1. CLINICAL, TECHNICAL, AND RESEARCH AIMS

A fundamental problem in neuroscience and medicine is to understand the mechanisms for loss of consciousness under general anesthesia. Studying loss of consciousness under general anesthesia is a complex problem. The phenomenon of general anesthesia has five components: loss of consciousness, amnesia, loss of pain perception, and immobility, while maintaining hemodynamic stability (Barash et al., 1997). Induction and different planes of general anesthesia produce highly stereotyped changes in electroencephalogram (EEG) patterns (Rampil, 1998; Sloan, 1998; John et al., 2001; Pockett, 1999; Plourde et al., 1998). Loss of consciousness under general anesthesia is measured clinically by observing the loss of response to external stimuli. The failure to respond to external stimuli could be a result of disruption of afferent sensory pathways, central processing, efferent motor pathways, or some combination of these three. We wish to conduct a series of studies using concurrent EEG and functional MRI that will characterize changes of function under general anesthesia in a number of afferent, efferent, and central processing pathways, including the somatosensory system, the auditory system, and cognitive systems subserving implicit memory formation. By observing functional changes in somatosensory, auditory, and cognitive systems relative to the time point of loss of consciousness and changes in stereotyped EEG patterns, we wish to begin
developing neurophysiological correlates that can describe the state of unconsciousness under general anesthesia, and provide a neurophysiological basis for monitoring depth of anesthesia during surgery, and for design of improved anesthetic drugs.

Establishing an EEG-fMRI paradigm for studying anesthesia poses a number of clinical and technical challenges. Methods for concurrent EEG-fMRI suitable for anesthesia studies have been developed in the author’s Ph.D. thesis. We propose the following Clinical, Technical, and Research Aims for this HST 203 Preceptorship that will address several important clinical and clinically-oriented technical and research concerns for these studies:

**Clinical Aim:** Become familiar with the clinical practice of anesthesia, paying particular attention to patient safety, clinical monitoring standards, and methods for monitoring depth of anesthesia.

**Technical Aims:** 1) Develop a data acquisition system for recording and integrating physiological monitoring signals such as electrocardiogram (ECG), blood pressure, and end-tidal CO₂ with EEG signals; 2) Assemble and test a computer-controlled drug delivery system using a laptop, infusion pump, and STANPUMP infusion software.

**Research Aim:** Perform a review of neuro-anesthesia literature to confirm the widely-held clinical assertion that Propfol, the most common hypnotic agent used to induce general anesthesia, maintains cerebro-vascular coupling and is therefore suitable for study with fMRI.

**John Walsh, M.D.,** an Instructor in the Department of Anesthesia and Critical Care at the Massachusetts General Hospital, has been selected as the clinical advisor for this preceptorship. In addition to being a full-time clinical anesthesiologist, Dr. Walsh is also an expert in pharmacokinetic modeling of anesthetic drugs.
Vitaly Napadow, Ph.D., an Instructor in Radiology at the Massachusetts General Hospital, has been selected as the technical advisor for this preceptorship. Dr. Napadow is an expert in device development and data acquisition for functional MRI studies.

2. PLAN OF STUDY

Clinical Aims: The clinical aims for this preceptorship will be achieved by following Dr. Walsh as a medical student would during the course of his normal clinical practice during several days distributed throughout the preceptorship. Each clinical session will focus on a different clinical service of anesthesia, including anesthesia for general surgery, cardiovascular anesthesia, neuroanesthesia, and outpatient anesthesia. Approximately four clinical sessions will be scheduled during the preceptorship period.

Technical Aim 1 (Integrated data acquisition of physiological signals with EEG): Several afternoons of full-time effort will be devoted to modify an existing EEG data acquisition system to include physiological signals. The EEG data acquisition software, written in National Instruments LabView, will be modified to acquire several channels of analog data from an InVivo Magnitude MRI patient monitor via a National Instruments DAQCard 6024E data acquisition card. Development, evaluation, and testing of this system will be supervised by Dr. Napadow.

Technical Aim 2 (Computer Controlled Drug Infusion System): A computer-controlled drug infusion system will be assembled based on the STANPUMP infusion program (Shafer et al., 1988). A Dell Inspiron 3500 will be used to run STANPUMP and will be interfaced with a Harvard 22 infusion pump, and will be tested with several pharmacokinetic parameter sets to confirm that the proper amount of drug is administered. A few afternoons of full-time effort will be assigned to this task and will be supervised by Dr. Walsh.
**Research Aim:** The neuroanesthesia literature will be studied in detail to review the effects of Propofol on cerebro-vascular coupling. Several afternoons of full-time effort will be assigned to this task and will be reviewed by Dr. Walsh.

The preceptorship activities outlined above will take place between mid-April and mid-May 2005.

3. **Outline for Final Paper**

The final 10-15 page paper to fulfill the preceptorship requirements will integrate the experiences of the above clinical, technical, and research aims and will include the following components:

- Introduction: What is general anesthesia?
- Monitoring depth of anesthesia
- A neurophysiological model for loss of consciousness under general anesthesia
- Review of animal studies on the neural mechanisms of anesthesia
- Review of functional imaging studies of loss of consciousness under general anesthesia
- Discussion of flow-metabolism coupling under propofol
- Development of an experimental paradigm for studying loss of consciousness under general anesthesia using concurrent EEG and fMRI.

This report will provide the scientific background for a comprehensive series of studies focused on developing neurophysiological correlates and mechanisms for anesthesia. These neurophysiological correlates could provide the basis for development of site-specific anesthetic drugs with fewer side-effects, as well as functionally-specific approaches to EEG-based anesthetic monitoring.

References:


