Brief communication

Use of handheld computers for assessment of prefrontal cortex function in patients with phenylketonuria


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Abstract

Assessment of prefrontal brain cortex function can be helpful in treatment monitoring in patients with phenylketonuria. We aimed to assess the usefulness of computerized neuropsychological tests developed for handheld computers for this purpose. We observed worse test performance among persons with blood phenylalanine concentrations exceeding the recommended range. Use of handheld computers was assessed by patients and by doctors as interesting, not time-consuming and convenient. This method can be helpful during routine follow-up visits.

Keywords: Neuropsychology; Development; Inborn errors of metabolism; Dietary treatment

Background

Phenylketonuria (PKU) is the most common inborn error of metabolism in human. Discontinuation of dietary treatment can lead to mental retardation, epilepsy, and other neurological disorders especially in young children [1]. After the 10th year of life the toxic influence of phenylalanine rapidly decreases probably because of bigger brain maturity [2]. On the other side adolescents with phenylketonuria usually relax the diet after the 10th year of life. At this age, the compliance falls and problems with diet control increase, what worsens the treatment effects [3].

Initial symptoms of excessive brain phenylalanine concentration are psychoneurological disorders related to the so-called prefrontal brain cortex. They include prolonged reaction time, deterioration of the short-term memory, and worsening of impulsive behavior control [4–6]. Prefrontal dysfunction results from decrease in brain tyrosine concentration and a subsequent decrease of dopamine concentration in the prefrontal cortex occurring parallel to hyperphenylalaninemia. Neuropsychological examination of the prefrontal cortex, although potentially very useful especially in teenagers and adults with PKU, is usually time-consuming, requires sophisticated equipment and can be therefore of limited use during routine follow-up visits of patients with PKU. Thus, the aim of the study was to assess the usefulness of selected computerized neuropsychological tests developed for simple handheld computers for detection of prefrontal cortex dysfunction in PKU teenagers.

Methods

A computerized neuropsychological testing program (PKUtest) was developed for PalmOS System,
Impulsive behavior control test

The tested person has to press a button immediately after rectangle appearing on the screen (the rectangle appears in random time intervals). Mean reaction time and its standard deviation are calculated.

Short-term memory test

The tested person has to memorize a sequence of 4, 6, or 8 digits appearing on the screen every 0.5 s, preceded and followed by a star to eliminate the effect of preferred memorizing of the first and the last digit. Then, a control digit appears and the tested person has to decide if it was present in the sequence showed before (pressing “yes” or “no”). The test consists of 144 trials. Total number of errors is measured.

Impulsive behavior control test

66 rectangles and 33 circles appear on the screen every second in a random order. The tested person has to press a button immediately after rectangle appearing but not to press if a circle appears. Total number of errors is measured.

which is used in handheld computers. The test battery consisted of tests assessing simple reaction time, short-term memory, and impulsive behavior control. The description of the neuropsychological tests is given in Table 1.

Normal mentally developed PKU patients (treatment started in the 1st or 2nd month of life) aged 10–30 years were tested in six Polish metabolic centers during their routine follow-up visits by means of the PKUtest installed on monochromatic Palm Zire handheld computers. The simple reaction time test and impulsive behavior control test were performed twice to allow the patients learning of the test solving technique. Because of the same reason the short-time memory test included a training module.

Blood phenylalanine concentration was routinely assessed during the visit in each patient.

The results of the neuropsychological tests were compared between the following sub-groups of patients: (1) with blood phenylalanine concentrations within the recommended range (for patients aged 10–12 years 2–6 mg%, 13–18 years 2–12 mg%, and adults 2–15 mg%) and (2) exceeding the recommended limits.

Results and discussion

Seventy-five patients took part in the study. Blood phenylalanine concentration remained within the recommended range in 28 (37.3%) of them, whereas in 47 (62.7%) it was higher than recommended and exceeded the upper limit by 1.1–19.9 mg% (mean 7.4 mg%).

Although patients with blood phenylalanine concentration higher than recommended tended to have longer reaction time (mean reaction time 320 ms versus 299 ms in the patients with proper blood phenylalanine results) and reaction time standard deviation (69 versus 63 ms, respectively), this difference did not reach statistical significance (mean reaction time difference 21 ms, p = 0.1 in Student’s t test). The results of the short-time memory test did not differ (mean number of wrong answers 31 versus 30). Statistically insignificant results of the above tests seem to be due to a relatively low number of participants of the study. However, patients with blood phenylalanine concentration exceeding the recommended limits achieved significantly worse results in the impulsive behavior control test in comparison to the “proper phenylalanine results” group (mean number of errors 9.7% versus 6.1%, p = 0.045 in Student’s t test).

Use of handheld computers was assessed by the patients as very interesting. The testing procedure took typically 30 min per patient.

The participants of the study were selected from the group of early and continuously treated persons with PKU and with normal psychological development. In this situation the results of the study cannot be extrapolated to late-treated PKU patients or persons with lower IQ level. Such persons could have problems in managing neuropsychological test solving technique and could be possibly more susceptible to the toxic effect of higher phenylalanine levels.

Although our results are preliminary and larger patients groups need to be tested to confirm the observed differences, our experience encourages use of handheld computers in neuropsychological testing. Especially teenagers, who like to play computer games, are very interested in use of such portable electronic tools. This fact could be useful in improvement of the treatment process in this group of PKU patients, as adolescents and adults demonstrate the greatest compliance problems.

Summarizing, in our opinion neuropsychological computer programs developed for handheld computers can be effectively used for monitoring of prefrontal cortex function in patients treated for phenylketonuria. As validation of the new test is necessary to clearly demonstrate its power, a multi-centre, possibly international study is intended which could additionally give the opportunity to evaluate the handheld computers as a diagnostic tool for other colleagues in charge for treatment of PKU patients.

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References


