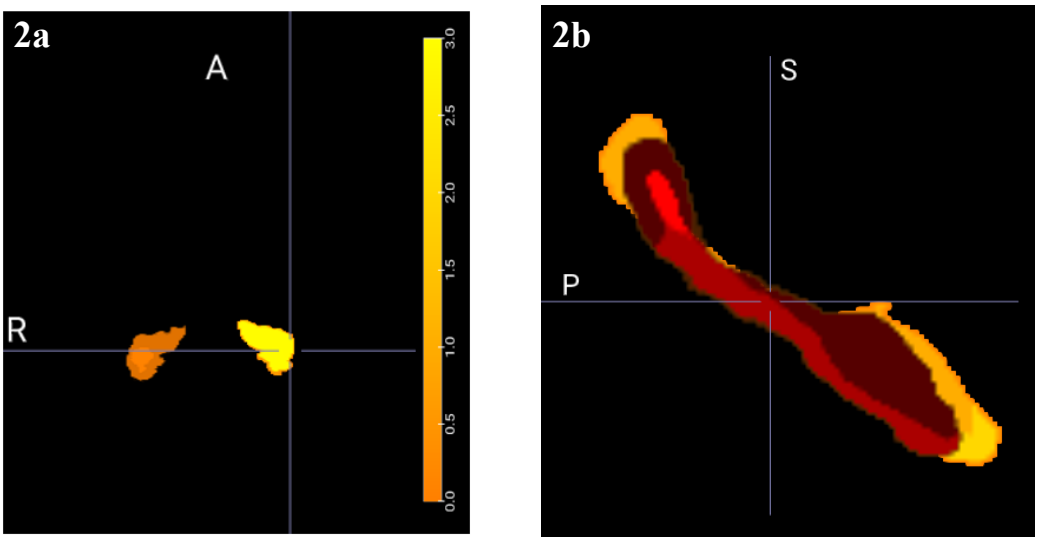


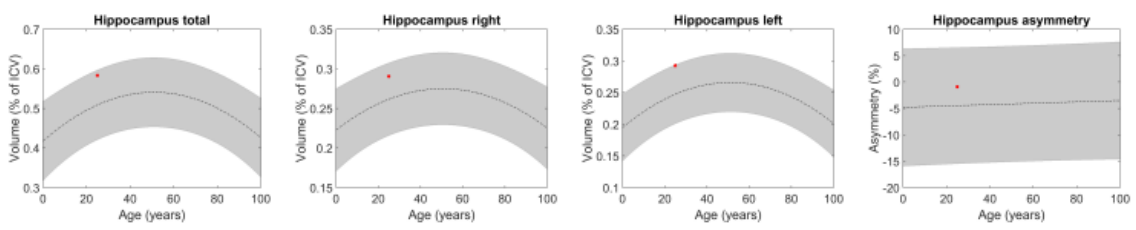
Figure 2a. Left (Yellow) and Right (Orange) Hippocampus in native region.
2b. An image of the left (Orange) and Right (Red) Hippocampus positioned in a sagittal view, The left hippocampus has a larger volume.

Discussion

In this case report, the left hippocampus volume was larger than the right volume, with a history of the patient never exercising or exercising regularly. An increase in hippocampal volume can occur in people who do frequent exercise and can increase the expression of BDNF in the hippocampus [12,13]. In general, the hippocampus can be asymmetrical on both sides and larger on the right side. An enlarged hippocampus is associated with longer-lasting spatial memory [14]. Where according to neurotrophic theory, high BDNF expression will increase Long-Term Potentiation (LTP). Although asymmetry in the hippocampus is normal, but there are no studies that say the volume of the left hippocampus is larger than the volume of the right hippocampus in a normal people. In another study by Özdemir et al., for both gender male and female, the right hippocampal volume was larger than the left volume in healthy people [15,16]. In volumetric calculations with Volbrain application, the left hippocampus in our patient had an above-normal volume in the left hippocampus (Table 1) (Figure 3), allowing this patient to respond well to the given treatment. Crosstalk between BDNF and HPA Axis may contribute to the pathophysiology of psychiatric disorders such as Major Depressive Disorder (MDD), and may be involved in the therapeutic mechanisms of antidepressant medications. In another study on the topic of MDD, patients treated with venlafaxine had increased levels of BDNF and response to treatment, whereas BDNF expression could increase hippocampal volume [6].

Table 1. Hippocampus measurement results using the 3 segment Kulaga-Yoskovitz method with Volbrain software.

Expected volumes



Segmentation protocol: Kulaga-Yoskovitz[2]

Volumes[3]	Total (cm^3/%)	Right (cm^3/%)	Left (cm^3/%)	Asym.(%)[4]
Hippocampus	7.33 (0.5840)	3.65 (0.2908)	3.68 (0.2933)	-0.8565
	[0.42 - 0.59]	[0.21 - 0.31]	[0.20 - 0.29]	[-15.48 - 6.51]
CA1-3	4.56 (0.3632)	2.33 (0.1855)	2.23 (0.1777)	4.3130
	[0.25 - 0.38]	[0.13 - 0.20]	[0.11 - 0.18]	[-25.70 - 6.94]
CA4-DG	0.79 (0.0629)	0.38 (0.0300)	0.41 (0.0329)	-9.2255
	[0.03 - 0.07]	[0.02 - 0.04]	[0.02 - 0.04]	[-30.87 - 38.77]
Subiculum	1.98 (0.1579)	0.94 (0.0752)	1.04 (0.0827)	-9.4098
	[0.11 - 0.17]	[0.05 - 0.08]	[0.06 - 0.09]	[-11.68 - 18.48]

Figure 3. Volume chart and general standard of hippocampal volume by Volbrain software.

Correlation of HPA Axis in depressive disorders with BDNF

Most studies show that early life stress causes permanent changes in the HPA Axis and can lead to the development of anxiety in adults. The most consistent findings in the literature show increased HPA axis activity associated with hypercortisolemia and reduced inhibitory feedback. These findings suggest that this dysregulation of the HPA Axis is due in part to an imbalance between the glucocorticoids (GR). Glucocorticoids regulate BDNF at various levels in the signaling pathway, with the strongest evidence for the effect of glucocorticoids on BDNF mRNA expression [6]. The negative feedback HPA Axis process in people with depression triggers a hyperactivity reaction, so glucocorticoids at blood levels will reduce GR receptor expression, which triggers the opposite TrkB BDNF pathway in the hippocampus, resulting triggering a loop that will increase the expression of proBDNF, which activate the apoptotic process and reduce the volume of the hippocampus as shown in **Figure 4.**

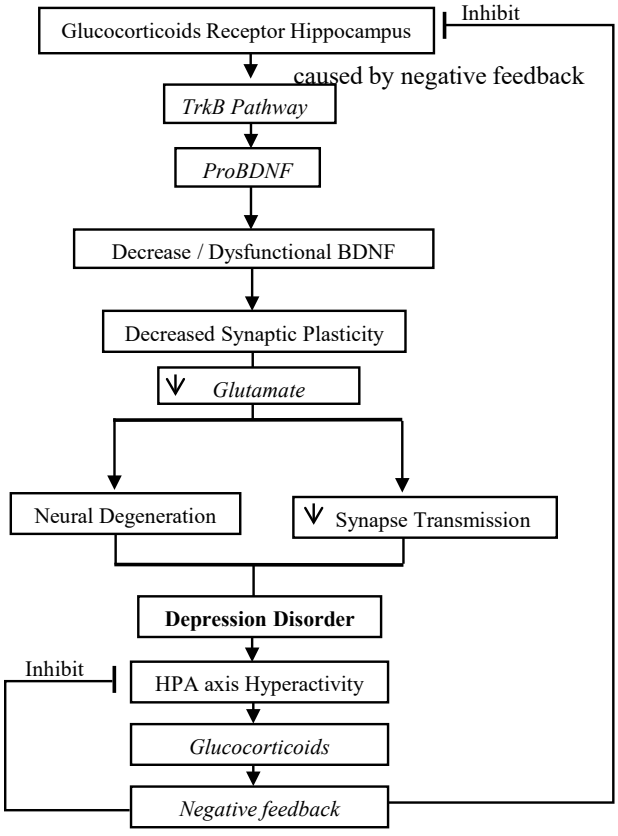


Figure 4. Conceptual Framework of Looping Negative Feedback.

Previous study explained, dysfunction or decrease in BDNF causes damage to synaptic plasticity, decreased excitability of neurons and glutamate; and eventually leads to depression [17]. If we connect depressive disorders, BDNF/ProBDNF expression, Neural Plasticity, they have a relationship that will continue to occur or what is called Looping Negative Feedback as shown in (Figure 4) it will cause atrophy of the hippocampus.

In this case report, a female patient was diagnosed with MDD 6 months ago and had a history of attempted suicide in 2016, something unusual were found, because there is an enlargement of the left hippocampus when compared to the right. In this case report, we have two hypotheses, the first is that the treatment given has been successful in increasing the expression of BDNF and has a picture of increasing the volume of the hippocampus even though the patient had stopped taking the drugs 4 months. Second thought, it could be that the right patient's hippocampus is actually bigger than the left one before, but it was not detected because the patient already had a history of trauma and attempted suicide in 2016 so that it seems the patient's left hippocampus looks larger where the right hippocampus has experienced atrophy earlier [14,18]. Previous studies explained, regarding atrophy of the hippocampus, hippocampus atrophy were found in a case study of MDD where the patient's symptoms are the first episode of a depressive disorder [19, 20]. In this case, we propose the potential effectiveness and feasibility of radiology as a support, as well as follow-up treatment in patients with psychiatric disorders.

Conclusions

We report a case where a person with depression should be screened and planned for early treatment. In the field of radiology, psychoradiology plays an important role in the main clinical situation in guiding decisions, especially treatment planning, as well as monitoring the results of care carried out in patients with psychiatric disorders.

Learning Points

(1) The field of psychoradiology has an important role in supporting early diagnosis to the therapeutic stage especially in psychology, but this field is still too new and unfamiliar on medical science.

(2) Although the hippocampal volume is normal in asymmetrical shape, we must carefully consider whether there are abnormalities, especially behavioral and emotional changes.

(3) BDNF is a factor that affects the plasticity of neurons and requires future research in terms of advancing the formation of neurogenesis and anti-aging.

(4) MRI is a non-invasive imaging technique that can evaluate the volume of the hippocampus and can monitoring therapy in psychiatry.

Data Availability

Data are available on request.

Conflict of Interests

There is no conflict of interest regarding the publication of this article.

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