Presentation 11- Robert Haley

Plan for Gulf War Illness and Chemical Exposure Research Program

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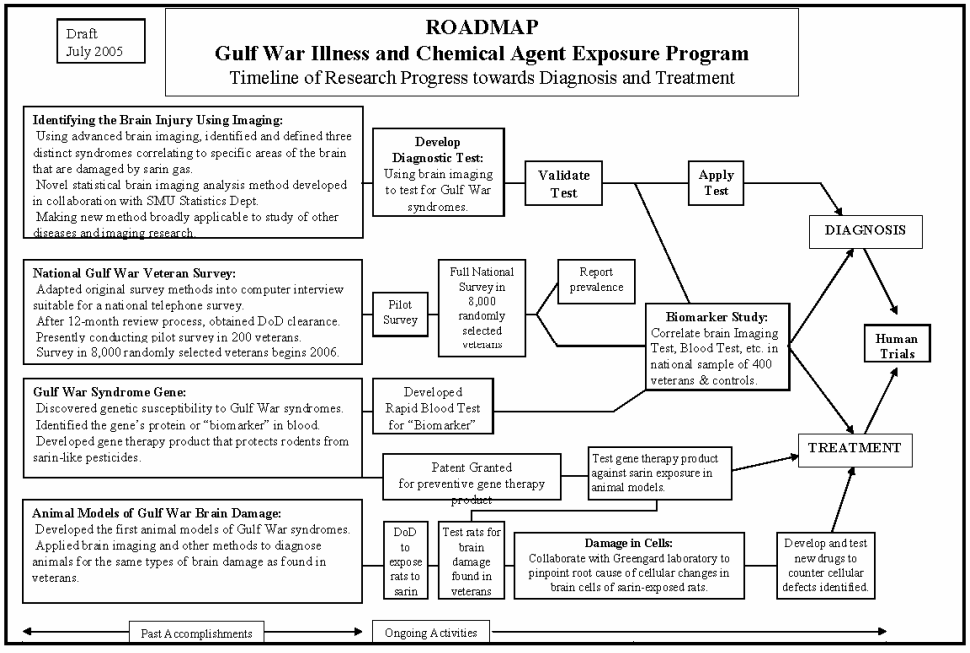
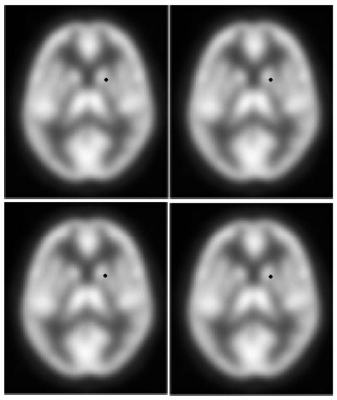
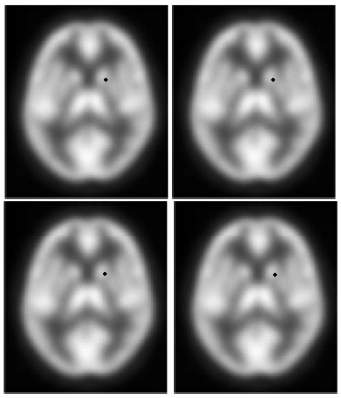


Analysis of Group Differences in Brain Imaging Experiments

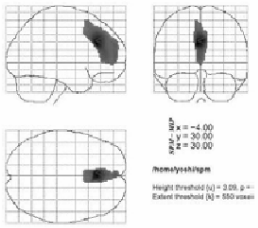
Group 1



Group 2



Statistical Parametric Mapping (SPM)



Detects group differences of 15% or more.

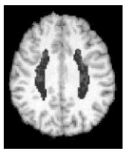
The Statistical Development Team

Wayne Woodward Bill Schucany Dick Gunst Robert Haley

Pat Carmack Jeff Spence

SPM Approach	New Approach
• Spatial normalization	• Spatial normalization
• Count normalization to the whole brain average $CBF_v/CBF_{wb} = nrCBF_v$	• Count normalization to a white matter volume $CBF_v/CBF_{wm} = nrCBF_v$
• Brett transformation of Talairach coordinates to MNI space (brain surface)	• Carmack transformation of Talairach coordinates to MNI space (ventricular surface)
• Smoothing with an 8-14 mm gaussian kernal over all 200,000 voxels	• Geostatistical spatial modeling to extract larger uncorrelated blocks for analysis
• Group comparisons with canned GLM programs	• Group comparisons with SAS modeling

Count Normalization to a White Matter Standard Region vs the Global IC Average



Centrum semiovale

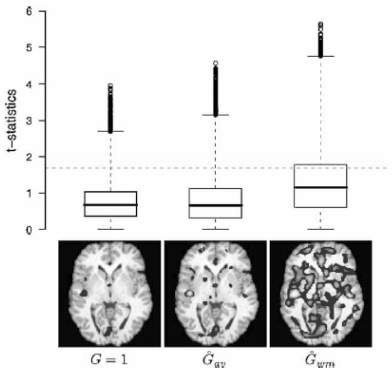


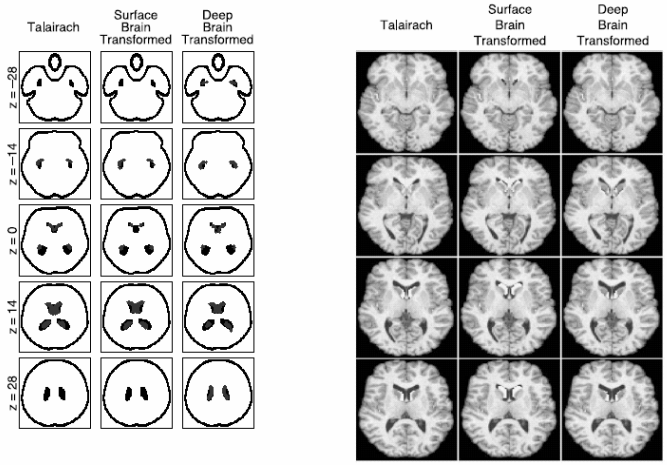
Table 2
Results of SPM analysis (cluster-level P values) using three measures of global signal

Location	$G = 1$		$\hat{G}_{av}$		$\hat{G}_{wm}$	
	Cluster size	$P_{corrected}$	Cluster size	$P_{corrected}$	Cluster size	$P_{corrected}$
Lt. Mid. Frontal	–	–	–	–	82	0.029
Lt. Insula	–	–	5	0.835	86	0.025
Lt. Sup. Frontal	–	–	–	–	94	0.018
Rt. Sup. Frontal	–	–	2	0.931	85	0.026
Lt. Med. Fronta	–	–	–	–	88	0.023

In each case, the t statistic threshold is 4.22 on 34 degrees of freedom.

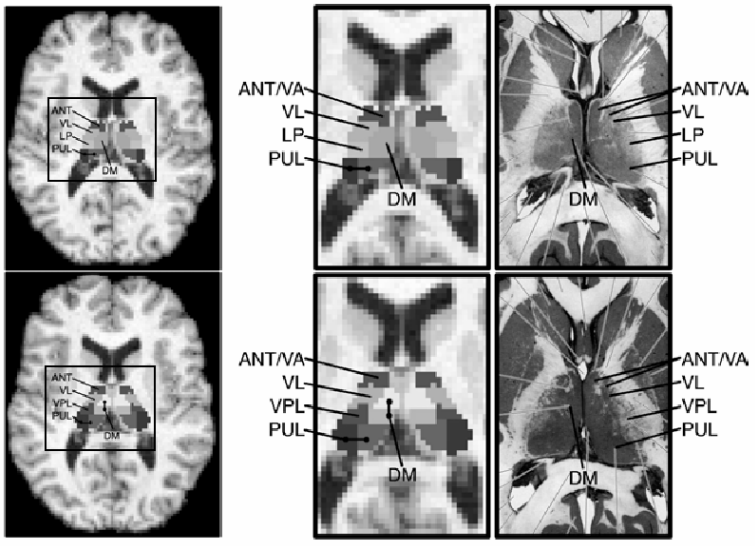
Spence et al. ***NeuroImage*** 2006 (in press)

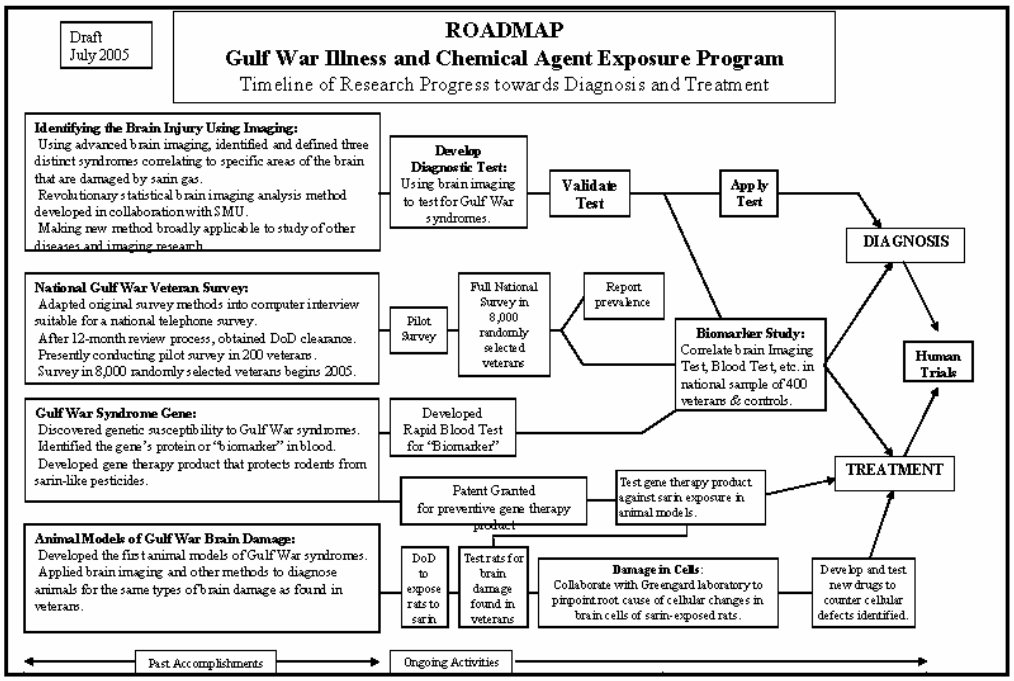
Improved Algorithm for Locating Deep Brain Structures: The Carmack Transformation

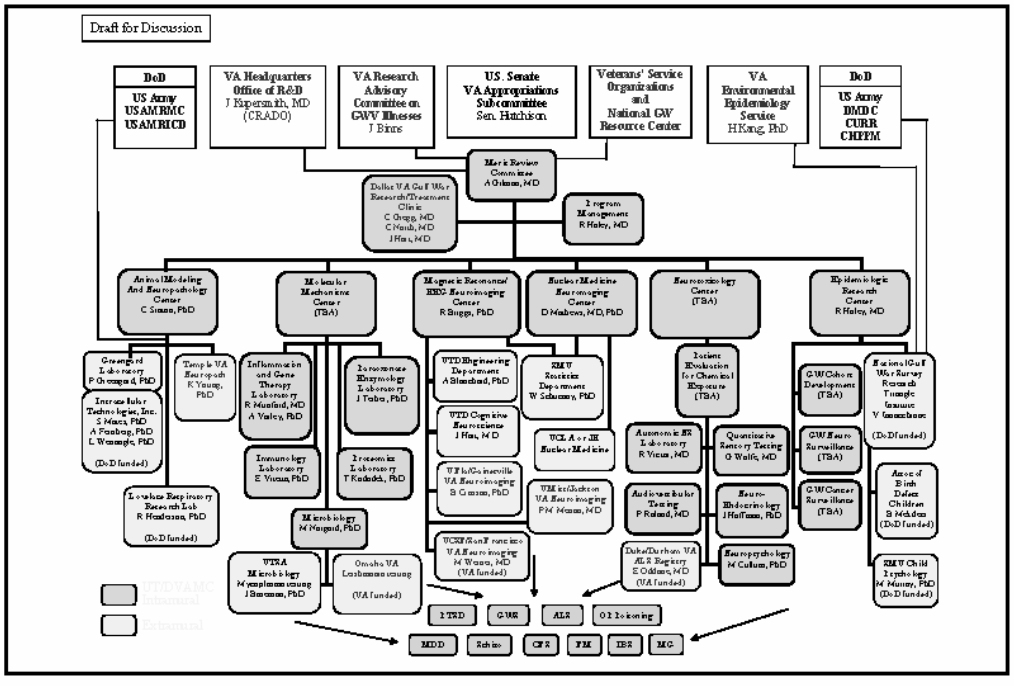


Carmack et al. ***NeuroImage*** 2004; 20:367-371

Anatomic Accuracy Achieved by Spatial Modeling of High Resolution SPECT using the Carmack Transformation: Thalamic Nuclei




Draft
July 2005
ROADMAP
Gulf War Illness and Chemical Agent Exposure Program
Timeline of Research Progress towards Diagnosis and Treatment
Identifying the Brain Injury Using Imaging:
Using advanced brain imaging, identified and defined three distinct syndromes correlating to specific areas of the brain that are damaged by sarin gas.
Revolutionary statistical brain imaging analysis method developed in collaboration with SMU.
Making new method broadly applicable to study of other diseases and imaging research.
Develop Diagnostic Test:
Using brain imaging to test for Gulf War syndromes.
Validate Test
Apply Test
DIAGNOSIS
National Gulf War Veteran Survey:
Adapted original survey methods into computer interview suitable for a national telephone survey.
After 12-month review process, obtained DoD clearance.
Presently conducting pilot survey in 200 veterans.
Survey in 8,000 randomly selected veterans begins 2005.
Pilot Survey
Full National Survey in 8,000 randomly selected veterans
Report prevalence
Biomarker Study:
Correlate brain Imaging Test, Blood Test, etc. in national sample of 400 veterans & controls.
Human Trials
Gulf War Syndrome Gene:
Discovered genetic susceptibility to Gulf War syndromes.
Identified the gene's protein or "biomarker" in blood.
Developed gene therapy product that protects rodents from sarin-like pesticides.
Developed Rapid Blood Test for "Biomarker"
Patent Granted for preventive gene therapy product
Test gene therapy product against sarin exposure in animal models.
TREATMENT
Animal Models of Gulf War Brain Damage:
Developed the first animal models of Gulf War syndromes.
Applied brain imaging and other methods to diagnose animals for the same types of brain damage as found in veterans.
DoD to expose rats to sarin
Test rats for brain damage found in veterans
Damage in Cells:
Collaborate with Greengard laboratory to pinpoint root cause of cellular changes in brain cells of sarin-exposed rats.
Develop and test new drugs to counter cellular defects identified.
Past Accomplishments
Ongoing Activities


Draft for Discussion
DoD
US Army
USAMRMC
USAMRICD
VA Headquarters
Office of R&D
J Kupersmith, MD
(CRADO)
VA Research Advisory Committee on GWVI Illnesses
J Binns
U.S. Senate
VA Appropriations Subcommittee
Sen. Hutchison
Veterans' Service Organizations and National GW Resource Center
VA
Environmental Epidemiology Service
H Kang, PhD
DoD
US Army
DMDC
CURR
CHPPM
Merit Review Committee
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J Han, MD
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Molecular Mechanisms Center
(TBA)
Magnetic Resonance/ EEG Neuroimaging Center
R Briggs, PhD
Nuclear Medicine Neuroimaging Center
D Mathews, MD, PhD
Neurocognition Center
(TBA)
Epidemiologic Research Center
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Greengard Laboratory
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Temple VA Neuropath
K Young, PhD
Immune Modulator Technologies, Inc.
J Mears, PhD
A Fraser, PhD
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(DoD funded)
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A Yaksh, PhD
Immunology Laboratory
E Vivas, PhD
Neuroscience Electrophysiology Laboratory
J Tobin, PhD
Proteomics Laboratory
T Kodadek, PhD
VTD Engineering Department
A Blanchard, PhD
VTD Cognitive Neuroscience
J Han, MD
VA Nuclear Medicine
VA Neuroimaging
S Gibson, PhD
VCU/Johnson VA Neuroimaging
W Scharmen, PhD
VCU Radiation VA Neuroimaging
P Mansi, MD
VCSF/San Francisco VA Neuroimaging
M Weiner, MD
(VA funded)
Autonomic RX Laboratory
R Vivas, MD
Auditory Motor Testing
P Roland, MD
Duke/Durham VA ALS Registry
E Oddone, MD
(VA funded)
Quantitative Sensory Testing
G Wolfe, MD
Neuro-Endocrinology
J Huffman, MD
Neuropsychology
M Cullum, PhD
GW Cohort Development
(TBA)
GW Neuro Surveillance
(TBA)
GW Cancer Surveillance
(TBA)
Autism/Gulf War Survey Research Triangle Institute
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(DoD funded)
Autism of Birth Defect Children
S Mehdian
(DoD funded)
KMW Child Psychology
M Mumby, PhD
(DoD funded)
Lovelace Respiratory Research Lab
R Henderson, PhD
(DoD funded)
Microbiology
M Maigard, PhD
VTRA Microbiology
Mycoplasma assay
J Baseman, PhD
Omaha VA Leishmaniasis assay
(VA funded)
UTD/VA MC
Intramural
Extramural
I TBD
GWI
ALS
O1 Screening
MDD
Schizo
CFS
FM
IBS
MC