The Impact of Addition of N2O on BIS, PSI, and Entropy during a Stable Sevoflurane Anesthetic.

Background
N2O is a commonly used anesthetic agent that has significant amnestic and analgesic properties. Studies in volunteers breathing up to 70% N2O have shown no change in Bispectral Index (BIS) from normal awake values (95-100), despite loss of responsiveness to commands and apparent sedation. Furthermore, in previous studies we have shown that addition of N2O to a stable sevoflurane anesthetic did not change BIS nor Patient State Index (PSI) despite near doubling of MAC. Entropy is a new measurement based on spectral entropy which measures disorder in the cortical EEG and frontalis EMG. State Entropy (SE) is derived from EEG (0.8 -32 Hz) and Response Entropy (RE) from a combined measure of EEG and FEMG activity (0.8 – 47Hz). Unlike BIS and PSI, Entropy does not compare electric signal to an existing library, and thus is potentially more applicable to a wider variety of patients receiving a wider variety of anesthetic agents.

Methods
General anesthesia was induced and titrated to maintain normal blood pressure and pulse during laparoscopic surgical procedures. Laparoscopic operations were selected due to a relatively stable level of surgical stimulation. After 10 min with no change of more than 10% in heart rate, mean blood pressure, end-tidal anesthetic concentration, and measure of consciousness, baseline data were recorded. N2O was then added to the inspired gas mixture to achieve an end tidal concentration of >65%. When end-tidal N2O was >65% and after 10min of blood pressure and pulse stability, data were again collected. N2O was discontinued, and after end-tidal N2O was <5% and following 10min of physiologic stability, data were re-collected. Sample size (n=20 per group) was designed to detect a 10 unit change in measure of consciousness with alpha = .05 and statistical power = .80. Data are summarized as mean SD and were compared with an analysis of variance for repeated measures. All patients were paralysed during data collection.

Results
There were no differences in variables reflecting cardiovascular function throughout the study in any of the groups. Supplementing sevoflurane with >65% N2O increased MAC from 1.3 ± 0.05 to 2.2 ± 0.10, but did not alter BIS or PSI (p-value for differential MAC is <0.001). Entropy, however, dropped significantly, with a change in state entropy (SE) from 29.2±6.1 to 19.1±3.8 and response entropy (RE) from 29.7±6.2 to 19.5±4.0.

Conclusion
Supplementing sevoflurane with >65% N2O affected neither BIS nor PSI despite nearly doubling MAC. Entropy, however, decreased as anesthetic depth increased. Since N2O is often used in combination with volatile anesthetics, it is important to know that N2O has variable effects on these derived measures of consciousness. Entropy may be a more robust measure of consciousness for a more diverse spectrum of patients and anesthetics.