Statistical Re-Analysis of the Cholinergic Challenge Experiment:

Comparison of CBF Measurements by SPECT and MRI-Based Arterial Spin Labeling (ASL)

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Rationale

- Hypothesis: damage to cholinergic receptors from repetitive exposure to cholinesterase-inhibiting chemicals may explain chronic symptoms of ill Gulf War veterans
- Expect ill and healthy GW veterans to respond differently to a short-acting cholinergic stimulus
  - assessed by 1998 SPECT study of physostigmine infusion
- Do current studies validate the original?
  - 2008 SPECT replication,2008 ASL assessment of same protocol

Methods

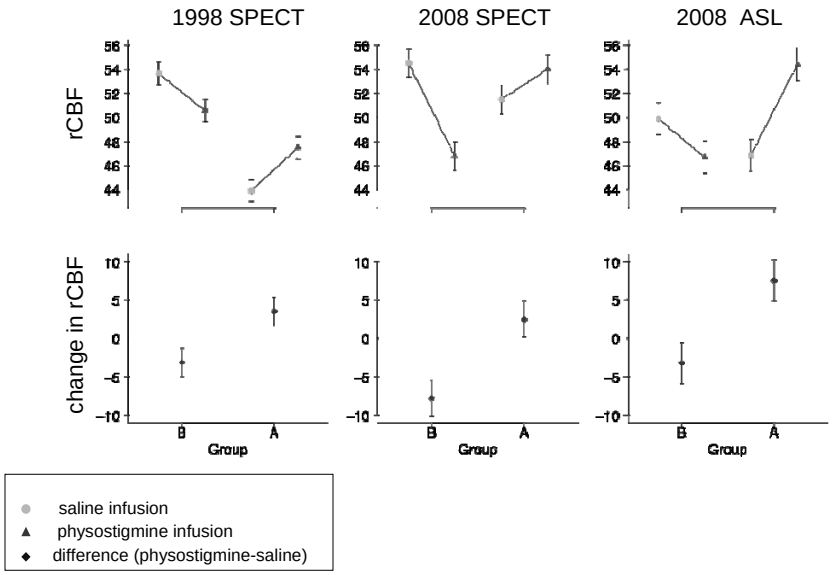
- 1998 SPECT
  - Session 1: scan follows1-hr saline infusion
  - Session 2: scan follows1-hr physostigmine infusion 48 hrs later
- 2008 SPECT and ASL
  - two sessions as above, 48 hrs apart
  - 30-min infusion protocol changed to accommodate simultaneous ASL scan, validated by a pilot infusion study measuring rCBF by ASL in the hippocampus

Summary of Findings

Brain Regions reacting most abnormally	Sess 2 - Sess 1 mean response of CBF to physostigmine
L & R amygdala corticomedial and basolateral groups R hippocampus anterior and posterior L basal ganglia inferior caudate head pallidum and part of putamen	B → decreased* A → increased*

*Normal response

Compare the Findings by 2 Methods



Conclusions

- 2008 SPECT study replicates 1998 SPECT study
  - Finds same phase-reversal response to physostigmine
  - Same deep brain regions found to respond abnormally
- ASL measures the same abnormal regional physostigmine effects as SPECT

  (with better statistical power locally)
  - Effect negative in group B and positive in group A
  - Same deep brain regions
- MRI-Based ASL method can replace SPECT
  - Cholinergic challenge can be done in 1.5 hrs on 1 day rather than 8 hours over 2 days.