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Computerised evaluation of cognitive and motor function

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Abstract—*In this paper, we present a clinical study of computerised tracking in the evaluation of cognitive and motor function. We investigate its use in the assessment of effectiveness of antiepileptic drugs (AEDs) as well as in the process of following the progress of Alzheimer's disease (AD). To simplify the experiments, we introduce real-time adaptation of the target speed. In the study with epileptic patients, three result groups are compared: blood levels of AEDs, scores on standard neuropsychological tests, and scores on computerised tracking and reaction time tests. It is found that the computerised tests are repeatable, reliable and sensitive and may therefore be useful in the evaluation of epilepsy treatment. For example, while the blood levels associated with AEDs lie in the therapeutic range, variations in the optimal speed (OS) between 0.9 and 1.1 (expressed in relative units) are recorded. To significantly simplify the protocol for AD patients while preserving its main features, we introduce signal–processing techniques into the data analysis. Local signal property characteristics for AD are found which indicate that the preview tracking of an AD patient is similar to the non-preview tracking of a healthy control. This result is expected since the working memory, which is involved in movement planning, is impaired in AD. In non-preview tracking, healthy control subjects are mostly in tracking mode 1 and have a mean mode duration of 600 ms. In preview tracking, AD patients are mostly in mode 2 with a mean mode duration of 600 ms.*

Keywords—*Biomedical computing, Clinical engineering, Signal analysis, Data acquisition, Human performance analysis, Computerised tracking, Epilepsy, Alzheimer's disease, Working memory model*

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1 Introduction

AT LEAST several areas of medical research and practice would benefit from an inexpensive, repeatable, reliable and sensitive measurement of cognitive and motor function. These include the assessment of epilepsy therapy, monitoring of Alzheimer's disease (AD) and assessment of the rehabilitation process after head injury. In addition, it would allow for the simple screening of elderly people for dementia or problems in driving a car.

Recently, an increasing number of neuropsychological tests have been computerised (FLETCHER, 1997), (TETEWSKY, 1999), allowing for the processing of huge amounts of data. Computerised tracking tasks, in which a subject attempts to follow a randomly moving object on a computer screen, give a measure of motor speed. Tracking tasks administered with simultaneous tests of reaction time (RT) also provide information on the capacity of the central executive component of the working memory (WM) to distribute and co-ordinate processing resources (BADDELEY, 1993).

In this paper, we present the results of two studies, one with epilepsy patients, the other with AD patients.

In the former study, we investigated the effects of antiepileptic drugs (AEDs) on motor and cognitive function using tracking tasks, with or without simultaneous RT testing. These computerised tests were compared to standard neuropsychological measures (grooved pegboard and symbol-digit modalities tests) and performance on these tests was correlated to blood levels associated with the taking of AEDs.

In the latter study, we conducted similar tests with AD patients. Due to the characteristic inability of the patients to understand, learn and remember what they were told to do, we found it necessary to introduce signal processing into the data analysis. We were thus able to significantly simplify the experimental protocol.

The tests in both studies were designed on the basis of the theoretical and experimental work by BADDELEY *et al.* (1991).

Section 2 explains how AED treatment and AD influence the cognitive and motor function; section 3 introduces tracking and reaction time experiments; section 4 provides more details on the experimental equipment and protocol; while in sections 5 and 6, we discuss the experimental results from both studies.

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2 Factors influencing cognitive and motor function

2.1 *Antiepileptic drugs*

Epilepsy is a chronic neurological disorder, manifested by sudden and recurrent disturbances in mental function, consciousness, sensory activity or body movements. Rather than being a specific disease, it is a complex of symptoms resulting from excessive excitation of cerebral nerve cells. More than two-and-a-half million persons of all ages in the USA alone have epilepsy.

While some forms of epilepsy can be traced to specific brain injuries or tumors, most cases are of unknown origin. As a result, the treatment of epilepsy is directed to reducing the frequency of seizures, rather than eliminating the actual causes. Many of the AEDs were found by mere trial-and-error testing, and their mechanisms of action are incompletely understood.

Probably the most important reason for evaluating the influence of AEDs on cognitive and motor function is that the action of AEDs is not limited to the symptoms of epilepsy: neuropsychological dysfunction, from mild to severe, often occurs with AED therapy, because AEDs have many short-term and long-term toxic effects.

2.2 *Alzheimer's disease*

Alzheimer's disease is a common form of dementia—a medical condition giving rise to severely impaired memory and reasoning ability, associated with damaged brain tissue. It was first described by A. Alzheimer in 1906, and is characterised by neurotic plaques and neurofibrillary tangles in the brain, severe loss of neurons, and reduced weight and size of the brain. It is progressive, irreversible and incurable.

Ageing is the largest risk for becoming demented (1% prevalence at age 65, 5% at age 75, and 15–25% at age 85). As the disease progresses, memory loss becomes more severe, and the patient's perceptual, language and motor skills deteriorate.

3 Tracking, reaction time and dual task paradigm

3.1 *Tracking*

Tracking covers a wide range of activities, such as catching a ball or a frisbee, keeping a spotlight on an actor as he walks on a stage, pointing a camera at a hummingbird, even whistling, singing or playing in tune, to name but a few. More complex tracking tasks include driving and parking a car or flying and landing an aircraft.

Common to all of these is the process of following a target (ball, frisbee, actor, hummingbird), or keeping controlled parameters (car or plane position and speed) within prescribed limits.

The laboratory tracking experiments included: following a target on a computer screen using a mouse, a light-pen or some other interface device, or tracking a wiggling line on a moving paper using a pen. Depending on the purpose of the experiment, the design was able to include preview of the target motion, feedback on the subject's performance, etc.

Everyday activities can be described in many ways, but two processes are of great importance: making choices and acting towards the chosen goal. Although these processes are not separable, they are often considered as such, with experiments having been conducted to determine how people carry out purely decision tasks or purely action tasks. Owing to the complex interactions between making decisions and taking actions, such experiments cannot give a reliable estimation of the subject's ability to solve realistic problems. Tracking tests offer an inexpensive yet reliable way of simulating complex tasks, especially if combined with other tasks.

Tracking tests were developed for training purposes during and after the Second World War. Since then, they have been used in psychological and engineering studies, but the use of tracking in clinical studies came only in the 1970s.

Examples of the clinical use of tracking include studies of Parkinsonism (FLOWERS, 1978), monitoring recovery from head-injury (JONES, 1986) and investigations into dementia (BADDELEY *et al.*, 1991).

3.2 *Reaction time*

Helmholtz was the first to measure the speed of neural conduction. Measuring the time needed for a mental operation to be performed was solved soon afterwards by Donders, who devised a simple subtractive method. He measured the time needed for a person to react to a light stimulus (simple reaction time) as well as the time needed for one of two possible reactions, with a choice dependent on the colour of light (choice reaction time). Donders' view that these mental operations are sequential and the corresponding times additive was confirmed by Sternberg in his 1968 experiments with variable length lists. The tests we use are similar in principle to Donders' original tests.

3.3 *Dual task paradigm*

To determine which component of the working memory (WM) is affected most in AD patients, Baddeley and his colleagues developed the dual task paradigm, which they used to selectively load components of the WM. For the primary task, they used tracking of a square on a computer screen using a light pen. They repeated this test until the target speed was found such that the tracking was on target 60% of the time. In this way, the difficulty of the primary task was equalised for all subjects. A secondary task was then added to the primary task and the drop in performance due to this addition was measured and used as an indicator of the abilities of the central executive component of the WM. The time needed to react to a tone was one of the secondary tasks they found useful. Our tests are very similar to Baddeley's original tests. Our improvements include real-time target speed adaptation and the use of a commercially available laptop computer (low price, conveniently portable for clinical settings) for test implementation. We also used the laptop's built-in mouse buttons for the reaction time tests and the track-ball instead of a light pen.

4 Experimental equipment and protocol

4.1 *Hardware considerations*

The tests were implemented on a standard commercially available laptop computer. The choice of the pointing device in the tracking task was not difficult, because only two devices, the external mouse and the track-ball, offered the following desired features: a simple one-to-one correspondence between the position of the device and the position of the pointer on the screen, practically immediate response, availability of easy-to-use programming routines, reliability, and the possibility of a quick change in the case of malfunction. The track-ball was preferred because very few subjects were expected to be familiar with it. If we had used a mouse, it would have made the tests easier for those subjects who had experience with it.

4.2 *Tracking experiments*

In the tracking experiments, a subject was asked to use his or her dominant hand to roll the track-ball, with the aim of following the target on the computer screen. The target was a wiggling white line while the pointer was a red spot that could be moved left or right using the track-ball.

The target motion was governed by the sum of 20 sinusoidal signals with non-harmonically related frequencies, different amplitudes and phases. The resulting signal was pseudorandom, in the sense that during the 60 s of the test there was no periodicity. Owing to hardware speed limitations, the measurements were taken every $T_s = 37$ ms, hence the sampling frequency was $f_s = 1/T_s = 27$ Hz.

In all the experiments with epilepsy patients, the tracking tests contained a preview of the future target positions. In the experiments with AD patients, we conducted both preview and non-preview tracking tests.

As described in Section 3.3, in the dual task paradigm it is important to adapt the target speed to the individual abilities of the subject, usually to the target speed at which the subject's tracking is on target approximately 60% of the time. We effected such adaptation using our novel real-time adaptation scheme. All tracking experiments began with the same target speed, which we shall refer to as the *unit relative speed*, characterised by a maximum frequency of 1.2 Hz. For other target speeds, the maximum signal frequency was proportionally higher. The real-time speed adaptation to the individualised target speed was based on the subject's performance in the immediate past and was achieved using the weighted root mean square error (WRMS) as the error estimator, with an empirically chosen forgetting factor of 0.96, which with $f_s = 27$ Hz enables us to make the target speed adjustments every 5 s. Depending on whether the subject's performance was better, worse or on target approximately 60% of the time, we increased, decreased, or kept the current target speed unchanged. Typical results of the real-time target speed adaptation are shown in Fig. 1. We have found this simple adaptation scheme to be very reliable.

4.3 *Reaction time experiments*

We implemented two types of RT test: *simple* and *choice* reaction times. In all of these tests, no matter whether they were done as single tasks, or as secondary tasks in the dual task tests, the subject was required to use the non-dominant hand to press the built-in mouse buttons on the laptop computer as soon as the colour changed on the computer screen.

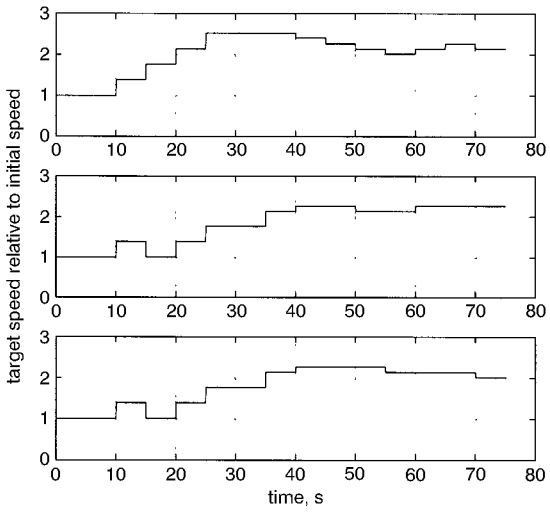

Fig. 1 *Target speed adaptation. Three separate trials are shown*

In the simple RT test, empty boxes appeared on the screen first. After 3 s the boxes became grey, signalling the need for increased attention. After random intervals of 0.5, 1.0 or 1.5 s, the boxes changed to red, and the program tested the state of the mouse buttons every 2 ms. When the subject pressed any of the buttons, the reaction time of that trial was recorded, and the boxes were coloured as background (dark blue) to look empty. This process was repeated, i.e. after 3 s, boxes were coloured grey, etc.

In the choice RT test, everything was the same except that after turning grey, the boxes were randomly coloured, either green or red. The subject was asked to press the left button for green and the right button for red. The difference between the average choice and simple reaction times is an indicator of the speed of central information processing.

In both tests, a new trial was initiated after 3 s. If the subject did not respond within 3 s, the current trial was interrupted. Similarly, if an incorrect button was pressed, a 'wrong' sound was heard, and after 3 s a new trial would begin. It should also be noted that the number of trials was taken to be 12 as a trade-off between two conflicting requirements: too many experiments would cause fatigue, while too few measurements would cause the sample mean to significantly vary between the blocks of trials. The choice of 12 trials also corresponds to the duration of the tracking tests (around 60 s).

4.4 *Protocol*

In addition to the tests described earlier, the protocol included two standard neuropsychological tests of cognitive and motor function: the grooved pegboard test and the symbol-digit modalities test.

The grooved pegboard test involves putting 25 small keys into the key-holes of different orientations. The result of this test is the time needed to complete the task, and is mostly influenced by the subject's speed and co-ordination of motion. In the symbol-digit modalities test, the subject is asked to fill in the missing digits corresponding to the symbols above the spaces. The table of correspondence is printed at the top of the paper. The result of this test is the number of digits written in 90 seconds. This result is mostly influenced by the subject's mental speed, but also by the motor speed and co-ordination.

The protocol of the experiment was as follows:

- Patients, referred to us by their physicians at the time of their regular visits, were asked a few questions, such as their name, age, phone number, and for information about their epilepsy. If a patient had a photically induced epilepsy, or had had a seizure during the previous 24 hours, he or she was not allowed to be a subject. The same applied if the patient had problems with alcohol or drugs. If all the inclusion criteria were satisfied, the consent forms were duly filled out, and the purpose of the study was explained, along with the confidentiality issues.
- The experiments were performed in the following order:
  1. Computer testing ((a) adaptive tracking, (b) simple RT, (c) tracking with simple RT, (d) single tracking; (a') adaptive tracking, (b') choice RT, (c') tracking with choice RT, (d') single tracking)
  2. Grooved pegboard test (preferred hand first, followed by non-preferred hand)
  3. Computer testing (same as 1)
  4. Symbol-digit modalities test
  5. Computer testing (same as 1 and 3)
- Blood concentration of drugs was measured immediately after the test.

The testing session lasted for approximately 45 min in total. Special care was taken to make the room quiet and to reduce the lights.

5 Results

5.1 *Study with epileptic patients*

The aforementioned computerised tests were shown to be repeatable, i.e. tests repeated after six months and one year, showed the performance of the subjects to be very similar to their original performance (KISAČANIN *et al.*, 1997). They were also reliable, i.e. the subjects' performance on the computerised tests correlated well with their performance in standard neuropsychological tests: For $n = 7$ control subjects, we found a correlation of $\sim 85\%$ between the grooved pegboard test and the optimal speed (individualised target speed) and $\sim 87\%$ correlation between the symbol-digit modalities and choice RT test (KISAČANIN, 1998).

We then compared the test performances to the blood levels associated with the taking of AEDs. Fig. 2 shows the optimal speed (OS), simple and choice reaction times (SRT and CRT), as well as the difference between them (DRT) against the measured blood levels of carbamazepine for four patients: EF (age 54, denoted by 'o'), CM (age 38, denoted by '+'), DN (age 31, denoted by '*'), and LH (age 25, denoted by 'x').

All tests relied on the natural variability of blood levels, i.e. no changes in therapy were requested from the patients.

While the OS showed no noticeable trend, the reaction times tended to increase slightly as the carbamazepine blood level increased.

The graphs in Fig. 3 show the test results of a 22-year-old patient, SW, who was on phenytoin. The chronologically first test (the one to the right, with the greater phenytoin level) was

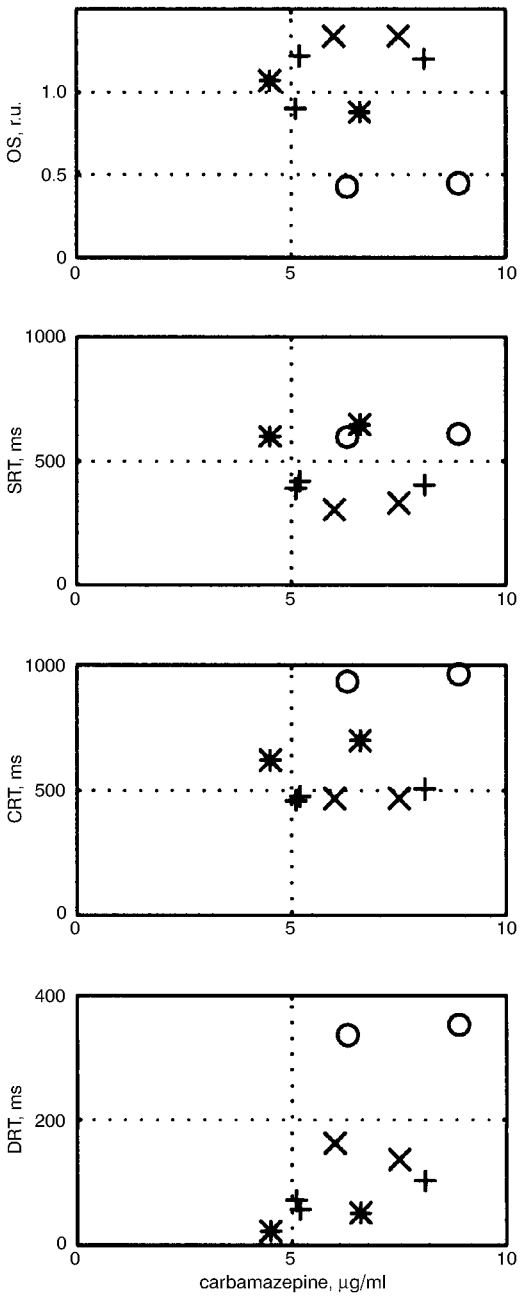

Fig. 2 *Performance on computerised tests against blood level of carbamazepine. Data are presented for four patients: EF (age 54, o), CM (age 38, +), DN (age 31, *) and LH (age 25, x)*

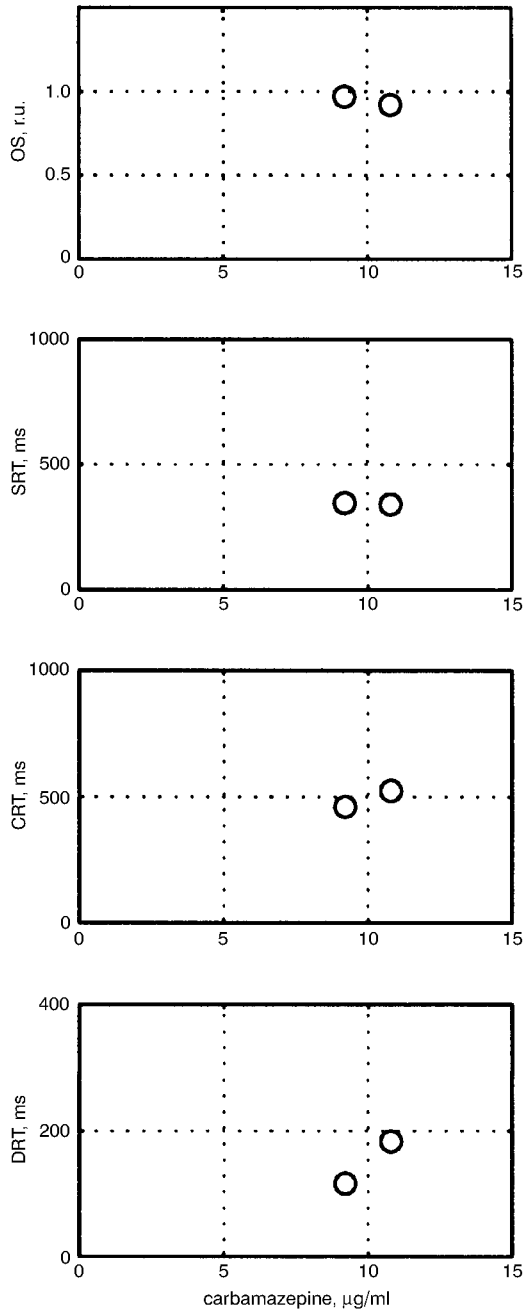

Fig. 3 *Performance on computerised tests against blood level of phenytoin. Data are for SW (age 22). At time of test with greater phenytoin level, therapy also included valproic acid*

conducted at a time when SW was also taking valproic acid. A decrease in the blood level was followed by slightly better test performance.

In addition to the above, we should stress that we found no evidence that epileptic patients performed any worse in the dual task tests than did healthy controls (KISAČANIN *et al.*, 1997). Future test protocols can therefore be made shorter by excluding the dual task tests.

5.2 *Study with AD patients*

Traditionally, tracking has been analysed using overall test performances such as the mean-square error over the entire duration of the test.

In the following, we present the results obtained by looking at the local features of the signals recorded during the experiments. This approach was applied to both the data from experiments with AD patients as well as to the data from healthy controls.

The reason for this new approach came from the problems we encountered in tests with AD patients: the dual task tests were too difficult for them. To provide a performance indicator for the central executive, we used the data from single task tracking tests and compared certain characteristics of tracking carried out by AD patients to those of healthy controls: the tracking modes (local delay times scaled by the individual OS) and mean durations of these modes (KISAČANIN, 1998). Our expectation that we would find differences was based on BADDELEY's model of the working memory and its role in motion planning and utilisation of available information about the future.

Fig. 4 indicates how often the tracking mode of a healthy control was one of the following:

−3	'vastly ahead'	(ahead $\geqslant$ 11 samples),
−2	'significantly ahead'	(ahead 6–10 samples),
−1	'slightly ahead'	(ahead 2–5 samples),
0	'on target'	
1	'slightly behind'	(behind 2–5 samples),
2	'significantly behind'	(behind 6–10 samples),
3	'vastly behind'	(behind $\geqslant$ 11 samples).

The results for both preview and non-preview tracking are shown. Note that in the preview tracking, with the future positions of the target shown on the screen, the healthy control was mostly 'on target', but that there are noticeable percentages when the subject was 'slightly ahead' or 'slightly behind' the target. This is not the case when the same subject sat the non-preview tracking test. In that case, the most common modes were 'slightly behind' and 'significantly behind'.

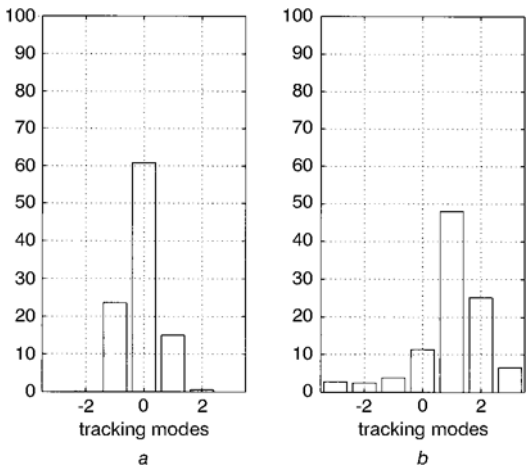

Fig. 4 *Percentages of time in different tracking modes: "−3" (vastly ahead) to "3" (vastly behind) for both (a) preview (speed 1.00) and (b) non-preview (speed 1.00) tracking by healthy control. In preview tracking, subject was mostly on target whereas in non-preview tracking subject was slightly or significantly behind*

It is interesting to compare these findings to the data from preview tracking experiments with AD patients. The best performance among them is found in the three tests with patient FF (Fig. 5). The performance of AD patients on preview tests was worse than the performance of healthy controls on non-preview tracking.

We tried to determine other signal parameters that would distinguish AD patients from healthy controls, but the delay between the target and pointer was the only parameter that did not show an overwhelming variability. This is due to the difference between the following two time constants: the reciprocal of the maximum signal frequency ($T_1 \geqslant 1/2$ Hz $= 500$ ms) and the typical delay at which we wish to find measurable effects ($T_2 \simeq T_s = 37$ ms). Since any parameter identification requires direct or indirect inversion of the matrix $G = H'H$, where H is a Toeplitz matrix with the input signal as the first column, a good indicator of the sensitivity of the identified parameters to the quality of tracking is the condition number (KAY, 1993) of G:

$$\kappa(G) = \frac{\sigma_{\max}(G)}{\sigma_{\min}(G)}$$

where $\sigma_{\max}(G)$ and $\sigma_{\min}(G)$ are the largest and smallest singular values of G, respectively. In our case, $\kappa(G) = 2.99 \cdot 10^4 \gg 1$. Note that if the input signal were white random noise (containing all possible frequencies), the condition number of G would be ~ 1.

Since delays were found to be the only meaningful local signal properties, we analysed the mean durations of the tracking modes to see if any further results could be obtained. From the theory of Markov chains (RABINER, 1989), it is known that if p_{ii} is the probability of transition from state i to itself and the sampling period is T_s, the expected uninterrupted duration of that state is

$$T_i = \frac{T_s}{1 - p_{ii}}$$

If the values for p_{ii} are estimated to be the frequencies of any observed transitions, we obtain the graphs in Fig. 6. Observe that

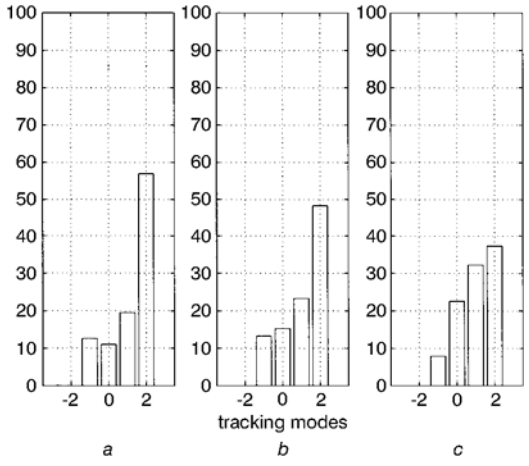

Fig. 5 *Time percentages in different modes for all three tests by FF with outliers at −3, −2, and 3 removed, leaving time percentages in different modes during good tracking, rather than during entire test. All tests had target preview, at individualised optimal speeds (0.18, 0.62 and 0.24 initial speeds for (a), (b) and (c), respectively). Also shown are the results of mini-mental tests (22, 23 and 20 for (a), (b) and (c), respectively) showing mild dementia*

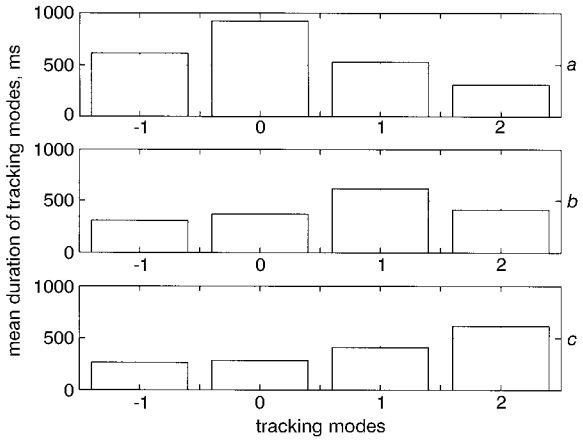

Fig. 6 *Mean durations of tracking modes for healthy subject (both preview and non-preview tracking) and AD patient (preview tracking only): (a) healthy control, with preview, (1.00); (b) healthy control, no preview, (1.00); (c) AD patient, with preview, (0.62)*

the good modes in the preview tracking of an AD patient are less stable than the good modes of a healthy control in non-preview tracking.

6 Conclusions

Starting from BADDELEY's dual task paradigm, we introduced a real-time adaptation scheme and the use of commercially available equipment (a conveniently portable and inexpensive laptop computer). In the course of our studies, we found that our tests were repeatable (tests repeated after several months gave very similar results to tests carried out when the controls and patients sat them for the first time), reliable (good correlation with standard neuropsychological measures of cognitive and motor function) and sensitive (the performance on computerised tests may provide useful information about the influence of therapy on the cognitive and motor function of patients).

We also found that AEDs did not affect the functioning of the central executive component of the working memory. Future studies need therefore only include tracking and RT tests, because other tests are either redundant (these two tests correlate well with the standard neuropsychological measures) or unnecessary (no effects of AEDs on the WM are expected).

Introduction of signal processing into the data analysis of our AD experiments allowed us to significantly simplify the protocol without sacrificing its main feature: testing the performance of the central executive. In particular, we analysed the tracking modes and their durations.

We found that AD patients, compared to healthy controls, lagged behind the target most of the time, and had a short mean duration of good tracking modes. In other words, their preview tracking was very similar to the non-preview tracking of healthy controls. This was consistent with the suspected role of the central executive in motion planning and its impairment in AD.

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