An Objective Method to Quantify Hippocampal Dentation on T2-Weighted High Resolution MR Images

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Hippocampal dentation (HD) is a feature of hippocampal morphology that refers to surface convolutions seen in the CA1/subiculum region of the inferior aspect (Figure 1) of the hippocampus [1]. HD has been found to vary in prominence from quite bumpy to quite smooth in healthy controls. HD is best visualized in High Resolution Multiple Image Co-Registration and Averaging (HR-MICRA) images [2]. We have previously quantified HD using our visual rating system (subjective method) and found that variation in hippocampal dentation in a healthy population showed a positive association with aspects of episodic memory. To be specific, HD from the left hippocampi showed positive correlation with verbal as well as visual memory scores. Similarly, HD from the right hippocampi showed positive correlation with visual memory score [3]. However, up to now HD has been quantified only using subjective visual rating systems. Further, manual HD quantification is time consuming and prone to inconsistency across raters [4]. Therefore, an objective measure to quantify HD is needed to advance the study of this morphologic feature. In this work, we have developed an objective method to quantify HD by transforming a strip of a 3D surface mesh into a dimensionally reduced 2D plot followed by area under the curve (AUC_{HD}) calculation (Figure 1).

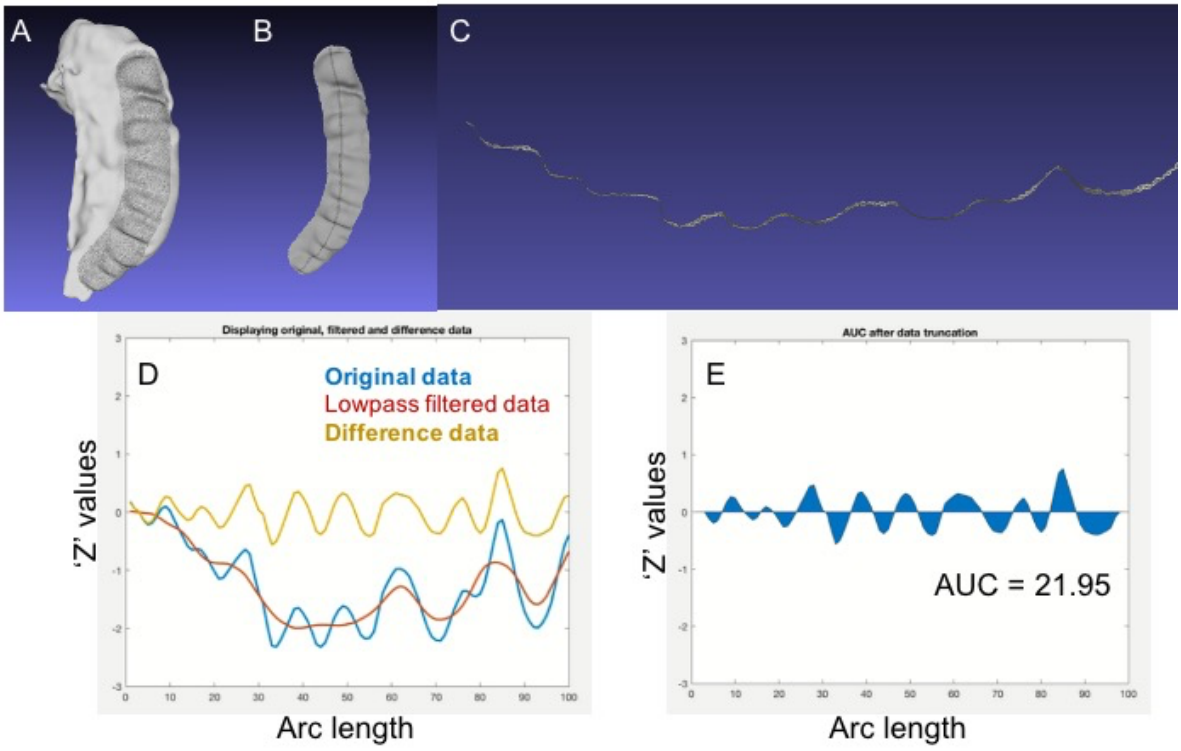

Figure 1. Demonstration of an objective HD quantification method. (A) An overlay of open cut surface of HD on the whole hippocampus, (B) an overlay of a strip of 3D surface mesh on the open cut surface of HD, (C) a strip of 3D surface mesh in its side view, (D) a 2D plot of dimensionally reduced original, lowpass filtered and difference data and (E) an area-under-the-curve (AUC_{HD}) calculation for the 2D plot of difference data.

T2-weighted HR-MICRA images (0.5×0.5×0.75mm) acquired from 20 healthy controls were resampled to ~0.25mm isotropic and segmentation of the hippocampi was performed using Automatic Segmentation of Hippocampal Subfields [5]. Surface meshes were generated from the segmentations followed by Taubin smoothing. Using MeshLab, a "swath" containing the entirety of HD was selected from each whole hippocampal surface mesh and reoriented to align its principal axis in the x-y plane. A strip was traced on the swath to get a set of points that reflects the essential topology of HD, and further simplified to get a single curvilinear set of points [6]. Savitzky-Golay low pass filtering (FIR filter with order=1, frame length=11 and cutoff frequency=3db) was performed to extract the general shape of the hippocampus and was subtracted from the simplified strip to create a curve that reflects only undulations in surface contour (i.e., HD). Area under the curve (AUC_{HD}) was calculated from the difference data to quantify HD (Figure 1). Student's t-Test was performed to detect a difference between the left and right hippocampi. A Pearson's Correlation Coefficient was calculated to test the correlation of AUC_{HD} with visual dentation scores and neuropsychometric testing (NPT) measures including the Rey Complex Figure Recognition Test, California Verbal Learning Test (CVLT)-II trials 1-5 and CVLT-II long delay free recall.

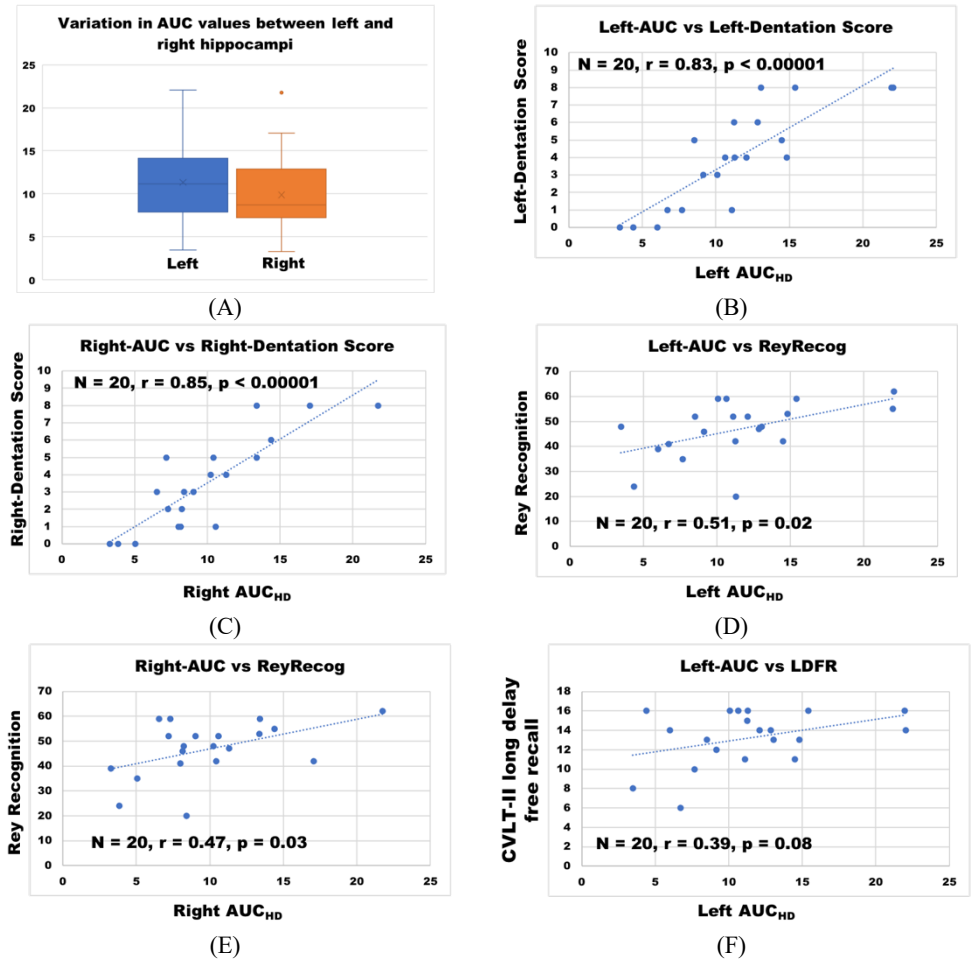

Figure 2. Analysis of AUC values. (A) Boxplot representation of AUC_{HD} values between left and right hippocampi, (B-C) correlation analysis of AUC_{HD} values (objective method) with dentation score (subjective method), (D-E) correlation analysis of AUC_{HD} values with visual memory (Rey Recognition), (F) correlation analysis of left AUC_{HD} values with verbal memory (CVLT-II long delay free recall).

Results show that our super resolution based segmentation approach demonstrates HD much more clearly. The AUC_{HD} values were significantly different between left and right hippocampi ($p = 0.03$) (Figure 2(A)). The left and right AUC_{HD} values (objective method) showed a strong positive correlation ($p < 0.0001$) with visual dentation scores (subjective method) (Figure 2(B-C)). We also found that the left ($p = 0.02$) as well as right ($p = 0.03$) AUC_{HD} values showed a positive correlation with visual memory score (Rey Complex Figure Recognition Test) (Figure 2(D-E)). However, left AUC_{HD} values showed a positive trend with verbal memory score (CVLT-II long delay free recall), but was not statistically significant ($p = 0.08$) (Figure 2(F)).

In this work, we have developed an objective method to quantify HD using HR-MICRA images and compared its performance with the subjective method. Some of the managerial insights of this work are as follows.

- This is the first objective method to quantify HD on healthy controls using high resolution images.
- The newly developed objective method could demonstrate HD much more similar to our previously published subjective method [3].
- The higher AUC_{HD} values on the left (11.34 ± 4.92) compared to the right (9.88 ± 4.47) hippocampi suggests that there is greater degree of specialization on the left hemisphere.
- Also, there is a significant correlation between AUC_{HD} values and visual memory but not verbal memory score unlike our subjective method. This implies that further improvement is required in the objective method towards precise quantification of HD.

ACKNOWLEDGMENTS

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AN OBJECTIVE METHOD TO QUANTIFY HIPPOCAMPAL DENTATION ON T2-WEIGHTED HIGH RESOLUTION MR IMAGES

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Introduction

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However, up to now HD has been quantified only using subjective visual rating systems. Further, manual HD quantification is time consuming and prone to inconsistency across raters [4]. Therefore, an objective measure to quantify HD is needed to advance the study of this morphologic feature.

In this work, we have developed an objective method to quantify HD by transforming a strip of a 3D surface mesh into a dimensionally reduced 2D plot followed by area under the curve (AUCHD) calculation
(Figure 2).

Methods

T2-weighted HR-MICRA images (0.5×0.5×0.75mm) acquired from 20 healthy controls were resampled to ~0.25mm isotropic and segmentation of the hippocampi was performed using Automatic Segmentation of Hippocampal Subfields [5]. Surface meshes were generated from the segmentations followed by Taubin smoothing. Using MeshLab, a “swath” containing the entirety of HD was selected from each whole hippocampal surface mesh and reoriented to align its principal axis in the x-y plane.

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Area under the curve (AUC_{HD}) was calculated from the difference data to quantify HD (Figure 2). Student’s t-Test was performed to detect a difference between the left and right hippocampi. A Pearson’s Correlation Coefficient was calculated to test the correlation of AUC_{HD} with visual dentation scores and neuropsychometric testing (NPT) measures including the Rey Complex Figure Recognition Test, California Verbal Learning Test (CVLT)-II trials 1-5 and CVLT-II long delay free recall.

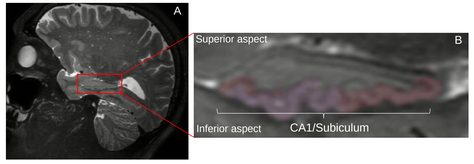
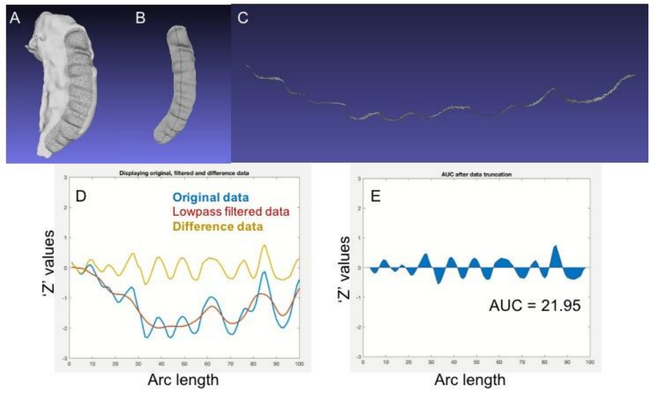


Figure 1. Illustration of human Hippocampal Dentation. (A) high resolution T2 weighted MR image in the sagittal plane showing hippocampus (highlighted using red box) and (B) zoomed in view of hippocampus exhibiting tooth like pattern of HD in the CA1/Subiculum region.

Results

- Results show that our super resolution based segmentation approach demonstrates HD much more clearly.
- The AUC_{HD} values were significantly different between left and right hippocampi (p = 0.03) (Figure 3(A)).



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- The left and right AUC_{HD} values (objective method) showed a strong positive correlation ($p < 0.0001$) with visual dentation scores (subjective method) (Figure 3(B-C)).
- We also found that the left ($p = 0.02$) as well as right ($p = 0.03$) AUC_{HD} values showed a positive correlation with visual memory score (Rey Complex Figure Recognition Test) (Figure 3(D-E)).
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Conclusions

- In this work, we have developed an objective method to quantify HD using HR-MICRA images and compared its performance with the subjective method. Some of the managerial insights of this work are as follows.
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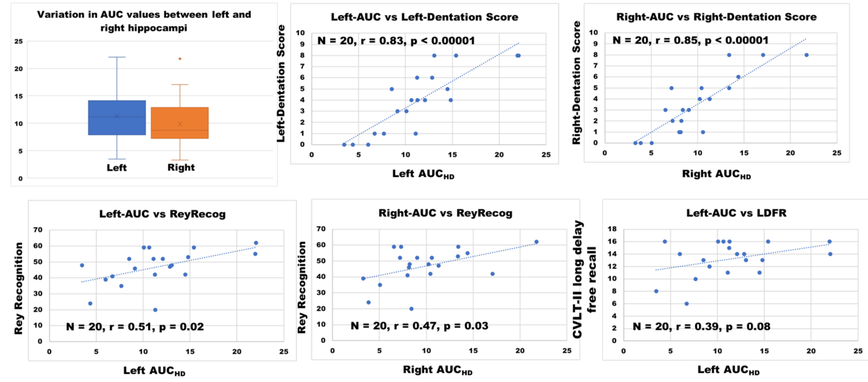

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