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Utilization of the auditory consonant trigram test to screen for cognitive impairment in patients with multiple sclerosis: comparison with the paced auditory serial addition test

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Several screening methods have been evaluated, but most of them are insensitive to MS-related cognitive impairment. The Auditory Consonant Trigram (ACT) test, which contains core features required for a working memory task, has been used to test neuro-cognitive function in different samples of patients to examine the status of working memory. The aim of the present study was to investigate the correlation between ACT and the Paced Auditory Serial Addition Test (PASAT), and the usefulness of ACT for evaluating the cognitive impairment in MS in a brief visit. A total of 109 consecutive patients with definite MS were included. The patients were administered ACT, PASAT and EDSS. Mean PASAT score and mean ACT score were 46.19±8.51 and 45.30±9.07, respectively. Correlations between EDSS and PASAT, and EDSS and ACT were moderately strong. The correlation between ACT and PASAT was very strong ($r = 0.831$, $P < 0.01$). The mean time required to perform ACT was significantly shorter than PASAT (7.25±4.72 and 14.70±6.97 minutes, respectively). In conclusion, as a relatively brief measure of working memory, ACT was well accepted by MS patients and has a strong correlation with PASAT. Thus, ACT might be used for rapid evaluation of cognitive impairment in patients with multiple sclerosis.
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Key words: *multiple sclerosis; auditory consonant trigrams; paced auditory serial addition test; cognitive impairment; screening test*

Introduction

Cognitive impairment may have a significant impact on social and occupational functioning in multiple sclerosis (MS),[1] and occurs in 40–60% of patients.[1,2] Several screening methods have been evaluated in MS. For example, the most common used one, the Mini-Mental State Examination (MMSE)[3] is insensitive to MS-related cognitive impairment, except in the most severely impaired patients.[4]

The Auditory Consonant Trigram (ACT) test[5,6] has been developed to assess short-term memory, divided attention, and information-processing capacity in adults.[7] It contains core features required for a working memory task and is being used as a measure of verbal working memory. Impaired performance on ACT has been observed under conditions such as Alzheimer's disease,[8,9] Korsakoff's syndrome,[10] anterior communicating artery aneurysms,[11] or traumatic brain injury.[12]

The Paced Auditory Serial-Addition Test (PASAT)[13] imposes high demands on the subject's working memory capacity, requiring controlled information processing (attention), visual memory, good auditory functioning and calculating ability.[14]

The aim of the present study was to investigate the correlation between ACT and PASAT, and the usefulness of ACT for evaluating the cognitive impairment in MS in a brief visit.

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Material and methods

Patients

A total of 158 consecutive patients with definite MS in terms of McDonald's criteria[15] were included. The sex ratio was around two females to one male reflecting the distribution in the general MS population (101 female patients). Most of patients ($n = 109$) had a relapsing–remitting course. Thirty-two patients had a secondary progressive course and 17 had a clinically isolated syndrome. Mean age was 33.18±8.67 (range 19 and 55), mean duration of disease was 7.11±7.54 (range 1 and 29), and mean EDSS score was 4.02±2.17 (range 1.5 and 6.5).

Patients who had not experienced a relapse and were stable in ongoing MS medications within the last three months were enrolled in the study. Patients with definite MS on the basis of McDonald's criteria (other than primary progressive MS patients) were included. Patients under the age of 18 and above 55 were not included.

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ACT and PASAT

In the ACT, three consonants are presented. The subjects should remember these consonants after intervals of 0, 9, 18 and 36 seconds. During the intervals of 9, 18, and 36 seconds, the subjects were required to count backwards aloud by threes from different numbers; e.g., 100-97-94. To calculate the total score, the number of consonants recalled correctly on each trial, including those from the 0-second delay trials, was summed. The maximum score obtainable was 60.

The PASAT consists of 61 random digits, which are sequentially presented from audiotape. The subject is instructed to add the last digit to the preceding one, for every number he/she heard. The resulting sum has to be vocalized before the next digit is presented. The 3-second/digit version of PASAT (PASAT-3) was used in the present study. For PASAT, the maximum score obtainable was also 60.

Procedure

ACT, PASAT and EDSS were assessed at the same time of the day, i.e., at 09.00 and 10.00 hrs. Two trained neurologists administered the PASAT and ACT. A rest period of 10 minutes was allowed between the two tests. The Turkish version of the ACT test was used, which was adopted into Turkish recently.[16] The same neurologist performed the EDSS. The number of correct sums given in the PASAT-3 and ACT (out of 60 possible) was used for analysis.

Analysis

Pearson's correlation test was conducted to assess correlations between ACT, PASAT and EDSS. Correlations were also performed to assess the relationship between the two tests and demographic and clinical features, e.g., age and duration of disease. The difference between male and female patients was investigated using the chi-squared test. Student's *t*-test was used for evaluating the difference between the mean time required performing PASAT and ACT. ANOVA was performed for detecting the difference of PASAT and ACT scores among the groups of disease courses.

Results

The mean PASAT score was 46.19±8.51 (range 28 and 59), and the mean ACT score was 45.30±9.07 (range 30 and 57). There were no significant sex differences for both tests. In the subgroups, in terms of disease course, the mean PASAT scores were 48.78±7.77 in patients with relapsing–remitting MS (RRMS), 49.85±8.92 in patients with clinically isolated syndrome (CIS) and 34.76±10.18 in secondary progressive MS (SPMS) patients. ACT in these groups was 47.11±6.31, 49.02±10.34 and 36.08±9.80, respectively. Again, there were no significant differences in PASAT and ACT scores between the patients with RRMS and CIS ($P>0.05$). The difference between the patients with RRMS and SPMS in terms of PASAT ($P=0.006$) and ACT ($P=0.009$) were significant. As expected, the differences between SPMS and CIS group were more prominent for both PASAT ($P=0.004$) and ACT ($P=0.008$).

There were negative and moderately strong correlations between the EDSS and PASAT, and EDSS and ACT ($P<0.01$). In other words, as EDSS scores increased, progressive decrease was found in the PASAT and ACT scores, indicating poorer performance on the functional measures within the two tests. The correlation between ACT and PASAT was very strong ($r=0.831$, $P<0.01$).

There was moderate correlation between EDSS and disease duration ($r=0.410$, $P<0.05$). The correlation between disease duration and ACT, and disease duration and PASAT was very weak and was not statistically significant. The results of correlation analysis are summarized in Table 1.

The mean time required to perform PASAT was 14.70±6.97; this was significantly shorter for ACT (7.25±4.72, $P=0.016$) (Table 1).

Discussion

In the present study, there is a significant and strong correlation between ACT and PASAT. In addition, the time required to perform ACT is significantly shorter than that required for PASAT. There have been no studies that detect the correlation between ACT and PASAT. However Stuss's study on traumatic brain injury found that only ACT was sufficiently sensitive to differentiate the concussed patients from the control group.[12] Combining with the stressfulness of PASAT,[12] ACT might be used for detecting cognitive impairment briefly, in patients with MS.

Impaired performance in ACT is observed under a variety of conditions. It has been suggested that the test is particularly sensitive to frontal lobe or frontal/brainstem deficits.[17] PASAT and ACT appear to assess similar aspects of cognition such as speed of information processing and short-term memory. Suggestion of Kopelman and Stanhope is to relate ACT to generalized deficits in information processing rather than to specifically frontal functions.[19] In comparison to PASAT, Stuss *et al.* found ACT a relatively brief measure of short term or working

Table 1 Results of ACT and PASAT scores, correlations and time required for tests

Mean ACT score (±SD)	47.11±6.31 (32–55)
Mean PASAT score (±SD)	48.78±7.77 (28–58),
Correlations (*r*)	
EDSS–ACT	−0.467
EDSS–PASAT	−0.557
ACT–PASAT	0.826
EDSS–disease duration	0.433
ACT–disease duration	−0.256
PASAT–disease duration	−0.263
Time required (minutes±SD)	
ACT	8.05±2.86 (4.90–13.20)
PASAT	13.65±4.77 (4.30–18.30)
P	0.017

memory in traumatic brain injury.[12] It has also been suggested that it is less affected by moderator variables such as age and education, and it is less stressful than PASAT.[12] For conditions such as MS that do not affect mortality but do produce morbidity, perhaps the most important factor is the impact of disease on patients' quality of life.[20] Cognitive decline is one of the main agents of quality of life impairment.[18] Thus, the detection of cognitive impairment in a brief visit is very important in MS. PASAT has been used to detect cognitive impairment in the last decade in MS patients. However, there are some drawbacks to PASAT: it is stressful for patients[12] and is a time-consuming process. This study is the first one to detect the correlation between ACT and PASAT in MS, and investigate the usefulness of ACT as a screening test besides PASAT in patients with MS.

In a previous study, correlation between EDSS and PASAT has been shown in relapse periods in patients with MS.[21] In that study, EDSS had the weakest relationship with PASAT among the three components of Multiple Sclerosis Functional Composite (e.g., PASAT, Nine Hole Peg Test and Timed 25 Walk Test) which might confirm the knowledge of poor assessment of cognitive decline of EDSS.[21] In fact, clinical rating scales, such as EDSS, were designed to measure abnormalities observable during the neurological examination, and not to be sensitive to the cognitive deficits typical of MS. In the present study, correlations between EDSS and PASAT, and EDSS and ACT were similar. This result supports the suggestion that ACT, similar to PASAT, may remove the inadequacy of EDSS in determining cognitive impairment.

The correlation between EDSS and disease duration has been demonstrated,[21] and is not surprising. But the correlation between disease duration and ACT, and disease duration and PASAT was very weak. Although cognitive impairment does not occur in only advanced stages of MS, and is one of the more common disease manifestations in MS, early studies suggested that cognitive function was reasonably stable in most MS patients.[22] The weak relationship between disease duration and cognitive impairment may be related to the inadequate conventional methods of establishing disease duration. Recent studies of axonal transection[23] and brain atrophy[24] have shown that the disease process may start many years before clinical symptoms.

In conclusion, as a relatively brief measure of working memory, ACT was well accepted by MS patients. In comparison to PASAT, which is a component of MSFC and measures working memory, ACT has a strong correlation with PASAT. Thus, ACT might be used for rapid evaluation of cognitive impairment in patients with multiple sclerosis.

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