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Interuncal Distance as a Measure of Hippocampal Atrophy: Normative Data on Axial MR Imaging

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PURPOSE: To assess the effects of age and gender on the interuncal distance measured from MR images. **METHODS:** High-field strength MR images (axial) of 75 volunteers, 21–82 years old and free of neurologic disorders, were used to measure the interuncal distance. **RESULTS:** The interuncal distance increased with age ($r = 0.66$, $P < .0001$). The mean (SD) interuncal distance for all subjects was 21.4 (4) mm with a range of 12 to 29 mm. **CONCLUSIONS:** The interuncal distance in healthy subjects is unlikely to exceed 30 mm. Our data may be of clinical significance in view of a previous report stating that the interuncal distance may be enlarged in pathologic hippocampal degeneration, such as in patients with Alzheimer disease.

Index terms: Hippocampus; Brain, measurements; Dementia; Brain, atrophy

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Degenerative changes in the hippocampal formation may play a role in the pathogenesis of several disorders, notably Alzheimer disease (1), amnestic syndrome (2), temporal lobe seizure (3), and schizophrenia (4). Normative data on age and gender-related variations of this region in normal subjects will facilitate investigation of disorders related to the hippocampal formation.

Recent studies have detected reductions in hippocampal volumes on magnetic resonance (MR) images of patients with Alzheimer disease, amnestic syndrome, temporal lobe seizure, or schizophrenia (5). However, such volume-rendering procedures are not widely available and can be cumbersome as a supplement to routine clinical interpretation, and volumes may vary with the landmarks selected. Recently, Dahlbeck et al (6) reported that the interuncal distance measured on MR may provide a more direct reflection of hippocampal atrophy in Alzheimer disease than methods previously reported. In their study, the interuncal distance was greater than 30 mm in Alzheimer patients but was smaller than 30 mm in 10 matched controls.

Materials and Methods

Subjects

75 volunteers were determined to be free of significant neurologic or psychiatric illness. The 75 subjects (34 men) ranged in age from 21 to 82 years with a mean age (SD) of 52.5 (18) years (see Table 1). These individuals were not selected specifically to look at the interuncal distance but were part of an ongoing research study on normal brain aging (7).

MR Measurements

MR imaging was performed on a 1.5-T scanner. The subjects were positioned in a quadrature head coil with the canthomeatal line at 0 degrees from the vertical axis and the laser of the imaging section centered at the nasion. Five-mm thick axial section (intersection gap, 2.5 mm) were obtained parallel to the canthomeatal line using flow compensation and a variable bandwidth pulse sequence. T1-weighted images 500/20 (TR/TE) were used to measure the interuncal distance. Measurements were obtained with a computer-generated transparent scale calibrated to 0.5 mm at the level of the suprasellar cistern. All measurements were made blinded to the subject's age and using head-

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TABLE 1: Age and gender-specific interuncal distances in healthy subjects

Age Range	Interuncal Distance (mm)					
	Males		Females		Combined	
	N	Mean ± SD	N	Mean ± SD	N	Mean ± SD
20–30	8	19.1 ± 3	7	17.4 ± 3	15	18.3 ± 3
31–40	6	22.1 ± 2	5	17.2 ± 3	11	19.9 ± 3
41–50	3	18.1 ± 1	5	17.0 ± 3	8	17.4 ± 3
51–60	4	23.5 ± 3	5	21.2 ± 3	9	22.2 ± 3
61–70	7	25.6 ± 3	10	22.1 ± 4	17	23.5 ± 4
71+	6	25.6 ± 3	9	24.6 ± 3	15	25.0 ± 3

mounted magnifying glasses. Data reported reflect actual brain sizes.

Statistical Analysis

Data were analyzed using PC-SAS (SAS Institute, Cary, NC) software. The two-tailed Student *t* test procedure was used to evaluate significant differences between groups, and the Pearson correlation coefficient was used to evaluate correlations between variables. Subjects were also divided into young (< = 50 years) or old (> 50 years) to provide normative data that may be useful for investigating early and late-onset Alzheimer disease.

Results

For all subjects the mean (±SD) estimated interuncal distance was 21.4 (±4) mm with a range of 12 to 29 mm. The mean interuncal distance was 23.8 (±3) mm for subjects older than 50 years and 18.6 (±3) mm for those younger than 50 years. Subjects older than 50 years of age had significantly larger interuncal distance ($t = -7.2$, $df = 73$, $P < .0001$) than younger subjects. Age was correlated with the interuncal distance ($r = 0.66$, $P < .0001$) for all subjects, and when analyzed for males ($P < .0001$) and women ($P < .0001$). Male subjects did not differ from female subjects in mean age ($t = 0.76$, $df = 73$, $P = .45$). Mean interuncal distances tended to be larger in men than women ($t = -2.17$, $df = 73$, $P = 0.03$). Table 1 shows age and gender specific data.

Discussion

The main finding in this study was that the interuncal distance increased with advancing age within the range of 12 to 29 mm in these subjects. The uniform MR methodology, the prospective selection of healthy volunteers, and the large sample size add credence to our findings.

Our findings have potential clinical implications. Dahlbeck et al (6) reported that an interuncal distance value of 30 mm separated controls from Alzheimer disease, with the latter exceeding this value. LeMay et al measured interuncal distances using CT (8). Although our study suggests that this distance may not exceed 30 mm in normal aging subjects, additional studies are needed to replicate and to address the specificity of Dahlbeck's findings. Our study will serve as normative data for comparison with findings in patients with suspected hippocampal degeneration.

There are some potential limitations in interpreting the results of our study. The MR protocol in our normal subjects was designed to match that currently in use for routine clinical brain MR studies at our institution and hence the images were not graphically prescribed to any internal brain landmarks. We also did not control for head size. We do not feel that lack of this measure confounds the results of our study. LeMay et al (8) have documented that linear measurements lack predictive power and are thus inadequate to correctly classify an individual case as control or Alzheimer disease. Thus additional studies of the interuncal distance in other patients such as Parkinson disease, epilepsy, and other dementia are indicated to confirm the report by Dahlbeck et al (6). A future study of interest would be to correlate volumetric hippocampal data, acquired using thinner interleaved sections obtained using internal landmarks, with the interuncal distance and with pathologic data. This would be essential to determine whether differences in interuncal distance reflect hippocampal pathology.

The hippocampal formation is suspected of being involved in several disorders. Quantitative studies of this region may provide valuable insights into the pathogenesis or early detection of these disorders, and MR provides a noninvasive method for testing this hypothesis.

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