HST.583 Functional Magnetic Resonance Imaging: Data Acquisition and Analysis
Fall 2008

Midterm Exam
HST.583
November 5, 2008

Instructions:
There are 7 problems, points for each problem are indicated. Please immediately confirm you have all 5 pages! This is a closed book/ closed notes exam. You have one hour.

Read the whole exam first. **Write legibly**. Describe what you are thinking. Even if the final answer is wrong, you will be given credit for your reasoning and approach to the problem. Be efficient, assess what you can answer right away; divide your time so that you can cover all the problems, allocating less time to the easiest parts. Don't spend too much time on a single question. **Try not to leave questions blank; we cannot give partial credit without something written down.**

Problem 1 (25 points):
Spatial attention has been hypothesized to be an emergent function of a "Tri-nodal Cortical Network".

a) Name each of the three cortical regions that comprise the "Tri-nodal Cortical Network" for spatial attention (5 points)

Frontal eye fields, posterior parietal cortex and cingulate gyrus

b) Design your own or describe a published experimental paradigm to probe the attention network. Your answer must include a clearly stated hypothesis (5 points), a briefly, but accurately described paradigm (5 points), and predicted or reported outcome (5 points).

Several described in textbook and in Brad Dickerson's lecture notes; levels of arousal, visual or spatial directed attention, domain or modality specific attentional modulation

c) Choose an appropriate acquisition sequence for collecting this scan noting type of sequence, and relevant parameters (5 points)

For example:
Gradient echo EPI at 3T, TR = 2000 ms, TE = 30 ms, 20 slices, 5 mm thickness, 1 mm gap, FOV = 220 mm, matrix size = 64x64, BW = 2520 Hz/pixel, etc.

Problem 2 (15 Points):
Standard functional imaging at the Martinos Center uses an echo planar (EPI) imaging paradigm (30 slices, 4 mm slice thickness, TE = 30 ms, TR = 2000 ms, matrix size = 64x64).

a) What is the phenomenon that causes EPI distortions called? (5 points)

Magnetic susceptibility, which leads to B_o-field inhomogeniety

b) What regions of the brain are most susceptible to these distortions. Explain. (5 points)

orbitofrontal, medial-temporal- areas that are at air tissue interfaces.

c) What relaxation parameter allows the generation of contrast through the BOLD effect? (5 points)

T2; the paramagnetic nature of deoxyhemoglobin will slightly alter the local magnetic field, leading to spin dephasing. This is a concentration-dependent phenomenon; as the amount of dHb changes, so will the local T2*. **T2 is also acceptable**; SE-BOLD also produces functional contrast that is more sensitive to changes around smaller vessels (why?).*

Problem 3 (20 points):
After a short fMRI scan during which your subject performed a carbon dioxide inhalation task (block design paradigm in which she alternates between breathing room air and breathing room air enriched with 10% carbon dioxide), she takes a coffee break. The caffeine in her coffee is a known vasoconstrictor (i.e. decreases the radius of arterioles).

a) Will caffeine cause a global increase or decrease in baseline cerebral blood flow (CBF)? Explain. (5 points)

CBF is proportional to r^4, so a vasoconstriction will decrease blood flow.
The major way blood flow is regulated in the brain is by vasoconstriction/ dilation of arterioles perfusing tissue and capillary beds. A change in arteriolar diameter results in a change in vascular resistance, leading to a change in flow. Vasodilation decreases vascular resistance, resulting in an increase in blood flow. Vasoconstriction increases vascular resistance, resulting in a decrease in blood flow.

b) Carbon dioxide inhalation is thought to (increase/ decrease/ not affect) oxygen metabolism ($CMRO_2$). Explain. (5 points)

Carbon dioxide inhalation should not alter $CMRO_2$. Carbon dioxide is a potent vasodilator and will cause arteriolar smooth muscle to relax, thereby increasing CBF; however, it should not alter neuronal activity in an appreciable way. $CMRO_2$ is thus not expected to change. This is a key assumption made in Hoge and Davis' seminal work, and is one that is still made in state-of the-art studies. The hemoneural hypothesis, if correct, may challenge this idea.

Happily caffeinated, she returns to the magnet and you resume scanning using the exact same carbon dioxide inhalation task. Assume that the absolute change in CBF during carbon dioxide inhalation is the same as in the original scan (i.e. before coffee).

c) Do you expect the BOLD percentage change during carbon dioxide inhalation to (increase/ decrease/ stay the same), compared to the original scan (i.e. before coffee)? (10 points)

To help you answer this problem, consider the BOLD/flow relationship derived by Hoge and Davis; feel free to plot this curve if it helps you answer the problem.

*Since CO_2 is a potent vasodilator ΔCBF should be **positive** during CO_2 inhalation blocks. We are also told that ΔCBF will stay the same before and after caffeine ingestion. Since CBF_o decreases due to caffeine, and ΔCBF is positive and stays the same, the percentage change ($\Delta CBF/ CBF_o$) **increases**.*

*The flow-BOLD relationship is drawn below. A increase in ($\Delta CBF/ CBF_o$) moves us to the right and up on the curve. Therefore, the percentage BOLD response ($\Delta BOLD/BOLD_o$) also **increases**.*
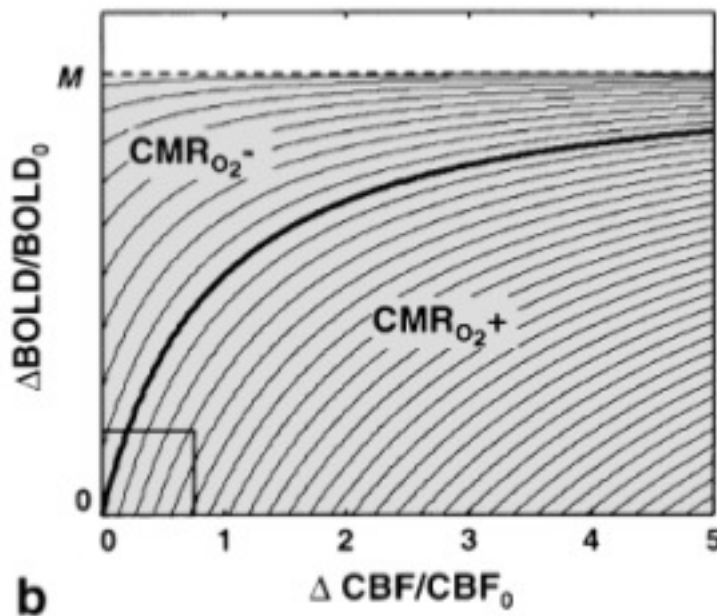

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Problem 4 (10 points):
The post stimulus undershoot (PSU) is a consistent feature of the BOLD hemodynamic response.   Provide a possible explanation for the PSU that considers dynamic changes in physiology during activation. Feel free to use hand drawn diagrams and/or graphs.

One possible explanation: after neural activity ceases, blood flow returns to baseline faster than the venous vasculature can shrink back to its original size (venous vessels are compliant and increase in volume in response to increased pressure and flow). Since flow returns to baseline more quickly than blood volume, there ends up being a greater amount of deoxyhemoglobin present transiently. Once volume returns to baseline, the BOLD signal does as well (as seen below).
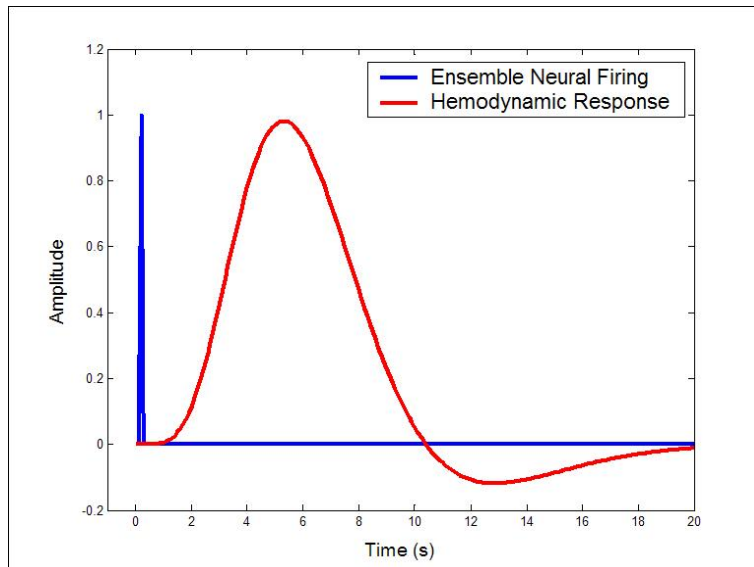
Problem 5 (5 points)**:**
What are two different types of experimental manipulation used in fMRI tasks for relating specific mental processes to specific brain regions? For each, give an example from something presented in class or a published study.

Answer:
I was initially looking for:
1) Hold the stimulus constant and vary the task:
For the self reference task, the stimulus (trait adjectives) is held constant and the task varies between self reference and semantic questions.

2) Hold the task constant and vary the stimulus
For the SIRP task, the task (maintain information in WM) is constant and the stimulus varies (parametric modulation of working memory LOAD)

I also accepted (because the wording of the question is sufficiently vague that nearly all of you interpreted it this way!):
1) Block design

2) Event related

Problem 6 (15 points)**:**
It is well known that fMRI data is very noisy. Considerable effort is being made on multiple fronts to improve activation detection sensitivity (improve signal to noise). For each of the domains listed describe one way to improve sensitivity to fMRI signal changes and explain why it would work.

a) Image acquisition

b) experimental design

c) image analysis (post-processing)

Answer:
a) *Higher field strengths, Multi-channel imaging coils, Restrict head motion, Monitor respiratory and cardiac signal to use as regressors, Gate to cardiac signal, Choose better TE to optimize BOLD contrast, averaging, larger voxel size*

b) *More trials, Longer blocks, Design experiments s.t. design vectors are orthogonal to drift vectors, Create tasks that better isolates cognitive area of interest, fast event related with more trials*

c) *Smooth data (optimize smoothing kernel), Temporally filter data to remove autocorrelation, Use FIR analysis if HRF is not well known, Use model-free analysis if there is no prior info about expected signals, ROI based analysis*

Problem 7 (10 points)**:**
Diffusion Weighted Imaging is used to investigate white matter integrity and pathology associated with normal aging and neurological disorders such as multiple sclerosis that are known to disrupt axonal function and/or myelination.

a) What would you expect to observe about FA values in areas of disruption along a white matter tract, such as the cortico-spinal tract? Explain. (5 points)

(thanks to Borjan Gagoski for part of the answer text)
Goes down relative to the FA value of a healthy subject at that same point along the tract.
Fractional anisotropy (FA) is a metric of the variance of the eigenvalues fo the tensor D. White matter tracts have high FA values since they are directional, i.e. the diffusion along a specific direction is evident. Multiple Sclerosis (MS) patients that have a disruption along a WM tract will therefore have <u>low</u> FA values at that point.

a) What would you expect to observe about FA values in areas of disruption along a white matter tract at the site of crossing with an unaffected tract? Explain. (5 points)

Goes up relative to the FA value of a healthy subject at that same point of crossing between the two tracts.

The FA value would be roughly the same as the FA value of the unaffected tract since the contribution of the disrupted path to the FA measure is minimal.

Reference for your information:
Ciccarelli O, Werring DJ, Wheeler-Kingshott CA, Barker GJ, Parker GJ, Thompson AJ, Miller DH. Investigation of MS normal-appearing brain using diffusion tensor MRI with clinical correlations. Neurology. 2001 Apr 10;56(7):926-33.