Validation of a screening instrument to detect cognitive and psychoaffective deficits in children and juveniles with Multiple Sclerosis - The MUSICADO study

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Introduction
Cognitive and psychoaffective deficits may already appear in the early years of the disease in children affected by multiple sclerosis (MS). The most affected areas include attention, visual-perceptual abilities, executive functions and - in contrast to adults - verbal skills. Fatigue and Depression are also frequent. However, these deficits remain unrecognized as a lack of specific screening tools during regular clinical visits for children and adolescents.

Aim of the study
The aim of this study is to validate a modified screening tool (MUSIC = MULTiple Sclerosis Inventory of Cognition) which is already in use in adults and to adapt this screening-instrument for children and juveniles (MUSICADO = MULTiple Sclerosis Inventory of Cognition in ADOlescents). Additional standardized clinimetric tests will be used in order to validate this measure, and a questionnaire for depression and fatigue will also be added.

MUSICADO
On the basis of well established test paradigms five subtests were developed which assess cognitive functions that can be impaired in MS (see Table 1, fig. 1A and 1B). MUSICADO will also contain a short fatigue questionnaire which can be scored and interpreted independently.

Patients (MUSIC-study)
For the normation of the MUSIC, a total of 185 control subjects (control group (CG), mean age 36.9 years, SD=10.9, range 19-62) who were classified as cognitively unimpaired by means of standard psychometric tests were included in the study. Furthermore, 80 patients with MS (mean age 39.2 years, SD=11.3, range 18-61; median of disease duration 10 months, range 0 – 300 months) were enrolled in the study. All patients underwent detailed neurological and neuropsychological examination.

Methods (MUSIC study in adults)
On the basis of discriminant analyses raw scores were weighted, and a maximum transformed score of 30 was defined for MUSIC (Table 1). CG data (mean scores and standard deviations) was then used to define transformation of raw scores, cut off scores for impairment and score ranges for different severities of dysfunction.

Inclusion criteria for the MUSICADO validation study
Altogether n=100 patients from 28 participating centers from Germany (n=26) and Austria (n=2), aged 12-18 years, fulfilling the revised MacDonald-criteria, will be included. A matched cohort of healthy controls will serve to calculate ortho- and pathonorms. The study protocol has been approved by the ethic-committees of the participating centers.

Table 1: Description of MUSIC subtests (adult version)

<table>
<thead>
<tr>
<th>Subtest</th>
<th>description</th>
<th>cognitive domain assessed</th>
<th>max. raw score</th>
<th>max. transformed score</th>
</tr>
</thead>
<tbody>
<tr>
<td>word list A</td>
<td>a word list with 10 items and free recall in two trials</td>
<td>verbal short term memory</td>
<td>20</td>
<td>4</td>
</tr>
<tr>
<td>word list B</td>
<td>another word list with 10 items and free recall in one trial</td>
<td>interference in memory</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>word generation</td>
<td>name as many items that can be bought in a supermarket in 1 minute</td>
<td>executive function, word finding</td>
<td>n.l.</td>
<td>4</td>
</tr>
<tr>
<td>naming</td>
<td>confrontation naming (Figure 1A), time is taken</td>
<td>speed of information processing, naming</td>
<td>n.l.</td>
<td>6</td>
</tr>
<tr>
<td>interference</td>
<td>interference task (Stroop paradigm (Figure 1B), time is taken</td>
<td>interference</td>
<td>n.l.</td>
<td>5</td>
</tr>
<tr>
<td>word list A delayed</td>
<td>delayed recall of list A</td>
<td>verbal long term memory</td>
<td>10</td>
<td>7</td>
</tr>
</tbody>
</table>
| Total score: 30 points

Conclusion
MUSICADO-project is aimed to develop an economical and efficient screening-tool to detect cognitive impairment in juvenile MS patients at an early stage of the disease. The test should be easy to administer and well accepted by the young patients. Moreover, the test should offer a classification algorithm to discriminate age-appropriate from mildly, moderately or severely impaired individuals.

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