Neurological phenomena during emergence from enflurane or isoflurane anaesthesia

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During emergence from anaesthesia, transient neurological signs that would usually be considered pathological may appear. The objective of this randomized, patient (n = 30) and observer-blinded study was to compare prospectively the incidence and duration of post-anaesthetic neurological abnormalities in healthy patients undergoing minor elective procedures following thiopentone and succinylcholine induction, and enflurane-N_2O or isoflurane-N_2O anaesthesia. Patients were studied for 60 min after anaesthesia. Arousal state, muscle tone, deep tendon reflexes, plantar reflex, sustained clonus, shivering, intense muscular spasticity and temperature were assessed. Results of neurological examination were correlated with the patient's state of arousal. Transient emergent neurological abnormalities occurred more frequently following enflurane-N_2O anaesthesia than isoflurane N_2O anaesthesia. This was statistically significant ($P < 0.05$) for quadriceps hyperreflexia, upgoing toes (positive Babinski reflex) and intense muscular spasticity. Neurological abnormalities occurred most commonly 5-20 min after anaesthesia and all abnormalities resolved within 60 min. Following enflurane anaesthesia, as patients became more alert the incidence of abnormalities declined, while the arousal state did not affect the incidence of abnormalities after isoflurane. There was no significant difference between axillary temperatures of those patients who shivered and those who did not. In conclusion, temporary emergent neurological abnormalities occurred more often following enflurane-N_2O than after isoflurane-N_2O anaesthesia.

A la fin de l'anesthésie, il est possible d'observer des signes neurologiques anormaux durant la phase d'émergence. Lors d'interventions mineures et après une induction au thiopental et succinylcholine, nous avons randomisé 30 patients quant à l'anesthésique à employer en sus du N_2O, soit l'enflurane ou l'isoflurane. Nous avons demandé à une observateur neutre de mesurer la fréquence et la durée des anomalies neurologiques à l'émergence. Pendant 60 minutes, il évaluait la température, le tonus musculaire, les réflexes tendineux et plantaires et notait la présence éventuelle d'un clonus soutenu, de tremblements, de spasticité musculaire, le tout, en parallèle avec le niveau de conscience. L'hyperréflexie quadricipitale, la spasticité intense et un réflexe plantaire en extension (Babinski positif) sont survenus plus fréquemment avec l'enflurane-N_2O qu'avec l'isoflurane-N_2O ($P < 0,05$). Les anomalies neurologiques survenaient surtout entre 5 à 20 min après la fin de l'anesthésie et s'estompaient en deçà d'une heure. Dans le groupe enflurane-N_2O, les anomalies disparaissaient à mesure que s'améliorait le niveau de conscience des patients mais cette relation n'était pas manifeste dans le groupe isoflurane-N_2O. Par ailleurs, la température axillaire était la même, que les patients tremblent ou pas. La combinaison enflurane-N_2O entraîne donc plus d'anomalies neurologiques transitoires à l'émergence que l'isoflurane-N_2O.

Key words
ANAESTHETICS, VOLATILE: enflurane, isoflurane;
COMPLICATIONS: neurologic, shivering.

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It is well recognized that during emergence from anaesthesia certain transient neurological signs that would usually be considered pathological can appear.[1-3] These include upgoing toes, transient hyperreflexia, clonus, and decerebrate posturing. Shivering is also commonly seen after anaesthesia.[4]

Because of differences in chemical structure and EEG characteristics, it is reasonable to suspect that enflurane and isoflurane may produce different neurological profiles on awakening from anesthesia. Enflurane and isoflurane are isomers and therefore have identical atomic composition, but the orientation of halogen atoms with reference to the oxygen atom differs and may account for some of the different neurological effects. It has been reported, in a small group of patients,[3] that anaesthesia with enflurane-nitrous oxide results in a higher incidence of certain transient neurological abnormalities than does

anaesthesia with halothane-nitrous oxide. The objective of this randomized, observer- and patient-blinded study was to compare prospectively the incidence and duration of post-anaesthetic neurological abnormalities in healthy patients undergoing elective surgical procedures who had received either an enflurane or isoflurane anaesthetic.

Methods

After receiving institutional Ethics Review Committee approval, 30 ASA physical status Class I and II patients, aged 16 to 65 yr, with normal preoperative neurological examination, undergoing minor elective surgery (which for the majority of patients studied was dental extractions) were studied. Patients received no premedication and anaesthesia was induced with thiopentone (5 mg·kg^{-1}), and succinylcholine (1 mg·kg^{-1}) was used to facilitate tracheal intubation. Patients were randomized to enflurane or isoflurane groups, and subsequently received either enflurane N_2O/O_2 (60/40 per cent) or isoflurane N_2O/O_2 (60/40 per cent) for maintenance of anaesthesia. The concentrations of enflurane and isoflurane used in individual patients were titrated by the anaesthetist to achieve surgical anaesthesia. Patients were allowed to breath spontaneously.

Postoperatively, a single neurological examiner, blinded to the type of anaesthesia used, studied the patients. Patients were studied immediately upon cessation of the anaesthetic, and at 5, 10, 15, 20, 30, 40 and 60 min following anaesthesia. Level of consciousness was assessed by the presence or absence of a lash reflex, pupillary light reflex and state of arousal as measured on Rosenberg's 0–3 scale: 0 = no response to the command "Open your eyes and raise your arms"; 1 = slow inappropriate response; 2 = slow appropriate response; 3 = prompt appropriate response.[3] Muscle tone, deep tendon reflexes (which were considered hyperactive if associated with clonus), the plantar reflex, presence of sustained clonus on forced ankle dorsiflexion which persisted for more than five seconds, shivering and intense muscular spasticity were assessed at each interval. Intense muscular spasticity was defined as sustained hypertonicity, most easily observed in the jaw, neck and pectoral muscles, flexors of the upper limbs and extensors and adductors of the lower limbs.[2] Shivering was defined as a rhythmic contraction of muscle groups with irregular intermittent periods of relaxation.[1] Because patients were at different stages of recovery at any given time following anaesthesia, the results of the neurological examination were correlated with the patient's state of arousal.

Axillary temperature was also recorded at each assessment time, as was the presence of shivering. Comparison between the two groups used chi square analysis (Table II, Figures 1 and 2) and Student's t test where $P \leq 0.05$ was considered statistically significant.

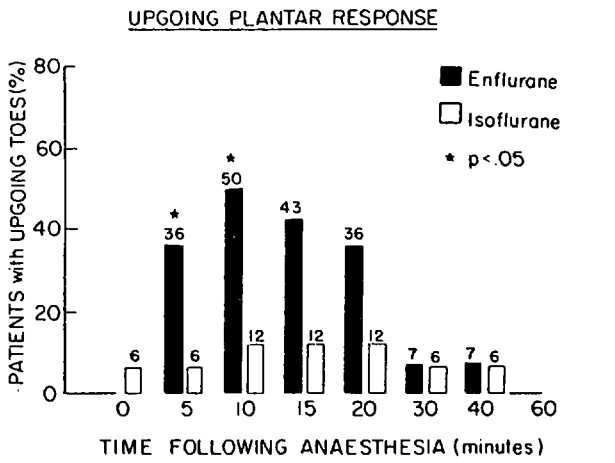

FIGURE 1 Percentage of patients with upgoing toes at each assessment time following anaesthesia. Numbers on top of the bars represent the percentage of patients in each group.

Results

There were 14 patients in the enflurane group and 16 in the isoflurane group. There were no significant differences between age, sex, and duration of anaesthesia in the enflurane or isoflurane group (Table I). Table II shows the incidence of transient postoperative neurological abnormalities. Generally, all abnormalities listed occurred more frequently following enflurane anaesthesia, and this was statistically significant for quadriceps hyperreflexia, upgoing toes, and intense muscular spasticity. These neurological findings were not always symmetrical. Occasionally a patient would have an upgoing toe on one side, while the plantar response on the other side was equivocal or normal. These occasional patients were included in the abnormal category. There was no significant difference between the axillary temperatures of those patients who shivered and those who did not.

Figure 1 shows the percentage of patients with upgoing toes at each assessment time following anaesthesia. This sign occurred more often following enflurane anaesthesia

TABLE I Patient data: (mean ± SEM)

	Enflurane	*Isoflurane*
Age (yr)	31.8 ± 3.9	26.3 ± 3.6
Duration of anaesthesia (min)	55.0 ± 5.0	51.6 ± 4.8
Sex: Male *n*	8	7
Female *n*	6	9

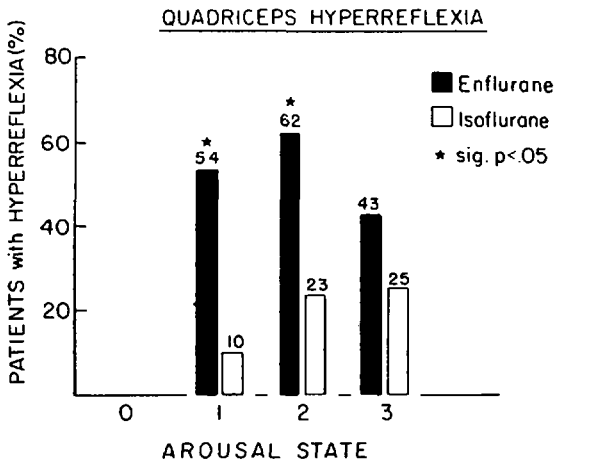

FIGURE 2 Percentage of patients with quadriceps hyperreflexia at various arousal states. Numbers on top of the bars represents the percentage of patients in each group.

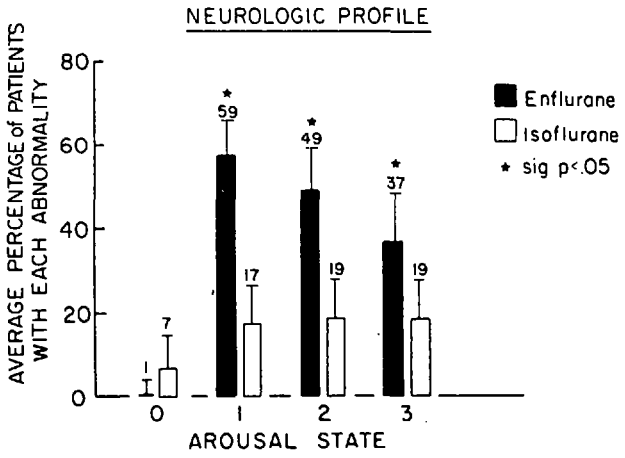

FIGURE 3 The percentage of patients demonstrating each of the six neurological abnormalities tabulated in Table II was averaged for each arousal state to obtain a neurological profile. Numbers on top of the bars represents the percentage of patients in each group. Lines on top of the bars represent one SEM.

at almost all assessment times and this was significant at five and ten minutes. This graph reveals that neurological abnormalities occurred most commonly 5–20 min after anaesthesia and that all abnormalities resolved within 60 minutes.

Figure 2 shows the percentages of patients with hyperreflexia at different states of arousal. Hyperreflexia occurred more commonly after anaesthesia with enflurane than isoflurane at arousal state 1 and 2. Hyperreflexia was absent in arousal state zero, and abnormalities occurred most commonly in arousal states 1 and 2, when patients were in the early stages of awakening from anaesthesia.

The percentage of patients demonstrating each of the six abnormalities in Table II was averaged for each arousal state to obtain a neurological profile and these results are shown in Figure 3. When all abnormalities studied were taken into account, more abnormalities were observed following enflurane anaesthesia during arousal states 1–3 than following isoflurane anaesthesia. Following enflurane anaesthesia, as patients became more alert the incidence of abnormalities declined. The arousal state did not affect the incidence of abnormalities after isoflurane.

TABLE II Incidence of transient abnormality

Neurological sign	*Enflurane* $n = 14$	*Isoflurane* $n = 16$
Increased muscle tone	71%	50%
Quadriceps hyperreflexia*	71%	38%
Upgoing toes*	57%	25%
Sustained ankle clonus	57%	31%
Intense muscular spasticity*	64%	12%
Shivering	79%	56%
Time to arousal state 2	16 ± 11 min	10 ± 10 min
Time to arousal state 3	25 ± 15 min	19 ± 15 min

*$P < 0.01$.

Discussion

This study demonstrated that transient neurological abnormalities occurred more frequently following enflurane-N_2O than after isoflurane-N_2O anaesthesia. With enflurane, a higher incidence of neurological abnormalities occurred in arousal state one, and the incidence decreased as patients became progressively more alert, while with isoflurane there was a more uniform distribution of neurological abnormalities among arousal states.

The complex mechanism underlying these transient abnormalities remains to be established, but may result from differential recovery rates of various CNS centres following anaesthesia. For example, the upper motor neuron signs could be related to recovery of the reticular activating system before recovery of higher CNS centres. The inhibitory cells of the reticular activating system depend on impulses from higher centres for their function, while the facilitatory cells have their own spontaneous activity.[1,5] Therefore, during recovery, there is a period of facilitation of the anterior horn cells in the absence of modulating inhibition which results in spasticity. Alternatively, a direct excitatory or disorganization effect on CNS mechanisms could be responsible for these postanaesthetic abnormalities.

In conclusion, transient neurological abnormalities occurred more often following enflurane-N_2O than isoflurane-N_2O anaesthesia. Accordingly, isoflurane may be a more suitable anaesthetic agent than enflurane, when close postoperative monitoring of neurological function is required.

References

1 *Soliman MD, Gillies DM.* Muscular hyperactivity after general anaesthesia. Can Anaesth Soc J 1972; 19: 529–35.

2 *Brichard G, Johnstone M.* The effect of methylphenidate (Ritalin) on posthalothane muscular spasticity. Br J Anaesth 1970; 42: 718–21.

3 *Rosenberg H, Clofine R, Bialik O.* Neurologic changes during awakening from anesthesia. Anesthesiology 1981; 54: 125–30.

4 *Smith RM, Bachman L, Bougas T.* Shivering following thiopental sodium and other anesthetic agents. Anesthesiology 1955; 16: 655–64.

5 *Shimoji K, Fujioka H, Fukazawa T, Hashiba M, Maruyama Y.* Anesthetics and excitatory/inhibitory responses to midbrain reticular neurons. Anesthesiology 1984; 61: 151–5.