Application for Round 3 QIBA Project Funding

Title of Proposal: fMRI Digital Reference Objects for Profile Development and Verification		
QIBA Committee/Subgroup: fMRI Technical Committee		
NIBIB Task Number(s) which this project addresses: Objectives 1,2,3,4,5 (from SOW)		
Project Coordinator or Lead Investigator Information: E. DeYoe		
Last Name: DeYoe	First Name: Edgar	Degree(s): PhD
e-mail:	Tel #:	
Institution/Company: Medical College of Wisconsin		
Amount Requested:		

Project Description

Previous work by this committee has identified many possible sources of variance in fMRI and has established metrics of reproducibility for one representative image analysis protocol. However, methods used for clinical fMRI typically vary from site to site and it is not known: (1) which methodological factors significantly affect reproducibility, sensitivity and bias, (2) which methods in current use are best suited for obtaining consistent quantitative results, or (3) how our methodological considerations impact clinical performance of fMRI as a biomarker. The current proposal covers the first year of a 2-year project to address these issues. The centerpiece of the project will be to create standard datasets or "digital reference objects" (DROs) with realistic known signal qualities and noise features. Aim 1 will combine existing human fMRI data sets plus simulation software to create a range of DROs that will allow us to manipulate sources of variance and systematically assess the technical performance of different fMRI data analysis methods. These DROs will be used in Aim 2 to compare the performance of different fMRI data processing methods in current use at different experienced clinical sites. As optimal existing methods are identified, we will begin the process of isolating and characterizing specific individual sources of variance by comparing reproducibility, sensitivity, bias, and linearity for Aim 1 DROs that vary systematically in signal and noise properties.

This project will be coordinated across two sites: Medical College of Wisconsin and Duke University. Aim 1 will be headed by MCW and Aim 2 by Duke though both sites will work collaboratively on both aims. Overall, the first year of this project will generate valuable reference data resources for distribution to clinics, industry, and other fMRI users, and it will fill critical knowledge gaps concerning fMRI methodology and sources of variance that, ultimately, will be incorporated into an optimized fMRI profile and protocol. The second year of this project (not detailed in the current proposal) will continue this effort and may also address the impact of the optimized methods on clinical performance.

Primary goals and objectives

Aim 1. Tools for Profile Assessment - Generation of fMRI Reference Data Sets and QA metrics
To provide a basis for comparing fMRI methods, we will create a set of standardized fMRI reference datasets (DROs) with known "ground truth" related to the time-course, amplitude and spatial distribution of BOLD-like signals embedded in "noise". DROs will incorporate realistic brain activity signals as well as several types

of noise and common fMRI signal artifacts. In round-1, signal and noise properties will be sampled from existing fMRI data sets in order to accurately represent real data, then in round-2, a set of DROs will also be synthesized in order to provide a more systematic manipulation of signal-to-noise, spatial topography (within the brain) and noise/artifact features. This will permit precise specification of the "ground truth" that different analytic methods in Aim 2 must try to recover. For each combination of signal and noise properties, 2 DROs differing only in random noise patterns will be developed to assess repeatability.

In conjunction with the development of the DRO's we will also select, implement and test several raw data, quality assurance metrics with the goal of using them to characterize the properties of the DRO's and to provide minimum data quality recommendations needed to achieve profile claims. Such metrics will include signal-to-noise ratio (SNR), degree of contamination by head motion, heart and respiration signals, and measures of spatial inhomogeneity (e.g. ghosting, artifactual contrast variations, etc.). These will complement an existing set of processed-data, reproducibility metrics developed previously and to be further expanded with the addition of sensitivity, bias, and linearity metrics.

Aim 2. Profile/Protocol Optimization - Influence of Methodological Factors

Previous work developing the current fMRI profile has revealed a variety of image analysis methods in common use, many of which have been identified as potential sources of variance in fMRI maps. Aim 2 will use the standard human reference data sets and DROs from Aim 1 to assess to what degree different sources of variance in fMRI signals and analysis methods affect reproducibility and other response metrics related to the Profile claims. To compare methods, 5 independent clinical sites with imaging expertise will download the round-1 DRO's and reference data and use their own automated methods to analyze each data set. The Duke and MCW sites will use the analysis pipeline tested in our previous fMRI reproducibility project. All results will be uploaded to Duke where QA metrics and response metrics will be calculated for all data sets and compared across the methodologies used by the different clinical sites. The goal of Phase 1 is to identify existing methodological sequences that yield the best precision and reproducibility, and which can be combined into an optimized analysis protocol and fMRI profile. In phase 2 we will use the complete set of Aim 1 DRO's to systematically assess the impact of specific methodological sources of variance on reproducibility and bias. Phase 2 will begin in year 1 (in parallel with the multi-site field testing) and continue into year 2 of this project.