MENTAL FUNCTION AFTER GENERAL ANAESTHESIA FOR TRANSURETHRAL PROCEDURES

C. SMITH, M. CARTER, P. SEBEL AND P. YATE

SUMMARY

We have assessed the influence of age and preoperative mental status score on postoperative mental function, using a choice reaction time test. One hundred and twelve patients (mean age 70 yr, range 48–88 yr) were given a standardized general anaesthetic for transurethral procedures. Mental status before anaesthesia was measured with the Clifton Assessment Procedure for the Elderly (CAPE). Reaction time was measured before anaesthesia and for up to 3 days after anaesthesia. Variability in reaction time performance was increased 24 h after anaesthesia in transurethral patients, but not in a control group of orthopaedic patients (P = 0.0006). Factors contributing to increased variability of reaction time after operation in a multiple regression analysis were reduced CAPE score before operation (P < 0.0001), extent of surgery (P = 0.023), postoperative pain (P = 0.007) and postoperative sedative drugs (P = 0.009). Factors not contributing included age, diagnosis of cancer, number of previous operations in past 5 years, duration of anaesthesia, minimum mean arterial pressure, minimum and maximum perioperative Pco2 values, postoperative pyrexia and poor sleep.

KEY WORDS


Transient mental impairment after anaesthesia has been reported in all surgical patients, which increases the burden of care [1–5]. Although clinical observation indicates that elderly patients suffer from relatively more transient mental impairment, studies have revealed inconsistent findings [5–8]. It has been reported that deficits in orientation and concentration occurred 2 days after anaesthesia in a group of patients of mean age 69 yr, but not in a younger group (mean age 50 yr) [6]. In contrast, other studies have found no correlation between age and postoperative mental function measured in several ways [7, 8]. However, all these studies have been deficient in some respects.

We have reported previously preliminary results in elderly patients undergoing transurethral surgery with standardized anaesthesia which suggested that a low score on a mental status test, rather than chronological age before operation, predisposes to postoperative mental impairment [9]. We now report the results of a larger study. Mental function was assessed for up to 3 days after operation using a reaction time test shown previously to be sensitive to the effects of anaesthesia for up to 2 days after operation in middle-aged patients [10]. The study was designed to observe if age, preoperative mental impairment and other risk factors predispose to postoperative mental impairment measured by reaction time. Confounding clinical factors were measured and reaction time measurements were made also in a small control group of hospital patients who had not recently had an operation.

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PATIENTS AND METHODS

The study was approved by the Ethics Committee of the local district health authority. We studied 112 patients of mean age 70 yr (range 48–88 yr), undergoing endoscopic urological procedures (table I). Patients who, in the opinion of the anaesthetist, required spinal anaesthesia were excluded. Patients were premedicated with temazepam 20 mg by mouth 1 h before operation. Anaesthesia was induced with thiopentone and maintained with nitrous oxide and halothane or enflurane in oxygen. We intended originally that all patients in the study should receive halothane, but decided to change to enflurane after 14 patients had been studied, after further concern about halothane and liver damage [11]. Alcuronium was used for neuromuscular block for procedures expected to last longer than 20 min; otherwise the patients breathed spontaneously.

On the day before surgery, patients were screened using the Information—Orientation subscale of the Clifton Assessment Procedure for the Elderly (CAPE) [12]. This 12-item mental status test was used to screen for a subgroup of elderly patients with possible preoperative mental impairment. In addition, patients were asked to rate any pain or discomfort and quality of previous night's sleep on a fixed-point scale. The research nurse who carried out all performance testing and recording of other variables throughout the study also noted any signs of confused behaviour, particularly in relation to understanding the instructions on a visual four-choice reaction time test which was used to assess postoperative recovery objectively. In this task, run by a BBC B computer, reaction time was separated from motor time. Twelve practice trials were given, followed by two blocks of 40 trials and the reaction time data were stored on disc. Subsequently, the computer printed a record of all individual trials and calculated a mean, median and SD score from 70 responses, ignoring the first five trials in each block. Reaction time was re-tested 1, 2 and 3 days after anaesthesia, or until the patient was discharged: all 112 patients were tested 24 h after anaesthesia; most patients undergoing only investigation or minor surgical procedures were then discharged.

Extent of surgery was scored: 1 = investigation only; 2 = bladder biopsy, resection of small bladder tumours and miscellaneous procedures; 3 = resection of large bladder tumours and prostates.

Twenty-six orthopaedic patients (mean age 64 yr) at least 12 days post-surgery served as controls (table I); they also were screened with the CAPE and had subjective assessments and reaction time tested at the same days and times of day. It was difficult to study elderly control hospital patients who had not recently had an operation or were comparable in physical fitness to the patients undergoing transurethral procedures. Therefore 10 ambulant elderly volunteers, of mean age 75 yr, from a local social club for the elderly also were screened with the CAPE and tested twice, once to act as a baseline and again to correspond to 1 day after anaesthesia (table I).

The following variables were recorded during anaesthesia: arterial pressure and heart rate at 1-min intervals; duration of anaesthesia, defined as time from induction to discontinuation of nitrous oxide; anaesthetic incidents, e.g. hypotension; bladder irrigation during surgery.

In 78 patients, arterialized venous $P_{CO_2}$ was measured before and during anaesthesia at 15-min intervals with a Radiometer ABL 3 blood-gas analyser [13]. This was not performed on a random sample of patients, but was undertaken if there was sufficient time available in the operating theatre.

### Statistical analysis

Independent $t$ tests were used to test if transurethral and control groups were comparable in age and baseline reaction time score. Reaction time performance after anaesthesia was very variable in the transurethral group. Therefore change in reaction time performances from baseline to after anaesthesia was examined within this period.
group and the small control group using Friedman non-parametric analysis of variance followed by Wilcoxon matched pairs tests. Mann–Whitney U tests were used also to test for differences in reaction time performance between groups. Multiple regression was carried out on change in SD of reaction time score using the multiple regression and best subset regression program from the BMDP statistical package [14].

(The computer program for the reaction time test and data analysis are available on request at a small charge.)

RESULTS

Preoperative CAPE scores for transurethral patients and orthopaedic controls are shown in table I, and other measurements made before, during and after anaesthesia are given in table II. On the basis of hospital records and patient reports, 46% of transurethral patients with reduced CAPE scores had evidence of cardiovascular disease, compared with 34% of maximally scoring patients (chi-square test, \( P = 0.4 \)). Seven patients acted as subjects twice, as they required repeat operations within the study, and five patients received non-standard anaesthesia. The data were analysed both retaining and excluding these subjects.

An independent \( t \) test (using the appropriate separate estimates of variance, as there was a significant difference in variance between the groups, Levene \( F \) for variances \( P = 0.0002 \)), carried out on the ages of transurethral patients and orthopaedic patient controls, indicated no significant difference in mean age. In addition to age being more variable, there was a greater proportion of females in the control group (table I). However, independent \( t \) tests showed there was no significant difference between transurethral patients and controls in baseline reaction time measured by median score (\( P = 0.28 \)) or SD score (\( P = 0.98 \)) (table III).

Fifty-seven and 35 patients, respectively, were available for testing 2 and 3 days after anaesthesia (table IV). Inspection of individual trials of reaction time together with means for the block of trials indicated that, when mean reaction time was increased after anaesthesia, this occurred not because each trial was longer, but because the frequency of particularly long responses was increased. Reaction times exceeding 1 s occurred and, in one patient, were frequent and persisted until the 3rd day after anaesthesia. Medians and SD of 70 reaction time trials are therefore presented [15] (table III). A Wilcoxon matched pairs signed rank test performed on the difference in median and SD of reaction time from baseline to 24 h after anaesthesia showed a statistically significant increase in the SD of reaction time scores in transurethral patients, but not in orthopaedic controls (\( P = 0.0026, n = 112 \); excluding repeat patients and patients receiving non-standard anaesthesia, \( P = 0.0006, n = 100 \)). However, the same paired comparison of median reaction time was not significantly different in patients or orthopaedic controls, for either the total of 112 patients, or the 100 patients after exclusions. Comparison between transurethral patients and orthopaedic controls of difference from baseline reaction time scores using Mann–Whitney U tests showed no significant difference in SD (\( P = 0.08 \)) or median scores. There was no significant difference in median reaction time or SD of reaction time between baseline and day 1 testing in the group of ambulant controls (table III). Only five patients undergoing transurethral procedures were rated as showing signs of confusion after anaesthesia. Inspection of reaction data indicated that only two of these also showed deficit in reaction time performance.

Friedman non-parametric analysis of variance was carried out on SD and median measures of reaction time for baseline and days 1, 2 and 3 after anaesthesia, in patients and orthopaedic controls for complete cases. Wilcoxon matched pairs tests were carried out comparing differences between day 1 and baseline, day 2 and baseline and day 3 and baseline. Again, there was a statistically significant increase in the SD of reaction time score between baseline and day 1 after anaesthesia for

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<tr>
<th>TABLE II. Measurements made before, during and after anaesthesia in 112 patients undergoing transurethral procedures (mean (SD), or number)</th>
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<tr>
<td>Weight (kg) ((n = 106))</td>
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<tr>
<td>Duration of anaesthesia (min) ((n = 110))</td>
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<tr>
<td>Mean arterial pressure before anaesthesia (mm Hg) ((n = 106))</td>
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<td>Minimum mean arterial pressure during anaesthesia (mm Hg) ((n = 106))</td>
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<td>Minimum arteriovenous PCO(_2) (kPa) ((n = 78))</td>
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The 57 patients tested for 2 days after operation (Friedman Test Statistic = 22.99, \( P = 0.00001 \); Wilcoxon matched pairs test \( P = 0.0001 \)) and the 35 patients tested 3 days after operation (Friedman Test Statistic = 16.97, \( P = 0.007 \); Wilcoxon matched pairs test \( P = 0.002 \)). There were no significant differences between day 2 and 3 performances for the SD measure, compared with baseline in either patients or orthopaedic controls. For the median measure of reaction time, there was a significant decrease in final day 3 performance compared with baseline in patients (Friedman Test Statistic = 11.9, \( P = 0.01 \); Wilcoxon matched pairs test \( P = 0.0053 \) (\( n = 35 \)) and orthopaedic controls (Friedman Test Statistic = 12.8, \( P = 0.007 \); Wilcoxon matched pairs test \( P = 0.01 \) (\( n = 19 \))). However, for day 2 performance this was significantly decreased from baseline only in orthopaedic controls (Friedman Test Statistic = 12.17, \( P = 0.002 \); Wilcoxon matched pairs test \( P = 0.01 \) (\( n = 21 \))). Median reaction time data for days 1 and 2 after anaesthesia are shown in Table V.

Multiple regression and best subset regression were performed on change in SD of reaction time score 1 day after anaesthesia (Fig. 1). This was carried out excluding patients tested twice, those having non-standard anaesthesia and the positive outlier of +1197. Factors contributing to increased variability of reaction time after operation were: reduced CAPE score before operation (\( P < 0.0001 \) (95% confidence interval (CI) = -93 to -34)); extent of surgery (\( P = 0.023 \) (95% CI = 3–48)); occurrence of pain after operation (\( P = 0.007 \) (95% CI = 14–87)) and administration of sedative drugs after operation (\( P = 0.009 \) (95% CI = 30–200)). The contribution of halothane.
anaesthesia was also statistically significant \( (P = 0.02 \ (95\% \ CI = -102 \ to \ -90)) \). However, as all the halothane cases were at the beginning of the series, a time dependent variation may have contributed. Further regression analysis leaving out the next two positive outliers of +423 and +355, who both had less than maximum CAPE scores, gave the same best subset of predictor variables with reduced CAPE score contributing significantly \( (P < 0.0001 \ (95\% \ CI = -68 \ to \ -21)) \). The same best subset and significance of change in CAPE was observed also when the negative outlier of \(-634\) was removed. Factors making no additional statistically significant contribution were age \( (P = 0.25) \), diagnosis of cancer \( (P = 0.91) \), number of previous operations in past 5 years \( (P = 0.99) \), pyrexia after operation \( (P = 0.51) \), duration of anaesthesia \( (P = 0.91) \), minimum mean arterial pressure \( (P = 0.98) \), self-rated quality of previous night’s sleep \( (P = 0.18) \), and whether or not patients received bladder irrigation \( (P = 0.48) \). In addition, a separate regression analysis on patients who had \( P_{co_2} \) values measured shown that minimum \( (P = 0.80) \) and maximum \( (P = 0.10) \) recorded \( P_{co_2} \) values also made no additional statistically significant contribution. Figure 1 indicates patients with a known psychiatric disorder or history of stroke, and those having anaesthetic incidents. There were few of these patients, but inspection of the data for these individuals suggested that depressive illness, cerebrovascular disease and peri-operative extremes of hypotension and hypercapnia may also contribute to impaired reaction time after operation.

**DISCUSSION**

Variability in reaction time performance was increased the day after anaesthesia in patients undergoing transurethral surgery. There was also evidence suggesting that learning of the task was impaired for up to 2 days after anaesthesia. The data are consistent with an earlier reaction time study in middle-aged patients, which used a similar control group of orthopaedic patients, and halothane anaesthesia, and in which performance was impaired for up to 48 h after anaesthesia [10]. However, only means of blocks of reaction time trials were reported, and it was not possible to compare our data directly. More recent studies reporting reaction time performances after alcohol or other drugs [15] in individuals indicate that an increase in the number of long responses also occurred, and that the mean measure was therefore a second order measure of drug effect [15].

The power of the study to examine the duration of changes in performance was reduced because the majority of transurethral patients were tested only at 24 h after operation. Similarly, assessment of the size of the performance deficit at 24 h in the transurethral group was compromised by having only a small control group of hospital patients. Also, there was marked improvement as a result of practice in some elderly patients. However, it is concluded that the 24-h performance deficit was related to the fact that transurethral patients had undergone surgery the day before, as there was no evidence in hospital or ambulant controls for increased variability in reaction time on the second occasion of testing. Further, transurethral surgical patients, in common with hospital controls, showed no difference in variability of reaction time 3 and 4 days after baseline testing. Even with transurethral procedures, it is difficult to establish that anaesthesia \textit{per se} caused performance deficit, because of various confounding factors. However, we did take account of extent of surgery when analysing results.

Studies in young normal volunteers undergoing longer periods of anaesthesia but without surgery demonstrate that performance may be impaired for up to 1 week, depending on the solubility and metabolism of the general anaesthetic used [16].
Halothane would be expected to produce more mental impairment than enflurane, and this was suggested in the present study, but the evidence was weak. Chronological age was not a predictor of impaired performance and this is consistent with previous findings [7, 8]. In another study [6] which did show a positive correlation between age and performance deficit measured by tests of orientation and concentration, there was no control group, and a lack of standardization in anaesthetic and surgical procedures. Preoperative CAPE score correlated negatively with performance deficit 24 h after anaesthesia and this was statistically highly significant. The subscale of the CAPE we used is a short, screening version which can distinguish between groups of patients with different degrees of mental impairment [12], but is most successful if mental impairment is extreme, which was not the case in our patient sample. It is acknowledged that there is no validated screening test to measure mild mental impairment, but it is considered that questions of information and orientation are diagnostic [17]. It therefore appears reasonable to suggest that, as a group, patients scoring less than maximally on the CAPE are less capable mentally than a group who score maximally. Similarly, at this mild level of impairment it is not possible to determine cause. Forty-six percent of patients with reduced CAPE scores had evidence of cardiovascular disease, which was not significantly different from the incidence in maximally scoring patients (34%) and comparable to the proportion (37%) in general surgical patients older than 65 yr [18].

From surveys in the general population and diagnoses in hospital series of demented patients, it has been estimated that the prevalence of dementia may be as high as 10% in people aged more than 65 yr, with Alzheimer's disease accounting for up to 50% of cases and multi-infarct dementia for about 30% [19]. However, our study and others suggest that demented patients are less likely to be referred for surgery [18]. Our series included only one overtly demented patient with a CAPE score of 7, and apraxia, who was excluded. The association of reduced CAPE score and postoperative mental impairment is consistent with clinical observations after surgery indicating failing mental status as a predisposing factor [20]. Also, it has been reported that two patients described as having "organic brain disease" demonstrated a markedly impaired ability on a battery of performance tests following spinal with light general anaesthesia for prostatectomy [21]. The results of the present study indicate the importance of measuring variables which may confound performance, such as sedative drugs and postoperative pain. Similarly, the results emphasize the importance of measuring all clinical details. Whilst hypotension and changes in PCO2 were not associated with performance deficit in the whole series, there was evidence, as shown in earlier work [22, 23], that extremes of hypotension and hypercapnia may be associated with performance deficit. It was of interest that the patient with depression also showed a large performance deficit. It has been suggested in other studies that depression, antidepressant drugs, or both may predispose to impaired performance after anaesthesia and this merits further study [5].

In conclusion this study has indicated that chronological age does not contribute to any postoperative performance deficit, but that preoperative mental impairment has a large influence. It has also indicated other risk factors worthy of examination in follow-up studies of patients undergoing longer and more complicated anaesthesia alongside more extensive surgery, where the complex clinical situation makes investigation more difficult, but where the anaesthetic risks are greater. Such studies should include more detailed screening of preoperative mental impairment.

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REFERENCES


