Sevoflurane Causes a Significant Increase in Hippocampal Glutamate in Neonatal Piglets

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Background

Glutamate, the major excitatory neurotransmitter in the brain, is critical for normal neuronal signal transduction. Glutamate must be present in the synaptic cleft at the correct concentration if neuronal toxicity is to be avoided, making it a novel target for studies investigating the mechanism(s) of anesthesia-induced developmental neurotoxicity (AIDN). Novel technologies, such as enzyme-linked microelectrode arrays (MEAs), can be used to monitor glutamate activity in intact animals in real time. With extremely high spatial (100 μm) and temporal (10Hz) resolution, MEAs are well suited for the evaluation of acute and chronic changes in glutamate concentration.

Methods

- 4 piglets were anesthetized and prepared as previously described1
- Following craniotomy, an MEA is placed in the hippocampus using a stereotactic apparatus and atlas
- Following MEA placement, glutamate levels were allowed to equilibrate prior to recording
- Continuous glutamate activity (10 Hz) was recorded under sevoflurane anesthesia at 1 minimum alveolar concentration (MAC) for 3h, followed by 2 MAC for 1h
- MEA placement in the hippocampus was verified histologically

Results

- Each animal showed a marked increase in glutamate over the course of the anesthetic in an apparent dose-dependent fashion (Figures 1&2)
- Baseline levels of glutamate (levels during the first 30 min) were 27.8±0.8 μM.
- Glutamate reached peak levels of 58.6±0.8 μM after 1 MAC sevoflurane.
- Additional exposure to 2 MAC sevoflurane for 1h increased glutamate levels to 76.1±0.8 μM. (Figure 3, p<0.0001)

Discussion

- These data establish for the first time the feasibility of in vivo electrochemical recording in the in the neonatal piglet brain – a novel application of cutting-edge technology
- Patterns of glutamate spiking activity and kinetic profiles observed can be used to quantify changes in response to anesthesia
- Observations suggest a significant increase in glutamate in neonatal animals in the setting of a sevoflurane anesthetic
- Future studies will establish the contribution of surgical stress to glutamate dysregulation and correlation of glutamate levels with cellular toxicity and changes in behavior, and elucidation of glutamate activity in awake, behaving animals.

Methods

- 2-3 day old piglets were studied after preparation as previously described1
- Glu MEAs were prepared as previously described, with two enzyme-free ‘sentinel’ sites and two enzyme coated (Glu Oxidase) ‘glu sensitive’ sites.2
- MEAs are coupled with constant potential amperometry (+0.7 V vs. Ag/AgCl), the FAST-16 system (Quanteon L.L.C.)
- Continuous glutamate measurements were recorded under 1 MAC sevoflurane (3h) and 2 MAC sevoflurane (1h)

Results

- Average glutamate concentration during the period of 1 MAC vs. 2 MAC sevoflurane for 4 animals. * indicates significance, P<0.0001

References


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