



Profile of Hippocampal Volume of Adults in North Sumatera

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Abstract

BACKGROUND: Hippocampus is a brain region that includes in the limbic lobe. It is formed by two groups of neurons that look such as letter C, which were facing each other – dentate gyrus and Ammon's horn and played an essential role in the development of memory.

AIM: The objective of this study is to find the volume of the right and left hippocampal volume and the measurement of the total volume. To the best of our knowledge, this is the first study in Indonesia that measures the hippocampal volume of healthy adults.

METHODS: We collected 54 subjects of healthy adults in Medan Indonesia, with the inclusion criteria: Age 15–40 years, cooperative and willing to be interviewed, and did not have a family history of mental disorders. Exclusion criteria for the control group were excluded from the study: Having a history of previous mental disorders and a general medical condition that affected brain structure, and obesity. We used MINI ICD-10 structured clinical interview to rule out the mental disorders. Hippocampal measurement was done by manual segmentation using AnalyzePro software that was developed by Mayo Clinic and followed the protocol of manual segmentation of hippocampal measurement from the Alzheimer's Disease Neuroimaging Initiative: Magnetic resonance imaging methods.

RESULTS: We found that the total hippocampal volume was 3979.77 ± 678.51 mm³.

CONCLUSION: Our findings of hippocampal volume were smaller than other Asian people. Few conditions had been thought related to it, that is, chronic stress exposure inducing prolonged hypothalamic-pituitary-adrenal axis activation that leads to loss of hippocampal neurons and neural level conditions resulting from gene-environment interaction. This smaller hippocampal volume can also predict verbal memory function in the future.

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Introduction

Hippocampus is a part of the brain that belongs to the limbic lobe. This part is folded in the temporal and dorsal lobes of the important cortical structure of the rhinal sulcus. Hippocampus is formed from two groups of nerves that look like the letter C, which was facing each other– dentate gyrus and Ammon's horn. Ammon's horn has four regions, namely, cornu ammonis (CA) 1, CA2, CA3, and CA4. Hippocampus has a key role in the development of memory. The volume of the hippocampus is found to decrease in psychiatric disorders [1]. Circuits formed by the hippocampus, fornix, mammary bodies, mammothalamic tracts, anterior thalamic nuclei, cingulate gyrus, and projecting back into the hippocampus form the Papez circuit. In 1937, Papez explained that this circuit was the substance of "a harmonious mechanism functioning at the centre of emotions" [2]. Magnetic resonance imaging (MRI) is a non-invasive action and an essential component for the study related to the brain [3]. Since the early 1990s, a gradient-recalled echo sequence has been developed in three dimensions. This technique is called the Magnetization-Prepared Rapid Gradient Echo Imaging (MP-RAGE) sequence that

perfectly demonstrates T1-weighted contrast with the very thin imaging portions [4]. This study was conducted to determine the hippocampal volume of healthy adults in Medan, North Sumatra, Indonesia, because the study on hippocampal volume in healthy adults in Indonesia has never been done.

Methods

Study subject

This study was a cross-sectional analytic study, and an MRI examination was carried out at Siloam Medan Hospital, which had a Phillips Achieva 1.5T MRI machine. Fifty-four subjects were collected within 4 months, with inclusion criteria; aged 15–40 years, cooperative, and willing to be interviewed to rule out a history of mental disorders using the MINI International Neuropsychiatric Interview for International Classification of Disease and Related Health problems 10th edition, and did not have a history of general medical conditions and obesity.

MRI test

Subsequent examinations were carried out by accompanying the subjects to do an MRI test at the hospital to assess the condition of the brain structure, which was then interpreted by a radiology specialist (A.R). The recording of brain structure was recorded by measuring values in millimetres. The same image and sequences which were used for the subjects were obtained through a 1.5 T MRI machine using T1-weighted coronal, sagittal, and axial pieces and 3-dimensional MP-RAGE sequences. The AnalyzePro software [5] was used to process the imaging result.

Manual tracing for determining hippocampal volume

Manual tracing was done by M.M.A. using AnalyzePro software and accompanied by A.R. AnalyzePro, which is a software for visualization, manipulation, and measurement of leading biomedical imaging. The software had been carefully designed to allow the exploration of biomedical imaging data. Integrated modules can be found in the software for multi-dimensional display, image processing, segmentation, measurement, and registration of biomedical image modalities. AnalyzePro was developed by the Biomedical Imaging Resource at the Mayo Clinic, which is the biomedical imaging research facility [5].

Before segmentation with manual tracing was carried out, MRI images were aligned in three dimensions with the AC-PC axis to standardise differences in the position of the head when the image was taken [5], [6]. The limits of the hippocampus were defined by manual tracing using the Alzheimer's Disease Neuroimaging Initiative method; it was when a rostral piece was visible in the coronal section to the hippocampal tissue below the amygdala, and by checking it through sagittal and axial sections. The first tissue that could be detected was the alveus in three dimensions, a layer of white matter that covers the grey matter part of the hippocampal head. Meanwhile, the caudal part of the hippocampus was when a solid grey matter mass was visible inferomedially, leading to trigone from the lateral ventricle [5], [7].

Results

From this study, 54 subjects were collected, most of the subjects were male, 30 (60.29%), the left hippocampal volume that was larger than the right, $2014.55 \pm 337.04 \text{ mm}^3$, and the total volume of the hippocampal was $3979.77 \pm 678.51 \text{ mm}^3$.

Table 1: Hippocampal profile

Normal Adults	n = 54
Sex	
Male	30 (62.96%)
Female	24 (37.04%)
Age (years)	29.38 ± 5.75
Hippocampal volume	
Right	$1965.22 \pm 393.40 \text{ mm}^3$
Left	$2014.55 \pm 337.04 \text{ mm}^3$
Total	$3979.77 \pm 678.51 \text{ mm}^3$

The complete results of this study are shown in Table 1 below, and the example of the hippocampal segmentation results of the AnalyzePro software is shown in Figure 1.

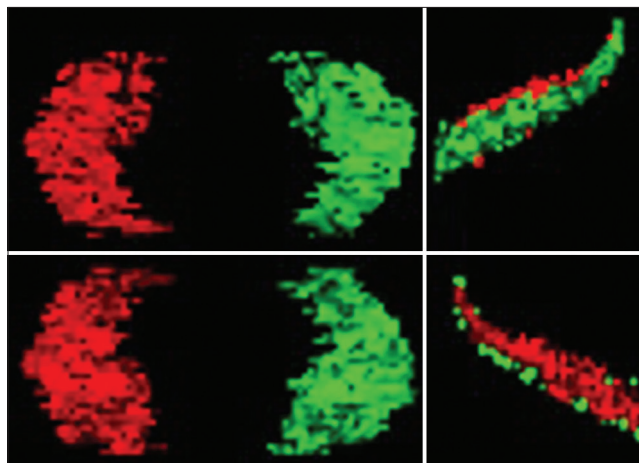


Figure 1: The example of one segmentation of a healthy adult hippocampal using AnalyzePro software

Discussion

Hippocampus is an essential part of the limbic structure [8], has a significant role in memory, and is vulnerable to increasing age [9]. In contrast to the previous studies, this study found that the volume of the left hippocampus was larger than the right hippocampus. The asymmetry of the hippocampal volume was due to the strength of the magnetic field, which was an essential moderator for this [10]. The total hippocampal volume found in this study was $3979.77 \pm 678.51 \text{ mm}^3$, this volume was more significant than the normal hippocampal volume in the United Kingdom that was $3863.94 \pm 411.56 \text{ mm}^3$ [11]; yet, it was smaller than the results reported by Honeycutt and Smith which was $5860 \pm 667 \text{ mm}^3$ [12], by Ismail *et al.* [13] in Egypt for the age group of 20–39 years that was $5641 \pm 449 \text{ mm}^3$, Mohandas *et al.* in India that found 4938 mm^3 for men and 4585 mm^3 for women [14], and Embong *et al.* in Malaysia that was $6690 \pm 660 \text{ mm}^3$ [15].

According to Nobis *et al.* [11], several things affect the hippocampal volume; they are age, hypertension, body mass index, education, and smoking status. In this study, age, hypertension, and body mass index were controlled; yet, the level of education and

smoking status was not asked. Prolonged exposure to chronic stress will activate the hypothalamic-pituitary-adrenal axis so that it will result in loss of hippocampal neurons and reduce its volume [16]. Hippocampal volume decreased can be a predictor for the decrease of verbal memory [17] and memory loss; yet, the statement of the greater hippocampal volume and the greater memory performance is also not supported by the results of the previous studies [18]. One thing that is needed to be noted is the variety of anatomical boundary determination used in the previous studies resulting in the differences in the volume of hippocampus produced [12].

Although each subject did not undergo a medical examination, previous medical history obtained during interviews with the subjects did not have any effect on the hippocampal volume report. The limitation of this study is that the subjects were healthy adults. Thus, this condition makes it difficult to generalise the results in patients with brain disease; yet, this study provides data of software that is available to measure hippocampal volume manually. Second, our study was done in North Sumatera and only represented the people that lived in it. In the future, heterogeneous subjects are needed from all of the areas in Indonesia so that they can serve as a database for the people of Indonesia.

Conclusion

Hippocampus is an essential part of the brain, and our study showed that the hippocampal volume of the people in North Sumatera is smaller compared to other parts of Asia, that is, India and Malaysia. This study is expected to have a positive impact since it can serve as a reference for future studies. It is expected that in the future, there will be further studies that use subjects with more diverse age variations, education level, smoking status, and use methods longitudinally.

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