Algesimetry: Concepts For Intelligent Anesthesia Monitors

E Kochs, G Schneider

Abstract

General anaesthesia can be divided into the main components hypnosis, antinociception and stability of the autonomous nerve system. The analgesic component can only be monitored by the influence on the autonomous nerve system (increase in heart rate, blood pressure, tearing) or the hypnotic component. Surgery-induced changes of the anaesthetized patient are reflected by changes of the AEP and EEG. During anaesthesia, the somatosensory evoked potentials (SEP) change with different levels of analgesia. Increasing levels of sedation also induce changes of the pain-evoked potential.

INTRODUCTION

General anaesthesia can be divided into the main components hypnosis, antinociception and stability of the autonomous nerve system. A variety of drugs can be used to obtain these goals. During modern balanced anaesthesia, a combination of drugs is used, with each of the drugs altering mainly one of the three components. This means, according to specific requirements hypnotic drugs, analgesic drugs or "if necessary" muscle relaxants or cardiovascular drugs are administered. The components of anaesthesia and the influence of drugs can be monitored with varying precision. Stability of the autonomous nerve system can be quantified by haemodynamic measurements and observation of e.g. tearing and sweating. The effect of muscle relaxants can be quantified by measurements of neuromuscular transmission. Numerous studies describe changes in EEG activity under the influence of anaesthetics and opioids. These pharmakodynamic effects are non-specifically induced changes of cortical function, reflecting a global effect rather than antinociceptive components. Individual reactions to painful stimuli are a problem of conscious perception and thus reactions differ between awake and anaesthetised subjects [1].

ALGESIMETRY

Quantification of the sedative and hypnotic component is achieved with increasing precision using auditory evoked potentials (AEP) and EEG-derived parameters [2, 3]. The analgesic component can only be monitored by the influence on the autonomous nerve system (increase in heart rate, blood pressure, tearing) or the hypnotic component.

Insufficient antinociception may result in patient reactions despite of sufficient pre-stimulus anaesthesia [4]. Surgery-induced changes of the anaesthetized patient are reflected by changes of the AEP [5] and EEG (Figure 1) [6].

Figure 1

Figure 1: Surgery-induced changes in brain electrical activity during isoflurane/nitrous oxide anaesthesia
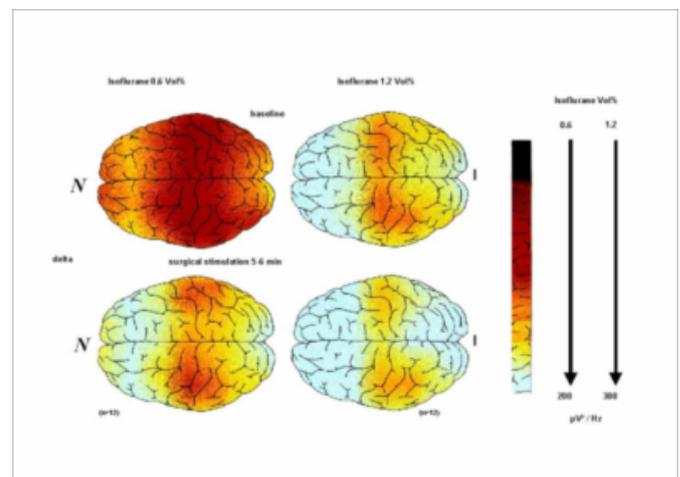
Even though detection of changes are important, prevention of these changes by sufficient antinociception would be more desirable. In experimental settings, changes of brain activity can be monitored using positron emission tomography (PET) (Figure 2).

Figure 2

Figure 2: Activated brain areas during pain stimulation and remifentanil analgesia and corresponding VAS-scores: In volunteers without remifentanil infusion (control) rCBF increased in response to painful stimulation. Successive reduction in pain-related activation was observed with increasing doses of remifentanil (thalamus, insula, Nc. lenticularis, anterior and posterior cingulate cortex (ACC, PCC)) but not in the insula which seems to be most resistent to the effects of remifentanil.
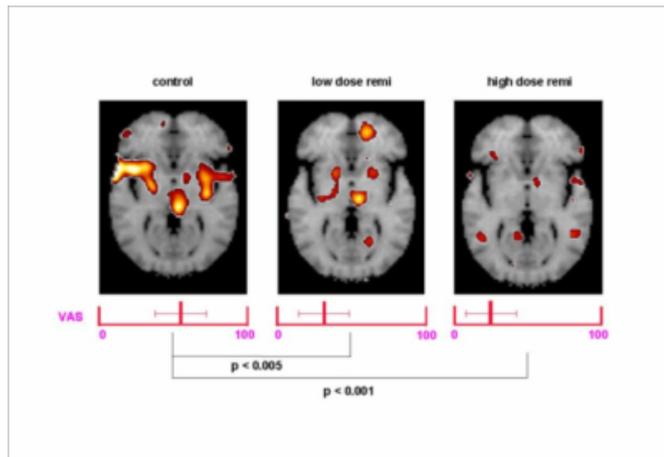
During anaesthesia, the somatosensory evoked potentials (SEP) change with different levels of analgesia [7]. Under subanesthetic anaesthetic concentrations of ketamine these changes correlate with changes of pain perception whereas changes in the spontaneous EEG correlate with changes of the hypnotic level [8]. In patients undergoing surgery under general anaesthesia, varying surgical stimulus intensity is reflected by changes of the SEP (Figure 3) [9].

Figure 3

Figure 3: SEP and haemodynamic reactions during isoflurane/N2O anaesthesia: Baseline (BL), during positioning (PR), skin incision (S1), periostal stimulation (S2) and 10 min. following S2 (S3).
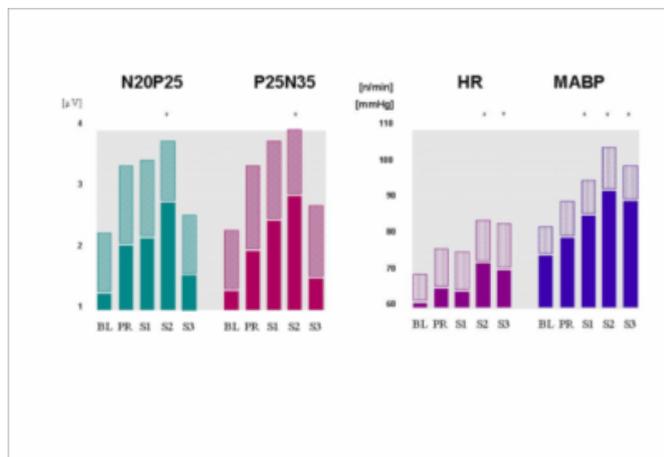
Electrical SEP stimulation, however, does not only activate pain-related C- and AΔ-fibers but also mixed sensory (AΔ-) fibers. I.e. electrical SEP do not reflect a pure pain reaction. As the evoked signal does not allow to differentiate between non-specific sensory activation and specific nociceptive response, exclusive activation of receptors of nociception is crucial (i.e. touch or pressure receptors should not be triggered simultaneously). Modification of the electrical stimulus by removing a small core of epidermis from the skin allows intradermal stimulation at the depth of pain receptor nerve endings [10]. Still, exclusive stimulation of C- and AΔ- fibers can not be guaranteed. The stimulus applied should be quantifiable in terms of intensity and duration, easily applied, removed and repeated without causing tissue damage. Pure pain-stimuli for the measurement of evoked potentials can be induced by mechanical, chemical or heat stimuli. The application of chemically induced stimuli are not very precise in terms of timing, except for nasal application of CO_2 [11]. The application of precisely controllable laser-heat stimuli is a validated method with flexibility in application of the stimulus (localisation), precision in its timing (within milliseconds) and specificity of stimulation (exclusively nociceptive pathways - C and AΔ) [12]. Amplitude localisation of pain-evoked potentials is different from SEP, using electrical stimulation of the nerve [13]. First studies correlated pharmacodynamic profiles of analgesic drugs with pain-evoked potentials in awake and anaesthetised subjects [12, 14]. Differentiation between the analgesic and the hypnotic effect may not be achieved by laser-evoked potentials alone [15]. In fibromyalgia patients, laser-evoked potentials as a measure of pain perception and auditory evoked potentials as a measure of sedation and hypnosis have been used simultaneously as a diagnostic tool [16]. Increasing levels of sedation also induce changes of the pain-evoked potential [17]. This may be a reflection of a decrease in pain perception induced by sedation [18]. Further research will be necessary to evoke earlier components of the pain-induced potential, as these may reflect activity in the nociceptive system rather than the effect of conscious pain perception [19].

This knowledge must be obtained to fully understand perception of pain and possibly develop a monitoring tool for the antinociceptive component of anaesthesia.

This paper was presented at the 23rd Annual Meeting of the European Academy of Anaesthesiology (EAA): Molecular Biology, Ethics and the Future of Anaesthesia Research. August 30 - September 1, 2001, Graz, Austria

CORRESPONDANCE:

Eberhard Kochs, M.D., Ph.D. Director Department of

Anesthesiology Klinikum rechts der Isar Technical

University Munich Ismaninger Str. 22 D-81675 Munich

Germany Tel.: +49 (0)89 4140-4291 Fax: +49 (0)89

4140-4886 E.F.Kochs@lrz.tum.de

References

1. Bromm, B., Das spontane und das reizevozierte EEG in der Narkose. Anasthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie, 1992. 27(2): p. 76-83.

2. Kochs, E., Kann das EEG einen Beitrag zur Narkosetiefenbestimmung leisten? An?hesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie, 1994. 29(6): p. 319-21.

3. Schneider, G. and P.S. Sebel, Monitoring depth of anaesthesia. European Journal of Anaesthesiology, 1997. 15(Suppl): p. 21-28.

4. Kochs, E., et al., Middle latency auditory evoked responses and electroencephalographic derived variables do not predict movement to noxious stimulation during 1 minimum alveolar anesthetic concentration isoflurane/nitrous oxide anesthesia. Anesthesia & Analgesia, 1999. 88(6): p. 1412-7.

5. Thornton, C., et al., Effect of surgical stimulation on the auditory evoked response. British Journal of Anaesthesia, 1988. 60(4): p. 372-8.

6. Kochs, E., et al., Surgical stimulation induces changes in brain electrical activity during isoflurane/nitrous oxide anesthesia. A topographic electroencephalographic analysis. Anesthesiology, 1994. 80(5): p. 1026-34.

7. Kochs, E., et al., Modulation of pain-related somatosensory evoked potentials by general anesthesia. Anesthesia & Analgesia, 1990. 71(3): p. 225-30.

8. Kochs, E., et al., Analgesic efficacy of low-dose ketamine. Somatosensory-evoked responses in relation to subjective pain ratings. Anesthesiology, 1996. 85(2): p. 304-14.

9. Rundshagen, I., E. Kochs, and J. Schulte am Esch, Surgical stimulation increases median nerve somatosensory evoked responses during isoflurane-nitrous oxide anaesthesia. British Journal of Anaesthesia, 1995. 75(5): p. 598-602.

10. Bromm, B. and W. Meier, The intracutaneous stimulus: a new pain model for algesimetric studies. Methods & Findings in Experimental Clinical Pharmacology, 1984. 6(7): p. 405-10.

11. Hummel, T., et al., Chemo-somatosensory event-related potentials in response to repetitive painful chemical stimulation of the nasal mucosa. Electroencephalography & Clinical Neurophysiology, 1994. 92(5): p. 426-32.

12. Bromm, B. and R.D. Treede, Laser-evoked cerebral potentials in the assessment of cutaneous pain sensitivity in normal subjects and patients. Revue Neurologique, 1991. 147(10): p. 625-43.

13. Kany, C. and R.D. Treede, Median and tibial nerve somatosensory evoked potentials: middle-latency components from the vicinty of the secondary cortex in humans. Electroencephalography & Clinical Neurophysiology, 1997. 104(5): p. 402-10.

14. Handwerker, H.O. and G. Kobal, Psychophysiology of experimentally induced pain. Physiological Reviews, 1993. 73(3): p. 639-71.

15. Roth, D., et al., Analgesic effect in humans of subanaesthetic isoflurane concentrations evaluated by evoked potentials. British Journal of Anaesthesia, 1996. 76(1): p. 38-42.

16. Lorenz, J., Hyperalgesia or hypervigilance? An evoked potential approach to the study of fibromyalgia syndrome. Z Rheumatol, 1998. 57(Suppl 2): p. 19-22.

17. Petersen-Felix, S., et al., Psychophysical and electrophysiological responses to experimental pain may be influenced by sedation: comparison of the effects of a hypnotic (propofol) and an analgesic (alfentanil). British Journal of Anaesthesia, 1996. 77(2): p. 165-71.

18. Zacny, J.P., et al., Propofol at conscious sedation doses produces mild analgesia to cold pressor-induced pain in healthy volunteers. Journal of Clinical Anesthesia, 1996. 8(6): p. 469-74.

19. Zaslansky, R., et al., Pain-evoked potentials: what do they really measure? Electroencephalography & Clinical Neurophysiology, 1996. 100(5): p. 384-91.

Author Information

Eberhard Kochs, Prof., Dr., Dipl.-Phys.

Director, Department of Anesthesiology, Klinikum rechts der Isar, Technical University Munich

Gerhard Schneider, M.D.

Department of Anesthesiology, Klinikum rechts der Isar, Technical University Munich