Screening for cognitive impairment in Multiple Sclerosis
Proposal of an expert-based two-step approach

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Background:
Cognitive impairment in the early phase of multiple sclerosis (MS) is a common finding. Occurring in up to 65% of MS patients and also independently of physical disability, these deficits can cause significant limitations in activities of daily living, such as employment status. Recent studies observed cognitive decline even in patients with probable MS, early onset MS, or in clinically isolated syndromes suggestive of MS. As a large proportion of these patients are engaged in vocational activities, often working in a demanding environment, cognitive impairments at all stages of the disease may become a crucial factor to patients’ professional as well as social life, thus reducing their quality of life substantially. Hence, there is a strong need for a short, validated and widely accepted tool to identify patients with cognitive deficits in an early stage since this may have implications for treatment and rehabilitation. Nevertheless, there are some practical issues which might prevent a proper recognition and subsequent management of these problems. First, there are only few validated instruments to assess cognitive deficits in MS patients. Secondly, a standardized assessment of cognition in MS, while time consuming, lacks an appropriate remuneration.

Objectives:
1. To define and recommend a brief cognitive screening test for routine testing in daily practice to identify cognitive impairment in MS patients.
2. To propose an algorithm to assess cognitive deficits in MS patients.

Methods:
An expert committee consisting of neuropsychologists and neurologists representing clinicians and private practice neurologists was convened.

On a basis of a literature survey several neuropsychological assessment tools for the measurement of cognitive deficits in MS were reviewed. Subsequently the identified tests were critically discussed concerning statistical prerequisites (objectivity, reliability, validity, sensitivity, specificity). In a follow-up meeting it was concluded by consensus that, in addition to methodological standards the diagnostic approach should also consider practical issues, such as patient acceptability, brevity, and practicability to be implemented in a practice setting. Consequently, some MS-specific neuropsychometric screening tools meeting these criteria were first selected and then, prioritized according to their methodology-usability-trade-off.

These selected screening tools were also submitted to a feasibility analysis among the members of the group. Based on a 5-point scale the single tests were evaluated regarding their practicability and efficiency.

Results:

Screening
Based on pertinent reviews and clinical experience from the individual participants (hospital- and private practice-based) it was concluded that cognitive function should at least be screened with appropriate tools if extended assessment is not possible. Among the discussed neuropsychometric tests (MMSE, MoCA, BRB, FST, PASAT, MUSIC, SDMT) the following tests were identified to meet the specificity-methodology-usability-trade-off satisfactorily:

1. Symbol Digit Modalities Test (SDMT)
2. Multiple Sklerose Inventarium Cognition (MUSIC)

In the feasibility analysis both tests proved to be suitable for application in daily routine (Table 1).

Recommended Screening Tests:
1. SDMT
   The Symbol Digit Modalities Test (Fig. 1) detects cognitive impairment in less than 5 minutes, including instructions, practice, and testing. It evaluates visual scanning, visual attention and processing speed, and probably also episodic memory. The test has demonstrated remarkable sensitivity in detecting not only the presence of brain damage, but also changes in cognitive functioning over time and in response to treatment. The SDMT involves a simple substitution task that MS patients can easily perform. Using a reference key, the examinee has 90 seconds to pair specific numbers with given geometric figures. The sensitivity and specificity of a computerized version of SDMT is 71% and 84%, respectively.

   Because examinees can give written or spoken responses, the test can be used with almost anyone, including those with motor disabilities or speech disorders. Because it involves only geometric figures and numbers, the SDMT is relatively culture free as well, and can be administered to people independent of the spoken language.

2. MUSIC
   The MUSIC (Multiple Sklerose Inventarium Cognition) test (Fig. 2) consists of five cognitive sub-tests and a fatigue scale. The sub-tests assess short- and long-term memory, information processing speed, attention and fatigue. The test was specially developed for MS and is a reliable and quick (10-12 min.) way of mapping the most frequent core deficits in MS cases. The test is standardised and normalised and can also be converted into a points system to permit ongoing assessments to be made.

   This test contains 5 cognitive sub-tests, which measure: short-term memory, long-term memory, information processing speed, attention and fatigue. The test is simple to administer and can be used with patients who have mild to moderate cognitive impairment.

Algorithm (two-step approach)
Within the expert group appropriate timing for screening an individual for cognitive impairment was addressed.

1. The expert group suggested to screen MS-patients at the time of MS diagnosis with at least one of the proposed screening tests.

   It should be considered, that neuropsychological test performance, including tests such as SDMT or MUSIC can be influenced by physical symptoms of MS (relapse), the presence of concurrent neurological disorders other than MS, concurrent medications (corticosteroids), and symptom depression, fatigue, disability.

2a. For patients with appropriate test performance at screening, repeated testing should be performed if the patient reports cognitive decline or the treating physician suspects cognitive impairment.

   If cognitive dysfunction is diagnosed by screening, the cognitive performance may be further tested in detail by comprehensive psychometric batteries.

Conclusion:
Cognitive impairment is a common feature of MS. It may occur even in early phases of the disease and has often a significant negative impact on daily life. There is a strong need to identify patients with cognitive deficits early since this may have implications for pharmacologic treatment and/or neuropsychological training.

Our evidence and expert-based proposal of an algorithm aiming to detect cognitive disturbances in individuals with MS as early as possible combines both evidence-based as well as practical issues. As a result, it became apparent that only few screening tools were suited to meet these criteria. SDMT and MUSIC were identified as appropriate screening-tools based on requirements. Thus, the expert group proposes a two-step approach, considering a cognitive screening with one of these tests at the time of MS diagnosis. In a second step the cognitive performance may be further explored in detail by comprehensive psychometric batteries when cognitive dysfunction is diagnosed by screening. If no cognitive impairment is detected by SDMT and/or MUSIC, a re-evaluation should be considered when patients subjectively report cognitive decline or the physician suspects evolving cognitive impairment.

The proposed algorithm should help to identify MS patients with cognitive deficits at an early stage in order to adapt individually/adapted strategies of treatment or other interventions.

References:
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