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Original Article

Hippocampal sulcal cavities in healthy individual: high resolution magnetic resonance imaging using 3.0 MRI

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Abstract: Most of the studies on hippocampal sulcal cavities (HSCs) have been focused on the hippocampal lesions, lacking of systemic investigations on the normal individuals. In this study, we aimed to investigate the detection rate and number of HSCs together with the correlation between HSCs and the gender, sides, hippocampal volume, and age. In total, 187 healthy subjects underwent 3.0 Tesla magnetic resonance scan. Chi square test was utilized for the comparison of HSCs detection rate among the male and female individuals. Student's t-test was used to compare the HSCs number between the subjects with different ages as well as different body sides. Analysis of variance was performed for the comparison of primary hippocampal volume, corrected hippocampal volume, and age. Person regression analysis was utilized to analyze the correlation between HSCs number and the primary hippocampal volume, corrected hippocampal volume, and age. The incidence of HSCs was 95% among the 187 subjects. There was no significant gender difference in the incidence of HSCs (P=0.448). There was no statistically significant difference in the number of HSCs on the left and right sides (P=0.093). There were statistically significant differences in mean age between groups (P<0.01). Pearson correlation analysis was performed on HSCs with age, hippocampal original volume and corrected volume, and the correlation coefficients were 0.316, -0.005 and 0.055. Healthy population has a high HSCs incidence, which had no significant gender-related difference. There is no significant difference of HSCs number between the left and right sides. HSCs showed a low correlation with age and no correlation with hippocampal volume.

Keywords: Magnetic resonance imaging, hippocampus, hippocampal sulcal cavities

Introduction

Magnetic resonance imaging (MRI) with excellent tissue comparison capacity has been commonly used for the imaging of hippocampal morphology [1-5]. The advances of MRI and higher image resolution techniques, hippocampal morphology, and internal structure can clearly determine hippocampal sulcal cavities (HSCs). Most studies suggest that HSCs are considered as normal variations originating from embryonic folding of the hippocampus [6]. Whereas, partial studies indicate that HSCs are speculated to be dilated perivascular spaces [7, 17]. Others speculate that HSCs might be ischemic and/or anoxia-related lesions [8]. Previous literature reported that HSCs were correlated with cognitive function [9, 10, 21]. However, recent studies denied the correlation between HSCs and cognitive function [11, 12]. Some literatures reported that HSCs were correlated with Hippocampal volume and age [5, 11, 15]. Some literature showed no correlation between HSCs and hippocampal volume and age [6, 24]. Most of the studies on HSCs have been focused on the cognitive function related diseases in the aged population, while rare studies focus on that in the normal individuals. In this study, we aimed to investigate the detection rate and number of HSCs together with the correlation between HSCs and the gender, sides, hippocampal volume, and age.

Materials and methods

Study population

The inclusion criteria were as follows: 1) no contraindications for MRI (e.g. metal in or on their bodies, claustrophobia); 2) no psychiatric

or neurological disorder; neuropsychiatric examination showed no positive findings; 3) no head trauma, diabetes, hypertension or other immunological, hematologic or metabolic diseases; 4) no smoking or alcohol; 5) no aberrant changes in the routine MR scan (i.e. T1WI, T2WI and FLAIR). Each subject signed the informed consent. The study protocols were approved by the Ethical Committee of Shandong Provincial Qianfoshan Hospital, Shandong University.

Among 196 healthy subjects, 9 of which were not included due to heavy moving artifacts, only 187 cases were included in the study. There were 81 men and 106 women. The mean age was 48.15±19.5 years (range: 2-88 years).

MRI imaging protocol

All MRI examinations were performed on a 3.0T imager (Siemens Medical System Germany). The protocol included T1 weighted 3D fast-field echo sequence (TR/TE7.1/3.2, FOV 200×200, slice thickness 1.0 mm, no gap, whole brain scan), 3DT2 weighted sequence (TR 1200 ms, TE 268 ms, FOV 200×200, slice thickness 0.6 mm, no gap, whole hippocampus scan).

Hippocampal volume determination and calibration

The original data (3DT1) was transferred to the image workstation. Then the hippocampal boundaries were depicted using the mouse, to obtain the area of the corresponding layer, followed by multiplying the layer thickness to obtain the volume of the layer, as well as calculating the hippocampal volume by adding up the volume of each layer. To eliminate the effects of individual cranial size on hippocampal volume, all hippocampal volumes were corrected by phase division according to the previous description [13]. All images were reviewed by two experienced neuroradiologists blinded to this study. Detailed communication was held in cases of disputes until consensus.

HSCs definition

HSCs were defined according to the previous literature [12, 14] by the following properties: 1) hypointense signal on T1-weighted images, hyperintense signal on T2-weighted images; 2) located in regions adjacent to where stratum radiatum lacunosum moleculare might be present; 3) not connected with the temporal horn of the lateral ventricle, which, in case of doubt, was checked in the sagittal plane; and 4) preferably presented on multiple consecutive slices. They were described as round or curvilinear in coronal orientation and crescent shaped in axial orientation. Based on these standards, the number of individuals with detected HSCs, together with the number of HSCs at the left or right sides. All images were reviewed by two experienced neuroradiologists blinded to this study. Consensus was obtained after communication of the disputes.

Grouping

According to the detected number of HSCs, the 187 subjects were divided into four groups: Group 1, those who showed no HSCs; Group 2, those with 1-5 HSCs; Group 3, those with 6-10 HSCs; and Group 4, those with >10 HSCs.

Statistical analysis

Statistical analyses were performed on SPSS 18.0 software (Chicago, IL, USA). The detection rate of HSCs among the male and females was compared using the Chi square test. Student's t-test was utilized for the comparison of HSCs among the male and female counterparts, as well as the HSCs number of the bilateral body sides. One-way analysis of variance (ANOVA) was utilized to compare the mean hippocampal volume and age between groups. Least significant difference (LSD) analysis was used for the multiple comparisons between groups. Pearson correlation analysis was performed to evaluate the correlation between hippocampal volume, age, and HSCs. $P<0.05$ was considered to be statistically significant.

Results

Comparison of HSCs detection rate in gender

Among the 187 individuals, HSCs were detected in 178 (95%; male: 76; female: 102). Among the 81 male individuals, 76 showed HSCs (93%). In the 106 female individuals, 102 (96%) showed HSCs. There was no statistical difference among the HSCs detection rate in the male and female individuals ($P=0.448$, **Table 1**).

Table 1. Detection rate of HSCs

Gender	HSCs (+)	HSCs (-)	Total	
Male	76	5	81	
Female	102	4	106	χ^2=0.577
Total	178	9	187	*P*=0.448

Table 2. HSCs number in different gender and body sides

Variable	N	HSCs	*P*
Male	81	568	0.02
Female	106	918	
Right side	187	765	0.093
Left side	187	721	

Comparison of HSCs number in different gender and body sides

There were 1,486 HSCs identified in total, including 721 on the left side and 765 on the right side, respectively. No statistical differences were noticed in the number of HSCs between the left and right sides (*P*=0.093, **Table 2**). The total number of HSCs in male and female counterparts was 568 and 918 respectively. The number detected in the female was higher than that in the male counterparts (*P*=0.02, **Table 2**).

Comparison of hippocampal volume and median age in different groups

Based on the HSCs number, the individuals were divided into 4 groups with a number of 9, 53, 69, and 56, respectively. There were no statistically differences in the original and corrected hippocampal volume between groups (*P*=0.943, *P*=0.287, **Table 3**). There were statistical differences in the age between groups (*P*<0.01, **Table 3**). Pair-wise comparison of age indicated that there was significant differences in the age between the first group and the third group (*P*=0.013), as well as between the first group and the fourth group (*P*<0.01). Statistical differences were noticed in the age between the second group and the fourth group (*P*< 0.01), as well as between the third group and the fourth group (*P*=0.005).

Pearson correlation analysis

Pearson correlation analysis was performed on HSCs with age, hippocampal original volume and corrected volume. The correlation coefficients were 0.316 (**Figure 1**), -0.005 (**Figure 2**), and 0.055 (**Figure 3**), respectively. There was a low correlation between HSCs number and age (*P*<0.01). There was no correlation between HSCs number and primary hippocampal volume and corrected volume. **Figures 1-3** were the scatter plot diagrams of HSCs number correlating with age, primary hippocampal volume, and corrected hippocampal volume.

Discussion

Based on the literature review, there were different reports on the incidence of HSCs. For example, Sasaki et al. [22] reported an HSC incidence of about 39% for the 109 subjects. Yoneoka et al. [17] showed that the incidence of HSCs was 36.4% in 22 volunteers. Li et al. [7] reported that the incidence of HSCs in 130 subjects was 64%. In a meta analysis [10], the incidence of HSCs was 63.96%, while the incidence of patients and healthy controls were 66.36% and 46.53%, respectively. In the study by Maller et al. [14], the incidence of HSCs in healthy subjects was 51.2%. Van Veluw et al. [6] performed a MR scan on 56 subjects and found that the prevalence of HSCs was 97%. The differences between sample size, MRI field intensity, scanning sequence, and slice thickness may explain for the large variances of the HSCs detection rates. According to our experiences, the detection rate of HSCs was higher in the subjects with higher field intensity and the resolution, as well as a thinner scanning layer. The device was MRI device with high electric field intensity, involving the three-dimensional thin slice scan. The HSCs detection rate was about 95%. In addition, there was no significant difference in the male compared with the female counterparts in terms of HSCs detection rate. Similarly, there was no difference in the HSCs number between the left and right body sides. This was in line with the previous findings [11, 22]. The number of females showing HSCs was higher than that of the male individuals, which may be related to the enrollment of more females than the male counterparts. In addition, the race and living environment of subjects may also affect the incidence of HSCs.

There were no statistical differences in the primary hippocampal volume and corrected hippocampal volume in the subjects with different

Table 3. Analysis of variance between primary hippocampal volume, corrected hippocampal volume and age

Group	HSCs number	Cases	Primary hippocampal volume (mm^3)	Corrected hippocampal volume (mm^3)	Age (yr)
Group 1	0	9	4599.86±598.91	1683.62±340.12	31±16.61
Group 2	1-5	53	4541.07±717.84	1571.42±326.34	42.91±23.58[b]
Group 3	6-10	69	4553.43±501.49	1653.75±236.34	47.35±17.21[a,c]
Group 4	>10	56	4665.17±595.68	1659.09±262.78	56.86±19.50[a]
F			0.128	1.266	8.221
P			0.943	0.287	0.000

[a]P<0.05 versus Group 1; [b]P<0.05 versus Group 4; [c]P<0.05, versus Group 4.

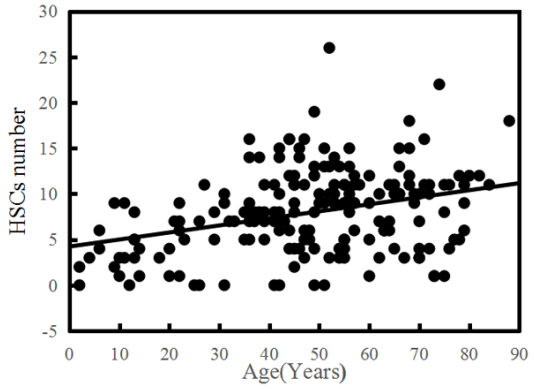

Figure 1. Pearson correlation analysis indicated a lower correlation between HSCs number and age (correlation coefficients, 0.316).

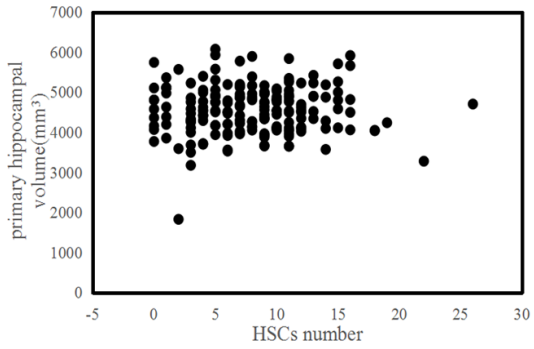

Figure 2. The HSCs number showed no correlation with the primary hippocampal volume (correlation coefficients, -0.005).

number of HSCs. Correlation analysis indicated that there was no correlation between HSCs number and hippocampal volume. This was consistent with the previous description [6]. However, in a SMART-Medea study and PREDICT-MR study [12], there was significant difference in hippocampal volume between those with no HSCs and those with at least 2

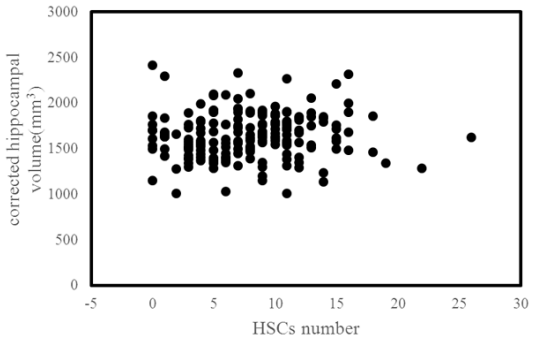

Figure 3. No significant correlation was noticed between HSCs number and corrected hippocampal volume (correlation coefficients, 0.055).

HSCs. We found low positive correlation between HSCs and age, which was consistent with these studies. In a previous study, Barboriak et al. [5] determined the number of HSCs in 92 individuals, which indicated that the HSCs score increased in the aged population. Yoneoka et al. [17] demonstrated that the frequency of HSCs showed elevation in 74 individuals. Jerome et al. [14] reported that there was a correlation between HSCs detection rate and age, and the HSCs number increased with the aging process. In contrast, there are some disputes on some studies. For example, there was no correlation between HSCs and age in some studies [6, 24].

For the development of HSCs, it has been well acknowledged as an anatomical variation [15, 16]. In the embryological perspective, it has been speculated that HSCs may occur due to incomplete fusion of the HC sulcus during development, which then led to a congenital cystic remnant of the sulcus at its lateral margin. The human HC was visible during the first trimester and folded to form the HC fissure in the second trimester. The walls of this fissure

fused by 30 weeks, although small residual cavities occurred if development was disrupted. Therefore, these pockets of fluid that could be found along the course of the sulcus and were referred to as "vesicles" and/or at the very lateral aspect, aptly assume the name of HC residual cavities. Yoneoka et al. [17] suggested that there were deep hippocampal veins and hippocampal ventral artery passing through HSCs. HSCs were dilated perivascular spaces (dPVS), also known as dilated Virchow-Robin spaces (dVRS) [7]. Some authors [21] speculated that HSCs might be small vessel diseases, while some studies [8, 18, 22] indicated that it might be related to the ischemic and anoxemic lesions. In this study, we included 9 individuals aged 10 years or less, and 8 were confirmed with HSCs. This implied that HSCs may present in the young individuals. This supported the hypothesis that HSCs was a type of anatomical variation. HSCs number was correlated with the age, which may be resulted from the decline of cerebral parenchima in the aged population. There might be potential space in the young age, which became visible with the decline of the peripheral brain tissues with the aging process. In a previous study [22], HSCs were more common in the individuals with impaired cognitive function. Meanwhile, there was a negative correlation between HSCs number and brain volume. With the increase of age, the expression regulation of a certain gene or a certain biomarker dysregulation may lead to brain tissue aging, which then resulted in cognitive dysfunction. The increase of the HSCs may be caused by cognitive function injury, rather than the cognitive function injury by HSCs.

Indeed, there are some limitations in this study. We included more female individuals than the male counterparts, which may bring bias to the statistical analysis. In addition, we only evaluated the detection rate and number of HSCs, which was lacking of evaluation for the HSCs volume.

Conclusion

In summary, healthy population has a high HSCs incidence. It has no significant gender-related difference. There is no significant difference of HSCs number between the left and right sides. HSCs showed a low correlation with age and no correlation with hippocampal volume.

Disclosure of conflict of interest

None.

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