CHANGES IN VISUAL REACTION TIME FOLLOWING CEREBRAL ANGIOGRAPHY

Preliminary Communication

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SUMMARY

An instrument for measuring visual reaction time (VRT) was constructed and later tested on 18 control volunteers. It was established in these subjects that the mean VRT did not vary by more than 6% over a period of 5 days. The equipment was then employed to measure changes in VRT following carotid angiography under general anaesthesia in a series of 48 patients. Of these, 22 patients had no demonstrable lesion and showed no change in VRT; 26 patients had an intracranial lesion and revealed an increase in VRT on the first day after angiography. Possible causes of the changes in VRT are discussed and further investigations are suggested.

A number of writers have published details and figures concerning the neurological complications of carotid angiography. (Dunsmore, Scoville and Whitcomb, 1951; Rowbotham et al., 1953; Coddon and Krieger, 1958; Brendler and Hayes, 1959; Field, Robertson and de Saussure, 1962; Perret and Nishioka, 1966).

In an attempt to evaluate the influence of some variable factors on the incidence of complications following angiography, we conducted a pilot survey of 146 patients having cerebral contrast studies under a relatively standard general anaesthetic technique. Of these patients three poor risk subjects died within 21 days from the progressive disease which had occasioned the investigations and one patient suffered a transient neurological deficit prior to successful clipping of an aneurysm. In the remaining 142 patients no neurological sequelae were observed. The failure of this investigation to yield useful information suggested the necessity of seeking a finer measure of cerebral function which could be performed easily and which would give readily quantifiable results.

Several techniques of assessing cerebral function after anaesthesia have been described. Some were concerned with "street fitness" after anaesthesia and have been summarized by Dixon and Thornton (1973). Others attempted to detect intellectual impairment in the period following a particular anaesthetic sequence (Allen and Morris, 1962; Wollman and Orkin, 1968; Rollason et al., 1971). We were sufficiently impressed by the method of using a simple visual reaction time as described by Wollman and Orkin (1968) to apply this technique to patients undergoing carotid angiography.

METHODS

A reaction timer was designed to fulfil the following criteria:

(1) High resolution and accuracy of timing.
(2) Patient compatibility.
(3) Operator convenience.
(4) Freedom from freak performance caused by observation of the operator by the patient.
(5) Portability for use at the patient's bedside.

The instrument (fig. 1) was constructed in two linked units employing the circuit shown in figure 2. The patient unit has a xenon flash-tube and a low-force microswitch (the "patient reaction" switch). The observer unit has a push-button which energizes the flash-tube after a short random period to ensure that the patient cannot anticipate the appearance of the light. The delay in milliseconds between the light becoming visible and the subject depressing the microswitch key is taken as the reaction time. This is read off in the control unit from a digital timer the accuracy of which is ensured by the use of a 100 K Hz quartz crystal oscillator as the time standard.


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FIG. 1. Circuit diagram of the reaction timer.

FIG. 2. The reaction timer. The observer unit on the left is linked to the patient unit which has a flash-tube and switch-key. In use the two units are separated by the length of the coiled cable.

The detailed operation of the timer is explained by the flow-diagram in figure 3 and the function of the stimulus control unit is more fully given as follows:

When the Q (read as “not Q”) output of the delay monostable is reduced to its “low” state during the first delay period, the transistor connected to it turns off, allowing a current to charge the 25 μF capacitor. When it turns on again, the IN914 diode prevents this from discharging.

When the positive “stimulus” signal is presented the two transistors connected to it conduct the charge from the 25 μF capacitor into the gate of the IRC30 thyristor (electronic switch). The previously charged 0.22 μF capacitor is discharged by way of this thyristor and the starting coil of the xenon flash-tube. The flash-tube is now ionized and the charge stored in the 4 μF capacitor flows through it, giving a short intense flash. The energy of this flash is a little under 125 millijoules.

All of the gates and frequency dividers are standard DTL (diode-transistor logic) integrated circuits. The flash-tube is a Thorn-AEI FA10 unit. Either integrated circuit timers or integrated circuit monostables may be used for the delay and reset monostables. A suitable a.c. power supply is required to provide +250 volts at 50 mA, +100 volts at 10 mA and +6 volts at 0.5 Amp.

Control tests.
A class of 18 student nurses volunteered to act as control subjects; their average age was 19 years. Each nurse attended on five successive days for measurement of her visual reaction time (VRT). Tests were conducted in a small quiet room and
one observer carried out all the examinations. A run of 20 reaction times was taken to obtain a mean for each nurse on each visit. The 18 means were then used to give a grand mean for that day (360 observations). Calculation was made of the percentage deviation for each day from the mean figure for the initial day.

The results of the tests are shown in Table I. It will be seen that the mean VRT remained fairly constant between 200–212 msec, the variation being statistically not significant. A negative deviation of between nil and 6% was observed for days 2–5 when related to day 1.

It was decided that the equipment was sufficiently reliable for the purposes required providing that a figure of at least 6% was allowed for "normal" deviation. In clinical practice we assumed deviations from day to day of up to 10% as being within the limits of experimental error.

A group of patients undergoing carotid angiography were studied. It was necessary to exclude those who were unco-operative. Patients who were found to have a preoperative reaction time of more than twice the mean value for the nurse control group on day 1 were not accepted for the complete study. This excluded the more ill patients who might have had a grossly increased reaction time in the period following angiography. It was thus hoped to ensure that the test should remain a satisfactory measure of finer cerebral disturbance.

The initial tests were carried out after the patients had been in hospital for 24 hours. Provided that the more obvious distractions were excluded, it was found that the tests could be performed best in surroundings to which the subject had become accustomed. If not in a single room, the bed was screened off and, after reassurance of the patient, a pre-angiography test was performed. After angiography, reaction times were tested at about the same hour each day under similar general conditions.

**Technique of anaesthesia and angiography.**

Anaesthesia was administered by one anaesthetist (L.J.D.). Premedication was with atropine 6 μg/kg given 1 hour before angiography. When headache was a problem, codeine phosphate 0.75 μg/kg was added to the premedication. Anaesthesia was induced with thiopentone 4 mg/kg i.v. followed by suxamethonium 1 mg/kg to facilitate endotracheal intubation with auffed armoured orotracheal tube. Anaesthesia was maintained with 50% nitrous oxide in oxygen supplemented with 0.5% halothane and a trace quantity of trichloroethylene.

Percutaneous carotid puncture was performed using a Lindgren needle which was left in situ during the investigation and flushed with normal saline at a temperature of 37°C. Meglumine iothalamate 60% w/v (Conray 280) was the contrast medium employed.

At the end of the procedure 100% oxygen was
administered while digital pressure was maintained on the puncture site. Following removal of the endotracheal tube the patients were kept under constant observation until they were awake and moving all limbs. Subsequently they were examined regularly for a period of up to 4 days in addition to having their daily reaction times measured.

RESULTS

There were no complications during the procedure in any of the 48 patients studied and in the 4-day period following angiography there was no evidence of neurological deficit. One patient with an intracranial tumour could not co-operate sufficiently to allow a satisfactory reaction time test on the third postoperative day. Some of the patients were available for testing on only one or two days because of the need for operative intervention, and some others were discharged early from hospital.

The results are given in tables II and III. In order to correspond with the nurse controls both series of test days were given the same set of sequential numbers, day 1 to day 4, day 1 being the day before angiography. There were 26 patients with positive intracranial findings and 22 in whom no lesion was found. (The latter group was checked 6 months later to ensure that there were no signs of intracranial disease.) The mean age of the positive group (47 years) was slightly greater than that of the negative group (44 years) but there was no statistically significant difference between the respective VRT values of 272 and 274 msec. By contrast the control subjects had a day 1 mean value of 212 msec, a difference probably in part the result of age. The 22 patients who had no lesion had postoperative VRT values marginally less than those on day 1 but the difference was not significant.

Of the patients with positive findings 11 had a space-occupying lesion and 7 had an aneurysm. The latter had all suffered subarachnoid haemorrhage. The mean VRT of the 22 patients increased from 272 msec on day 1 to 313 msec on day 2, decreasing to 299 and 273 on days 3 and 4 respectively. The delay in VRT of 41 msec on day 2 was significant (P<0.05) but the subsequent differences were not.

There were insufficient numbers in the positive subgroups to justify statistical analysis of the differences between day 1 and subsequent days. However, the tumour group showed a successive delay of 37%, 28% and 11% in VRT compared with 16%, 2% and 5% for the same postoperative days in the aneurysm group.

DISCUSSION

Allowing for the differences between the day 1 control values and pre-angiography values it would appear that the 22 disease-free patients behaved in a manner similar to the control series. It can probably be accepted, therefore, that the techniques of anaesthesia and angiography were without adverse effect where no lesion was demonstrated.

Conversely the prolongation in VRT which was characteristic of a majority of patients having a definable lesion suggests a postangiography deterioration in cerebral function lasting at least 24 hours. This finding of a delayed VRT was not an invari-

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**TABLE II. Visual reaction times (msec) of patients having angiography studies. n=number of patients examined. Significance of the difference between means and percentage difference of days 2 to 4 in relation to day 1 is included.**

<table>
<thead>
<tr>
<th></th>
<th>Day 1 before operation</th>
<th>Day 2</th>
<th>Day 3</th>
<th>Day 4</th>
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<tbody>
<tr>
<td><strong>Negative findings group. Mean age 44</strong></td>
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<tr>
<td>Mean</td>
<td>274</td>
<td>262</td>
<td>250</td>
<td>251</td>
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<tr>
<td>SD</td>
<td>60</td>
<td>58</td>
<td>59</td>
<td>51</td>
</tr>
<tr>
<td>SEM</td>
<td>13</td>
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<td>22</td>
<td>22</td>
<td>18</td>
<td>14</td>
</tr>
<tr>
<td>P</td>
<td>—</td>
<td>n.s.</td>
<td>n.s.</td>
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</tr>
<tr>
<td>%Δ</td>
<td>—</td>
<td>-4</td>
<td>-9</td>
<td>-8</td>
</tr>
<tr>
<td><strong>Positive findings group. Mean age 47</strong></td>
<td></td>
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<tr>
<td>Mean</td>
<td>272</td>
<td>313</td>
<td>299</td>
<td>273</td>
</tr>
<tr>
<td>SD</td>
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<td>87</td>
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</tr>
<tr>
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</tr>
<tr>
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able feature. Thus in 9 of the 26 abnormal patients the percentage delay was less than the 10% accepted as within the error of the measurement. On the other hand, the increase in reaction time of the positive findings group was probably not as great as one might expect from a strictly random group of such patients undergoing angiography. The reasons for this are the exclusion of the more seriously ill patients and the need for operative intervention within 24 hours of angiography.

The difference in the figures for patients with tumours as compared with those with aneurysms is not in accord with clinical experience in this unit, where temporary neurological deficit after angiography tends to occur more often in patients with subarachnoid haemorrhage than in those with space-occupying lesions. It may be that patients with tumours are more likely to develop subclinical cerebral dysfunction but less likely to exhibit overt post-angiography sequelae.

It would be inappropriate in this study to speculate at what level in the sensorimotor continuum the delay in VRT occurs. However, it is necessary to consider the reasons why such a change may take place in order to eliminate possibly undesirable features in the technique of anaesthesia employed.

Hypotension resulting from the use of halothane (Lewis and Moore, 1968) and the injection of contrast medium (Roberts, Young and Windsor, 1967) may result in a mean aortic pressure which is too low for adequate cerebral perfusion. The decreased cerebrovascular resistance caused by volatile anaesthetic agents does not necessarily offset the effects of this diminished blood pressure (Jennett et al., 1969) in patients with a cerebral tumour and raised intracranial pressure; indeed an increased pressure within the skull may have already endangered cerebral perfusion. In this series if the arterial pressure decreased, values below 100 mm Hg (systolic) were avoided by discontinuing halothane and atropine was given to correct a decrease in pulse rate. Decreases in arterial pressure were seen more frequently in patients with cerebral aneurysm who, paradoxically, had less delay in VRT after the procedure. As a corollary to diminishing cerebrovascular resistance, the use of halothane might be expected to reduce local spasm in patients with a history of recent subarachnoid bleeding. Gilbert, Brindle and Galindo (1966) suggested that this could be one of the beneficial effects of the administration of halothane associated with spontaneous ventilation. It is a common observation, however, that this effect is not always demonstrable radiographically.

The adequacy of carbon dioxide elimination may be questioned when spontaneous ventilation is permitted in the presence of an agent such as halothane. We were unable to carry out blood-gas analysis except in 7 patients in whom a single spot check was performed 30 min after induction of anaesthesia. The mean $P_{a\text{CO}_2}$ was 44 mm Hg with a range of 33–65 mm Hg; the highest value was found in a normal patient. If a raised $P_{a\text{CO}_2}$ were to occur this might further increase intracranial pressure and cerebral oedema in patients with a space-occupying lesion. Our findings of a delayed VRT following angiography may support the opinion that anaesthesia using spontaneous ventilation with a volatile agent is undesirable in patients with a brain tumour (Barker et al., 1968).

The possibility of damage by the chemical effect of contrast media has been suggested in relation to some of the drugs used (Broman and Olsson, 1956). In the present series meglumine iothalamate was employed which was shown to be a more satisfactory agent than contrast media in earlier use (Hinck and Dotter, 1962). Patients with an intracranial aneurysm had bilateral angiography in which at least four injections of Conray 280 were made; they showed less delay in VRT when compared with the tumour group who tended to have only two injections of contrast medium.

In no patient was there any evidence of a hypoxic episode. They all received a mixture containing 50% oxygen which (in those patients who had blood-gas estimations performed) was shown to maintain the $P_{a\text{O}_2}$ well above the normal value. It can be postulated, however, that during the cerebral transit time of the bolus of contrast medium there was a haemodilutional hypoxaemia throughout the distribution of the internal carotid artery. The excessive use of saline to maintain the needle patency could have a similar effect, although in this unit saline is used very sparingly. No patient in this series had a haemoglobin concentration less than 11 g/100 ml prior to angiography.

The mechanism of the deterioration in fine cerebral function cannot yet be established on the information available. The factors in general anaesthesia that we can alter readily are the $P_{a\text{CO}_2}$ and, to some extent, the cerebral blood flow. The use of controlled ventilation with minimal amounts of volatile anaesthetics is now standard practice, in a number of centres, for patients having carotid...
angiography. It would be interesting to know if this technique tended to abolish or reduce the delay in VRT seen in patients with proven intracranial lesions under the conditions of this study. Such a trial is already in progress in our unit.

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REFERENCES


