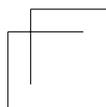
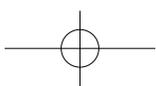
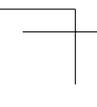
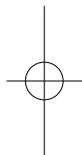
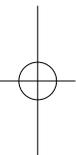
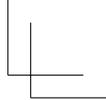


An offprint of
Journal of the Association of Community and Occupational Health Care No.302,2015
Oct.
(official Journal of the Association of Institution for Community and Occupational
Health Care)

Mild Traumatic Brain Injury: Multidisciplinary Approach and Multiple Neuroimaging Techniques

Toru Ishibashi
Kosaku Yasuda

Keiko Soma
Jun Shinoda



Mild Traumatic Brain Injury: Multidisciplinary Approach and Multiple Neuroimaging Techniques

Toru Ishibashi

Hirano Kameido Himawari Clinic, Tokyo, Japan

Keiko Soma

Department of Otolaryngology, Kawasaki Municipal Hospital, Kanagawa, Japan

Kosaku Yasuda

Yasuda Urology Clinic, Saitama, Japan

Jun Shinoda

Chubu Medical Center for Prolonged Traumatic Brain Dysfunction, Kizawa Memorial Hospital & Department of Clinical Brain Sciences, Gifu University Graduate School of Medicine, Gifu, Japan

Abstract

One objective of this study was to clarify the clinical features of mild traumatic brain injury from the standpoints of neuro-ophthalmology, neuro-otology, neuro-urology, orthopedics, neurosurgery, rehabilitation, and psychiatry using a multidisciplinary approach rather than discipline-specific approaches. We also determined imaging-positive rates of individual neuroimaging techniques for organic brain injury and the imaging-diagnostic rate of mild traumatic brain injury by multiple neuroimaging techniques. Six types of structural and functional neuroimaging methods were combined in mild traumatic brain injury patients who were assessed by the multidisciplinary approach. This retrospective study involved 106 mild traumatic brain injury patients (46 men, 60 woman, mean age, 45 years, range 22–76 years) diagnosed using both the multidisciplinary approach and multiple neuroimaging techniques. Objective tests performed by the above-mentioned specialists revealed that patients with mild traumatic brain injury exhibit a wide range of clinical features unique to each field. The imaging-diagnostic rate of mild traumatic brain injury by multiple neuro-

imaging techniques was numerically higher in patients assessed within 3 years after injury (57%) than in those assessed later (41%) ($P = 0.114$). The overall imaging-diagnostic rate was 46%. The multidisciplinary approach and multiple neuroimaging techniques were useful for a definitive diagnosis of mild traumatic brain injury.

Keywords: mild traumatic brain injury, multidisciplinary approach, neuroimaging techniques, traumatic axonal injury

Abbreviations: ABR, auditory brainstem response; CI, confidence interval; CRPS, complex regional pain syndrome; DSD, detrusor sphincter dyssynergia; ECD-SPECT, ethyl cysteinyl dimer single-photon emission computed tomography; EOG, electrooculography; FA-SPM, fractional anisotropy imaging analyzed by statistical parametric mapping; FDG, fluorodeoxyglucose; GCS, Glasgow Coma Scale; GOS, Glasgow Outcome Scale; MMT, manual muscle testing; MTBI, mild traumatic brain injury; NB, neurogenic bladder; SD, severe disability; TBI, traumatic brain injury; UDS, urodynamic study; UIC, uninhibited contraction; UIR, uninhibited sphincter relaxation; VEP, visually evoked potential

Introduction

Traffic accidents, which show an increasing trend worldwide, are among the major causes of traumatic brain injury (TBI). A report by WHO in 2007 estimated that road traffic collisions would become the third most common cause of illness in the world and the second most common cause of illness in developing countries by 2020 (World Health Organization, 2007). In the same report, WHO called TBI the silent and neglected epidemic and recommended that medical personnel should join forces to organize a worldwide fight against it (World Health Organization, 2007). The incidence of TBI varies among countries, but has been estimated to be in the range 150–300 per 100000 population per year in most countries (Tagliaferri et al., 2006). Mild traumatic brain injury (MTBI) occurs commonly, accounting for 90% of all cases of TBI.

The United States prepared its own diagnostic criteria for MTBI and enacted legislation beginning in the 1990s authorizing funding for prevention, surveillance, research, and improved care (American Congress of Rehabilitation Medicine, 1993;

Mild Traumatic Brain Injury: Multidisciplinary Approach and Multiple Neuroimaging Techniques

United States Congress House Committee on Commerce, 1996; National Center for Injury Prevention and Control, 2003; Department of Health and Human Services, 2013). European neurological societies have prepared their own treatment guidelines (Vos et al., 2002). In Japan, the Tokyo Metropolitan Assembly submitted a written appeal to the Japanese government in 2013 demanding the strengthening of measures against MTBI. Thus, MTBI is receiving increased attention in Japan and in other countries, although an important problem that needs to be addressed is that of underdiagnosis of MTBI (National Institutes of Health, 1998). Therefore, we conducted this study to understand the neurological consequences of MTBI in detail by applying a multidisciplinary approach; furthermore, we also attempted to improve the detection rate of organic brain injury and the imaging-diagnostic rate of MTBI by combining multiple neuroimaging techniques.

Subjects and methods

The subjects of this retrospective study were 106 patients diagnosed as having MTBI who were assessed by both a multidisciplinary approach and multiple neuroimaging techniques at our outpatient clinics during the 5-year period from 2008 to 2012. Two outpatient clinics were located in a university hospital, one in a municipal hospital, two in major urban hospitals, and four in urban outpatient clinics.

MTBI was diagnosed in accordance with the WHO's operational definition established in 2004 (Carroll et al., 2004). The causes of MTBI included traffic accidents (100 cases), falling objects (2 cases), acts of violence (2 cases), sports injury (1 case), and falling on the road (1 case). The patients ranged in age from 22 to 76 years (mean age, 45 years) and the male/female ratio was 46:60.

Patients routinely underwent six neuroimaging techniques [MRI, MR angiography, MR tensor tractography, fractional anisotropy imaging analyzed by statistical parametric mapping (FA-SPM), fluorodeoxyglucose PET (FDG-PET), and ethyl cysteinate dimer single-photon emission computed tomography (ECD-SPECT)] and routinely visited the orthopedics department for comprehensive neurological diagnostic examinations (i.e., evaluation of the deep reflexes, pathological reflexes, sensory disturbances, motor disturbances, sphincteric disturbances, cerebellar symptoms, cranial-nervous symptoms, cognitive dysfunction). Depending on the neurological abnormalities identified, patients were examined more closely by specialists in the

departments of neuro-ophthalmology, neuro-otology, neuro-urology, neurosurgery, rehabilitation, and psychiatry. Each patient with MTBI visited an average of 5.3 (range 3–7) specialist departments at the outpatient clinics. Table 1 shows the numbers of patients visiting each department and the tests carried out. Tests were carried out at the discretion of the specialists, so not all tests were carried out on all patients.

Table 1. The numbers of patients visiting each department and the tests carried out

Department	Patients (%)	Tests performed
Neuro-ophthal mology	87 (82%)	Visual acuity, visual fields, accommodation, conver- gence, eye movements, anterior eye segment, ocular media, and fundus
Neuro-otology	102 (96%)	Audiometry, stabilometry, olfactometry, and gustome- try
Neuro-urology	85 (80%)	Urodynamic studies were performed, including uro- flowmetry and cystometry, intra-abdominal pressure studies, detrusor pressure studies, and sphincter elec- tromyography
Orthopedics	106 (100%)	Comprehensive neurological diagnostic examinations were performed to assess the functions of the brain, spinal cord, and peripheral nerves
Neurosurgery	106 (100%)	Neuropsychological tests to examine the cognitive consequences of MTBI and various structural and functional neuroimaging studies
Rehabilitation	71 (67%)	Neuropsychological tests to examine the cognitive consequences of MTBI, laryngography, and electro- myography
Psychiatry	3 (3%)	Electroencephalography was performed to manage ep- ileptic seizures

Results

The causes of injury included falling on the road (1 case), falling objects (2 cases), acts of violence (2 cases), pedestrian–car collisions (4 cases), bicycle–car collisions (8 cases), motorcycle–car collisions (15 cases), and car–car collisions (73 cases). The car–car collisions comprised 42 rear-end collisions, 20 lateral collisions, and 11 head-on collisions. There was one sports injury, involving a snowboarder. Disturbed consciousness at the time of injury included 49 cases of loss of consciousness for 30 minutes or less, 61 cases of post-traumatic amnesia for less than 24 hours, and 93 cases of confusion or disorientation. Twenty-three patients were hospitalized on the day of the accident, while the other patients received treatment in outpatient settings. Eight patients were involved in one or more additional traffic accidents before or after the

Mild Traumatic Brain Injury: Multidisciplinary Approach and Multiple Neuroimaging Techniques
accident that was investigated in this study.

Ten patients suffered multiple injuries at sites other than the brain parenchyma in the accidents under focus in this study. These included one case of skull fracture, one case of alveolar bone fracture, one case of nasal bone fracture, one case of vitreous hemorrhage, two cases of lumbar transverse process fracture, two cases of sternal and rib fractures, and five cases of limb bone fracture. Tests at the department of neuro-urology revealed complicating spinal cord injury in 16 patients.

Two patients had a Glasgow Coma Scale (GCS, Teasdale et al., 1974) score of 13, 10 had a GCS score of 14, and 94 had a GCS score of 15 after 30 minutes or later upon presentation for health care. The GCS score of each patient was confirmed by medical interviews, ambulance transport reports recorded at the time of injury, and medical records at the medical institutions that the patients visited at the time of injury.

The Glasgow Outcome Scale (GOS, Jennett et al., 1975) score was evaluated when each patient was definitively diagnosed as having MTBI by the multidisciplinary approach based on the results of careful examinations performed in the relevant departments. According to the GOS, 14 patients were classified as having severe disability (SD), 48 as having moderate disability, and 44 as showing good recovery. Two patients who were classified as having SD needed to use a wheelchair after the injury.

Evaluation of 106 patients with MTBI using a multidisciplinary approach revealed that 99 patients (93%) had cerebral motor paralysis and/or sensory paralysis, 71 (67%) had olfactory disturbances, 10 (9%) had visual loss, 15 (14%) had concentric contraction of the visual fields, 28 (26%) had impaired smooth pursuit eye movements, 86 (81%) had gustatory disturbances, 51 (48%) had sensorineural hearing loss, 84 (79%) had neurogenic bladder, 105 (99%) had cognitive impairment, and 3 (3%) had epileptic seizures. The following sections give the results from the various departments.

Motor or sensory paralysis

Of the 99 patients with motor and/or sensory paralysis, 1 had monoplegia (left lower extremity; manual muscle testing [MMT] score of 3), 59 had hemiplegia (mean MMT score of 4), and 39 had quadriplegia (mean MMT score of 4). Seven of the patients did not have any motor or sensory paralysis at the initial examination.

Neuro-ophthalmology

Eighty-seven of the 106 patients underwent tests at the department of neuro-ophthalmology, and 58 of these 87 patients (67%) were found to have abnormalities. The test results are shown in Table 2. Ten patients (11%) had visual loss, but none of them had organic damage that could explain the visual loss. Eight of these ten patients had good visually evoked potential (VEP) results, raising the suspicion of psychogenic visual disturbance, while the cause was unknown in the remaining two patients.

Table 2. Incidence of individual impairments found in the 87 patients tested in the neuro-ophthalmology department

Impairment	Patients	Percentage
Visual loss	10	11%
Concentric contraction of both visual fields	15	17%
Partial contraction of a visual field	7	8%
External ophthalmoplegia	2	2%
Convergence insufficiency	9	10%
Impaired smooth-pursuit eye movements	28	32%
Impaired saccadic eye movements	5	6%
Gaze palsy	8	9%
Tonic accommodation	12	14%
Hemispatial neglect	3	3%

VEP was measured in all 15 patients with concentric contraction of both visual fields, to differentiate between disturbance inside the bilateral occipital lobes and psychogenic visual disturbance. Nine of the 15 patients had good VEP results. One of the remaining six patients was suspected of having bilateral optic neuropathy based on the VEP results. In the remaining five patients, reduced amplitude and delayed latency in VEP were observed; however, funduscopy revealed no optic atrophy or abnormalities of the pupillary response to light. Subsequent neuroimaging studies revealed no obvious abnormalities of the occipital lobe in any of these patients.

In addition, one patient had homonymous hemianopia, two had bilateral constriction of the upper visual field, one had bilateral nasal visual field constriction, one had right temporal hemianopia, one had an upper nasal field defect in the left eye, and one had a nasal field defect in the right eye and concentric contraction of the left visual field. No optic atrophy was observed in any of these patients. Eye movement testing revealed one case of abducens nerve palsy and one case of trochlear nerve palsy.

Twenty-eight patients (32%) had impaired smooth pursuit eye movements. Electrooculography (EOG) revealed the presence of a stair-like pattern in all the patients with impaired smooth pursuit eye movements. In two of these patients, EOG reexamination revealed improvement of the stair-like pattern 6 months after the initial examination. Impairment of brainstem and cerebellar functions was suggested in patients with impaired smooth-pursuit eye movements and those with impaired saccadic eye movements. Impairment of the brainstem or visual center function was suggested in eight patients who seemed to have the so-called gaze palsy, i.e., inability to track the target before the eyes. Impaired autonomic nervous function was suggested in 12 patients who complained of accommodation abnormalities, particularly unfocused vision, due to tonic accommodation. Three patients (3%) were diagnosed as having hemispatial neglect by neuropsychological tests carried out at the department of neurosurgery.

Neuro-otology

Of the 106 patients, 102 underwent tests, while the remaining 4 did not. The test results are shown in Table 3. Hearing loss, olfactory disturbance, taste disorder, and abnormal stabilometric values were commonly seen. Hearing tests showed that 16 patients with sensorineural hearing loss had normal auditory brainstem response (ABR), and these patients were diagnosed as having functional hearing loss.

Table 3. Incidence of individual impairments found in the 102 patients tested in the neuro-otology department

Impairment	Patients	Percentage
Sensorineural hearing loss	51	50%
Unilateral hearing loss	23	23%
Bilateral hearing loss	28	27%
Hyposmia or anosmia	71	70%
Hypogeusia or ageusia	86	84%
Abnormal stabilometric values	69	68%
Semicircular Canal paresis	14	14%
Nystagmus	5	5%

Two types of olfactory tests were performed: the Alinamin test and the odorant test. The results revealed that 71 of the 102 patients (70%) had hyposmia or anosmia. Sixteen of the 71 patients with olfactory disturbance showed normal Alinamin test results and abnormal odorant test results, indicating olfactory dissociation.

Two types of gustatory tests were performed: electrogustometry and the

taste disc test. The results revealed that 86 of the 102 patients (84%) had hypogeusia or ageusia. Of these, eight patients had unilateral gustatory disturbance and 78 had bilateral gustatory disturbance. Twenty-one of the 86 patients with gustatory disturbance showed normal electrogustometry results and abnormal taste disc test results, indicating gustatory dissociation. Of these 21 patients, 11 had hemiplegia and 10 had quadriplegia. All but one of the 21 patients had bilateral gustatory disturbances.

Neuro-urology

Eighty-five patients underwent tests at the department of neuro-urology. The frequency of each complaint is shown in Table 4. Pollakiuria, urinary incontinence, and urinary urgency were the most common complaints.

Table 4. Incidence of individual impairments found in the 85 patients tested in the neuro-urology department

Impairment	Patients	Percentage
Pollakiuria	63	74%
Nocturia	21	25%
Urinary incontinence	52	61%
Terminal dribbling	26	31%
Urinary urgency	46	54%
Diminished sex drive	12	14%
Constipation	33	39%
Diarrhea	16	19%
Alternating constipation and diarrhea	16	19%
Fecal incontinence	12	14%

Eighty-four of the 85 patients (99%) were diagnosed as having neurogenic bladder (NB) by urodynamics study (UDS). Tests at the department of neuro-urology excluded the presence of NB in the remaining one patient. One patient had hydronephrosis due to NB. Only one of the patients with NB self-catheterized: the other patients passed urine without assistance. Some patients needed drug therapy.

UDS suggested that 16 of the 85 patients (19%) had complicating spinal cord injury. In thirteen of these patients, both brain and spinal cord injuries were suggested to be involved in the development of NB. In another three patients, NB was mainly derived from spinal cord injury: cervical spinal cord injury in two patients and sacral spinal cord injury in the third patient. The patient with complicating sacral spinal cord injury had marked sensory disturbance in the sacral segments.

Neurosurgery

All 106 patients were assessed by neuropsychological tests and multiple neuroimaging techniques at the same medical institution. The results of the neuropsychological tests are shown in Table 5. Memory disturbance and attention deficit disorder were common in patients with MTBI.

Table 5. Incidence of individual cognitive impairments found in the 106 patients tested in the neurosurgery department

Impairment	Patients	Percentage
Reduced cognitive ability	14	13%
Reduced intellectual ability	32	30%
Memory disturbance	85	80%
Attention deficit disorder	82	77%
Disorientation	41	39%
Executive dysfunction	46	43%
Reduced ability to manage own affairs	55	52%
Word finding difficulty	34	32%
No abnormal findings	1	1%

Table 6 shows the imaging-positive rates, independent of the timing of imaging, for each of the multiple neuroimaging techniques. MR tensor tractography, FA-SPM imaging, and FDG-PET showed relatively high individual imaging-positive rates. Only in one patient did all neuroimaging techniques give normal neuroimaging findings.

Table 6. Individual imaging-positive rate independent of the timing of imaging (total: 106 patients)

	No. of patients		Findings
MRI (3.0 Tesla)	7	7%	Diffuse cerebral atrophy
MR angiography	0		Traumatic changes in major cerebral arteries
MR tensor tractography	61	58%	Reduction in local axonal fibers
FA-SPM imaging	60	57%	Significant decrease in the regional FA values
FDG-PET	65	61%	Decrease in regional glucose metabolism suggestive of diffuse brain injury
ECD-SPECT: traumatic changes	8	8%	Decrease in regional blood flow suggestive of diffuse brain injury
ECD-SPECT: depression	61	58%	Decrease in regional blood flow suggestive of depression

Considering that organic brain injury may heal with time, patients were divided into two groups: 35 patients in whom neuroimaging was performed within 3 years of injury and 71 in whom neuroimaging was performed more than 3 years after injury. The imaging-positive rate for each neuroimaging technique was compared between the two groups. The results are shown in Table 7. According to the results, the individual imaging-positive rate for each neuroimaging technique was different depending on the timing of imaging. Normal MRI suggested the progression of cerebral atrophy over time. MR tensor tractography, FDG-PET, and ECD-SPECT (depression) showed a decrease in the imaging-positive rate over time.

Table 7. Imaging-positive rate for each neuroimaging technique

Imaging modality	Imaging-positive rate (%)	
	Imaging ≤ 3 years post-accident (n = 35)	Imaging > 3 years post-accident (n = 71)
MRI	3	8
MR angiography	0	0
MR tensor tractography	66	54
FA-SPM	54	58
FDG-PET	71	56
ECD-SPECT	6	8
Depression on ECD-SPECT	69	52

Our diagnostic criteria using multiple neuroimaging techniques

In the comprehensive assessment using multiple neuroimaging techniques employed in this study, if MRI (3.0 Tesla) revealed no abnormalities, organic brain injury was considered to be present when obvious abnormal findings typical of diffuse brain injury were obtained by two or more other neuroimaging techniques. According to this criterion, 49 of the 106 patients (46%) who were assessed by multiple neuroimaging techniques were considered to have organic brain injury. The diagnostic rate of organic brain injury in the MTBI patients was 57% [20/35 patients, 95% confidence interval (CI) 39%–74%] in the group that was assessed within 3 years of the injury and 41% (29/71 patients, 95% CI 29%–53%) in the group that was assessed more than 3 years after the injury; however, this difference was not statistically significant ($P = 0.114$, c^2 test (two-sided)).

Rehabilitation

At the department of rehabilitation, 71 patients underwent laryngography, electromy-

Mild Traumatic Brain Injury: Multidisciplinary Approach and Multiple Neuroimaging Techniques

ography, or neuropsychological tests, according to their symptoms. Laryngography revealed delayed initiation of the swallowing reflex in 23 patients (32%) and delayed laryngeal elevation and laryngeal penetration in 9 patients (13%). Three patients were diagnosed as having a cervical nerve root lesion and one as having a lumbar nerve root lesion by electromyography. In addition, one patient was diagnosed as having brachial plexus injury of the left arm and one as having bilateral carpal tunnel syndrome. Of the 66 patients who underwent neuropsychological tests, 64 (97%) were found to have cognitive impairment.

Psychiatry

Two of 106 patients (2%) were found to have generalized convulsive seizures. One of these two patients with grand-mal seizures had been in a pedestrian-car collision and the other had been in a motorcycle-car collision. Both patients had lost consciousness at the time of injury. These two patients developed grand-mal seizures 2 years 3 months and 2.5 years after the injury, respectively. One patient with temporal lobe epilepsy was involved in a car-car collision, lost consciousness briefly at the time of the injury, and developed transient attacks of impaired consciousness shortly after the injury. A definitive diagnosis was made by electroencephalography 3 years after the injury.

Discussion

In this study, there was often a long interval between injury and definitive diagnosis: the shortest and longest intervals were 1.5 months and 16.5 years, respectively, with a mean interval of 3.5 years. There are various possible reasons for such a delay in the definitive diagnosis. Patients with MTBI are not always aware that brain injury has occurred because of the rather mild disturbance of consciousness at the time of the injury. Therefore, hospital visits are often delayed (National Center for Injury Prevention and Control, 2003). In addition, even if patients visit the hospital soon after injury, clinical symptoms of MTBI may not have developed at that time. MTBI is neuropathologically characterized by traumatic axonal injury, and it takes time for all the clinical symptoms of MTBI to become manifest because heterogeneous degeneration and regeneration of the injured axons march in temporal progression. Therefore, at first contact, doctors often cannot grasp the subclinical signs and symptoms of MTBI that have not become overt yet, even after neurological diagnostic examination

(Povlishock and Coburn, 1987; Gaetz, 2004; Blumbergs et al., 2008). Consequently, patients with MTBI are often labeled as having whiplash injury or traumatic cervical syndrome. In general, damage of the neck structures predominates over brain damage in orthopedic interventions after whiplash injury (Spitzer et al., 1995). It is worth noting that rotational acceleration of the head with no major direct head impact was shown to produce brain damage in monkeys (Ommaya et al., 1968).

The multidisciplinary approach employed in this study is useful for the early diagnosis of MTBI because injury of the brain may manifest with a wide range of symptoms. For accurate diagnosis of MTBI using this approach, it is important to conduct careful medical interviews with patients and to accurately ascertain the nature of the disturbed consciousness that occurred between the injury and the hospital visit. This is because, although the GCS is useful for assessing disturbed consciousness when patients with MTBI visit the hospital, it does not reflect the disturbed consciousness state immediately after a head injury is sustained. Therefore, if the disturbed consciousness that was present immediately after the injury has resolved and the patient is fully alert at the time of the hospital visit, MTBI may be missed in the absence of a careful medical interview. Furthermore, if patients with MTBI suffer from post-traumatic amnesia, they may not be able to accurately remember the disturbed consciousness that was present immediately after the injury and therefore fail to report it (Ruff, 2003).

Mechanisms of injury

In Japan, accidents involving pedestrians, cyclists, and motorcyclists, who are all viewed as being more vulnerable in traffic accidents, are the second most common type after vehicle accidents involving rear-end car collisions. Victims of accidents involving pedestrians, bicycles, and motorcycles have mean GOS scores of 4.5, 4.4, and 4.1, respectively, and the mean degree of residual impairment is more severe in accidents involving motorcycles than in the 106 patients who were assessed in this study (mean GOS, 4.3).

In the current study, there was only one sports injury, but there are likely to be many cases of sports injury that result in latent brain damage. Overseas, the occurrence of MTBI in various sports has been reported (Bailes and Cantu, 2001). In Japan, if MTBI is more generally recognized, in the future, more patients with sports injury will likely visit hospitals.

Complications related to motor paralysis

One patient had deafferentation pain associated with motor paralysis (left leg pain associated with left hemiplegia). In one patient who already had complex regional pain syndrome (CRPS) before the accident that caused the MTBI, CRPS intensified after the accident and thumb-in-palm developed, resulting in the loss of hand function.

Neuro-ophthalmology

Based on the results of neuro-ophthalmological tests and neuroimaging studies, eight of the ten patients with visual loss were diagnosed as having psychogenic visual loss, and the other two as having idiopathic visual loss. Recently, the concept of “medically unexplained visual loss” was introduced, mainly in Europe, for psychogenic visual dysfunction developing in adults; the cause of such visual loss remains to be precisely delineated (Griffiths and Ali, 2009).

Because the pathology of concentric contraction of the visual fields is neurologically and neurosurgically “a state of long-term intracranial hypertension,” and because occipital lobe lesions alone cannot cause concentric contraction of the visual fields, brain images were examined in 15 patients with concentric contraction of the visual fields. The results revealed no findings suggestive of intracranial hypertension in these 15 patients, and MRI, SPECT, and PET showed no lesions in the occipital lobe.

In this study, 28 patients were found to have impaired smooth pursuit eye movements and 5 had impaired saccadic eye movements. The findings in these patients suggested impairment of the brainstem and cerebellar functions. In regard to impaired smooth pursuit eye movements and impaired saccadic eye movements, it has been reported that in whiplash injury, moderate eye movement disorders suggest impairment of the proprioceptors of the head and neck, and that severe eye movement disorders indicate impairment of the brainstem and cerebellar functions (Hildingsson et al., 1989). Also, in the present study, tests at the department of neuro-urology revealed complicating spinal cord injury in 16 patients; impaired smooth pursuit/saccadic eye movements in head and neck trauma should be extensively investigated from the standpoint of injuries of the brain, spinal cord, and soft tissues around the cervical spine.

Neuro-otology

It has been reported that traumatic olfactory disturbance is associated with frontal lobe contusion on images in some patients and that this disturbance is common in severe head injury patients with severely disturbed consciousness. On the other hand, it has been reported that many patients with no MRI abnormalities have severe olfactory disturbance or anosmia. In the present study, all 106 MTBI patients had GCS scores in the range 13–15, indicating the absence of severely disturbed consciousness; however, olfactory disturbances were found at a high frequency (71/106 patients, 67%).

It is considered that traumatic gustatory disturbances are rare compared to traumatic olfactory disturbances, which occur at a high incidence. However, in the present study, traumatic gustatory disturbances were observed at a high frequency (86/106 patients, 81%). Of these 86 patients, 8 (9%) had unilateral gustatory disturbances, 78 (91%) had bilateral gustatory disturbances, and 21 (24%) showed gustatory dissociation.

In regard to the relationship between traumatic olfactory disturbances and traumatic gustatory disturbances, 65 of 106 patients (61%) had both olfactory and gustatory disturbances, this incidence being much higher than that of traumatic olfactory disturbances alone (8 patients; 8%) and of traumatic gustatory disturbances alone (22 patients; 21%). There are two hypotheses concerning patients with both olfactory and gustatory disturbances: one is that the olfactory and gustatory neural pathways are independently impaired, resulting in the coexistence of these impairments; the other is that, assuming the presence of a high-level center in the orbitofrontal area in which sensory inputs, such as olfactory, gustatory, visual and somatosensory inputs, converge and information is integrated, injuries in this area would cause both olfactory and gustatory disturbances (Soma and Kunihiro, 2012).

Olfactory and gustatory dissociation observed in olfactory and gustatory disturbances is considered to be caused by olfactory and gustatory identification deficits in the cortical olfactory and gustatory centers, respectively, of the brain. Overseas, screening tests of olfactory function have long been performed, because olfactory identification deficits are defined as an initial symptom of Alzheimer's disease.

It is thought that patients with sensorineural hearing loss who have normal ABR and have been diagnosed with functional hearing loss are not malingering, and

Mild Traumatic Brain Injury: Multidisciplinary Approach and Multiple Neuroimaging Techniques
that the symptoms are psychogenic or caused by attention deficits.

Neuro-urology

In one previous report, neuro-urological problems in patients with MTBI were perceived as sexuality problems, i.e., loss of libido or diminished sexual drive (Stoler and Hill, 1997). In the present study, the problem of neurogenic bladder (NB) in MTBI was investigated in detail by UDS. The results revealed a variety of abnormal findings of bladder sensation, detrusor function, and sphincter function, such as increased or reduced bladder sensation, abnormal detrusor activity (i.e., detrusor hyperreflexia, weak detrusor, or detrusor contraction after urination), abnormalities of the external urethral sphincter (i.e., uninhibited sphincter relaxation [UIR], sphincter activity to accelerate flow, detrusor sphincter dyssynergia [DSD]), and detrusor-bladder neck dyssynergia in MTBI patients with NB. At the same time, mechanisms to improve urination were found to function in MTBI patients with NB. In addition, the above abnormal findings were associated with neuro-urological complaints.

For example, weak detrusor activity is one of the causes of increased residual urine. Detrusor hyperreflexia leads to an increase in intravesical pressure in a manner like autonomous contraction, causing hydronephrosis. Uninhibited contraction (UIC) of the detrusor muscle leads to urgent urinary incontinence. Detrusor contraction after urination leads to a sense of incomplete urination and terminal dribbling.

UIR causes sudden urinary incontinence. DSD during detrusor contraction causes subjective dysuria at the start of urination and interruption of the urinary stream midway during urination. Sudden UIC and sudden UIR can lead to bladder hypersensitivity.

Hyperextension of the neck

Forensic medical experts have reported, based on judicial autopsy results, that if the cervical spine is forced to bend backward beyond the physiological tolerance in traffic accidents, the brain stem or the spinal cord will be transected (Simpson et al., 1989; Hiraiwa et al., 2004). In addition, according to another report, the cervical spine will extend by as much as 5 cm, if forced to bend forward (Oosterveld et al., 1991). From these reports, it is speculated that if excessive acceleration or deceleration energy is kinesiologically loaded to the head in the anteroposterior direction, sudden death occurs in some individuals, and others will have traumatic axonal injury in the brain

parenchyma as well as cervical spinal cord injury or cervical soft-tissue injury.

Neurosurgery

According to a previous report in which MTBI was evaluated using neuroimaging techniques, the imaging-positive rate is not necessarily high (Belanger et al., 2007). Based on this finding, to improve the diagnostic rate of MTBI by neuroimaging techniques, structural neuroimaging modalities, such as MRI (Nakayama et al., 2006; Wada et al., 2012), and functional neuroimaging modalities, such as FDG-PET, were combined in the present study. The diagnostic rate of organic brain injury in the cases of MTBI in the present study was 57% (95% CI 39%–74%) in patients who were assessed within 3 years of the injury and 41% (95% CI 29%–53%) in patients who were assessed more than 3 years after the injury. Thus, the imaging-diagnostic rate was numerically higher in patients who were assessed within 3 years of the injury, but the difference was not statistically significant ($P = 0.114$). The overall imaging-diagnostic rate was 46%. In the field of neuroimaging diagnostics, the various structural and functional neuroimaging methods that were selected for this study were applied to the diagnosis of MTBI, although the individual diagnostic neuroimaging methods have not been perfected yet. Under such circumstances, the multidisciplinary approach is considered to be helpful for the definitive diagnosis of MTBI (Ishibashi, 2009).

Acknowledgements

We sincerely thank Hisao Ohde, MD, of the Department of Ophthalmology, Keio University School of Medicine, for performing the tests in his respective fields.

Funding No competing financial interests exist.

◆ References

- American Congress of Rehabilitation Medicine. Definition of mild traumatic brain injury. *J Head Trauma Rehabil* 1993; 8: 86-7.
- Bailes JE, Cantu RC. Head injury in athletes. *Neurosurgery* 2001; 48: 26-46.
- Belanger HG, Vanderploeg RD, Curtiss G, Warden DL. Recent neuroimaging techniques in mild traumatic brain injury. *J Neuropsychiatry Clin Neurosci* 2007; 19: 5-20.
- Blumbergs P, Rilly P, Vink R. Trauma. In: Love S, Louis DN, Ellison DW, editors. *Greenfield's neuropathology*. 8th ed. London: Hodder Arnold; 2008. p. 733-812.
- Carroll LJ, Cassidy JD, Holm L, Kraus J, Coronado, VG: WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. Methodological issues and research recommendations for mild traumatic brain injury: the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. *J Rehabil Med* 2004; 43 (Suppl): 113-25.
- Department of Health and Human Services. Traumatic Brain Injury ACT of 2008: Overview. [Internet] [cited 2014 Oct 6] Available from: www.bianys.org/_literature_116303/Fed_TBI_act_overview. 2013.
- Gaetz M. The neurophysiology of brain injury. *Clin Neurophysiol* 2004; 115: 4-18.
- Griffiths PG, Ali N. Medically unexplained visual loss in adult patients. *Curr Opin Neurol* 2009; 22: 41-5.
- Hildingsson C, Wenngren BI, Bring G, Toolanen G. Oculomotor problems after cervical spine injury. *Acta Orthop Scand* 1989; 60: 513-6.
- Hiraiwa K, Sato T, Sasaki T, Kodama N. [Head injury: forensic medicine of traumatic verte-brobasilar arterial injury]. *Practical Currently* 2004; 14: 793-800. Japanese.
- Ishibashi T. [Mild traumatic brain injury]. Tokyo: Kanehara; 2009. Japanese.
- Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet* 1975; 1: 480-4.
- Nakayama N, Okumura A, Shinoda J, Yasokawa YT, Miwa K, Yoshimura SI, et al. Evidence for white matter disruption in traumatic brain injury without macroscopic lesions. *J Neurol Neurosurg Psychiatry* 2006; 77: 850-5.
- National Center for Injury Prevention and Control. Report to Congress on mild traumatic brain injury in the United States: steps to prevent a serious public health problem. Atlanta: Centers for Disease Control and Prevention; 2003. p. 1-45.
- National Institutes of Health. Rehabilitation of persons with traumatic brain injury. NIH Consensus Statement 1998; 16: 1-41.
- Ommaya AK, Faas F, Yarnell P. Whiplash injury and brain damage: an experimental study. *JAMA* 1968; 204: 285-289.
- Oosterveld WJ, Kortschot HW, Kingma GG, de Jong HA, Saatci MR. Electronystagmographic findings following cervical whiplash injuries. *Acta Otolaryngol* 1991; 111: 201-5.
- Povlishock JT, Coburn TH. Morphopathological change associated with mild head injury. In: *Mild head injury*. Levin HS, Eisenberg HM, Benton AL, editors. New York: Oxford University Press; 1987. p. 37-53.
- Ruff R. Sequelae of traumatic brain injury. In: Winn RH, editor. *Youmans neurological surgery*. 5th ed. Philadelphia: Saunders; 2003. p. 5181-201.

- Simpson DA, Blumbergs PC, Cooter RD, Kilminster M, McLean AJ, Scott G. Pontomedullary tears and other gross brainstem injuries after vehicular accidents. *J Trauma* 1989; 29: 1519-25.
- Soma K, Kunihiro T. [Smell and taste disorders after a traffic accident]. *Pract Otol (Kyoto)* 2012; 105: 1091-1100. Japanese.
- Spitzer WO, Skovron ML, Salmi LR, Cassidy JD, Duranceau J, Suissa S, et al. Scientific monograph of the Quebec Task Force on Whiplash-Associated Disorders: redefining "whiplash" and its management. *Spine (Phila Pa 1976)* 1995; 20: 1S-73S.
- Stoler DR, Hill BA. Sexuality. In: *Coping with mild traumatic brain injury*. New York: Avery; 1997. p. 79-87.
- Tagliaferri F, Compagnone C, Korsic M, Servadei F, Kraus J. A systematic review of brain injury epidemiology in Europe. *Acta Neurochir (Wien)* 2006; 148: 255-68.
- Teasdale G, Jennett B. Assessment of coma and impaired consciousness. A practical scale. *Lancet* 1974; 2: 81-4.
- United States Congress House Committee on Commerce. *Traumatic Brain Injury Act of 1996: report (to accompany H.R. 248)*. USA. 1996.
- Vos PE, Battistin L, Birbamer G, Gerstenbrand F, Potapov A, Prevec T, et al.: European Federation of Neurological Societies. EFNS guideline on mild traumatic brain injury: report of an EFNS task force. *Eur J Neurol* 2002; 9: 207-19.
- Wada T, Asano Y, Shinoda J. Decreased fractional anisotropy evaluated using tract-based spatial statistics and correlated with cognitive dysfunction in patients with mild traumatic brain injury in the chronic stage. *AJNR Am J Neuroradiol* 2012; 33: 2117-22.
- World Health Organization. *Traumatic brain injuries*. In: *Neurological disorders: public health challenges*. Geneva: World Health Organization; 2007. p. 164-75.

