Mild cognitive impairment (MCI) is a state where the cognitive functions are more impaired than what would be expected from aging alone but not enough to be described as dementia. In our material, there was an overrepresentation of men in the stable MCI group and an overrepresentation of women in the two other groups. Normalization of the data removed the gender-related differences in hippocampal volume and allowed for better utilization of the data. Hippocampal volumetry predicts conversion to dementia in MCI patients.

**MATERIALS AND METHODS**

The Göteborg MCI study is a clinically based longitudinal study that aims at identifying neurodegenerative, vascular and stress-related disorders prior to the development of manifest dementia. The subjects undergo biannual clinical assessment which among other things includes neurological, psychiatric and cognitive examinations and MRI.

The subjects with MCI (N=42) were independently classified as stable MCI (MCI-s, N=21) or converting MCI (MCI-c, N=21), using the Global Deterioration Scale. Healthy controls (N=26) were also included. There was a significant difference in sex distribution between MCI-c and MCI-s due to a bias in the sample.

Manual hippocampal volumetry using a custom method was performed on MR images at baseline and the two-year follow-up. Intracranial volumes (ICV) were estimated for all subjects using a previously validated method where the maximal intracranial areas are segmented in the coronal, sagittal and transversal planes.

**RESULTS - 1**

The results in Table 1 are absolute hippocampal volumes at baseline. They show that the patients in the converting MCI group have significantly smaller hippocampal volume than the stable MCI group, but only when looking at men and women together. Table 1 also shows that men are overrepresented in MCI-s and underrepresented in MCI-c. Women tend to have smaller ICV than men, and therefore smaller hippocampi as well. So, how much of the observed difference between MCI-c and MCI-s is due to a physiological sex difference? And does low ICV, in itself, contribute to the development of dementia?

**RESULTS - 2**

The ICV results (not tabulated here) showed that the only significant source of variation in ICV was the difference between the sexes. Normalization of hippocampal volumes with respect to ICV eliminated the difference between men and women. This makes it easier to interpret the pooled (men + women) data. The difference in hippocampal volume between the MCI-c and MCI-s groups is still significant (Table 2). This result is not contaminated by the normal gender difference in ICV.

**CONCLUSIONS**

Normalization allowed for meaningful comparisons between the full (both genders) clinical groups in spite of an overrepresentation of women in the converting MCI group. The findings confirm our hypothesis that hippocampal atrophy precedes cognitive decline in dementia but fails to support the idea that low ICV, as such, contributes to the development of dementia. Manual volumetry of the hippocampus can be a valuable instrument for predicting the course of MCI, but should be used together with a precise method for estimating ICV.