When comparing the patients with a primary-progressive course (n=11) to those with a relapsing-remitting course (n=349), the former were significantly more impaired in various domains (as indicated by asterisks).

However, the patients with primary-progressive course had a higher mean EDSS score and a longer duration of disease. When selecting a group of relapsing-remitting patients matched with respect to EDSS and duration of disease (n=11), no differences between primary-progressive and relapsing-remitting patients could be ascertained.

Summary

The computerized memory and attention test (MAT) proved to be a practicable tool for the assessment of cognitive performance in patients with MS. In the MS patients, we found a marked impairment of episodic short-term memory (ESTM), which correlated with disease severity and duration. This impairment may affect activities of daily living as well as the ability to work. In patients with primary-progressive MS, after correction for disease severity and duration, the impairment of episodic short-term memory was not stronger than in patients with a relapsing-remitting course of the disease.

Disclosure

This study was sponsored by Novartis GmbH Nürnberg through an unrestricted research grant. The MAT is property of Dynamikos GmbH.

Cross-sectional study in MS patients

A multicentric cross-sectional study in a large, unselected group of MS out-patients was performed at nine centers in Germany (1).

A neuropsychological assessment was done by means of the MAT. Additional clinical data were collected: duration and type of MS, EDSS score, medication, presence of fatigue or depression.

Data were centrally evaluated at the ISPG Mannheim (1).

So far, 446 patients (290 women, 156 men) were assessed. Their ages were between 17 and 60 years (mean ± SD: 39.6 ± 10.1). The majority of the patients had a relapsing-remitting course of disease (78 %). Mean EDSS was 2.8 (SD: 1.7).

Profile of memory and attention in MS patients

Memory and attention performance in the MS patients (n=446) compared to age-, sex- and education-matched controls (n=84).

The differences were significant for episodic working memory, episodic short-term memory and verbal short-term memory.

Evaluation of the MAT

The MAT was evaluated in a mixed group of 42 elderly healthy volunteers and 42 age-, sex- and education-matched patients with mild to moderate Alzheimer’s dementia at ages between 60 and 84 years (mean ± SD: 71.2 ± 7.2 years). The correlations of the subtests with the respective reference methods were between 0.63 and 0.84 (Pearson’s r). Controls and patients were separated with a sensitivity of 0.74 and a specificity of 0.71. The MAT was readily accepted by the elderly probands. A slight majority even preferred the computerized test to be tested by a person.

The memory and attention test (MAT) is a computerized test, which allows a standardized adaptive testing of the working and short-term memory for verbal, figural and episodic material as well as an assessment of selective attention.

The MAT is easy to apply. The visual or auditory tasks are presented by means of a laptop. The test person responds by pressing on two buttons of a touchpad. The findings in each person are compared to the data of an age-, sex- and education-matched control group.

The computerized memory and attention test (MAT) proved to be a practicable tool for the assessment of cognitive performance in patients with MS. In the MS patients, we found a marked impairment of episodic short-term memory (ESTM), which correlated with disease severity and duration. This impairment may affect activities of daily living as well as the ability to work. In patients with primary-progressive MS, after correction for disease severity and duration, the impairment of episodic short-term memory was not stronger than in patients with a relapsing-remitting course of the disease.

Disclosure

This study was sponsored by Novartis GmbH Nürnberg through an unrestricted research grant. The MAT is property of Dynamikos GmbH.

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STEP 1. Standardization and translation of test stimuli. For visual stimuli, determine if there are any semantic associations to stimuli in the culture or language under consideration. For verbal memory, match new words on word frequency and similarity of meaning. If these parameters cannot be applied scientifically, then expert review and performance on test by appropriate participants will be utilized to assess translation.

STEP 2. Standardization and Translation of Test Instructions. All information from the test manual necessary for administration and interpretation must be translated, back translated, and checked for errors.

STEP 3. Normalisation. Samples of 150 or more healthy persons are suggested for data applicable to all ages. At a minimum, 65 controls matched on demographics to a concurrent MS sample, or to samples in published descriptive MS studies, is needed.

STEP 4. Test-retest reliability. Assessment can be achieved by evaluating an MS and/or healthy volunteer sample on two occasions separated by 1-3 weeks. This is the gold standard separation where the only question is test reliability, controlling for maturation effects. A Pearson’s correlation coefficient >0.80 will usually be required. STEP 5. Criterion-related validity. This step can be pursued in conjunction with Step 3, in that an MS sample can be compared to a healthy control group that also serves for normalization.

Discussion: Preliminary plans are being made to validate BICAMS in a number of countries, which will constitute important steps towards an international assessment tool of cognition in MS.

Professor Benedict has acted as a consultant or scientific advisory board member for Bayer, Biogen Idec, Merck Serono, EMD Serono, Pfizer, Novartis; royalties from Psychological Assessment Resources, Inc; financial support for research activities from Shire Pharmaceuticals, Biogen Idec.

Professor Amato received personal compensation from Merck Serono, Biogen Dompé, Sanofi Aventis, Bayer Schering for serving on scientific advisory board and for speaking; Prof. Amato received financial support for research activities from Merck Serono, Sanofi Aventis, Biogen Dompé, Bayer Schering.

Dr Boringa has consulted for Bayer Helathcare and served on speaker bureau for Exenica Pharma Academy.

Professor Brochet has served on scientific advisory boards for Bayer Healthcare and Novartis; has received funding for travel or speaker honoraria from Bayer Healthcare, Merck Serono, Biogen Idec, Sanofi-Aventis, Novartis and Teva Pharmaceutical Industries Ltd./Sanofi-Aventis; his institution received financial support for research activities from Bayer Healthcare and Merck Serono.

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Dr Hämäläinen received personal compensation from Bayer Healthcare and Novartis for serving on scientific advisory boards; consulting for Sanofi-Aventis; served on speaker bureau for Bayer Healthcare and Sanofi-Aventis.

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P891

Memory and attention in patients with multiple sclerosis: relationships with depression and fatigue

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Background: Cognitive impairments have been frequently described in patients with multiple sclerosis (MS) and may involve memory and attention. Type and extent of memory and attention impairments in outpatients with MS were assessed and related to the presence of depression and fatigue.

Methods: Memory and attention performance were examined at a number of neurological practices and specialized MS outpatient clinics by means of the computer-based Memory and Attention Test (MAT). By means of the MAT, working and short-term memory for verbal, figural and episodic material as well as selective attention are assessed in a standardized adaptive fashion. The test can be performed by the patients without assistance and needs about 45 minutes. In this preliminary evaluation, we present the findings in 400 patients with multiple sclerosis and compare them with the findings in an age-, sex- and education-matched control group of 84 volunteers.

Results: The patients were 133 (33.3%) males and 267 (66.7%) females at ages between 17 and 70 years (M:40.1; SD: 10.9 years). The course of the disease was relapsing-remitting in most of the patients (78.0%); mean EDSS score was 2.8 (SD: 1.7).

The patients showed impaired performance in episodic working memory (p<0.01), figural short-term memory (p<0.05) and episodic short-term memory (p<0.05). Attentional performance was unimpaired. A fatigue syndrome was diagnosed in 106 of the patients (26.5%), a depression in 34 of the patients (8.5%).
In the patients suffering from fatigue, no particular impairments of memory and attention were observed compared to the other patients. However, in the patients with depression, memory and attention were stronger impaired than in the other patients; we found significant impairments in episodic working memory (p<0.01), verbal working memory (p<0.01) and selective attention (p<0.05). After exclusion of the patients with depression from the group comparisons, the differences between patients and controls were confirmed.

**Conclusions:** These findings suggest that two components of memory impairment may be distinguished in patients with multiple sclerosis. One component mainly affects working memory and selective attention and is made worse by the additional occurrence of depression. The other component mainly affects short-term memory and seems to be rather unaffected by the presence of depression or fatigue.

This project was supported by a research grant of Novartis GmbH, Nürnberg

**P892**

**Pilot outcomes of Tower of Hanoi test performance for executive function assessment in patients with multiple sclerosis**


*Palacky University (Olomouc, CZ)*

**Objective:** Tower of Hanoi puzzle (ToH) is a widely used neuropsychological tool to evaluate the integrity of the frontostriatal systems. Application is associated with planning ability and problem-solving task that reflects the executive functions (EF). EF are frequently impaired in all stages of multiple sclerosis (MS)

**Methods:** There was used a new way of application of ToH. We administrated first the simplest three, then the four and five disk version in 5 minute limits for each version. The number of movements, the solution time, the perseverations and the frequency of the rule breaks were registered. The minimum number of moves for a solution is \(2n - 1\). The “n” means the number of the disk. The core test battery also includes neuropsychological tests for cognitive functions assessment, behavioral and personality changes as well. EF were assessed in sample of patients with relapsing-remitting form of MS (RRMS, \(n = 32\), average age 40.1 years, SD±12.04) matched to healthy controls (\(n = 94\), the average age 72.67 years, SD±12.04). Finally we used the three and four disk version in 5 minute limits for each version. The number of moves for a solution is \(2n - 1\). The “n” means the number of the disk. The core test battery also includes neuropsychological tests for cognitive functions assessment, behavioral and personality changes as well. EF were assessed in sample of patients with relapsing-remitting form of MS (RRMS, \(n = 32\), average age 40.1 years, SD±12.04) matched to healthy controls (\(n = 94\), the average age 72.67 years, SD±7.10). Finally we used the three and four disk version of the ToH for statistically analysis.

**Results:** We found statistically significant differences in extended solution time and increased number of movements (p<0.01) in healthy controls in three disk version of ToH. On the other hand in the four disk version we did not found any statistically significant differences neither in solution time nor in number of movements. (p<0.01).

**Conclusion:** The executive functions are not involving too much in the three disk version of ToH. Even the results of four disk version of ToH are not proving significant differences between the MS and the control group, this result is pointing out the executive function impairment in RR MS patients. The executive abilities of the observed MS sample in average age of 40 correspondents to that in the healthy group in their seventies. Using the ToH puzzle we revealed an executive level decline in young MS patients up to one generation zone.

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The authors have nothing to disclose.

**P893**

**Relationship between memory outcomes and normalised regional brain volumes in paediatric-onset multiple sclerosis patients**


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**Background:** Learning and memory impairments are often reported in youth with multiple sclerosis (MS). The specific domains of memory function that are most vulnerable to impairment, and the underlying neural substrates associated with these impairments, however, are not well understood.

**Objectives:** To examine memory function and its relation to total brain volume and specific brain structures associated with memory in children and adolescents with MS.

**Methods:** Verbal and nonverbal memory was assessed in 31 youth with MS and 30 age- and sex-matched healthy controls using the Test of Memory and Learning (TOMAL-2). Concurrent MRI scans were performed for all participants on a 1.5T GE TwinSpeed Excite 12.0 scanner. A model-based segmentation method was used to measure volume of the hippocampus, amygdala, and thalamus in T1-weighted images. Regional and total brain volume measures were then standardized using data collected as part of the National Institutes of Health pediatric MRI study, yielding age- and sex-specific z-scores for all study participants. Performance on the memory tests were correlated with these standardized MRI metrics.

**Results:** Average age at MS onset (defined as disease onset) was 11.9 ± 3.8 years and average disease duration was 4.3 ± 3.1 years. Fewer than 10% of MS patients demonstrated impaired memory performance (defined as <1 SD below normative performance on any one test). The MS group had lower total brain volume (p<.001), amygdala volume (p<.005) and thalamic volume (p<.001) compared with controls. Groups did not differ significantly with respect to hippocampal volume. In the MS group, but not control group, memory performance correlated positively with regional brain volumes of the hippocampus, amygdala, thalamus, and with total brain volume. Memory for visual information was most strongly associated with thalamic and amygdala volumes, whereas word-list learning performance was most strongly associated with hippocampal volume.

**Conclusion:** While memory impairment and hippocampal atrophy were not implicated as prominent features of pediatric MS, a robust relation was observed between increased total hippocampal volume and better performance on a verbal learning task.