

# SPECT brain perfusion findings in mild or moderate traumatic brain injury

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## Abstract

**BACKGROUND:** The purpose of this manuscript is to present the findings in the largest series of SPECT brain perfusion imaging reported to date for mild or moderate traumatic brain injury. **PATIENTS AND METHODS:** This is a retrospective evaluation of 228 SPECT brain perfusion-imaging studies of patients who suffered mild or moderate traumatic brain injury with or without loss of consciousness (LOC). All patients had no past medical history of previous brain trauma, neurological, or psychiatric diseases, HIV, alcohol or drug abuse. The patient population included 135 males and 93 females. The ages ranged from 11–88 years (mean 40.8). The most common complaints were characteristic of the postconcussion syndrome: headaches 139/228 (61%); dizziness 61/228 (27%); and memory problems 63/228 (28%). LOC status was reported to be positive in 121/228 (53%), negative in 41/228 (18%), and unknown for 63/228 (28%). **RESULTS:** Normal studies accounted for 52/228 (23%). For abnormal studies (176/228 or 77%) the findings were as follows: basal ganglia hypoperfusion 338 lesions (55.2%); frontal lobe hypoperfusion 146 (23.8%); temporal lobes hypoperfusion 80 (13%); parietal lobes hypoperfusion 20 (3.7%); insular and or occipital lobes hypoperfusion 28 (4.6%). Patients' symptoms correlated with the SPECT brain perfusion findings. The SPECT BPI studies in 122/228 (54%) were done early within 3 months of the date of the accident, and for the remainder, 106/228 (46%)

over 3 months and less than 3 years from the date of the injury. In early imaging, 382 lesions were detected; in 92 patients (average 4.2 lesions per study) imaging after 3 months detected 230 lesions: in 84 patients (average 2.7 lesions per study). **CONCLUSIONS:** Basal ganglia hypoperfusion is the most common abnormality following mild or moderate traumatic brain injury ( $p = 0.006$ ), and is more common in patients complaining of memory problem ( $p = 0.0005$ ) and dizziness ( $p = 0.003$ ). Early imaging can detect more lesions than delayed imaging ( $p = 0.0011$ ). SPECT brain perfusion abnormalities can occur in the absence of LOC.

**Key words:** single photon emission, computed tomography, traumatic brain injury

## Introduction

Head trauma is an underestimated cause of chronic disability. It has been called the "Silent Epidemic" (1, 2). Under-estimation of the true numbers of head injury victims is attributed to imprecise information gathering, lack of recognition of late developing neurological and endocrinological symptoms, and not recognizing the true range of traumatic brain-injury related dysfunctions (3). A meta-analysis of prison inmates indicated that of 1,055 subjects, 489 had head injuries with 31% unattended by a physician and 60% not hospitalized and therefore not part of public health records. It was inferred that the incidence of head injuries should be upwardly adjusted. More permanent effects occurred from unattended and undocumented injuries (4). A conservative estimate puts the total number of TBI at over 2 million per year, with over 1.5 million in which the injuries are not severe enough to require hospitalization. Young individuals between ages 15–24 have the highest rate of injury. Physical, cognitive, and psychosocial-behavioral-emotional impairment are well known consequences of TBI, with over 25 billion dollars in economic costs (5). Morbidity from acute and chronic symptoms (headaches, pain, seizures, memory problems, dizziness etc.), has been well recognized post mild TBI (6,7). The wide range of physiological, neurological, neuropsychological, and emotional symptoms occurring after concussive head injury is associated with diffuse brain damage (8). The patient is rendered vulnerable to incidents creating further brain injury (9).

The pattern of brain injury and its correlation with the patient symptoms has not been traditionally possible because the mechanism of injury rarely involves a pure single force, and because of the unknown contribution of secondary sequella (8,9).

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It is important to be aware of the following physical and mechanical factors that contribute to brain injury. The brain is vulnerable to trauma because it is deformable, soft and somewhat inelastic. Permanent distortion and tissue destruction occurs locally or in widespread areas due to impact, cutting, absorption of energy, and restricted capacity to recover its original length, shape, or volume, after force is removed. As the brain moves against vessels exiting the skull (including the internal carotid artery), either vessels or brain parenchyma can be torn. Impact and/or rotation occurs in lateral and transaxial planes in the neck and head, creating shearing, stretching, crushing, and torsion within the brain and neck, and between brain and skull, and between cerebral planes at different radial distances from the center of rotation. Brain impact with the flat and sharp surfaces of the skull and dura mater creates lacerations and contusions. Impact and brain acceleration-deceleration causes brain motion-associated positive and negative pressure waves, causing cavitation between the skull and the brain. Rotation in the sagittal plane, unrestrained by the falx, may cause the brain stem to move in and out of the foramen magnum affecting nuclei controlling the vasculature (10, 11).

Brain trauma is not an event but a process occurring over time, sometimes many years (12). Physical forces, as previously mentioned, create primary damage. Secondary pathology is consequent to destruction of tissue and hemorrhage, i.e. mass effects and intracellular and vascular changes. The tertiary phase refers to late endocrinological dysfunction. The quaternary phase refers to late development of neurological symptoms (e.g., dystonias, premature dementia, and posttraumatic epilepsy) (8). This is probably associated with transneuronal degeneration. Neuronal atrophy after initial injury has been reported and is reflected in increased ventricle to brain ratio which may stabilize 9–12 weeks post injury (13).

SPECT brain perfusion imaging is highly sensitive for detecting regional cerebral blood flow (rCBF) disturbances in-patients with traumatic brain injury (1, 14–19). Brain SPECT has been playing an increasingly important role in evaluating patients complaints following mild TBI, and there is increasing evidence that rCBF SPECT plays an important role in medical, and socio-economic decision-making involving mild head injury patients (20). Many studies on patients with head injury have already demonstrated that brain perfusion SPECT can depict larger and more numerous lesions than on CT. Most of these studies, however, have addressed rather severe trauma cases (14, 15, 21–24). In mild TBI there is increasing literature showing the superiority of SPECT over CT in evaluating the brain (1, 25, 26). The role of CT in mild to moderate trauma is probably limited (27–29). While SPECT imaging does not replace traditional structural imaging modalities for the identification of major lesions, hematomas, or edema; brain SPECT plays an important role in assessing cortical, basal ganglia, and thalamic perfusion alterations resulting from trauma (30). It is hypothesized that SPECT detected lesions are consequent to the mechanical and physiological effects of an accident upon the neck and head, and the physiological consequences of stress (31). All the reports in the literature have several problems such as the small number of patients in each individual report, lack of correlation with neurobehavioral analysis, lack of longitudinal follow-up, the non-specificity of the findings and lack of comparison with normal controls, and comorbidity that interferes with the in-

terpretation of the findings (neurological or psychological diseases; previous history of brain trauma, etc.). In addition, there is no standard protocol followed by all investigators for SPECT acquisition, processing and interpretation of the data. There is also lack of quantitation of the regional cerebral perfusion using the current radiopharmaceuticals approved by the FDA.

The objective of this manuscript is to present the SPECT brain perfusion abnormalities in the largest series thus far reported in the literature. In addition, we are presenting other data related to frequency of cause of the accident and patients' complaints. We are also presenting statistical analysis of the data in order to show the value of early imaging over delayed imaging from the time of the accident and the correlation of the findings with the patients' symptoms.

## Materials and Methods

We retrospectively reviewed the record of all the patients who had a SPECT brain perfusion study between Jan 1994–Feb 1997. We identified 228 studies of patients who were status post mild or moderate TBI with or without LOC. Patients may or may not have received a CT or MRI. Any patients with a CT, or MRI, and showing important cortical atrophy or focal lesions were excluded from the study. Any patient with significant past medical history such as a previous cranial trauma, epilepsy, other previously known neurological disorders before the trauma, psychiatric diseases, HIV, drug or alcohol abuse were also excluded. In addition to the 228 studies, another 132 other SPECT brain perfusion studies were included to blind the reader and prevent bias towards the "selected group" during the review process. These additional studies included 42 studies with mild TBI and significant past medical history, 30 normal SPECTs for patients that were referred for other reasons, 30 abnormal SPECTs with documented neuro-vascular diseases, and 30 studies with severe TBI. All studies were randomized and were read twice by an expert nuclear medicine physician in the field of traumatic brain injury (HMA). No history was provided while reading the studies.

We divided the patients into 2 groups: early (i.e. imaged before 3 months after the injury), and delayed (i.e. imaged after more than 3 months but less than 3 years from the date of injury).

## SPECT Procedure

SPECT studies were performed following the IV injection of Tc-99m HMPAO (2-hour delay)<sup>1</sup>, or Tc-99m ECD<sup>2</sup> (one-hour delay). The patients were supine with eyes open in a dimly lit, quiet room. Scanning was performed on Triple head gamma camera<sup>3</sup>, using low energy, ultrahigh resolution parallel hole collimator. The data were collected as 64 X 64 matrix, 3.56 mm/pxl, a total of 120 projections at 40 seconds/view, with a radius of rotation not to exceed 14 cm, and as close to head as possible. The raw data was smoothed with Butterworth filtered Nyquist (cyc/cm) of 1.404, and high cutoff frequency of 0.56 cyc/cm. The reconstruction was performed with ramp filter Nyquist (cyc/cm) of 1.404, and high cut

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<sup>3</sup>TRIONIX — Twinsburg, Ohio, USA

frequency (cyc/cm) of 1.404. The uniform attenuation was applied. The images were then reoriented in the axial, coronal and sagittal planes. The final data was displayed 2 pixels thick (7.4 mm) on 10 graded color scale. The cerebellum was used as the reference site for 100% maximum value of the maximum cerebellar uptake, and studies with cerebellar abnormalities were excluded. The brain was divided into 24 distinct regions: R and L caudate nuclei; R and L thalami; R and L putamen; R and L anterior frontal lobes; R and L superior frontal; R and L inferior frontal; R and L anterior temporal; R and L medial temporal; R and L lateral temporal; and R and L cerebellum. The R and L insular region and R and L occipital regions. Any measurement of cerebral perfusion in the cortex or basal ganglia under 70%, or 50% in the medial temporal was considered abnormally decreased (32).

### Statistical Analysis

Statistical Analysis was done by a two-tailed T-test from available commercial software — EXCEL from Microsoft which returns the probability associated with a Student's T-test. The T-test studied a hypothesis which states that the two samples were likely to have come from the populations that have the same mean.

### Results

The patient population included 135 M, 93 F, whose age ranged from 11 to 88 years (mean 40.8). The etiology of brain trauma was a history of: MVA 103/228 (45%), blow to the head 82/228 (36%) and fall 43/228 (19%).

The most common complaints were characteristic of the post-concussion syndrome (PCS): headaches 139/228 (60.9%); dizziness 61/228 (26.7%); memory problems 63/228 (27.6%); sleep disorders 20/228 (8.7%); concentration problems 19/228 (8.3%); visual problems 18/228 (7.9%); balance problems 10/228 (4.4%); depression 6/228 (2.6%); and hearing problems 5/228 (2.2%). Normal studies accounted for 52/228 (23%), and abnormal studies for 176/228 (77%). The total number of lesions (hypoperfusion) in 176 abnormal SPECT brain perfusion studies was 612 averaging 3.5 lesions per patient, distributed as follows: basal ganglia and thalami (BG) 338 (55.2%); frontal lobes 146 (23.8%); temporal lobes 80 (13%); parietal lobes 20 (3.7%); insular and/or occipital lobes together 28 lesions (4.6%). A pattern of diffuse supratentorial hypoperfusion was observed in a total of 35 patients (20%). The insular and occipital abnormalities were grouped together because of the small number of lesions. Of considerable interest and significance is the finding that BG abnormalities were more common than the previously recognized frontal lobes ( $p = 0.006$ ) and temporal lobes abnormalities ( $p = 0.0003$ ).

### Association of the patients' most common complaints and abnormal SPECT

The association of presenting symptoms with abnormal SPECT was as follows: dizziness 51/61 (84%); headaches 103/139 (74%); and memory problems 46/63 (73%). Overall BG abnormalities were most common. The average number of lesions for given symptoms was as follows: headaches: 188 lesions were detected in 103 abnormal SPECT studies (1.83 lesion/abnormal study); dizziness: 95 lesions in 51 abnormal SPECT (1.86 lesion/abnormal study); memory problems: 115 lesions for 46 abnormal SPECT

(2.5 lesion/abnormal study). For the main presenting symptoms of headache, dizziness, and memory problems, frontal lobe abnormalities were: 0.63, 0.73, and 0.78 lesion/abnormal study, respectively; temporal lobe abnormalities were: 0.46, 0.63, and 0.65 lesions/abnormal study; respectively; parietal abnormalities: 0.15, 0.1 and 0.15 lesion/abnormal study, respectively. Association of memory problems with BG abnormalities was significantly higher than in those with complaints of headache ( $p = 0.0005$ ), and in those patients complaining of dizziness ( $p = 0.003$ ).

### Differences Between Early and Delayed Imaging

SPECT brain perfusion was done in 122/228 (53.5%) of cases within 3 months from the date of the accident, and the rest 106/228 (46.5%) had the study over 3 months from the date of the injury and less than 3 years. There were 382 lesions in 92 studies of patients who were imaged within 3 months from the date of trauma (average 4.2 lesions per study) and 230 lesions in 84 who were imaged after 3 months from the date of trauma (average 2.7 lesion per study). Diffuse supratentorial hypoperfusion was noticed in 12 (15%) in those patients imaged within 3 months versus 23 (24%) in those imaged more than 3 months. This might indicate that diffuse supratentorial hypoperfusion could be due to the fact that has been previously reported in the literature that brain injury following traumatic brain injury is a progressive process. There was a significant difference when patients were imaged earlier < 3 months from the time of the accident versus when imaged later > 3 months from the date of the injury. Early imaging identified more lesions than delayed imaging with a  $p = 0.0011$ . Because the 2 groups compared are different, we realized that this is not the ideal way of evaluating early versus delayed imaging. It is possible that patients with late examination had different neuropathology or subjective complaints warranting study but not necessarily involving lesions manifested by hypoperfusion. Longitudinal follow up of the two groups is recommended, which is currently under limited investigation in our lab. However, the large number of studies reviewed in our series makes the assumption based on our results plausible.

### Association with Loss of Consciousness

Loss of consciousness (LOC) status was reported to be positive in 121/228 (53%) and negative in 41/228 (18%) (status was not reported in the medical records for the remainder). The results for patients with reports of no history of LOC are: 28/41 (68%) of the SPECT studies was read as abnormal and 13/41 (32%) was read as normal. Reports of focal hypoperfusion abnormalities were as follows: frontal lobes 13/28 (46%); basal ganglia 14/28 (50%); temporal lobes 5/28 (18%); and, parietal 4/28 (14%). SPECT brain perfusion abnormalities can therefore occur in the absence of LOC. In this subset of patients, CT results were available in 32/41, all reported to be negative. This further confirms that SPECT brain perfusion is more sensitive in detecting lesions post mild traumatic brain injury. This subgroup of patients without LOC has been the subject of a separate publication (33).

### Intraobserver Agreement

The intraobserver agreement was 92% for the temporal, 88% for the frontal, 78% for the basal ganglia and parietal lesions and 100% for the diffuse supratentorial hypoperfusion.

### **Drawbacks of the Study**

One of our disappointments — although this was not the objective of this presentation — was our inability to compare the SPECT findings to CT findings. Data of CT findings were obtained from the referring physician, patient, or medical record in 162/228. All were either normal, or with no significant findings. Most were not available for us to review. With the rest 66/228 it was unknown if the patient had a CT and if the patient did have one, the results were not known. We generally assumed that patients who were referred for a SPECT brain perfusion study had no abnormalities on CT. We have therefore concluded that a comparison between the CT findings and SPECT brain perfusion would be unreliable in this report.

Another drawback is the findings were not correlated with neuropsychotic analysis which was not available to us.

### **Discussion**

SPECT brain perfusion studies have been playing an important role in understanding the patho-physiology, medical and socio-economic decision-making involving mild head injury patients (MHI) (33–38). It is highly sensitive for detecting regional cerebral blood flow (rCBF) disturbances in-patients with acute head injury (30). Many studies on patients with head injury have already demonstrated that brain perfusion SPECT can depict larger rather than smaller and more numerous lesions than on CT. Most of these studies however have addressed rather severe trauma cases (14, 15). In mild traumatic brain injury there is increasing evidence in the literature showing the superiority of SPECT over CT in detecting abnormal brain perfusion findings (1, 16–26). The sensitivity of CT in mild to moderate trauma is less than 25% (15). While SPECT imaging does not replace traditional structural imaging modalities for identifying major lesions, hematomas, or edema, brain SPECT does play an important role in assessing cortical, basal ganglia, and thalamic perfusion alterations resulting from trauma.

Our findings suggest that basal ganglia and thalamic perfusion abnormalities are more common than previously reported. Previous reports described frontal and temporal lobes to be the most common abnormalities (14–26). In our subset of patients who suffered traumatic brain injury without loss of consciousness, basal ganglia hypoperfusion abnormalities are second to frontal lobe abnormalities and more common than temporal lobe abnormalities. Our results further confirmed that the SPECT brain perfusion studies are more sensitive than X-ray CT in detecting brain lesions following mild/moderate traumatic brain injury. We previously reported that early imaging less than three months following the accident detects more lesions than in delayed imaging performed more than three months after the accident (39). The present findings offer new and objective evidence that „mild“ head injury may be accompanied by objective neurotrauma not revealed by other imaging procedures which are less sensitive to „minor“ head injury, especially in the absence of areas of hematoma, contusion, mass effects and edema.

It is noteworthy that BG and thalamic lesions are located in areas protected from lesser impact injury. It is important to be aware of the range of physiological and traumatic circumstances that are hypothesized to contribute to patient's symptoms and to

the SPECT-detected lesions in the mild TBI. These include: 1. Primary physical traumatic effects upon (a) the parenchyma of the brain; (b) the arteries in the neck and head; 2. Disturbance of brain autoregulation; 3. Intracellular damage (damage to the blood-brain barrier; neurotoxic cascades, etc); 4. Transneuronal degeneration and atrophy consequent to parenchymal trauma (direct injury and vascular dysfunctions); and 5. Diaschisis consequent to atrophy and dysfunction of nuclei subserving distant incoming circuits.

Because of many unclear issues in our practice and in dealing with patients with traumatic brain injury, we aim in this presentation to review some of the facts that have been reported in the literature related to the mechanism and pathology of traumatic brain injury.

### **Primary physical trauma**

The brain, floating in the CSF inside the skull, is known to be a penetrable, deformable, soft, and not very elastic structure. The skull and the scalp, in addition to the dura and dural extensions, serve as a cushion to the brain against impacting forces. When the forces of traumatic impact on the skull exceed local elasticity, this induces permanent deformation. Further trauma is caused by the brain being pushed against fixed structures such as the internal surface of the skull, meninges, and blood vessels. When one portion of an anatomic structure is fixed in place and the other is moved by impact, creating acceleration or deceleration, a shearing force occurs, a significant cause of trauma. The shearing effects take place within the layers of the brain, between the brain and its entering and exiting vascular supply, especially to the hypothalamus, infundibulum, pituitary gland seated in the sella turcica, and occasionally the cranial nerves. Movement of the brain is expected to damage the pituitary stalk, the perforating vessels to the hypothalamus from the anterior cerebral arteries and pituitary portal veins (40–44). Minor head injury has been identified experimentally as causing meningeal thickening, discoloration of the cerebral cortex from old extravasated blood, contusions and lacerations (34). Under impact conditions, the vascular tissues of the brain undergo sudden deformations beyond their recoverable limit. The vascular tissue is a very complex structure with different responses to rapid mechanically induced trauma. The three-dimensional vascular distribution of vessels in the brain contributes to the overall stability of the brain (45).

### **Cerebral perfusion and sympathetic innervation**

Vascular branches from the anterior, middle perfuse the basal ganglia and thalamus, and posterior cerebral arteries that arise from the Circle of Willis (46–47); the anterior and posterior choroidal branches form the major blood supply. The multiple branches of these complex structures render the blood supply vulnerable to physical trauma and disruption of autoregulation and mass effects.

Sympathetic fibers reach cerebral vessels by 3 routes: (a) the carotid artery territory via post ganglionic fibers that originate in the superior cervical ganglia; (b) innervation of the vertebrobasilar territory via fibers that arise from the stellate ganglion; (c) from the stellate ganglion following the tunica adventi of the common and internal carotid arteries possibly innervating the rostral part of the Circle of Willis (48). As the carotid artery emerges from the

cavernous sinus, it is surrounded by a sympathetic plexus (47). The vasomotor center (anterior lateral portion of the medulla) has noradrenergic fibers that excite the vasoconstrictor neurons of the sympathetic nervous system (SNS), effecting the vasculature of the brain. Cerebral blood vessels are also innervated by intraparenchymal fibers, which originate from the locus ceruleus. Intracerebral arterioles are supplied with perivascular sympathetic nerves, whereas cerebral microvessels, capillaries and venules may be supplied with or closely associated with intraparenchymal adrenergic nerves.

### **Vasospasm and disturbance of brain autoregulation**

Ordinarily cerebral autoregulation prevents major changes stemming from sympathetic stimulation. However, cerebral sympathetic stimulation can markedly constrict the cerebral arteries in order to prevent high pressure from reaching the smaller blood vessels and causing stroke (48–50). Early and late vasospasm, involving the large basal intracranial arteries (middle cerebral and basilar), is considered to be a significant entity in head trauma, occurring in up to 25% of patients with head injury (40). Cerebral arterial spasm can occur in patients whose CT scans did not show subarachnoid or intracerebral blood. It has been deemed unlikely that posttraumatic cerebral arterial spasm is caused by elevated intracerebral pressure. Onset of vasospasm can occur from 48 hours to 7 days later (49–50). Ischemia (associated with vasospasm or mass effects) impairs the metabolic need of the brain, setting into motion multiple mechanisms of toxic metabolite formation and cell destruction. Blunt trauma was found to be able to cause cerebral hypoperfusion. This association is statistically stronger for the most severely injured patients (50). The intracranial artery can be injured by direct damage to neck structures, i.e. impact, stretching, tearing or compression of the intracranial arteries and other cervical vessels (51, 52) caused by impact or hyper-extension/hyper-reflexion and rotation in various planes („whiplash”). Cerebro-arterial spasm can occur secondary to sudden traction on the carotid artery sheath at the base of the brain, with symptoms of vascular type of headaches, and feeling of being dazed or stunned (52). Shearing effects may injure the intracranial arteries as they emerge from the cavernous sinus, and can create diffuse brain injury since the brain moves past the arterial tree (53). The combination of carotid occlusion and brain impact is more severe than carotid occlusion alone. Traumatized cerebral vasculature seems unable to respond to reduced perfusion pressure associated with carotid artery occlusion (54).

Cerebral vasoreactivity is under the control of the SNS through complex CNS circuits (medulla oblongata; pons; hypothalamus), feedback through the extra-cellular fluid (electrolytes; hormones), temperature and negative feedback baroreceptor mechanism of the tractus solitarius (55). Cerebral vasospasm can be relieved through electrical stellate or cervical ganglia blocks (56). In a personal communication (Fritz Jenkner, MD, Vienna, Austria), hemispheric flow measured by electrical resistance („rheoencephalography”) increased towards normal levels after stellate block in 11 patients who had symptoms secondary to decreased cerebral flow for various reasons including head trauma.

Neuronal integrity is maintained through control of brain metabolism and blood gas level, affected by a variety of metabolic and neurogenic effect (56). SPECT signs of hypoperfusion have

been attributed to loss of cerebral autoregulation after head trauma including minor head injury (57). Vasospasm is described as occurring after 48 hours. Brainstem damage or subarachnoid hemorrhage is associated with vasospasm independently of dysregulation. Impaired cerebral autoregulation of vasomotor control occurs after minor head injury (58) and is associated with poor outcome. After impact injury (rat model) there is transient hypertension and increased blood flow, followed by blood flow reduction below control values within minutes (56–59). Ischemia and luxury perfusion occur at different post-trauma periods (60). Vasospastic ischemia is most common after injury but can occur throughout the acute recovery period. After head injury and hypoperfusion, cerebral metabolic rate of oxygen tends to be highest very early and decreasing over the first 1–5 days (61). While blood flow measurements vary with location, the PCS is associated with slowed cerebral circulation for up to 3 years (62). Arterial hypotension or increased intracranial pressure can result in lowered cerebral perfusion pressure. Sudden increases in blood pressure can be transmitted to the brain's microcirculation, contributing to secondary hemorrhage and edema. Loss of autoregulation may occur in some areas but not others (63).

### **Intracellular damage: Reperfusion injury to neck and cerebral vessels**

Reperfusion following resolution of ischemia or vasospasm leads to additional neurological injury: phagocytic damage to the endothelium and surrounding tissues; release of oxygen-derived free radicals (64). This creates damage to vascular, neuronal, and glial membranes, with excitotoxic, intracellular calcium overload and excitatory amino acid release, i.e. glutamate (65–67).

### **Neurobehavioral implications**

Lesions may account for some subtle neurobehavioral dysfunctions in the inter-connected thalamus and basal ganglia (68, 69). The BG is associated with multiple behavioral disorders that might occur following mild or moderate traumatic brain injury. BG circuits and connections (including the cortex) have been implicated in disparate functions dependent upon circuits and nuclei involved: these included repeated skilled movement and ideomotor apraxia (70). Depression among patients with left BG lesions may be due to disrupted ascending noradrenergic/serotonergic pathways (71); species specific sexual behavior (72); movement disorders and behavior problems (abulia or disinhibition) (73); dementia associated with involuntary movement disorders (74); in Parkinson's disease and Huntington's disease, intellectual and emotional disorders (75). The potential for BG lesions to be caused by transneuronal degeneration is raised by the finding that thalamic (subcortical) atrophy is related to injury severity, degree of brain atrophy and the presence of nonthalamic cortical or subcortical lesions, i.e. diaschisis (75, 76).

The thalamus participates in numerous neurobehavioral functions through its location in the limbic circuit, and as a relay for diffuse stimuli influencing arousal and topographic sensory stimuli, and output for motivational systems (76, 77). The intra-thalamic laminar nuclei (ILN) may be the thalamic pacemaker, and are involved in functions disturbed in TBI (wakefulness, desynchronized sleep and pain). They receive topographically organized projections from the cerebral cortex, reticular formation, basal

ganglia, cerebellum and the brainstem up to the midbrain and superior colliculus. The ILN projects to the cerebral cortex (primarily frontal, medial and dorsolateral cortex), the striatum and substantia nigra, limbic forebrain, amygdala and hippocampus.

We realize that this report lacks a direct comparison with a normal control group (a problem many institutions face), and that there is a high false positive rate and non-specificity of SPECT brain perfusion abnormalities in head trauma and other disorders. Nevertheless this group was a part of a much larger series, in which all studies were read blindly to the patients history and presenting symptoms as described above.

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