evaluation of symptoms upon the respondents. Although people with multiple sclerosis are in any event generally very aware of their changing symptoms, the regular evaluation and recording of these symptoms and their impact will not only have an effect on the perception of the symptoms themselves, but could also have an adverse effect upon the psychological adjustment of the respondent. There is an ethical issue here which deserves further consideration and evaluation. Nevertheless, the MSSID is a welcome addition to the toolkit of those who work, either clinically or in a research context, with individuals with multiple sclerosis.

J Neurol Neurosurg Psychiatry 2004;**75**:526–527.
doi: 10.1136/jnnp.2003.032367

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Memory complaints in the elderly

Grey hair and grey matter

L van de Pol, P Scheltens

Could treating memory disorders prevent dementia?

Memory complaints are very common in elderly people. In 1958 Kral[1] had already introduced the terms ''benign and malignant senescent forgetfulness,'' attempting to differentiate between ''normal'' and pathological decline in memory performance during aging. Since that time the discussion has been continuing and many definitions for a suspected ''transitional'' stage between normal aging and dementia have been proposed. In the currently widely used criteria of ''mild cognitive impairment'' (MCI) by Petersen *et al*,[2] one of the five key elements is objective memory impairment on testing, corrected for age and education, suggesting that age has an influence on memory performance. Yet little is known about the cognitive and structural changes that occur in the normal brain with aging. The study by Lyle *et al* in this issue tries to define magnetic resonance imaging (MRI) correlates of normal brain aging.[3]

The investigators carried out cranial MRI in 102 very old community dwelling individuals (aged 82 to 94 years). Using a multivariate model with hippocampal size, estimated visually and volumetrically, sociodemographic factors, and age related disease as predictors of memory performance, they found that left hippocampal measurements were predictive, especially on delayed retention of verbal material. Even in a subgroup of cognitively healthy elderly people (clinical dementia rating (CDR) = 0), left hippocampal measures remained predictive of delayed retention of verbal information. For those fond of visual rating of hippocampal atrophy, the results support the view that visual and volumetric estimates of hippocampal size perform equally well.[4]

These results strengthen the already widely known relation between the hippocampus and memory, but what do they tell us about (normal) aging? When comparing the cognitively healthy group (n = 57) with the group as a whole, the difference in influence of age on memory is striking. Age was a significant predictive factor in memory performance in the group as a whole, but lost its predictive value in the cognitively healthy group. In the light of this, is it possible that (a part of) the subgroup of CDR ⩾0.5 was mildly demented, and although these subjects were selected from the community, can they still be regarded as representatives of ''normal'' aging? If not, this might be considered an indication that age predicts memory deficits through the age related presence of hippocampal pathology. In this respect it would have been interesting to compare hippocampal sizes between the two groups. It has been shown repeatedly that hippocampal atrophy is a sensitive marker of early Alzheimer's disease pathology. Jack *et al* have observed a decline in volume of all medial temporal lobe structures, including the hippocampus, with advancing age, and were able to discriminate normal aging from early dementia among subjects with a CDR of 0.5.[5]

Studies correlating MRI and pathology in the very old are much needed. Hippocampal atrophy may be sensitive to Alzheimer's disease[6] but lacks specificity, and the pathological basis of radiologically observed hippocampal atrophy in normal aging is still largely unknown. It seems reasonable to assume that besides Alzheimer's disease pathology there may be other processes in aging that target the hippocampus, such as hippocampal sclerosis or vascular damage.

A better understanding of the basic mechanisms of cognitive function and its anatomical correlates in normal brain aging will help clinicians to diagnose and treat memory disorders in the elderly and possibly to prevent dementia as the ultimate consequence of longevity.[7]

J Neurol Neurosurg Psychiatry 2004;**75**:527–528.
doi: 10.1136/jnnp.2003.032391

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CSF analysis in subarachnoid haemorrhage

Recommendations for CSF analysis in subarachnoid haemorrhage

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Spectrophotometry of CSF involving bilirubin quantitation is the recommended method of analysis

In this journal in the late 1980s, two papers presented contrasting advice about the appropriate investigation of cerebrospinal fluid (CSF) in suspected subarachnoid haemorrhage when computed tomography (CT) of the head revealed no evidence of blood. The first concluded that it was the detection of red blood cells that was important in supporting a decision to proceed to cerebral angiography and not that of the red cell breakdown products, oxyhaemoglobin and bilirubin.[1] This was a conclusion based on the use of visual inspection to detect the colour (xanthochromia) imparted by oxyhaemoglobin and bilirubin. The second, based on a series of 111 patients in whom blood was found on CT, concluded that it was the presence of oxyhaemoglobin and bilirubin, as detected spectrophotometrically, that was important.[2] An editorial in The Lancet picked on the difference in examination principle (visual inspection versus spectrophotometry) as being fundamental to the contrasting conclusions.[3] The editorial concluded that spectrophotometry was the appropriate way in which to examine CSF when the occurrence of subarachnoid haemorrhage was in doubt. As was subsequently pointed out, the criteria recommended to determine a positive finding were ambiguous on two counts, and it was not clear that the conclusions reached from a study of patients where blood was detected could be extrapolated to those where blood was not visualised on imaging.[4] Moreover, although the subjectivity involved in visual inspection of CSF had been replaced by spectrophotometry, this still involved a subjective interpretation of the spectrophotometric scan without any guidance on what quantitative amounts of oxyhaemoglobin or bilirubin constituted a positive finding.

Against this background it was clear that even in the late 1990s there was much confusion about how CSF should be analysed and the results interpreted in CT negative suspected subarachnoid haemorrhage. Consequently, a working group convened to produce guidelines on CSF sampling, transport, handling, analysis, and interpretation. Central to this process was a retrospective multicentre review of over 700 cases where spectrophotometry had been undertaken, haem pigments identified, and bilirubin quantitated, and where the angiographic outcome was known in 87 cases. While recognising the limitations of such a process, which inevitably would have resulted in some patient selection and population bias, this was a significant improvement on the knowledge that existed at this time.

These guidelines have now been published.[5] The key recommendations are as follows:

- Spectrophotometry of CSF involving bilirubin quantitation is the recommended method of analysis.
- This should be done on the final bottle of CSF to be collected.
- An increased CSF bilirubin is the key finding which supports the need for further investigation. Bilirubin will usually be accompanied by oxyhaemoglobin.
- The occurrence of oxyhaemoglobin alone is most often artefactual, but occasionally may occur with subarachnoid haemorrhage.
- Absence of oxyhaemoglobin and bilirubin on spectrophotometry is not supportive of subarachnoid haemorrhage.

In addition, the group has worked closely with UK NEQAS for Immunochemistry to produce a robust external quality assurance (EQA) scheme through which laboratories can maintain appropriate analytical and interpretative standards.

We believe that the production of the guidelines and the introduction of the EQA scheme represent a significant step forward in ensuring an appropriate standard of CSF analysis. We urge all clinicians and laboratories to adopt these practices.

J Neurol Neurosurg Psychiatry 2004;**75**:528.
doi: 10.1136/jnnp.2003.023176

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