## Remifentanil and Nitrous Oxide Anesthesia Produces a Unique Pattern of Frontal EEG Activity

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**Introduction:** Remifentanil (remi) and nitrous oxide (N<sub>2</sub>O) are commonly used in combination, together with other anesthetics, for routine surgical anesthesia, yet the electroencephalogram (EEG) effects of these are poorly described. In addition, remi and N<sub>2</sub>O produce EEG effects that are difficult to analyze using traditional frequency-derived measures. The present study examined effects of these two agents on EEG signals recorded from 40 randomly chosen surgical patients.

**Methods:** EEG responses were recorded using a BIS monitor, following patient consent to a Stanford University approved protocol. Remifentanil concentrations were varied on a steady background of nitrous oxide (66%) and cortical responses to a train of four (TOF) stimulus were compared at different concentrations of remi.

**Results:** At surgical planes of anesthesia high amplitude slow waves (1 to 2 Hz) dominated the EEG, similar to effects seen with most anesthetics, but these slow waves were interspersed with rhythmic theta activity from 4 to 10 Hz that lasted a few seconds to several minutes before reverting to slow wave activity, that could also last several seconds to minutes. Changes in remi concentrations had little effect on background activity, marginally increasing slow waves, and did not change the alternating pattern of delta and theta activity. Chaos analysis of the same EEG signals showed a typical flatting of attractors that is seen with propofol as well as with volatile anesthetics. Attractor flattening was seen for both the delta and theta dominant EEG patterns, with little apparent difference, at surgical planes of nitrous oxide/remifentanil anesthesia. TOF stimulation produced cortical activation, seen as a marked decrease in signal amplitude and increase in higher frequency content, which was diminished by higher concentrations of remi.

**Conclusions:** We conclude that remi/ $N_2O$  anesthesia is associated with a unique oscillating pattern of delta/theta frequency activity that makes it difficult to correlate these frequency-derived measures with anesthetic depth. Chaos analysis, in contrast, consistently provided a good measure of anesthetic depth in these patients.

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