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Reaction Time Prolongation in the Early Stage of Presenile Onset Alzheimer's Disease

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Summary. Simple reaction times (RT) to clicks, flashes and numerical signals were measured in four groups of subjects: 21 patients with mild presenile onset dementia of the Alzheimer type (PDAT, mean age 56 years), 14 patients with chronic cardiovascular disease and incipient cognitive deficit (mean age 55 years), 15 healthy older controls (mean age 53 years) and 16 younger controls (mean age 23 years). Both patient groups had significantly prolonged RTs, the PDAT group especially to the numerical signal (149%), compared with the age-matched controls.

Key words: Presenile-onset dementia of Alzheimer type – Normal aging – Reaction times

Introduction

In the early stages of primary degenerative dementia of Alzheimer type (DAT) the clinical diagnosis can only be tentative. The essential feature of dementia was formulated in the Diagnostic and Statistical Manual of Mental Disorders (DSM III-R, American Psychiatric Association 1987) as an impairment of short- and long-term memory associated with impairment of abstract thinking, impaired judgement, other disturbances of higher cortical functions, or personality change. We previously tested labyrinth learning in a group of patients in an early stage of presenile onset dementia of Alzheimer type (PDAT) and found that the decrease in constructional ability and the slowing of operational functions is prior to and more marked than the decline of memory (Müller et al. 1990). The results of our reinvestigation of the patients after 1 year support this hypothesis (manuscript in preparation). The aim of this study was to compare the reaction time (RT) of PDAT patients with normal aging. A prolongation of RTs has already been found in senile onset DAT patients (Pirozzolo et al. 1981; Hellström et al. 1989).

Subjects and Methods

Sixty-six subjects belonging to four groups were investigated (Table 1). All the patients complained of memory and cognitive impairment at work and were neurologically, psychiatrically and psychologically investigated. They were classified according to the Washington University Clinical Dementia Rating (CDR) as described and reported by Berg et al. (1982), Hughes et al. (1982) and Burke et al. (1988). The PDAT patients belonged to stage CDR 1 (mild dementia); the control groups had no symptoms; the second patient group had chronic cardiovascular diseases (hypertension or angina pectoris or both) for more than 10 years (CVD group) with similar but weaker psychopathological complaints for more than 4 years. Ten of the latter group were classified as CDR 0.5 (questionable dementia), 4 as CDR 1 (mild dementia); 9 of them had symptoms of mild cerebrovascular insufficiency, but a typical multi-infarct dementia was excluded by an "ischaemic scale" from Wagner (1985).

The subjects were relaxed and habituated to the working conditions in a sitting position. They held the response key in the right hand and had to press it with the thumb as fast as possible when the signal occurred. An electronic clock measured the RT in milliseconds. Light flashes (1.5 Ws) from a photostimulator were seen

Table 1. The four subject groups

Symbols for the groups	Number of persons	Age (years) (SD)	Complaints for (years) (SD)	Presumptive diagnosis	CDR stage
○	16 (9 females)	21.9 ± 3.7	–	Healthy (YC)	0
●	15 (6 females)	51.6 ± 3.9	–	Healthy (EC)	0
▲	21 (12 females)	54.7 ± 4.1	2.6 ± 1.5	PDAT	1
△	14 (6 females)	54.2 ± 4.4	4.7 ± 2.1	CVD	0.5 and 1

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through closed eyes. Clicks (80 dB) were heard through bilateral ear phones. Numerical stimuli were observed on a four-digit LED display and the subjects had to respond when all digits showed zero at once. The stochastic intervals of all ten stimulus series were 3.9 ± 1.4 s (mean ± SD) for all modalities. During visual stimulation the subjects heard a mild white noise through the phones to avoid any acoustic distraction. All the other conditions were constant during measurements.

Group differences were proved with the non-parametric Mann-Whitney U-test; intraindividual differences were tested with the Wilcoxon test for matched pairs.

Results

The mean RTs of the four groups are shown in Fig. 1. The PDAT patients needed 23% more time to respond to flashes and 34% more to respond to clicks, but 49% more to respond to numerical signals compared with the older healthy control subjects. The CVD group needed 27%, 25% and 23% more time respectively. The older control subjects were only significantly slower (49%) than the younger in the task with numerical signals. There were no differences between the patient groups in flash or click RTs, but there were in the RTs to numerical stimuli ($P < 0.01$).

The acoustic RTs were 20–25 ms shorter than RTs to flash in the control groups and the CVD patients, but not shorter at all in the PDAT patients. The response had a greater variance, however, in both patient groups compared with the controls. Evaluation of serial RT changes revealed adaptation to repeated intervals of the same length and further increase of the RTs when the interval was unexpectedly shortened (the eighth click or flash, Fig. 2).

The intraindividual sequential analysis demonstrated that the habituational improvement during the first half-series is statistically as good in patients or even slightly better than in the control groups. The interval prolongation after the fifth stimulus caused a significant RT increase in both patient groups ($P < 0.05$), whereas the changes in the control groups were not significant. Moreover, the response latency to clicks further increased in the PDAT group ($P < 0.01$) when the next interval between the 6th and 7th click was reduced to 3 s. Shortening of the interval to 1 s caused RT prolongation in all groups ($P < 0.01$) and again only the PDAT group prolonged their RTs to clicks further in the subsequent change. This analysis revealed that the PDAT group was more disturbed by interval changes when clicks were used as stimuli.

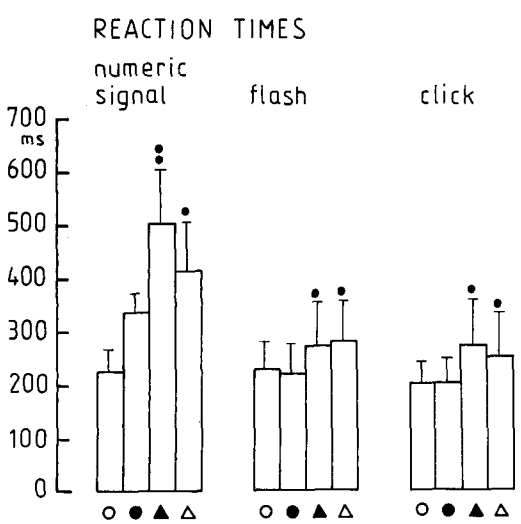

Fig. 1. Mean values and standard deviations of 10 reaction times (RTs) to numerical signals, clicks and flashes. • $P < 0.05$; •• $P < 0.01$ vs older control group (EC, ●). For symbols for the groups see Table 1

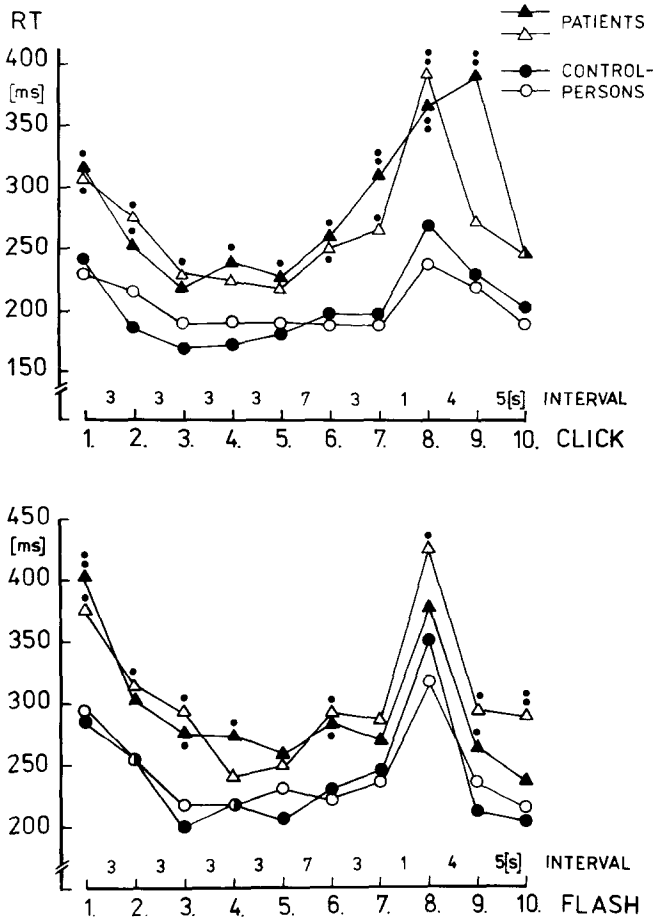

Fig. 2. Mean values of serial RTs of clicks and flashes in stochastic intervals. • $P < 0.05$; •• $P < 0.01$ vs older control group (EC, ●). For symbols for the groups, see Table 1

Discussion

The results support the notion that prolongation of even simple RTs is a reliable sign in the early stage of DAT, not only in the senile onset form as reported by Hellström et al. (1989) but also in the presenile onset. It has been questioned for a long time whether presenile and senile onset DAT belong to different entities. There are some data that DAT patients with presenile counterparts on age-adjusted measurements of sustained concentration and mental tracking (Loring and Largen 1985). On the other hand, epidemiological investigation revealed a logarithmic incidence increase of DAT with age and that

both senile and presenile onset of DAT belong to the same disorder (Mas et al. 1987).

The deceleration of brain operational speed with age in healthy subjects has been well documented (Bellis 1933; Pöthig and Roth 1980; Pöthig et al. 1985), but this decline is more or less mild and correlated with age. There were no differences in simple RTs to click and flash between younger and older (presenile) controls. The older controls had prolonged RTs, however, to the numerical signal, which required more sustained attentional and greater cognitive effort. This process needed 130 ms more than the response to clicks (65% increase) whereas the PDAT patients needed 230 ms more time to respond to the numerical signal (85% more) than to the click. In the labyrinth test the older group showed a tendency to prolonged step velocity compared with the younger group, but this was reduced during learning as fast as in the younger group, whereas the PDAT patients remained 40% slower (Müller et al. 1990). The CVD patients responded with the same RT increase to clicks and flashes as PDAT patients and also had 23% longer RTs to the numerical signal compared with age-matched controls. This group showed almost no change in labyrinth learning, but nearly the same amount of slowed step velocity as PDAT patients (Müller et al. 1990). The investigation of eye tracking performance revealed similar changes in both patient groups concerning the accuracy of smooth pursuit movements, with a clear difference of stronger attentional deficit in the PDAT group (paper submitted for publication). We assume that a number of symptoms of the CVD group indicate the very beginning of dementia, probably the Alzheimer type, which may develop independently of the cardiovascular disease or which may be advanced to an earlier age of onset by brain circulation disturbances. This hypothesis is supported by a correlation between severity of changes and the dementia rating in some of the CVD patients, four of them classified in CDR 1.

An interesting problem is the specificity of RT prolongation in dementia development. There are several reports on prolongation of RTs related to different brain injuries (Rüsch 1944; Klensch 1973; Nettelbeck 1980; Van Zomeren 1981; Elsass and Hartelius 1985; Tartaglione et al. 1986). In most cases of brain injury and disease a remission of illness was correlated with improvement of RTs. It would be of interest to know whether any kind of effective therapy in dementia leads to improvement of RTs, too. Nevertheless, the RT measurement can be used as a reliable diagnostic tool for judging organic brain processes such as primary degenerative dementia, among and together with other tests. The data support the hypothesis that impairment of operational brain functions occur prior to learning and memory decline.

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