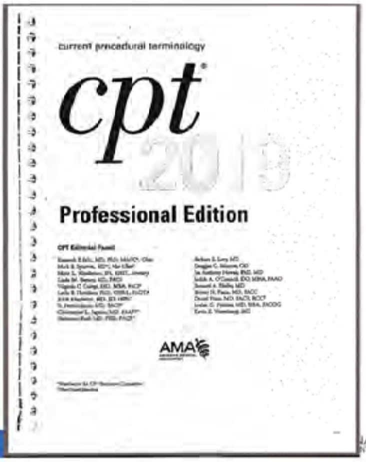

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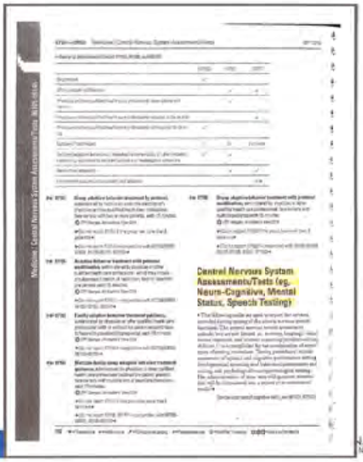
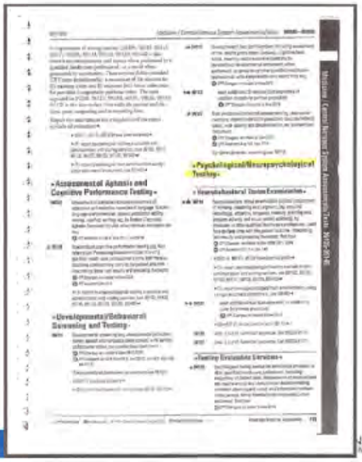


Central Nervous System Assessments/Tests (eg, Neuro-Cognitive, Mental Status, Speech Testing)



Assessment of Aphasia and Cognitive Performance Testing

Developmental/Behavioral Screening and Testing

Psychological/Neuropsychological Testing

Neurobehavioral Status Examination

Testing Evaluation Services

Preexisting Issues

Learning Disabilities

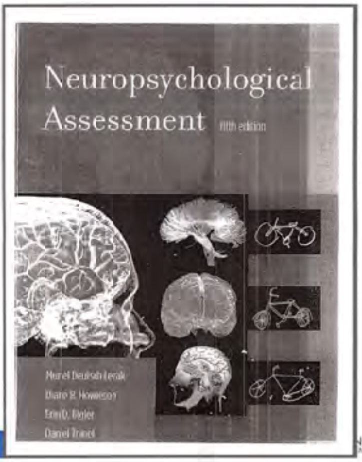
Previous TBI

Mental Illnesses

Substance Abuse

Evaluating patients with brain injuries who have a prior history of conditions such as learning disabilities or ADHD

"Related concepts germane to this discussion are presented in a book by Lezak, Howieson, Bigler, & Tranel entitled *Neuropsychological Assessment*, Fifth Edition, 2012, Oxford University Press."



Neuropsychological Assessment

fifth edition

Muriel Deutsch Lezak
Diane B. Howieson
Erin D. Bigler
Daniel Tranel

"There is often quite extensive testing utilizing cognitive and achievement-related procedures that may serve as a baseline for comparison to present results as well as a standard comparison to demographically corrected norms.

In addition, there are assessment procedures that may be utilized such as the Frontal Systems Behavior Scale that allow comparisons made by self and others regarding the patient's behavior before and after a given event.

These can be administered along with validity and reliability procedures even to others involved in their care that knew them, which may provide another objective, valid, and reliable measurement of change."

- Dr. Bradley G. Sewick, Ph.D.

Examining patients who have had prior traumatic brain injuries

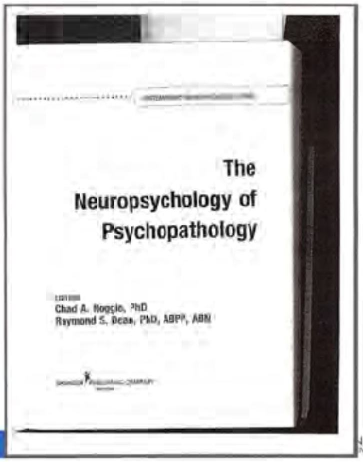
"Psychometric assessment...may again serve as a baseline for comparison purposes. When doing so, one must take into account expectations regarding degrees of recover and with recovery curves present in the literature for brain injuries of different severity. '...the presence of a prior brain injury is considered a risk factor rendering them more vulnerable to more complex and protracted recovery from future injury.'

Additional procedures can be utilized that compare a patient's functioning retrospectively prior to injury vs. during present status that may be completed by the patient and others familiar with them on a valid and reliable basis."

- Dr. Bradley G. Sewick, Ph.D.

Assessing patients with brain injuries who have a prior history of depression, schizophrenia, or other forms of psychopathology

The Neuropsychology of Psychopathology edited by Chad A. Noggle and Raymond S. Dean, published by Springer Publishing Company, New York, 2013.



The
Neuropsychology of
Psychopathology

Editors
Chad A. Noggle, PhD
Raymond S. Dean, PhD, ABPP, ABN

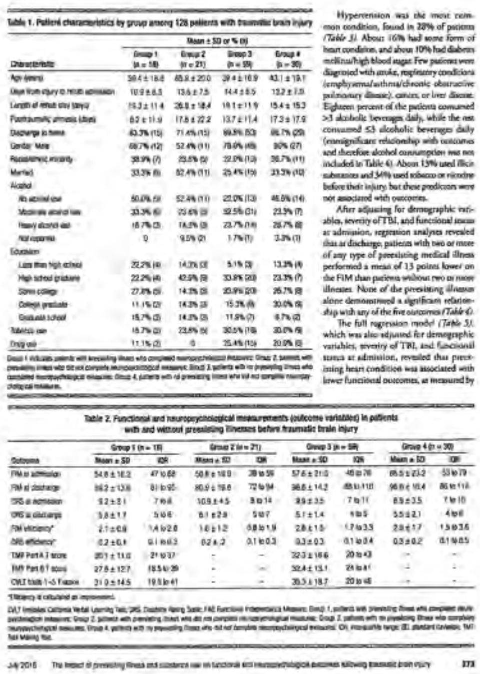
"Depending upon the severity and length of the condition, there may be impairments of a long-standing nature which should be considered. '...review prior psychiatric records...' Some conditions such as anxiety disorders and depression, if managed and mild, may have relatively little effect on neurocognitive functioning but if more severe and persisting and intractable, etc., may have a significant neurocognitive effect.

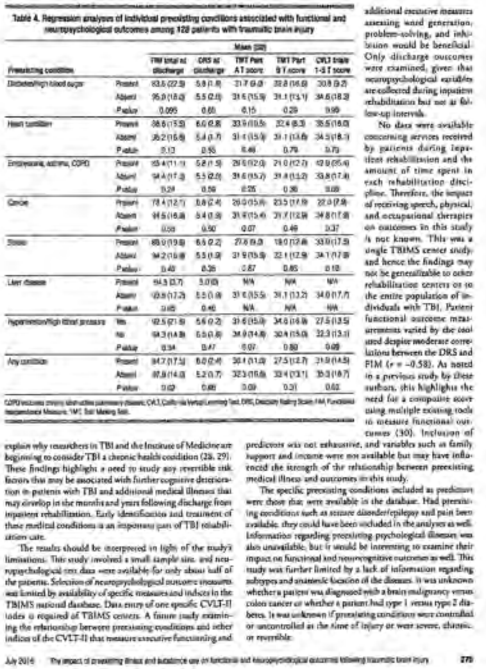
It is important, however, to understand the neuropsychological testing can identify focal brain damage associated specifically with brain injury and be very useful in disentangling effects that may be present from mental illness or psychopathology vs. brain trauma. '...comparisons to school records are likely useful as well.' '...retrospective pre-injury assessment methods may be useful for comparing to current status based upon objective, valid, and reliable ratings obtained from the patient and others.'"

- Dr. Bradley G. Sewick, Ph.D.

The impact of preexisting illness and substance use on functional and neuropsychological outcomes following traumatic brain injury

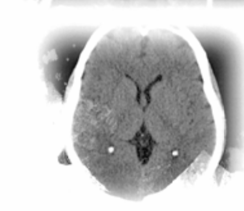
Marie N. Dahdah, PhD, Sunni A. Barnes, PhD, Amy Buros, MS, Andrew Allmon, BS, Rosemary Dubiel, DO, Cynthia Dunklin, BS, CCRC, Librada Callender, BS, CCRC, and Shahid Shafi MD, MPH





Other Forms of Proof

- MRIs
- CT
- DTI
- SPECT
- MEG
- PET
- fMRI
- CTA
- MRA
- EEG
- MRS



MRI	Magnetic resonance imaging	Bleeding, contusion, brain herniation. Special sequences like SWI susceptibility-weighted images can show small petechial hemorrhages, special sequences can help distinguish some cases of diffuse axonal injury
fMRI	Functional Magnetic resonance imaging	Measures blood flow to areas in the brain, not a static test. A task is given to the patient before testing and certain areas of the brain are evaluated (vision, analysis, memory…) fMRI mapping can help identify injuries and recovery.
CT	Computed tomography	To visualize fractures, bleeding.
CTA	Computed tomography angiography	To examine vasculature of the head and neck (narrowing, occlusion, aneurysm, dissection…)
MRA	Magnetic resonance angiography	To examine vasculature of the head and neck (narrowing, occlusion, aneurysm, dissection…)
DTI	Diffusion Tensor Imaging	Helps identify microstructural integrity of brain white matter
SPECT	Single-photon emission computed tomography	Relative blood flow rate within brain regions at rest and activity, visualization is qualitative, and interpretation varies between readers. More experimental than practical in clinical use.
PET	Positron-emission tomography	Can show hypometabolism in injured brain areas, can suggest physiologic dysfunction beyond the boundaries of anatomic lesions, like in the case of contusions.
MRS	Magnetic Resonance Spectroscopy	Still investigational test. Can show brain recovery based on change in brain biological markers areas of decrease of N-acetyl aspartate and increase of choline
MEG	Magnetoencephalography "Like an MRI EEG"	Still investigational test.
		Measures magnetic fields of nerve cells thus the electrical flow across nerve synapses, can help identify mild brain injury. Also used in autism and speech disorders research

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Prospective Evaluation of Technetium-99m-HMPAO SPECT in Mild and Moderate Traumatic Brain Injury

Axel Jacobs, Eric Put, Michel Ingels and Axel Bossuyt

Department of Nuclear Medicine, Virga Jesse Hospital, Hasselt, Belgium and Department of Nuclear Medicine, Free University of Brussels (V.U.B.), Jette, Belgium

We prospectively evaluated the contribution of ^{99m}Tc-HMPAO SPECT in patients who have sustained acute, mild or moderate head trauma. **Methods:** Forty-two patients formed the first subgroup of moderate trauma (ModTr) and 25 patients formed the second subgroup of mild trauma (MilTr). All 67 patients underwent an initial SPECT (Tinit) within 4 wk after a closed cranial trauma. After a mean interval of 3 mo from the time of Tinit, all patients were clinically re-evaluated; those with an abnormal Tinit underwent a repeat SPECT (Trpt) as well. All SPECT studies were visually graded by agreement of three observers adjudging a score ranging from 0 (no lesions) to 4. **Results:** For the group as a whole (ModTr + MilTr), the following results could be derived: (1) in 32/33 Tinit negative cases, clinical symptoms had resolved; (2) the positive predictive value of Tinit was only 20/34 (59%); (3) the sensitivity for the repeat SPECT was 19/20 (95%). **Conclusion:** Our results show that: (1) SPECT alterations correlate well with the severity of the trauma; (2) a negative initial SPECT study is a reliable predictor of a favorable clinical outcome; (3) in cases with a positive initial SPECT, a follow-up consisting of a combination of SPECT and clinical data is necessary; (4) in patients suffering from postconcussive symptoms, SPECT offers an instrument to objectivate sequelae.

Key Words: technetium-99m-HMPAO; traumatic brain injury; SPECT

J Nucl Med 1994; 35:942–947

Alterations in regional cerebral blood flow (rCBF) have been described after craniocerebral trauma (*1–6*). In a study of patients who were all in a state of diminished consciousness after having sustained a head trauma, Abdel-Dayem et al. (*1*) clearly proved that ^{99m}Tc-HMPAO SPECT is more sensitive than CT, enabling an earlier detection of a larger number of lesions. The authors also found that SPECT lesions were larger than the corresponding CT abnormalities, and that SPECT perfusion patterns could be helpful in predicting the prognosis of post-traumatic injuries.

Roper et al. (*7*) compared ^{99m}Tc-HMPAO SPECT and CT in 15 patients with an acute closed-head injury. This study suggested that SPECT is most useful in the detection of focal (rather than diffuse) blood flow alterations that are not seen on CT. It also suggested that two hemodynamically different traumatic contusions could be identified, those with a decreased CBF (detectable with SPECT) and those with a blood flow equal to that of the surrounding brain tissue.

Gray et al. (*8*) compared ^{99m}Tc-HMPAO SPECT to CT in a population of patients with a remote history of traumatic brain injury. Particularly in the subgroup of minor trauma, SPECT was more sensitive than CT, enabling the demonstration of regional brain dysfunction in the presence of morphological integrity.

The present study was set up to evaluate the incidence, the extent and the evolution of CBF changes after mild or moderate head injury and to determine whether SPECT can play a role in the objectivation of traumatic sequelae in patients presenting with postconcussive symptoms. We studied the relationship between SPECT results and the severity of craniocerebral trauma, and we evaluated the correlation between the evolution of CBF disturbances measured by serial SPECT and the clinical course.

MATERIALS AND METHODS

Patient Population and Study Design

The study population consisted of 67 patients, 41 male and 26 female, with a mean age of 35 yr (age range: 11–71 yr), all having sustained a closed-cranial trauma. In 95% of these cases, the trauma was caused by a car, motorcycle or bicycle accident. Subjects were excluded from the study if they had presented a previous cranial trauma, epilepsy or other neurological disorders, psychiatric disease, drug or alcohol abuse, a CT showing important cortical atrophy or focal lesions (such as arachnoid cysts) unrelated to the trauma, or an unreliable anamnesis concerning the trauma.

All 67 patients underwent an initial ^{99m}Tc-HMPAO brain SPECT study (Tinit) and a CT within 4 wk after the trauma (26 patients within 3 days; 24 patients between 4 and 7 days; 10 during the second wk; 7 patients between 2 and 4 wk after the trauma).

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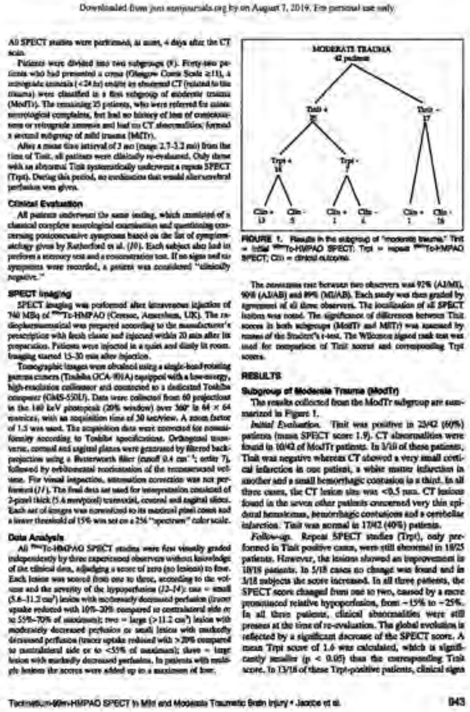

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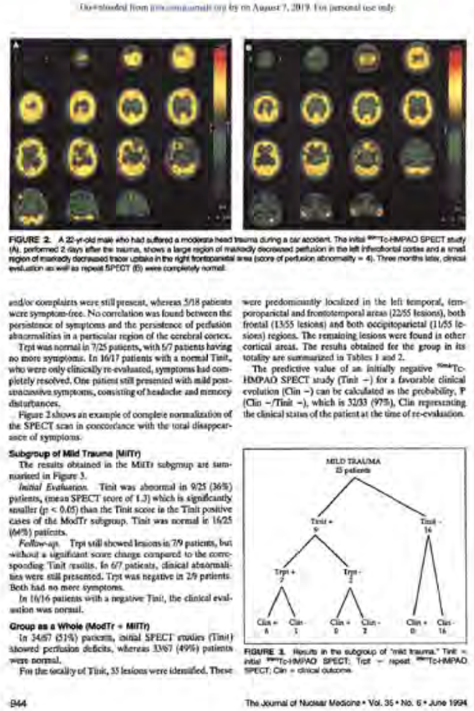

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CONCLUSION

REFERENCES

Objective Documentation of Traumatic Brain Injury Subsequent to Mild Head Trauma: Multimodal Brain Imaging With MEG, SPECT, and MRI

Jeffrey David Lewine, PhD; John T. Davis, PhD; Erin D. Bigler, PhD; Robert Thoma, PhD; Dean Hill, PhD; Michael Funke, MD, PhD; John Henry Sloan, MD; Sandra Hall, PhD; William W. Orrison, MD

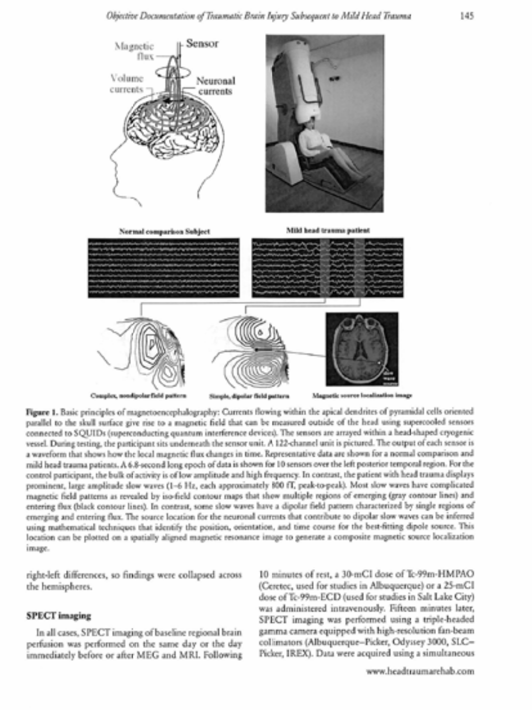
Evaluation of post–head trauma symptoms

METHODS

Participants

MEG examination

Magnetic resonance imaging



SPECT imaging

transmission and emission protocol. A total of 120 rotation steps were acquired using a 128 × 128 acquisition matrix. Images were reconstructed using a Butterworth or Weiner filter. Data were reformatted in axial, coronal, and sagittal planes, and evaluated for regions of hypoperfusion by a board-certified radiologist specializing in nuclear medicine. The radiology report and all images were available for review by the investigative team. Raters who were blind to other imaging and behavioral findings coded SPECT data sets as showing evidence of hypoperfusion in right/left frontal, temporal, parietal, occipital, or subcortical basal ganglia nuclei, or in a diffuse pattern consistent with generalized brain atrophy. Exploratory analyses showed no significant right-left differences, so findings were collapsed across the hemispheres.

Image integration

After MEG, MRI, and SPECT data were initially evaluated in an independent manner, image fusion was performed to explore the relations between modalities. Image fusion was accomplished by first sending DICOM images from the MR scanner to the MEG workstation. Using proprietary software (Neuromag Ltd), the fiducial points used during MEG to define the head-centered coordinate system were identified on the MR images. The software then aligned MEG and MRI coordinate systems so that MEG source locations could be plotted on the MR images to form magnetic source localization images. These images, with MEG source points now an inherent part of the data set, were then DICOM transferred to the SPECT workstation, which treated the magnetic source localization images as though they were simply MR images. A 9 df volume registration protocol with iterative processing was then used to align SPECT and MRI/MEG coordinate frames. The magnetic source localization images were reformatted in planes centered on the SPECT slices and image blending was performed.

RESULTS

Neuroimaging

Table 1 summarizes demographic, neuroimaging, and clinical observations for each patient. As previously mentioned, there were no significant laterality effects, so a region was coded as being abnormal if an abnormality was observed for either hemisphere. A descriptive summary of findings is provided below.

CT/MRI

Structural imaging performed at the time of accident revealed abnormalities in only 5 of the 30 patients (all with subdural hematomas). MR follow-up at the time of MEG and SPECT (performed, on average, 33.2 months after trauma) revealed chronic MR findings (mild atrophy) in only 2 of these 5 cases. There were also 2 cases with initially normal MR scans that showed mild cortical atrophy and some ventricular dilation at follow-up. Hence, there were 4 cases with evidence of atrophy on MRI at the time of MEG and SPECT imaging. No patient showed focal lesions or clear MR evidence of diffuse axonal injury. Ten patients had history of more than 1 traumatic event, including each of the 4 patients with chronic MR findings.

SPECT

Perfusion imaging using SPECT revealed abnormalities in 12 participants (40%), including each of the 4 with chronic MR findings and 8 others. SPECT was abnormal for 7 of 9 patients with histories of multiple mild traumatic events but only 5 of 21 patients with single traumas ($P < .05$ by the Fisher exact test, odds ratio [OR] = 11.2, 95% confidence interval [CI] = 1.7–100.1). In all cases with abnormal SPECT findings, focal perfusion deficits were seen in regions not explicitly identified as abnormal by MRI.

MEG

Six patients showed intermittent epileptic spikes, even though none had reported clinical seizures. MEG also revealed the presence of abnormal DSWA in 19 patients (63%). All 4 patients with structural findings and 9 of the 12 patients with SPECT findings showed MEG abnormalities. When focal MR or SPECT abnormalities were present, MEG always provided evidence of concordant electrophysiological dysfunction (except with respect to subcortical hypoperfusion). In most of these cases, MEG also revealed a more extensive picture of dysfunction than was shown by either MRI or SPECT.

There were 10 patients with normal MRI and normal SPECT who showed MEG abnormalities. Three patients with abnormal SPECT showed normal MEG and MRI examinations. As was seen for both MRI and SPECT, participants with a history of multiple traumas were more likely to show MEG abnormalities than patients with only a single traumatic event (9/9 vs 10/21, $P < .05$ by the Fisher exact test).

It should be noted that there were no significant differences in the slow wave sensitivity profiles across study sites or for the 122-channel recording system versus 306-channel recording system. Although the 122- and 306-channel sensor units differ significantly in the number of sensors, the actual area of coverage for the 2 units shows only a modest difference, with the increased number of sensors in the 306-channel unit being mostly a reflection of slightly increased packing density and addition of a magnetometer at each recording site. A set of exploratory data analyses failed to provide evidence that magnetometers were more sensitive to dipolar slow waves than planar gradiometers. The increased packing density for the 306-channel unit does give this unit a greater degree of spatial resolution than the 122-channel unit, but it does not appear to provide a significant increase in the efficiency of detection of dipolar slow wave events.

TABLE 1 *Data for individual participants*[*,†]

Age	Sex	No. of trauma	Initial MRI	Time	Current MRI	SPECT						MEG					Clinical profile					
						A	F	T	P	O	B	F	T	P	O	e	P	S	M	A	E	PS
36	M	1	Normal	30	Normal	Normal						Normal					P					
54	M	1	NA	45	Normal	Normal						Normal					P					
43	F	1	Normal	20	Normal	Normal						Normal					P					
34	M	1	NA	22	Normal	Normal						Normal										PS
31	M	1	Normal	34	Normal	Normal						Normal						S				
21	M	1	NA	40	Normal	Normal						Normal					P	S				
19	F	1	Normal	14	Normal	Normal						Normal							M			PS
57	M	1	NA	36	Normal	Normal						Normal							M	A	E	PS
61	F	1	NA	61	Normal						B	Normal						S				
31	F	1	Normal	86	Normal						B	Normal						S				
32	F	1	Normal	70	Normal		F				B	Normal					P	S			E	
26	M	2	Abnormal	20	Normal	Normal						F					P				E	
44	F	1	Normal	22	Normal	Normal							T		O							PS
45	F	1	Normal	31	Normal	Normal							T	P					M			
41	M	1	Abnormal	19	Normal	Normal							T			t			M		E	
37	M	1	Normal	21	Normal	Normal								P						A		
38	M	1	Normal	32	Normal	Normal						F				p				A	E	
40	F	1	Normal	23	Normal	Normal							T						M			
50	F	1	NA	40	Normal	Normal							T						M			PS
29	M	1	Normal	15	Normal	Normal							T	P						A		PS
27	F	2	Normal	32	Normal	Normal						F	T			t			M	A	E	PS
44	F	1	Normal	15	Normal			T			B		T					S				
53	M	2	NA	13	Normal				P					P						A	E	
67	M	2	NA	140	Normal		F					F	T	P		p					E	PS
23	F	1	Normal	21	Normal			T					T	P		t			M	A	E	PS
42	M	2	Abnormal	19	Normal			T		O	B		T	P	O		P		M	A	E	PS
21	F	2	Abnormal	14	Mild atrophy		F					F	T						M		E	
18	F	2	Abnormal	12	Mild atrophy	A	F					F	T	P		t	P				E	PS
36	M	3	Normal	22	Mild atrophy	A		T					T						M			PS
62	M	2	NA	30	Mild atrophy	A	F		P		B	F	T	P			P	S	M	A	E	PS

[*] MRI indicates magnetic resonance imaging; SPECT, single photon emission computed tomography; and MEG, magnetoencephalography.

[†] Demographic, clinical, and neuroimaging findings are provided. Reported information includes participant age (in years), total number of head trauma prior to imaging, whether MRI done at the time of trauma was normal, abnormal, or not available (NA) and the time (number of months) between the traumatic event and MRI/SPECT/MEG imaging. Current MRI findings are indicated as normal or showing atrophy (no patients showed focal encephalomalacia). SPECT findings are indicated as normal, or abnormal in the following ways: A indicates evidence of atrophy, ventricular dilation, and/or global depression of cortical perfusion; F, frontal hypoperfusion; T, temporal hypoperfusion; P, parietal hypoperfusion; O, occipital hypoperfusion; and B, basal ganglia subcortical hypoperfusion. MEG findings are indicated as normal or showing abnormal dipolar slow wave activity in the following regions: F indicates frontal; T, temporal; P, parietal; and O, occipital. When epileptiform activity was present, it is indicated in column "e" with the region indicated as follows: f indicates frontal; t, temporal; p, parietal; and o, occipital. Clinical findings are indicated in each of the following domains: P indicates psychiatric; S, somatic; M, memory problems; A, attention problems; E, problems in executive function; and PS, decreased processing speed.

Imaging summary

Overall, 73% of the patients showed abnormalities on 1 or more imaging tests, with only 4 subjects (13%) showing abnormalities on all 3 imaging tests. Figure 2 illustrates integrated MRI, SPECT, and MEG data from a patient with normal MRI but abnormal SPECT and MEG. Of the 3 imaging methods, MEG provided objective evidence of brain injury for the greatest number of patients (19/30). This "hit" rate was significantly superior to that for MRI (4/30, $P < .01$ by McNemar Test of Proportions), but only marginally better than that seen for SPECT (12/30, $P = .09$ by McNemar test of proportions). However, as discussed in more detail below, MEG and SPECT did not provide merely redundant information, especially when specific clinical profiles are taken into account.

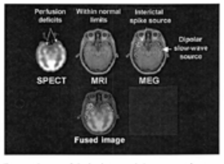


Figure 2. Integrated single photon emission computed tomography (SPECT), magnetic resonance imaging (MRI), and magnetoencephalography (MEG) in mild head trauma: Data are shown for a 23-year-old female participant who suffered a mild head trauma in a motor vehicle accident. She reported only a brief less than 1-minute loss of consciousness and her Glasgow Coma Scale was 15 at the time of hospital admission. MRI performed at the time of admission was interpreted to be within normal limits. Nevertheless, she reported a chronic postconcussive syndrome characterized by documented memory and attention problems and some general cognitive decline. Follow-up MRI, 21 months posttrauma, was within normal limits. SPECT revealed bitemporal hypoperfusion. MEG revealed right and left temporal focal slow waves and additional left parietal slowing. MEG also showed rare left temporal epileptiform spikes even though the participant had never been reported to show a clinical seizure. Subsequent to these studies, the patient was placed on valproic acid (Depakote). Follow-up neuropsychological testing conducted 6 months after initiation of Depakote revealed a significant improvement in memory function, although attentional skills and general processing speed did not improve.

Imaging in relationship to clinical profiles

Table 2 provides the odds ratio (OR) that brain imaging was abnormal, given the presence of persistent symptoms in psychiatric, somatic, and cognitive domains.

As can be seen, there were no significant general brain imaging correlates of persistent postconcussive psychiatric or somatic complaints, although there was a trend for SPECT to be abnormal in patients with somatic problems ($.05 < P < .10$, by the Fisher exact test). When considering the overall cognitive domain, only MEG findings were significant ($P < .001$). Given that cognitive problems were present, MEG was abnormal for 18 of 22 patients (86%), while only 1 of 9 patients without cognitive problems had an abnormal MEG.

One of the goals of this study was to examine the relations between specific clinical symptoms and specific regional patterns of brain imaging abnormality. Table 3 provides OR on these relations.

TABLE 2 *Odds ratios for finding imaging abnormalities given that postconcussive symptoms were present*[*,†]

	Psychiatric	Somatic	Cognitive
MRI	2.7	1.1	~‡
SPECT	2.3	5.7	1.5
MEG	0.3	0.1	**48.0**§

[*] Odds ratios are shown for finding imaging abnormalities in patients with post-concussive psychiatric, somatic, or cognitive symptoms. Significant relationships are in bold.

[†] MRI indicates magnetic resonance imaging; SPECT, single photon emission computed tomography; and MEG, magnetoencephalography.

[‡] The symbol (~) indicates infinite odds ratio because one of the cells in the calculation was 0.

[§] $P < .001$ by the Fisher exact test. All other observations are nonsignificant.

There were no significant imaging correlates of postconcussive psychiatric symptoms. As stated previously, when considering the presence of any abnormality on MRI, SPECT, or MEG, there was also a lack of significant imaging correlates of postconcussive somatic symptoms. However, when imaging profiles are analyzed with respect to a more detailed regional perspective, it becomes clear that there is an imaging correlate of postconcussive headaches. Specifically, there is a significant ($P < .001$) relation with basal ganglia hypoperfusion on SPECT. Seven of the patients in this study reported persistent severe headaches subsequent to mild HT, with 5 of these showing hypoperfusion of the basal ganglia. Of the 6 patients with basal ganglia hypoperfusion, only one did not show headaches.

The relations between cognitive problems and imaging profiles were complex. Each of the 4 patients with mild atrophy on MRI had some degree of cognitive dysfunction, but cognitive problems were also found for many patients without MRI findings. There were no significant relations between MR findings and specific cognitive symptoms.

Although SPECT revealed some hypoperfusion for 40% of the patients with any type of cognitive problem, associations between regional SPECT findings and specific cognitive symptoms were mostly weak. The only significant relation was between problems in executive function and hypoperfusion of the frontal lobes. Each of the 5 patients with frontal hypoperfusion showed problems in executive function. There were 8 patients with executive problems who did not show frontal hypoperfusion, but the overall relation was nevertheless significant ($P < .01$ by the Fisher exact test).

TABLE 3 *Odds ratios for finding specific imaging abnormalities given that a specific postconcussive symptom was present*[*,†]

		Psychiatric all	Somatic all	Cognitive			
				Memory	Attention	Executive	Speed
MRI	Atrophy	2.7	1.1	5.7	0.7	4.8	4.8
SPECT	Atrophy	2.7	1.7	3.4	1.2	2.9	—
SPECT	Frontal	4.7	2.7	1.0	0.5	~‡	0.8
SPECT	Temporal	0.8	1.1	5.7	2.7	1.4	4.8
SPECT	Parietal	2.5	0.8	1.5	~	~	~
SPECT	Occipital	~	0.0	—	—	—	—
SPECT	subcortical	3.0	56.0§	0.7	1.2	1.4	0.8
MEG	Frontal	2.1	0.5	1.2	0.9	~§	2.1
MEG	Temporal	0.4	0.3	13.0‖	1.4	2.2	8.0¶
MEG	Parietal	1.3	0.3	1.0	12.0‡	4.0	4.0
MEG	Occipital	2.5	0.0	0.4	2.5	1.3	~

[*] Odds ratios are shown for relationships between specific imaging observations and specific, post-concussive symptoms. Significant relationships are in bold.

[†] MRI indicates magnetic resonance imaging; SPECT, single photon emission computed tomography; MEG, magnetoencephalography; ~, infinite odds ratio because one of the cells in the calculation was 0.

[‡] $P < .010$ by the Fisher exact test.

[§] $P < .001$ by the Fisher exact test.

[‖] $P < .005$ by the Fisher exact test.

[¶] $P < .050$ by the Fisher exact test.

In general, MEG slow wave abnormalities were significantly associated with cognitive problems. As indicated in Table 3, there were several significant relations between specific regional findings and specific cognitive symptoms. Of the 12 patients with memory problems, temporal slow waves were seen for 10. Given a finding of temporal slowing (15 patients), only 4 were without memory problems. The relation between memory problems and temporal slowing is significant at $P < .005$. Memory problems were not associated with frontal, parietal, or occipital lobe slow waves ($P > .1$).

Of the 9 patients with attention problems, parietal slowing was seen for 6. When parietal slowing was present ($N = 9$), attention problems were seen for 67%. This relation is significant at $P < .01$. Attention problems were not significantly associated with frontal, temporal, or occipital slowing ($P > .1$).

Problems in executive function were significantly coupled to frontal slow waves ($P < .001$). Although 6 of 13 patients with executive problems did not show frontal slowing, in all 7 cases where frontal slowing was present, deficits in executive function were seen. Deficits in executive function were not significantly correlated with temporal, parietal, or occipital slowing. Interestingly, all 6 patients with epileptiform activity (independent of region) showed executive deficits, but only 4 of these also had frontal slowing. This suggests that general epileptiform activity can compromise the complex neural network that supports executive skills.

Decreased processing speed was seen for 10 of 15 patients with temporal lobe slowing, but only 3 of 15 patients without temporal lobe findings, indicating a significant association between temporal lobe findings and decreased processing speed ($P < .05$). Deficits in processing speed were not significantly associated with frontal, parietal, or occipital abnormalities.

DISCUSSION

Brain imaging, head trauma, and postconcussive symptoms

The patient data confirm and extend several prior observations on the relations among head trauma, traumatic brain injury, postconcussive symptoms, and structural and functional neuroimaging data. In the acute evaluation of patients with even mild HT, structural methods such as CT and MRI can play an important role in ruling out life-threatening brain injuries (eg, depressive skull fractures, subdural hematomas). The value of MRI in the evaluation of patients with persistent postconcussive symptoms several months after the traumatic event is less clear, although structural MRI is presently one of the most commonly employed imaging tools for these patients. The present data indicate that MRI findings (at least as applied here in a clinically routine manner) are significantly less likely to be abnormal in these patients than findings from functional methods.

In our patients, SPECT was more likely than MRI to be abnormal ($P < .01$ by McNemar test of proportions), with some hypoperfusion seen for 12 of the 30 patients. Prior attempts to examine the relation between SPECT findings and specific postconcussive symptoms have yielded mixed and inconsistent results.[13,21,28–30] Critical factors may include the time between injury and imaging, the neuropsychological tests used, and sample size limitations. The present study had one of the largest reported study populations, yet, with the exception of a moderately significant ($P < .01$) relation between frontal hypoperfusion and deficits in executive function, and a highly significant ($P < .001$) relation between persistent postconcussive somatic symptoms (headaches) and subcortical basal ganglia hypoperfusion, no significant relations were seen between specific SPECT findings and other specific symptoms. The relation between frontal lobe abnormalities and problems on tests of executive function is well documented, but at present, we lack understanding of the physiological processes by which basal ganglia hypoperfusion and posttraumatic headache might be coupled. Also, it should be noted that, whereas this observation attained statistical significance, there were only 5 patients with both basal ganglia hypoperfusion and persistent headaches.

Although MEG findings were not strongly associated with psychiatric or somatic symptoms, there were highly significant relations between regional MEG abnormalities and specific cognitive problems. At significance levels of $P < .01$, temporal lobe MEG abnormalities were associated with memory deficits, parietal abnormalities were associated with attention problems, and frontal abnormalities were associated with problems in executive function. These patterns of MEG abnormalities are consistent with the organization of known cortical systems supporting mnemonic, attention, and executive abilities,[31] and they strongly suggest that MEG observations truly reflect traumatic brain injury to the implicated processing systems.

It was also observed that reduced processing speed was associated with temporal lobe slow waves. At present, the full significance of this relation is uncertain, but, like that between temporal lobe slow waves and mnemonic dysfunction, it may partly reflect underlying damage to limbic structures (see the discussion of slow waves, below).

Although no patients showed clear posttraumatic seizures, MEG identified epileptiform abnormalities in 6 cases, as a result of which physicians placed 3 patients on anticonvulsant medications (Depakote or Tegretol). In 2 cases (each with temporal lobe activity), this led to significant clinical improvements, especially in mnemonic function. These observations suggest that, even in the absence of clinical seizures, epileptiform activity can have a negative impact on cognitive functioning that may warrant pharmacologic management.

In considering the utility of multimodal imaging in mild HT, MRI data were fully redundant with data from SPECT and MEG in the sense that each patient with an MRI finding also had abnormalities on functional imaging. In contrast, SPECT and MEG provided some differential data. There were 5 patients with SPECT abnormalities without MEG findings, and 10 patients with MEG findings in the absence of SPECT abnormalities.

Whenever SPECT identified focal cortical abnormalities, MEG identified concordant slow waves. However, MEG failed to reveal a slow wave correlate for hypoperfusion of the basal ganglia. The strength of the MEG signal recorded outside of the head depends on many factors including the number of brain cells that are synchronously active, the geometric configuration of the dendritic trees of these cells, and the distance to the MEG sensors.[32] Through the application of special signal processing techniques (eg, signal-space projection strategies[33]), MEG can, in some circumstances, provide direct evidence for dysfunction of subcortical structures. However, for the most part, MEG is relatively insensitive to subcortical dysfunction, except through indirect observation of the impact of subcortical dysfunction on cortical activities. In the case of basal ganglia hypoperfusion, there seems to be little electrophysiological impact on cortex, at least with respect to generation of focal slow waves.

MEG, executive function, and frontal lobe vulnerability in head trauma

Several lines of data converge to suggest that the frontal lobes are especially vulnerable to head trauma. It is therefore somewhat surprising that MEG (the most sensitive of the employed imaging methods to problems in executive function) revealed frontal abnormalities in only 7 of the 30 trauma patients. Encouragingly, each of the patients with frontal findings showed evidence of deficits in executive functions, but there were 6 additional patients with clear problems in executive function where MEG failed to show any frontal abnormalities.

There are several possible explanations for the rarity of frontal MEG abnormalities. One possibility relates to an inherent limitation of MEG—a lack of sensitivity to intradendritic currents oriented perpendicular to the skull. The frontal lobes, in particular, have large regions where cortical pyramidal cells are oriented in a mostly radial direction, so MEG may be relatively blind to abnormal signals from certain large patches of frontal cortex. A partial solution to this problem that will be employed in future studies is inclusion of simultaneous quantitative EEG recordings. EEG shows a complementary sensitivity profile to MEG, with relatively greater sensitivity to radial versus tangential currents.

Another possible reason is that frontal dysfunction following mild HT is not well characterized by dipolar slow waves. Examination of nondipolar events, or abnormalities in higher frequency bands (eg, theta, alpha, and beta), might provide a better assessment of frontal dysfunction (see the discussion of slow waves, below).

On the other hand, SPECT also failed to reveal frontal problems in the majority of our patients. This suggests that we may have had a slightly atypical group of trauma patients, or that the selective vulnerability of the frontal lobes to damage by mild trauma is less than suspected. Many of the data supporting the susceptibility of the frontal lobes in mild trauma are inferentially based on the frequent presence of problems in executive function. Whereas it is well established that patients with frontal lobe lesions show deficits in executive function, the converse statement that deficits in executive function are an exclusive reflection of frontal damage is not well established. In our study, 100% of the patients with clear frontal abnormalities on either SPECT or MEG showed problems in executive function, but several patients with executive problems did not show frontal abnormalities. These data combined with those from other functional imaging studies indicate that brain regions beyond the frontal cortex contribute to performance on "executive" tasks.[34]

On the nature and value of slow waves

As previously described, the MEG slow wave analyses performed in this study focused only on those events with a dipolar field pattern. Although single dipole modeling is generally found to be unsatisfactory for modeling the true complexities of spontaneous data,[23] the present results support prior observations that this strategy can be effective in the identification of focal pathology in a wide range of conditions.[21,33–42] The fundamental rationale for the dipole strategy is that abnormal signals from dysfunctional regions are occasionally so large that they dominate the recorded magnetic signals, with the simple dipole model being only minimally perturbed by lower amplitude activity from normal tissue. With respect to nondipolar slow waves, the present study ignored these because we have found it difficult to reliably model such slow waves using even a multiple dipole approach. Nevertheless, complex slow waves may still represent important signs of pathology that merit attention. Fehr and coworkers[43] have used minimum-norm current reconstruction strategies to examine complex slow waves in schizophrenia. Future studies in head trauma should explore the utility of this approach.

An additional analysis strategy that may prove fruitful involves spectral assessment of absolute and relative power and coherence in various frequency bands.[25,43] The advantages of spectral methods are their computational simplicity, objectivity, and model independence. However, these methods can miss clinically significant pathophysiology that has a rare paroxysmal (burst-like) character. A short-duration burst of focal slowing may be of clinical significance, but one or a few bursts of slow waves against an otherwise normal background may not cause significant perturbation of power spectra derived over an extended time period.[23]

The multimodal integration approach employed in this study helps provide information on the neurobiological basis of MEG-identified slow waves. In prior studies of patients with focal encephalomalacia from stroke or moderate-severe head trauma, MEG frequently identified focal slowing only at the margins of the lesions.[25,38] This indicates cell loss and disruption of local interconnections as one likely cause of slow waves. The present study reveals that slowing is also seen in cortical regions that appear structurally intact but with decreased blood flow on SPECT. Additional evidence that a perfusion deficit alone can give rise to slow waves comes from observations in patients with transient ischemic attacks where we and others have found focal slowing.[33,39] Although the present study suggests that decreased perfusion of the basal ganglia does not appear to give rise to cortical slow waves, prior animal and human studies show that disruption of thalamocortical projections can cause focal slow waves in the relevant cortical projection zones. So, some subcortical disruptions do produce cortical slow waves, whereas others do not.[44]

Interestingly, and perhaps importantly, slow wave patterns in the MEG appear to vary according to the nature of the generating condition. Based on the MEG data presented here and in other studies,[23,25,38,39] slowing associated with encephalomalacia and/or perfusion deficits tends to be of a rather continuous nature, whereas that associated with disruption of thalamocortical connections is more burst-like.[25,44] In the present study, MEG slow waves were seen in several patients without MRI or SPECT findings. In most of these cases, a burst-like pattern was observed, suggesting a disruption of thalamocortical connections that was not identified by conventional imaging. Both animal and human literature support the view that mild HT can cause a disruption of axonal connections that is not detectable using conventional MR imaging.[45–47] In future studies, application of newer MR scanning sequences such as magnetization transfer and diffusion imaging may help clarify the situation as these methods are believed to be more sensitive to white matter damage than the traditional sequences used here.[45,47]

Whereas disruption of thalamic input to the cortex can lead to focal slow waves, based on data from patients with stroke, tumors, and multiple sclerosis, it does