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Alzheimer's & Dementia 3 (2007) 23–27

Alzheimer's & Dementia

Computerized diagnosis of mild cognitive impairment

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Abstract

Background: We previously described software that we have developed for use in the evaluation of mild cognitive impairment (MCI). Our previous study included an aged nondemented population with memory complaints (n = 41) that was relatively homogenous in terms of education, clinical history, neurological examination, and Mini-Mental Status Examination (MMSE) scores. Performance patterns in the computerized tests separated the subjects into two groups, and we hypothesized that one group might have had incipient dementia.

Methods/Results: In the present study we report a follow-up of 35 of the subjects 2 years later. Eight subjects who were thought to have incipient dementia at baseline could be evaluated in the follow-up, and six of them have deteriorated according to both MMSE and neurologists' evaluations and have now fulfilled clinical diagnostic criteria of dementia. The other two deteriorated only according to their computer performance. Of the 27 remaining subjects, only one now fulfilled clinical diagnostic criteria for dementia, although the present computerized examinations identified 10 subjects whose performance has deteriorated compared with the previous session.

Conclusion: The follow-up examination thus supported our hypothesis that human-computer interaction features can contribute to the detection of incipient dementia.

Keywords: Computerized neuropsychological test; Human–computer interaction; Mild cognitive impairment; Dementia; Mini-mental state examination; Alzheimer prediction

1. Background

Alzheimer's disease (AD) typically presents with complaints of memory decline, later encompassing additional cognitive domains. Complaints of memory impairment are, however, common in old age and have a heterogeneous nature [1]. The need to diagnose AD early becomes imperative because of the development of new therapies. Currently used diagnostic techniques include neuropsychological evaluation and biologic markers. Tests that are now being examined include cerebrospinal fluid markers such as A1-42 or tau [2] and magnetic resonance imaging [3,4], which are expensive and not widely available.

The transitional phase between healthy cognitive ageing and dementia has been designated mild cognitive impairment (MCI) and has received a lot of attention during recent years. However, MCI is heterogeneous in terms of etiology and outcome [5], and its definition is arbitrary [6,7]. In the literature, a score in neuropsychological tests of 1.5 standard deviations below the normal average that corresponds to the individual's age has been suggested for the diagnosis of MCI [8], but this arbitrary criterion has not yet been validated sufficiently. Performance in tests also depends on gender, education, and previous intellectual level [8–10]. In some tests allowance is made for these factors, but the majority, eg, the Mattis Dementia Rating Scale [11] and the Alzheimer's Disease Assessment Scale (ADAS) [12], do not, resulting in imprecise diagnosis. This is also the case for the most commonly used cognitive test, the Mini-Mental Status Examination (MMSE) [10,13].

Neuropsychological tests have not yet been verified as reliable predictors of cognitive decline from MCI to AD. The preclinical stage of MCI might demonstrate malfunc-

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1552-5260/07/$ – see front matter
doi:10.1016/j.jalz.2006.10.001

tioning in a variety of cognitive performances, although memory seems to be the most frequent complaint that points to an MCI state [7,14]. Psychomotor speed [15], verbal ability and reasoning [16], visuospatial skills [17], and attention [18] can also be affected early. It has also been implied that episodic memory impairment precedes the diagnosis of AD by several years and might thus serve as a marker of cognitive decline [19], particularly in combination with an apolipoprotein E (*APOE* e4 allele [20,21]).

One of the most significant problems facing the clinician confronting a person diagnosed as having MCI is to predict whether that person is developing a dementing disorder, because many subjects remain stable or even improve. In an attempt to provide an answer to this problem, computer-based methods have been developed by several groups [22,23]. These methods are more objective in the administration of the tests and usually have several alternate forms, thus minimizing a learning effect. Moreover, depending on their design, the requirement for an administrator might be less than in conventional tests.

In the present article we report a follow up of a method developed by us [24], with computerized neuropsychological tests with innovative analysis of time-related performance patterns. We aimed to construct a battery of neuropsychological tests in which a response pattern might identify those harboring incipient dementia among subjects with subjective memory complaints (SMC). We hypothesized that the computer method could help to identify early stages of cognitive decline and predict imminent conversion to dementia [24].

The baseline examination, previously reported by us [24], defined two clusters (normal and abnormal performance) in an SMC population that seemed otherwise homogeneous according to the clinical measures, including their MMSE scores. The clusters were defined with our sophisticated analysis by the scores of both Recall a Pattern test and Digit Symbol Substitution test (DSST), both of which are widely used in pen and paper tests. Subjects who had abnormal scores in both tests were suspects for future decline. Many subjects, however, had abnormal scores in only one of those tests.

The aim of the present study was to re-examine the subjects who have participated in the previous study, both clinically and by repeating the computer evaluation, to determine to what extent the computer analysis did predict cognitive decline.

2. Methods

2.1. Subjects

Our previous study included 41 subjects who were referred because of subjective memory decline [24]. Inclusion criteria were (1) consent to participate in the study, (2) not being demented, with MMSE scores higher than 25, and (3) good or corrected sight and hearing. All had similar clinical history, and their neurological examination was normal. The ages of the subjects were in the range of 50 to 87 years (median, 71). All had at least secondary education.

Control volunteers (n = 48) were age-matched to the test group and had no complaints of memory or other cognitive problems. The normal elderly controls included 26 men; 29 had no previous computer experience; and their age ranged between 50 and 88 years (median age, 73.5).

Although the test is available in several languages, only the Hebrew version was used in the present study.

2.2. Test procedures

The follow-up examinations were performed 2 ± 0.3 years after the first session. All subjects in the test group went through a neurological examination, MMSE and the computerized assessment, in both baseline and follow-up examinations. In both sessions, the subjects' computer results were stored under code names and kept separate from the clinical evaluation data. Only on completion of the follow-up evaluations were the computer tests analyzed and compared with both clinical data and the baseline examination data results.

2.3. Comparison with clinical data

A diagnosis of dementia was based on detection of significant memory impairment and an additional cognitive deficit in the neurological evaluation [24]. The computer scores and the MMSE scores in both baseline and follow-up sessions were each compared with the clinical diagnosis at follow-up (demented or not).

3. Results

3.1. Controls

The test results statistics in the control group were similar to the ones reported previously [24]. The reaction times (RT) statistical measures (mean and standard deviation) of elderly subjects who had computer experience (n = 19) were significantly better ($P < .01$) than those of computer-naïve subjects (n = 29) in all subtests. The difference became insignificant ($P > .26$) when the normalization and correction of RT (NCRT) algorithm [24] was used. Three control subjects had abnormally low scores in a single subtest.

3.2. Memory-impaired subjects

The follow-up examination included 35 of the 41 memory clinic subjects examined in our baseline study (Fig. 1). Of the missing subjects, one has since died, another developed severe motor impairment, one could not be located, and three others refused to participate. Those six subjects did not have any distinct characteristics of age, gender,