Effects of different concentrations of sevoflurane and desflurane on subcortical somatosensory evoked responses in anaesthetized, non-stimulated patients

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Twenty-four patients were recruited and given either sevoflurane or desflurane as their sole anaesthetic. Each patient was given sequentially increasing or decreasing doses at 0.5 MAC intervals, and the median nerve somatosensory evoked response recorded after an equilibration at each concentration. The N20-P25 and P25-N35 amplitudes decreased with increasing agent concentration. However, for both agents the P15-N20 amplitude response was quadratic in shape. The peak inflection points were at 3.2% for sevoflurane and 4.9% for desflurane. There were no differences between the ascending and descending groups. This increase in activity in the midbrain at 'surgical' end-tidal anaesthetic concentrations suggests more complex neuroelectrical responses to anaesthesia than simple global suppression.

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The somatosensory evoked response (SER) is a stimulus related potential of the central nervous system derived from the electroencephalograph (EEG). It is routinely used in spinal and head and neck surgery to assess perioperatively the functional integrity of ascending pathways during surgery (see Fig. 1). Increasing suppression of cortical SER as indicated by decreasing wave amplitude and increasing latency with increasing anaesthesia is widely reported during anaesthesia with volatile anaesthetics, barbiturates, benzodiazepines and opioids.1–5 This effect has also been noted in subcortical waves but these waves are said to be more resistant to anaesthetic suppression.6

We studied the effects of different concentrations of desflurane and sevoflurane on early SER waves. The amplitudes P15-N20, N20-P25, and P25-N35 were studied. These amplitudes are thought to represent activity in the pontothalamic, thalamic and thalamic/primary sensory cortex portions of the pathway, respectively,7–9 although the exact site of the generators is a subject for ongoing debate in the EEG literature. Our patients were not undergoing surgery during data acquisition and were ventilated with a laryngeal mask airway (LMA™) to minimize external stimuli.

Patients and methods

After local ethics committee approval 24 patients gave written, informed consent and were recruited to the study. All were ASA I and II and attending our hospital for elective surgery. No premedication was used. On arrival in the anaesthetic room full non-invasive monitoring was applied and intravenous (i.v.) access obtained. Inhalational induction of anaesthesia was performed with either sevoflurane or desflurane. Once the subjects were anaesthetized muscle relaxation was obtained with vecuronium 0.1 mg kg⁻¹ and a LMA of appropriate size sited. Patients were then ventilated to normocapnia using oxygen and the relevant agent only. End-tidal carbon dioxide and volatile agent were measured continuously with a calibrated Datex™ Capnomac Ultima™ monitor (Datex, Helsinki, Finland).

Patients were randomized to receive five sequential concentrations of sevoflurane or desflurane. To correct for possible time trends and to ensure adequate equilibration at each anaesthetic level patients were also randomized to receive the agent in an ascending or descending order. The levels were set at approximately 0.5 MAC intervals, and each end-tidal concentration was maintained for at least 10 min to allow equilibration prior to data collection. At the
end of data collection the patients were transferred to the operating theatre and the operation started.

**Data collection**
The median nerve was stimulated at the wrist with an electrical pulse delivered at a rate of 2.2 s⁻¹ and at an intensity adjusted to just above the motor threshold (11–13 mA). The SER was derived from the electroencephalogram, and recorded using silver/silver chloride electrodes attached at Fz and C3. SER data were collected over the last 2.6 min of each agent concentration period (356 EEG sweeps) on a system developed in our unit. These were averaged and analysed offline. The amplitudes $P_{15}$-$N_{20}$, $N_{20}$-$P_{25}$ and $P_{25}$-$N_{35}$ were measured at each anaesthetic concentration.

**Results**
Patient subgroups were similar in terms of age, sex and weight (see Table 1).

The SER amplitudes were plotted against end-tidal agent concentration for sevoflurane and desflurane, and are shown in Figs 2 and 3. The data from the ascending and descending subgroups for each agent were compared using a two sample $t$-test to assess for differences, and in each case were not significantly different (sevoflurane $P=0.37$; desflurane $P=0.98$).

For both agents a dose related decrease in amplitude with increasing anaesthetic end-tidal concentration was seen in the $N_{20}$-$P_{25}$ and $P_{25}$-$N_{35}$ amplitudes. The $P_{15}$-$N_{20}$ amplitude for both agents increased with increasing agent concentration before falling – a quadratic curve. Quadratic regression curves fitted each patient data-set significantly better than a straight line ($P<0.001$ in both cases). The inflexion point for these curves were at 3.2% (95% confidence intervals 2.9–3.4%) for sevoflurane, and 4.9% (95% confidence intervals 3.1–6.8%) for desflurane. The evoked potentials for one patient in the sevoflurane group are shown (see Fig. 4; only four of the five concentration curves are shown for clarity).

The mean inflexion points were compared for the two agents in terms of MAC, using 1 MAC=sevoflurane 2% desflurane 6%. There was a significant difference.
between the two agents (inflection point for sevoflurane 1.5 MAC, desflurane 0.8 MAC, \( P < 0.01 \)).

### Discussion

Increasing concentrations of anaesthetic agent, both inhaled and i.v., are widely recognized to cause suppression of central nervous system electrical activity as measured by the EEG and EEG derived variables (e.g. evoked responses and the Bispectral Index). Subcortical evoked response amplitudes are known to be relatively resistant to the effects of anaesthesia. This is one of the reasons that later, cortical mid latency evoked response amplitudes are commonly used for depth of anaesthesia assessment.

Increases in P15-N20 amplitude after bolus doses of etomidate have been reported\(^{13-15}\) during surgery with non-standardized and varied doses of anaesthetic agents. This may represent the same phenomenon but the presence of other agents and variable surgical stimuli may be confounding. The technique was recommended to augment SER signals during surgery. Jantti and colleagues also reported an increase in this amplitude during sevoflurane anaesthesia\(^{16}\). They recorded data at burst suppression (1.5–2.5 MAC sevoflurane) rather than at specific anaesthetic end-tidal concentrations and found similar potentiation of this amplitude, but did not report amplitude changes over a range of concentrations in each subject.

There are several plausible reasons for this increase. The site of increased activity cannot be localized anatomically from these data, because the amplitude represents the activity attributable to the median nerve stimulus at the stated time after stimulation rather than at a known site in the midbrain. However, it is widely held that the generators of the P15-N20 amplitude are in the pontothalamic area.

Increasing electrical activity in the midbrain could be caused by a direct, anaesthetic mediated increase in inhibitory postsynaptic potential (IPSP) generation, or a more generalized interruption of intercellular communication. One interesting possibility involves recent in vitro work by Traub, Whittington and others, which shows that anaesthetic and analgesic drugs disrupt gamma frequency oscillations originating in the hippocampus and midbrain.\(^{17,18}\) These high-frequency signals are thought to represent the co-ordination of sensory input analysis between anatomically discrete areas of the brain. When disrupted, the gamma frequency output increases. This is thought to be due to anaesthetic and analgesic drugs
decreasing gamma-aminobutyric acid (GABA) type A receptor mediated inhibition of excitatory and inhibitory interneurons. This increase in gamma signal could explain the increased electrical activity in the midbrain seen up to the point where direct pathway effects (burst suppression of the EEG) are seen, causing the fall in voltage at higher anaesthetic concentrations. It also may explain the increasing sensory detachment leading to and including the state of anaesthesia. However there is no human in vivo evidence to support or refute this at present.

The peak values at the points of inflexion of sevo\nflurane and desflurane differ significantly when compared using MAC values. These data must be interpreted carefully as the desflurane group peak value is not central in the data points measured. However, MAC is primarily a motor descriptor of MAC values. These data must be interpreted carefully as the effects on neuronal transmission may differ.

In conclusion, we have found that the subcortical SER dose not respond in a uniform way to increasing anaesthetic concentration. The N20-P25 and P25-N35 amplitudes decrease with increasing anaesthetic concentration, but the P15-N20 wave is potentiated at clinically relevant end tidal sevo\nflurane and desflurane concentrations.

Further work is needed to more closely analyse the anatomical site, if any, of this increased signal.

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