

RAPID INDIRECT HIPPO- CAMPAL VOLUMETRY USING THE XYZ GEO METHOD: A USEFUL TOOL IN THE DIAGNO- SIS OF COGNITIVE IM- PAIRMENT

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Abstract: Goals: to demonstrate the validity of the XYZ Geo Method of rapid indirect volumetry^{37,38,39} using the simplified geometric formula of the XYZ/1910 ellipsoid, to obtain a volume of the anterior part of the hippocampus (Ammon's Horn + Body = AA) or the complete Hippocampus, including the tail (AA + Tail = Complete Hippocampus = HarP = Harmonized Protocol²⁴), very close to the real volume determined by the voxel method (planimetry). **Material and Method:** prospective study, which took place between January 2020 and July 2022, of 100 Dominican adults, divided into a control group of 60 patients with normal cognition divided into 3 age groups (20-40, 41 to 60 and 61 to 80 years). and a case group of 40 patients complaining of cognitive problems (aged 41 to 60 and 61 to 80). The Folstein Mini Mental State Examination (MMSE) adapted to Latino patients was administered.¹⁵. All benefited from a 1.5 Tesla MRI with 1-1.5 mm slices for three-dimensional reconstruction including non-contrast T1, FLAIR, T2 and TOF sequences. The Principal Investigator (PI) performs real volumetry of the Anterior and Complete Hippocampus using voxels (planimetry), processing these Magnetic Resonance images on the Elekta Workstation Gamma Plan 10 platform of the Dominican Gamma Knife Center of CEDIMAT in the Plaza de la Salud de Santo Sunday, Dominican Republic. Next, the PI performs the indirect volumetry of these structures by applying the simplified formula of the Ellipsoid, following the guidelines of the XYZ Geo Method for rapid indirect volumetry of intracranial structures³⁹, determining their largest diameters Axial (X), Sagittal (Y) and Vertical (Z) on the aforementioned Platform. For each of these patients, blindly with respect to the PI results, the Research Assistants (RA), using the Magnetic Resonance CD in which the RadiAnt DICOM Viewer software

with capacity for millimeter measurement is encrypted, determine rapid indirect volumetry of the Anterior Hippocampus (AA) and complete Hippocampus (HarP) applying the aforementioned methodology. The data collected was processed using measures of central tendency and dispersion in the Microsoft Excel 2016 platform. **Results:** The indirect volumetry of the hippocampi studied carried out by the PI using the simplified geometric formula of the ellipsoid had an average approximation of 101.7% with respect to the real volume determined by voxels. The measurement carried out by the RAs approached 99.6% of the real volume of the hippocampi studied. The average time to perform the actual volumetry of the Anterior Hippocampus (AA) by the PI was more than 11 minutes, while using the formula for rapid indirect volumetry the hippocampal volume could be calculated in less than a minute. **Conclusion:** indirect volumetry of the hippocampus applying the guidelines of the XYZ Geo Method³⁹ and using the simplified geometric formula of the ellipsoid, it is a reliable and rapid alternative to determine the health and integrity of this important anatomical marker of cognitive and seizure health, even if it is used by non-neurospecialist doctors.

Keywords: Direct Volumetry, Indirect Volumetry, Hippocampus

INTRODUCTION

To know the volume of the hippocampus is useful for managing neurological pathologies such as dementia and temporal lobe epilepsy, which manifest clinically with cognitive impairment or seizures of special presentation. Currently there are several methods that allow calculating the volume of the hippocampus through MRI Images, among which the following stand out: Manual Voxels Volumetric Method (MVVM) using

a stereotactic platform for high-definition image processing.^{1,2,3,4,5,6,24} and Automated Software (AS)^{18, 19, 20, 21,22}. Each of these methods has advantages and disadvantages, MVVM requires time and experience of the observer, while AS requires obtaining expensive licenses. Result of research funded by a program of the Dominican Ministry of Sciences and Technology (FONDOCYT) recently published^{38,39}, the usefulness of the XYZ Geo Method was demonstrated, in which the applying the corresponding geometric formula, achieving in a few seconds a theoretical volume with a 93% approximation to the real volume of the intracranial lesion studied, without the need to paint it section by section as is done with the voxel method (planimetry).^{38,39}.

If we extrapolate this concept to the volumetry of the hippocampus taking into account that both its most voluminous anterior portion (Ammon's Horn + Body = AA) and if we add the tail (AA + Tail = Total Hippocampus = HarP= Harmonized Protocol²⁴) they have an ellipsoidal shape, we can infer that by applying the simplified volumetric formula of this geometric figure: XYZ/1910, we would obtain approximations to the real hippocampal volume equal to 100 + 10%. In world literature, there have been contributions from multiple countries on the particular volumetry of the hippocampus of their inhabitants.^{1,2,3,4,8,9}, to have an idea of what the expected normal and/or pathological volume is. After reviewing the corresponding literature, we confirmed that in our country, the Dominican Republic, nothing has been published in this regard. In daily clinical practice, an important concern of neurologists, neuroradiologists, neurosurgeons, psychiatrists and psychologists is to know the anatomical integrity of the hippocampus and particularly its volumetry, to determine whether or not there is atrophy, sclerosis or

dysembryoplasia. Manual volumetry using the voxel method (planimetry) can only be performed by very well-trained individuals who have stereotactic image processing platforms at their service.^{1,2,3,4,5,6,24}. The other option is to have Automated Software (AS) for volumetry, which is expensive and not widely available in our environment.^{18, 19, 20, 21,22}. To resolve these situations, it is necessary to have a simplified and reliable method of hippocampal volumetric calculation, which can be used by the specialist in Neuroradiology, Neurology, Neurosurgery, Neuropsychology, Psychiatry, or by the resident in training of these disciplines, on the diagnostic platform in which you are studying the image, whether in the emergency room, in your office or at the patient's side, and have an idea very close to reality of the volume of the most prominent anterior portion of the Hippocampus (Ammon's Horn + Body = AA) and even including its tail (AA + Tail = Full Hippocampus = HarP), which both have an ellipsoidal shape. We call the entire Hippocampus HarP (abbreviation for Harmonized Protocol) in this work, to pay tribute to the enormous effort deployed by the researchers of the "Working Group on the Harmonized Protocol for Manual Hippocampal Segmentation."²⁴ that served as a guide and inspiration for this research contribution. In it, we validate our basic hypothesis that by applying the XYZ Geo method³⁹, using the simplified geometric formula of the ellipsoid, we can satisfy the sometimes urgent and pressing need for rapid reliable hippocampal volumetry that frequently arises in any subspecialty treating cognitive problems or temporal lobe epilepsy.

MATERIAL AND METHODS

This prospective study was carried out at the Dominican Gamma Knife Center belonging to the Center for Diagnostic, Advanced Medicine and Telemedicine (CEDIMAT), located in the Plaza de la Salud in the city of Santo Domingo, Dominican Republic.

A total of 100 participants were recruited, distributed in 3 age groups made up of cognitively normal individuals (20 to 40, 41 to 60, 61 to 80 years) who attend outpatient neurology or neurosurgery consultations for any reason, except for cognitive dysfunction. All groups were made up of 20 individuals each. They were compared with another group made up of 40 patients with cognitive problems, aged between 41-60 and 61-80 years, periods of life in which dementia is usually detected. Before being included in the research, each patient was asked to read, understand, accept and sign an informed consent, which was signed by a responsible family member or caregiver in case the patient suffered from severe cognitive impairment. All patients included in the study underwent a 1.5 Tesla MRI, 1 to 1.5 mm slice thickness, with the capacity for three-dimensional reconstruction; obtaining in all cases the sequences: T1 without contrast, T2, FLAIR and Time Of Flight (TOF). The PI calculated the volume of the right and left hippocampi of each participant by obtaining manual volumetry using voxels on the stereotactic high-definition medical image processing platform: "Elekta Workstation Gamma Plan 10" (Sweden) of the Dominican Gamma Knife Center. The diameters X (horizontal axis), Y (anteroposterior axis) and Z (vertical axis) necessary for the implementation of the Method were then calculated by the PI, on the same platform: XYZ Geo³⁹ using the simplified formula of the ellipsoid, which is the geometric figure that best corresponds both to the shape of the anterior portion of the Hippocampus

(Ammon's Horn + Body = AA) and adding the tail (AA + Tail = Complete Hippocampus =HarP²⁴), (See Images 1, 2). The RAs, blinded with respect to the PI, performed indirect volumetry using the MRI CD containing the RadiAnt DICOM Viewer software and an ordinary Laptop (Image 3). Folstein's Mini Mental State Examination was administered to all patients. (MMSE)¹⁵ adapted to Latino patients, which is the most used scale for the basic diagnosis of cognitive problems. During the development of the Research we decided to integrate other investigative elements that seemed important to us to enrich the results: A-apply direct and indirect volumetry not only to the anterior part of the Hippocampus (Ammon's Horn + Body = AA), but to the entire hippocampal extension (AA + Tail =HarP²⁴), in all patients, both by the PI and the RA, to determine its relevance in the diagnosis of cognitive impairment. B-Chronometry of all volumetry processes to have an objective idea of the time savings that indirect volumetry implies over real volumetry. C-Take advantage of the fact that 10 of the 100 patients had undergone Gadolinium injection to determine the participation of the choroid plexuses and other vascular structures in the real volumetry of the hippocampi measured without contrast, data that we did not find in the literature in this regard. D-Basic physical examination and essential laboratory tests for determining biological markers of vascular or metabolic disease, which are directly related to vascular health and therefore the hippocampus, cognition³ or the comicality. All data collected was processed using measures of central tendency and dispersion in the Microsoft Excel 2016 platform.

RESULTS

We confirmed the reliability of the XYZ Geo method of rapid indirect volumetry using the simplified ellipsoid formula applied to the anterior (AA) and complete hippocampus (HarP) proposed in this research. The average volume of the 200 left Anterior Hippocampi (AA), after the Principal Investigator (PI) had painted its limits on the Gamma Plan X stereotactic platform of the Dominican Gamma Knife Center (planimetry), using the theoretical XYZ Geo method and the Manual, was 2.85 and 2.84 cc respectively, for an average approach of 100.29%. After carrying out the same process, the average volume of the Right Anterior Hippocampi (AA), using the XYZ GEO method and the Manual was 3.03 and 3.02cc respectively, for an average approximation of 100.75%.

The theoretical and manual measurements of the entire hippocampus (HarP) followed the same trend on both sides (See Table Number: 2).

The measurements made by the PI before painting the limits of the left AA had an average of 2.66cc for the Theoretical method and 2.84cc for the Manual (93.66% approximation). On the right: Theoretical Method 2.77cc, Manual Method 3.02cc. Average approach 91.72% Here also the theoretical and manual measurements of the entire hippocampus (HarP), followed the same trend on both sides (See Table 4).

The most significant result obtained in the research is the one seen in Table 3, which collects the results of Theoretical Volumetrics through the Application of the XYZ Geo Method by the Research Assistants (RA) working with the CDs where the 1.5 Tesla Magnetic Resonance images are located carried out at the CEDISA Imaging Company that has the RadiAnt software DICOM Viewer encrypted.

It can be noted that the average

approximation to the real volume of the Anterior Hippocampus (AA) is 99.59% for the Left Hippocampus and 99.63% for the right hippocampus. The average approach when this process was applied to the entire Hippocampus (HarP) was similar: 98.72% Left, 96.39% Right. Taking into account that these are general practitioners, with limited imaging, neuroanatomical and neurological experience, it can be presumed that this method of theoretical XYZ Geo volumetry in the hands of Neurology, Imaging or Neurosurgery residents could give similar or even better results.

As can be seen in Table 9, there is a tendency for the volume of the Anterior Hippocampus (AA) to decrease as the Minimal State Examination (MMSE) decreases. The right hippocampus in most cases is larger in volume than the left one, as reported in the literature 4,6. We can deduce according to our data that in the cognitively intact Dominican (MMSE 25 points or more) the volume of the Hippocampus Anterior (AA) must be above 2.69cc on the left and 2.86cc on the right.

When the volumes of the Anterior Hippocampus (AA) are compared with the MMSE (Table 9) we find that having a volume equal to or below 2.69 cc on the left and 2.86 cc on the right is related to frank cognitive impairment (MMSE equal to or less than 24 points) in the Dominican population. This finding is very important to take into account during the triage of patients suspected of having disorders in their cognition in the Dominican Republic.

The proposed indirect hippocampal volumetry method can be applied both in patients with normal cognition and in those with compromised cognition. As shown in Tables 2, 3 and 4 that appear in the Annexes, the Indirect Volumetry of the Anterior Hippocampus (AA) using the XYZ Geo Method is close to 100% of the Real Volume

calculated using the voxel method. Therefore, it can be inferred that it turns out to be a reliable method to calculate hippocampal volume in cognitively normal individuals and also in those with altered cognitivity.

We confirm that no diameter of the hippocampus taken in isolation is capable of predicting the trophic state of this very important part of the brain. However, as can be seen in Table 8: if the isolated Compare the case group with the control group. The diameters are slightly smaller with increasing age and cognitive impairment, although the difference is not significant. At the same time, a clear tendency is observed for most of the right diameters to be slightly larger than the left ones.

Among the reasons for wanting to measure both AA (Anterior Hippocampus) and HarP (AA + Tail = Complete Hippocampus) was to know if there was any difference when comparing the two volumes with the cognitive status of the patients after submitting them to the MMSE. As can be seen in Table 9, the volume of AA and HarP exhibit a relationship directly proportional to the MMSE: the lower the volume, the lower the score in the Test. It can be said that, by measuring AA, there is no need to measure HarP to know about the possibility of cognitive deterioration. **This is one of the most important findings of this research.**

To have a greater appreciation of the usefulness of rapid indirect volumetry from a practical point of view, we proceeded to accurately compare the average execution time of Real Volumetry applying the Voxel method versus that used in indirect volumetry using the XYZ method. Geo. The difference that can be noted by analyzing Table 5 in the Annexes is dramatic: AA Volumetry (Anterior Hippocampus) takes almost 12 minutes using the voxel method, while the indirect method takes 41 seconds on average. When HarP

(complete hippocampus, including tail) is measured using voxels, it takes a little more than 13 minutes versus 55 seconds on average using the indirect method.

We were able to clear up a mystery that is raised but not clarified in the literature: the effect that the injection of Gadolinium in the T1 sequence of Magnetic Resonance has on the real volumetry of the Anterior Hippocampus (AA) and the Complete Hippocampus (HarP). As can be seen in Table Number: 10, in all cases both areas of the hippocampus measured with contrast were slightly smaller in volume than the counterparts of the hippocampi measured without contrast. This difference, much less than 10% of the total volume, is produced, among other situations, by the addition of the choroid plexus and other vascular elements (arteries en passant) in the measurement without contrast, which is not done in the one with gadolinium since these structures can be clearly differentiated from the hippocampal mass.

As the difference between one volumetric measurement and another is of little relevance, reliable volumetric measurements can continue to be made in Magnetic Resonance without contrast, given that we have demonstrated in this investigation that the presence of the choroid plexuses and other vascular structures that are added to the volume of the hippocampus distort the real volume in a non-significant way.

In this work, it was possible to detect a significant difference in the MMSE score between the patients in the control group versus those in the case group. As noted in Table 1, of the patients belonging to the study group, 27.5% (11 cases out of 40) presented mild cognitive impairment evidenced by the MMSE test with a score between 24 to 20 points. Only 4 cases (10%) presented moderate to severe deterioration (MMSE 19 to 0 points). 62.5% of the case group had a

normal MMSE. Of the control group, only 5% had mild cognitive impairment. In relation to age, all patients with some degree of confirmed cognitive impairment were over 60 years old, except two. All patients who came for complaints related to memory (40 cases), whether or not they had confirmed cognitive impairment, were over 41 years of age.

On the other hand, when comparing physical and humoral vascular risk factors, a directly proportional correlation with cognitive impairment was not noted. As evidenced in Table 6, no specific trend is noted in the prevalence of vascular risk markers (arterial hypertension, carbohydrate dysmetabolism, obesity, hyperhomocysteinemia) between the control group and the case group. We only noticed a noticeable peak in the increase in Body Mass Index (BMI) in the group of cases aged between 41 and 60, especially among men.

When these vascular risk factors are compared with the MMSE score (Table 7), it is clear that there is no correlation between them and the presence of cognitive impairment in the population studied.

DISCUSSION

To determine the volume of a lesion is an imperative need in modern medicine to make any diagnostic or therapeutic decision.³⁸ Whether a tumor is being managed through surgery or radiosurgery, an intraparenchymal hemorrhage, a probable hippocampal atrophy in a patient suspected of having Alzheimer's Disease, a mesial temporal sclerosis in an epileptic, the application of the therapeutic protocol will depend on the dimension and structural integrity of the structure in question.

We already demonstrated in a previous Fondocyt investigation^{37,38} the enormous value of volumetry to decide the dose to be used in Radiosurgery of brain tumors and in

its development we were able to determine and communicate^{7,39} the usefulness of rapid indirect volumetry following the XYZ Geo method that uses the formula of the geometric figure to which the studied structure corresponds (ellipsoid, cube, cuboid, etc.), obtaining values close to 93% of the real volume determined by voxels (planimetry).

Since 1996, the use of the ABC/2 method has been the standard for volumetry of intracranial lesions.^{10,36} whose initial application was aimed at intraparenchymal hemorrhages. Based on a modification of the ellipsoid formula, this rapid volumetric modality, widely spread and used worldwide, has been questioned lately because its results in arteriovenous malformations are considerably different from the real volume.²³

It is our intimate conviction, after carrying out the real volumetry through voxels and theoretically applying the geometric formula closest to the studied structure of 403 intracranial tumors.^{37,38,39} that the most important source of error in these measurements is applying an incorrect geometric formula. If the measured lesion is cube-shaped and the geometric formula of the ellipsoid is applied, the result will be substantially different from the real volume. Hence, we coined the term the geometric figure that best adapts to the structure studied (Geo).

Given that the human hippocampus has an ellipsoidal shape, whether only its thick anterior portion is studied (Ammon's Horn + Body = AA) or including its tail (AA + Tail = HarP), and it is a structure whose volumetry is of capital importance in the positive diagnosis of Alzheimer's Disease and Temporal Lobe Epilepsy, we considered it pertinent to verify if by applying the simplified geometric formula of the ellipsoid (XYZ/1910) we could obtain a volumetric result close to 100 +/- 10% of the actual volume.

The hippocampus is a hidden structure of the temporal lobe, difficult to locate in Computed Axial Tomography, but very evident to delimit in 1.5 Tesla Magnetic Resonance images with thin slices of 1 to 1.5mm. Large Neuroresearch centers have specialized software to automatically perform reliable hippocampal volumetry^{18,19,20,21,22}. In our healthcare reality, these valuable instruments are not available.

For those of us who work in Radiosurgery, we have a stereotactic image processing platform to perform volumetry such as the Elekta Gamma Plan 10 Work Station, located at the Dominican Gamma Knife Center, which allows us to obtain very exact real volumes using the voxel method. (planimetry). This procedure consumes many minutes of the therapist's time and this platform is one of the few that exist in our country.

That is why we decided to implement a research project to validate the XYZ Geo Method for fast and reliable indirect hippocampal volumetry.

We were able to demonstrate that this method is close to 100% of the real volume whether an experienced operator (PI) uses a complex stereotactic platform or a sufficiently trained General Practitioner (RA) uses the encrypted software on the CD where the Resonance images are recorded. 1.5 Tesla magnetic using a conventional Laptop (Tables 2, 3, 4). The time savings is enormous (Table 5) and the precision is very satisfactory (Tables 2,3,4).

We realized that the entire hippocampus does not have to be measured to determine hippocampal atrophy and objectively establish cognitive impairment. The volumetry of the anterior portion of the hippocampus (Ammon's Horn + Body =AA) is sufficient to have an idea of the structural integrity of the hippocampus. Measuring the entire Hippocampus (AA + Tail = HarP) takes much

more time and is ultimately not essential (Table 9).

The use of Gadolinium for the exact real volumetry of the hippocampus is not necessary since the participation of arteries en passant and choroid plexuses in the total volume of the non-contrasted hippocampus is negligible, as can be seen in Table 10.

For the first time in our country, research has been carried out in which it has been possible to determine the real volume of the hippocampi of Dominican adults without and with cognitive impairment. We can firmly affirm that the Dominican adult of any sex, without cognitive problems (MMSE equal to or greater than 25 points), has an Anterior Hippocampus (AA) greater than 2.69cc on the Left and 2.86cc on the right. The complete hippocampus (AA + Tail =HarP) of a Dominican adult of normal cognition has a volume equal to or greater than 3.06 cc on the left and 3.21 cc on the right. (Table 9).

CONCLUSION

The method of indirect theoretical volumetry of the hippocampus, applying the simplified formula of the ellipsoid (XYZ/1910) yields results very close to 100% of the real volume determined on a stereotactic platform for the treatment of high-definition 1.5 Tesla Magnetic Resonance images in the hands from an experienced therapist (PI). By applying this same formula on a less sophisticated 1.5 Tesla MRI image processing platform such as a conventional laptop using the RadiAnt DICOM Viewer software encrypted on the CD that contains the MRI images at the command of a sufficiently knowledgeable general practitioner of the Method (RA), similar results are obtained very close to 100% of the real volume of the hippocampus. That is why we maintain that the XYZ Geo Rapid Indirect Volumetry Method using the simplified geometric formula of the Ellipsoid

(XYZ/1910) is an ideal and reliable tool to perform hippocampal volumetry used by both experienced therapists and those in training.

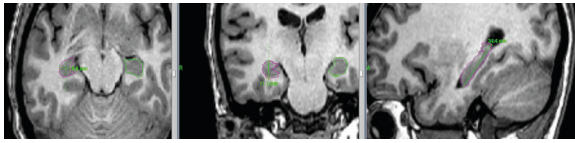


IMAGE 1: 1.5 Tesla MRI T1 without contrast Images showing from left to right the X, Z and Y axis of a right hippocampus (Anterior Portion = AA). Gamma Plan X Work Station (Elekta, Sweden).

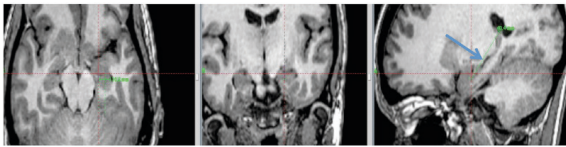


IMAGE 2: 1.5 Tesla MRI T1 without contrast Images showing a left hippocampus and the measurement of the Y axis of the whole hippocampus (AA + Tail = HarP) (Right image, Arrow). Gamma Plan X Work Station (Elekta, Sweden).

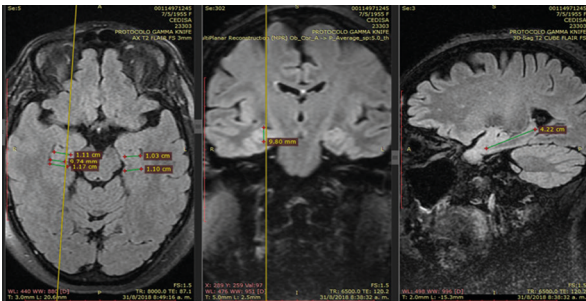


IMAGE 3: 1.5 Tesla MRI T1 without contrast Images showing from left to right the X, Z and Y axis of a right hippocampus (Anterior Portion = AA). RadiAnt DICOM Viewer software.

Table 1. Patient Demographic Profile and Folstein Mini Mental State Examination (MMSE)

	Frequency (age mean)	Normal MMSE (26-35)	Mild MMSE (24-25)	Moderate to Severe MMSE (19-23)
Control Group				
20 - 40 years				
Female	10(30.2)	10	0	0
Male	10(29.9)	10	0	0
41 - 60 years				
Female	10(52.5)	10	0	0
Male	10(50.9)	10	0	0
61 - 80 years				
Female	10(65.8)	7 (70%)	3 (30%)	0
Male	10(65.8)	10	0	0
Sub-Total	60(49.2)	57 (95%)	3 (5%)	0
Care Group				
41 - 60 years				
Female	11(52.5)	9 (81%)	2 (19%)	0
Male	9(51.9)	7 (77.8%)	2 (22.2%)	0
61 - 80 years				
Female	10(69.9)	5 (50%)	3 (30%)	2 (20%)
Male	10(73.2)	4 (40%)	4 (40%)	2 (20%)
Sub-Total	40(61.9)	25 (62.5%)	11 (27.5%)	4 (10%)
Total	100(54.3)	82 (82%)	14 (14%)	4 (4%)

Table 2. Real and Theoretical Volumetry by Manual Method and XYZ Geo. (Carried by the Principal Investigator after 3 measurements at different levels of the already delimited hippocampus and taking the closest result to the real volume).

	Manual Volumetry (cc)	Theoretical Geometric Volumetry (cc)	Percentage of Approach
	mean (IC)		% (IC)
Left Hippocampus			
AA	2.84 (2.70-2.99)	2.85 (2.70-2.99)	100.29 (99.21-101.37)
HarP	3.14 (3.00-3.29)	3.15 (2.99-3.31)	99.81 (97.93-101.69)
Right Hippocampus			
AA	3.02 (2.87-3.17)	3.03 (2.88-3.18)	100.75 (99.51-100.75)
HarP	3.34 (3.19-3.49)	3.30 (3.15-3.45)	99.38 (97.43-99.38)

Table 3. Real and Theoretical Volumetry by Manual Method and XYZ Geo (performed by Research Assistants and calculated only once, without prior knowledge of the real volume).

	Manual Volumetry (cc)	Theoretical Geometric Volumetry (cc)	Percentage of Approach
	mean (IC)		% (IC)
Left Hippocampus			
AA	2.84 (2.70-2.99)	2.82 (2.68-2.97)	99.59 (98.37-100.80)
HarP	3.14 (3.00-3.29)	3.11 (2.89-3.33)	98.72 (93.47-103.98)
Right Hippocampus			
AA	3.02 (2.87-3.17)	3.00 (2.85-3.15)	99.63 (97.96-99.63)
HarP	3.34 (3.19-3.49)	3.23 (3.07-3.38)	96.39 (94.78-98.39)

Table 4. Volumetry by Manual Method and XYZ Geo (performed by the Principal Investigator and calculated only once, before knowing the real volume.)

	Manual Volumetry (cc)	Theoretical Geometric Volumetry (cc)	Percentage of Approach
	mean (IC-ICS)		% (IC-ICS)
Left Hippocampus			
AA	2.84 (2.70-2.99)	2.66 (2.5-3.1)	93.66% (88.02-109.15)
HarP	3.14 (3.00-3.29)	2.9 (2.87 -3.02)	92.36 % (91.40-96.18)
Right Hippocampus			
AA	3.02 (2.87-3.17)	2.77 (2.69-3.2)	91.72 % (89.07-105.96)
HarP	3.34 (3.19-3.49)	3.05 (2.8-3.2)	91.32 % (90.7 - 92.8)

Table 5. Time of Real Volumetry and Time of Theoretical Geometric Volumetry by Manual Method and XYZ Geo

	Time of Real Volumetry (" ")	Time of Theoretical Geometric Volumetry (" ")
	(Min-Max)	
Left Hippocampus		
AA	11'46" (4'53"-20'16")	0'41" (0'12"-1'04")
HarP	13'10" (5'25"-24'07")	1'10" (0'30"-1'20")
Right Hippocampus		
AA	11'01" (4'40"-26'01")	0'33" (0'15"-0'59")
HarP	13'01" (3.19-3.49)	0'39" (0'17"-1'12")

Table 6. Lab Results and Vital Signs

Control Group	Heart Rate		Blood Pressure		HbA1C		Cholesterol		IMC		Homocysteine	
	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.
20 - 40 years												
Feminine	10	0	10	0	10	0	8	2	7	3	10	0
Masculine	10	0	10	0	10	0	9	1	7	3	6	2
41 - 50 years												
Feminine	10	0	10	0	10	0	8	2	5	5	8	0
Masculine	10	0	9	1	8	2	7	3	4	6	2	1
51 - 60 years												
Feminine	10	0	8	2	8	2	9	1	5	5	4	0
Masculine	9	1	8	2	9	1	9	1	5	5	3	0
Sub-Total	59 (98%)	1 (2%)	55 (92%)	5 (8%)	55 (92%)	5 (8%)	50 (83%)	10 (17%)	33 (55%)	27 (45%)	33 (92%)	3 (8%)
Case Group												
41 - 50 years												
Feminine	11	0	11	0	10	1	8	3	5	6	8	0
Masculine	9	0	9	0	9	0	6	2	2	7	4	0
61 - 80 years												
Feminine	7	3	8	2	10	0	6	4	6	4	5	0
Masculine	9	1	8	2	10	0	7	3	6	4	6	1
Total	36 (90%)	4 (10%)	36 (90%)	4 (10%)	39 (97%)	1 (3%)	28 (89%)	12 (31%)	19 (49%)	21 (51%)	23 (96%)	1 (4%)
Total	95 (95%)	5 (5%)	91 (91%)	9 (9%)	94 (94%)	6 (6%)	78 (78%)	22 (22%)	52 (52%)	48 (48%)	56 (93%)	4 (7%)

Table 7. Lab Results and Vital Signs Vs MMSE

MMSE	Heart Rate		Blood Pressure		HbA1C		Cholesterol		IMC		Homocysteine	
	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.	Norm.	Alt.
30	13	0	12	1	13	0	11	2	7	6	12	0
29	19	0	19	0	18	1	14	5	11	8	12	2
28	14	0	12	2	12	2	12	2	7	7	5	1
27	15	1	15	1	16	0	12	4	8	8	9	1
26	12	0	12	0	11	1	10	2	6	6	5	0
25	8	0	8	0	8	0	7	1	3	5	2	0
24	7	1	6	2	8	0	7	1	5	3	2	0
23 - 22	3	1	4	0	2	2	3	1	0	4	3	0
<19	4	2	3	3	6	0	2	4	5	1	5	0
Total	95 (95%)	5 (5%)	91 (91%)	9 (9%)	94 (94%)	6 (6%)	78 (78%)	22 (22%)	52 (52%)	48 (48%)	56 (93%)	4 (7%)

Table 8. Average XYZ Diameters of AA by Sex, Age and Group.

Control Group	X Izquierda (mm)	X Derecho (mm)	Y Izquierda (mm)	Y Derecho (mm)	Z Izquierda (mm)	Z Derecho (mm)
20 - 40 years						
Feminine	13.79	14.47	38.38	40.68	10.52	10.7
Masculine	14.34	13.72	38.06	39.77	10.87	10.87
41 - 50 years						
Feminine	13.05	14.34	38.03	39.22	10.28	10.39
Masculine	14.59	14.72	41.02	41.32	10.12	10.04
51 - 60 years						
Feminine	13.25	14.15	37.75	38.55	10.02	10.15
Masculine	14.78	14.93	39.33	39.89	10.27	9.99
Average Control Group	13.97	14.39	39.26	39.91	10.35	10.36
Case Group						
41 - 50 years						
Feminine	14.69	15.69	38.98	39.27	10.42	10.68
Masculine	14.28	13.84	38.06	40.88	10.27	10.37
61 - 80 years						
Feminine	12.61	13.04	36.53	37.73	9.82	9.61
Masculine	11.93	12.42	37.9	38.88	9.27	8.91
Average Case Group	13.38	14	37.87	39.19	9.95	9.89
General Average	13.68	14.2	38.57	39.55	10.15	10.125

Table 9. Relation Between MMSE and the Volume of AA and HarP.

MMSE	Left AA. Volume (cc)	Right AA. Volume (cc)	Left HarP Volume (cc)	Right HarP Volume (cc)
30	3.07	3.2	3.41	3.48
29	3.25	3.43	3.55	3.73
28	2.9	2.97	3.17	3.28
27	2.72	3.13	3.02	3.42
26	2.97	3.02	3.26	3.43
25	2.8	2.93	3.05	3.25
24	2.69	2.86	3.06	3.21
23 - 22	2.08	2.35	2.41	2.68
<19	1.77	1.9	2.06	2.21

Table 10. Real Volumetry of T1 with contrast Vs T1 without contrast (100 MRI without contrast and 10 MRI with contrast)

	T1 With Contrast (cc)	T1 Without Contrast (cc)	Choroid Plexus (cc)
Left Hippocampus			
AA	2.75	2.99	NA
HarP	2.98	3.25	0.15
Right Hippocampus			
AA	3.00	3.26	NA
HarP	3.38	3.48	0.08

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