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Elmukashfi's Protocol for Hippocampal Volumetry; 2022

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Abstract

There is a relation between many neuropsychiatric disorders and reduction in hippocampal volume. So, a protocol for researches in this area is highly needed. Study aimed to design and validate a protocol for hippocampal volumetry to facilitate manual segmentation of hippocampus region. It was a comparative study, carried at Diagnostic Imaging Clinic at Elmoalem Hospital; where 65 Sudanese individuals were surveyed in period (December 2021 –April 2022). Data was collected through master sheet for sociodemographic information, 3D magnetic resonance imaging for measuring hippocampus volume, and imaging acquisition. Software for measurements 3D slicer version (4.11) was used, where hippocampus is mapped by delineating its boundaries. Protocol was composed of mapping hippocampus.

Mapping hippocampus: identify sagittal view, lateral fissure, temporal horn of lateral ventricle, hippocampus region, temporal and occipital horn of lateral ventricle, choroid plexus of lateral ventricle. Among these slides hippocampus has been delineated.

Statistical Computing: Data was analyzed using SPSS version 23. Reliability test was performed by obtaining Cronbach's alpha. Protocol considered reliable if value of Cronbach's alpha is close to (+1). P-value ≤ 0.05 was considered statistically significant.

Validation of Protocol: Calculation of hippocampus volume is valid as total volume correlates strongly with both right and left measurements (correlation coefficient 0.76 and 0.87 respectively and p-value <0.001).

Reliability test was 0.85; which was close to (+1).

Conclusion and recommendation: This protocol represents a valid, reliable, and applicable method for measuring hippocampal volume. It could be a step to develop an international standard protocol for hippocampal volumetry.

Keywords: Elmukashfi's Protocol; Hippocampal Volumetry; Elmoalem Hospital; Structural MRI; Sudan.

1. Introduction

One of the most investigated part of the brain is the hippocampus region**.** It is an important part of the brain located medially within the temporal lobe, its associated with learning, memory, perception, and regulation of emotional behavior. Reduction in hippocampal volume is associated with many neuropsychiatric disorders such as depression, schizophrenia, epilepsy, Alzheimer's disease, dementia, hippocampal sclerosis, mesial temporal epilepsy, sleep disorders and PTSD **[1-23].**

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Magnetic resonance imaging (MRI) has become the best tool for measurement of the hippocampus as well as the gold standard method for the examination of macroscopic neuroanatomy in vivo, due to excellent levels of image resolution and between tissue contrast. A huge variety of software packages are available for viewing and appraising MR images, for reformatting the images in three dimensions so as to obtain sections with a particular orientation through the body and for making both simple and more sophisticated measurements of regions of interest, compartments and individual structures **[7,24,25].**

Hippocampal volumetry can be achieved by manual, semiautomatic, and fully automatic computer segmentation of sequential magnetic resonance images. Manual segmentation method was introduced in the late 1980s, and its precision was validated with a phantom. The advent of thin-slice three-dimensional (3-D) MRI with slice thicknesses of 1 to 2 mm and advanced measurement techniques for brain volumetry allow the detection of mild hippocampal atrophy and the prediction of Alzheimer disease, mild cognitive impairment, and epilepsy. Manual segmentation method is the gold standard method for measurement of hippocampal volume typically in the coronal view, it used by 90% of researchers; because it provides the accurate delineation of the boundaries of the hippocampus, but it needs expert training and reference to anatomical landmarks, also it tedious, resource intensive, time-consuming, and prone to human error especially in large set of data, unlike the automated methods which has high reproducibility and accuracy **[1,2,4,5,12,16,18,25-28].**

There are no clear protocols for hippocampal volumetry that all researchers can apply. This due to the great differences between studies; usually due to the studies inclusion or exclusion of different parts of the HC, i.e., the head, body and tail, also it can be due to magnetic resonance imaging (MRI) parameters, delineation of structures, and methods of normalization for brain volume. All of these factors may affect volumetric results **[1,8,25,26].**

The borders of the hippocampus are outlined differently by researchers. The anterior border is considered in some studies as the amygdaloid nucleus with a transitional cortex between the amygdalar cortical nucleus and the hippocampus, while in other studies it is considered as the temporal horn of the lateral ventricle. There is almost consensus on the temporal horn of the lateral ventricle as a mark for the lateral border. The medial border is defined as the ambient cistern anteriorly and the transverse fissure posteriorly, while sulcus hippocampi is mapped as a different medial border, and also the trigone of the lateral ventricle is considered as a third different border for the hippocampal tail, the quadrigeminal cistern as the medial border of the body and uncal recess as the medial border of the hippocampal head. The superior border is considered as the temporal horn and fimbria. While a vertical line from the medial end of the trigone of the lateral ventricle inferiorly to the parahippocampal gyrus, and a horizontal line from the superior border of the quadrigeminal cistern to the trigone of the lateral ventricle including the fimbria within the hippocampal volume. The inferior border is considered to be the white matter separating it from the parahippocampal gyrus. Another different landmark is the uncal sulcus anteriorly and parahippocampal gyrus posteriorly. When the uncal sulcus is not visible the medial part of the subiculum is used to be considered. The posterior boundary is defined as the first appearance of the ovoid mass of gray matter inferiomedial to the trigone of the lateral ventricle and as the section immediately before the most posterior part of the hippocampal tail **[29].** As the Harmonized Protocol Project **[30]**, this study aimed to design and validate a protocol for hippocampal volumetry to facilitate the manual segmentation of the hippocampus region for the researchers.

2. Material and methods

2.1. Study design

It was an observational comparative cross-sectional facility base study.

2.2. Study area

Diagnostic Imaging Clinic at Elmoalem Hospital; Khartoum; Sudan.

2.3. Study population

They were Sudanese individuals attending the Diagnostic Imaging Clinic at Elmoalem Hospital in the period (December 2021 –April 2022).

2.4. Sample size

Total coverage of those attending during this period.

2.5. Data collection and management:

2.5.1. Master sheet

Composed of socio-demographic data, was used to gather such information from the records of the patients (secondary data).

2.5.2. Measuring of hippocampus volume using 3D magnetic resonance imaging.

2.5.3. Imaging acquisition

MRI scanner is Toshiba medical system Ventage Elan 1.5 Tesla, 3D MRI scanning slice thickness of 2mm, in axial view.

2.5.4. Software for measurements 3D slicer version (4.11)

Program downloaded from website: (www.slicer.org), the National Institutes of Health (NIH) of the USA have been the major contributor, through a variety of competitive grants and contracts.

2.6. Protocol for hippocampal measurement

Measurement of the hippocampus is achieved by manual segmentation method using 3D slicer version (4.11), in which the hippocampus is mapped by delineating its boundaries.

2.6.1. Mapping of the hippocampus

Define the sagittal view, then start from the most lateral slide, define the lateral fissure which appears as the longest horizontal groove starting from the rostral aspect of the brain and continues to a variable distance. Move medially till a black shadow appears in the brain tissue below the lateral fissure; this is the temporal horn of the lateral ventricle. Move medially, the hippocampus region will appear as grey shadow. Move medially, the temporal and occipital horn of the lateral ventricle becomes identified as black shadow and the hippocampus region as grey shadow in between. The choroid plexus of the lateral ventricle will appear as small grey line connected to the hippocampus within the occipital horn. Among these slides the hippocampus has been delineated.

2.7. Statistical Computing:

2.7.1. Validation of Protocol

The calculation of hippocampus volume is valid as total volume correlates strongly with both right and left measurements

2.7.2. Reliability of the protocol

Reliability test is performed by obtaining the Cronbach's alpha in SPSS 28. The protocol will be considered reliable if the value of the Cronbach's alpha is close to (+1).

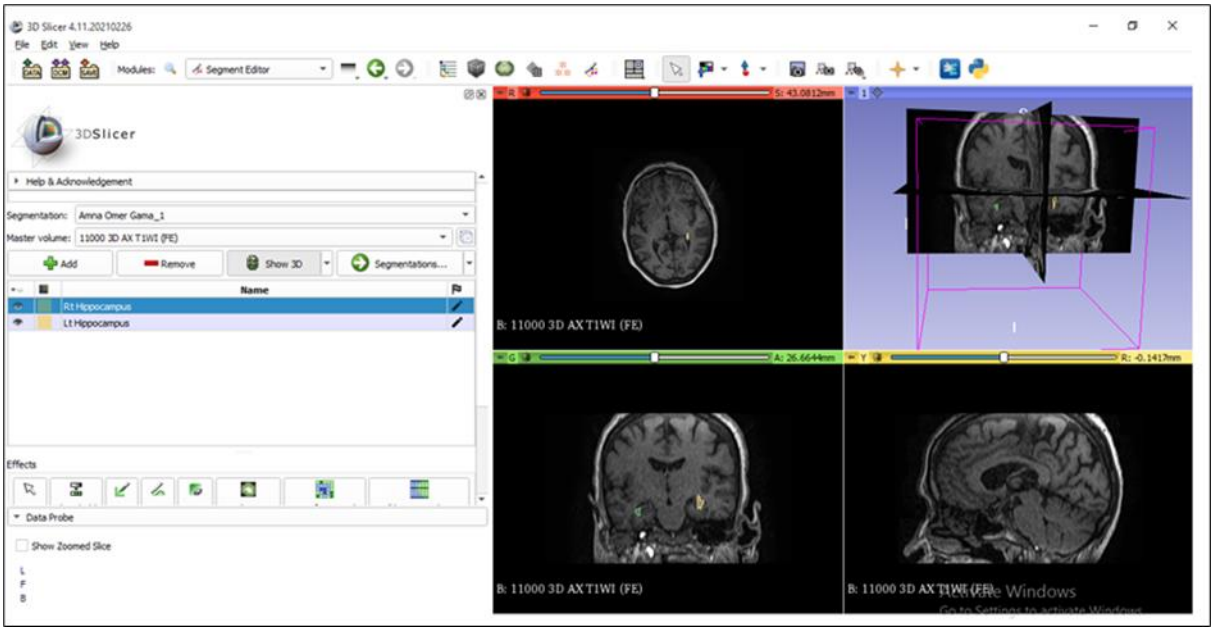

Figure 1 Right left hippocampal regions in 3D view; source; 3Dslicer version (4.11); Elmukashifi's protocol for Hippocampal voluntary among Sudanese attending Elmoalem hospital; Structural MRI; Sudan; 2022

2.8. Data management and analysis

Data was processed and analyzed using SPSS version 23. Descriptive data was done. Cross tabulation and Chi-square test were performed. P-value equal or less than 0.05 was considered statistically significant.

2.9. Ethical consideration

It was obtained from the Medical Postgraduate Studies Board; Faculty of Medicine; University of Gezira and from the Diagnostic Imaging Clinic at Elmoalem Hospital.

Data was kept secure and confidential in an efficient way that related to the study protocol and standards of good clinical practice.

3. Results

Sixty five respondents were surveyed. Forty of them were female. Without gender discrimination, the total hippocampal volume was 2118.7370 ± 1081.61581 mm^3 and the Rt hippocampal volume was larger than that of the Lt one. The male total hippocampal volume was 6315.13 ± 1348.64 mm^3 while that of the female was 3500.89 ± 765.76075 mm^3. The male's hippocampus volume was larger than that of the female. In the male group, the Lt hippocampal volume was larger than the Rt one; while it was vice versa for the female group. There was statistical relationship between the gender and the hippocampal volume, (*P-value* = 0.001); while there it was vice versa for gender and age group (*P-value* = 0.994). The total volume correlates strongly with both right and left measurements (correlation coefficient 0.76 and 0.87 respectively and p-value <0.001). This indicates the validity of this protocol. The reliability test of this protocol was found to be 0.85. So, it was considered a reliable method for hippocampal volumetry that facilitating manual segmentation of hippocampus region, as the value of the Cronbach's alpha was close to (+1).

4. Discussion

Magnetic resonance imaging (MRI) has become the best tool for measurement of the hippocampus. Although there are no clear protocols for hippocampal volumetry that researchers can apply, this due to the great differences between studies; usually due to the studies inclusion or exclusion of different parts of the HC, i.e., the head, body and tail, also it can be due to magnetic resonance imaging (MRI) parameters, delineation of structures, and methods of normalization for brain volume. All of these factors may affect volumetric results [1,7,8,24,25,26].

This protocol was designed to facilitate the measurement of hippocampal volume by researchers. This protocol used manual segmentation for the volumetry which is considered as the gold standard method for measurement of hippocampal volume, because it allows the accurate delineation of the boundaries of the hippocampus [1,4,5,30], this similar to many reports [2,5,6, 8,11,14,17,18,25, 27, 29,30].

Sagittal view was the standard view for hippocampal volumetry in this protocol, this consistent with many international reports [3,10,11,26], this could be due to easy differentiation between the hippocampus and the amygdala on sagittal view [5].

3D Slicer program was used in this protocol as a program of choice for hippocampal volumetry, this is similar to other studies [3,29]. It may be due to easy approach of the program.

The approach through this study showed a reliability test of 0.85 which was considered a good result, unlike many international studies [25,29,30]. This may be due to the sample size of the studies and the segmentation methods.

There was strong correlation of the total hippocampal volume with both right and left measurements (correlation coefficient 0.76 and 0.87 respectively and p-value <0.001); indicating the validity of our protocol. The value of the Cronbach's alpha was close to (+1); which was found to be 0.85; indicating that this protocol was a reliable method for hippocampal volumetry that facilitating manual segmentation of hippocampus region.

N.B.: I named this protocol after my family's name: (Elmukashfi's Protocol for hippocampal volumetry).

5. Conclusion

This protocol represented a valid, reliable, clear, easy and applicable method that facilitate the measurement of hippocampal volume. I hope it could be a step to develop an international standard protocol for hippocampal volumetry.

Compliance with ethical standards

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Statement of ethical approval

Ethical approval was obtained from the concerned bodies.

Statement of informed consent

Informed consent was obtained from the Director of the Diagnostic Center at Elmoalem Hospital.

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