Structural and functional neuroimaging in mild-to-moderate head injury

Zwany Metting, Lars A Rödiger, Jacques De Keyser, Joukje van der Naalt

Head injury is a major cause of disability and death in adults. Significant developments in imaging techniques have contributed to the knowledge of the pathophysiology of head injury. Although extensive research is available on severe head injury, less is known about mild-to-moderate head injury despite the fact that most patients sustain this type of injury. In this review, we focus on structural and functional imaging techniques in patients with mild-to-moderate head injury. We discuss CT and MRI, including different MRI sequences, single photon emission computed tomography, perfusion-weighted MRI, perfusion CT, PET, magnetic resonance spectroscopy, functional MRI and magnetic encephalography. We outline the advantages and limitations of these various techniques in the contexts of the initial assessment and identification of brain abnormalities and the prediction of outcome.

Introduction

Head injury is a leading cause of disability and death in adults, and most patients (85–95%) are classified as having mild-to-moderate head injury.1–5 Most of these patients recover within weeks to months without specific therapy. However, a subgroup continues to experience disabling symptoms that interfere with their return to work or resumption of social activities.6–10 The burden of these symptoms is not only personal but also socioeconomic, as they are most common in young patients in their 20s and 30s with full occupational status. It is of paramount importance to identify those patients who are prone to develop cognitive disability to promote early rehabilitation.11–15

In recent decades, major advances in the development of imaging techniques have contributed to the knowledge of the pathophysiology of head injury. The capabilities of structural imaging have been expanded by various techniques suitable for visualising haemodynamic and metabolic changes in the brain. Concurrently, the treatment of patients with trauma is increasingly guided by the rapid assessment of primary damage and prevention of further deterioration. Hence, selection of the technique most valuable in guiding management during the acute phase of injury is essential, as is the assessment of the additional value of the technique in predicting outcome.

In this article, we present an overview of the current imaging techniques in terms of their ability to reveal structural or functional brain abnormalities in patients with head injury. We focus on patients with mild-to-moderate head injury, defined by a Glasgow coma score of more than 8, as most patients sustain this type of head injury and, in contrast to severe head injury, scarce information is available on this topic. As some extensive reviews of imaging studies in children are already available, this review focuses on studies of mild-to-moderate head injury in adults.16–18 We discuss advantages and limitations of various techniques with regard to the initial assessment and identification of brain abnormalities and their role in the prediction of outcome.

Structural imaging

In traumatic brain injury, the mechanism of damage can be classified as primary and secondary. In general, structural imaging techniques are used to visualise primary brain injury. Primary brain injury occurs at the moment of impact, with diffuse axonal injury being the most important primary lesion.1,5–7,19 Diffuse axonal injury is a consistent finding in mild, moderate, and severe traumatic head injury, although the severity increases with that of the head injury.20–22 Primary brain injury also comprises focal abnormalities, such as contusions and haematomas, as a result of either direct external contact forces or from the movement of the brain within the skull.22,23 Secondary brain injury, on the other hand, develops within hours after impact as a result of primary injury and mainly consists of ischaemia;24–26 this is best visualised using functional imaging. In the emergency setting, clinical management is guided by the imaging of structural abnormalities requiring acute interventions. During follow-up, structural imaging techniques are most commonly used to explain post-concussional symptoms or to predict outcome. Structural imaging techniques in patients include CT and MRI.

CT

CT is one of the first developed and most commonly applied imaging techniques in the acute phase of head injury and can be used to detect haemorrhage, parenchymal injury, and skull fractures. CT is the most relevant imaging procedure for the detection of lesions eligible for surgical intervention, as it is rapidly and easily done, even in agitated patients.15,27–29

For mild and moderate head injury, there is no agreement about routine CT scanning. There is substantial variation among institutions in the ordering of CT for patients with mild head injury, ranging from 16% to 74%.29 When all patients with mild-to-moderate head injury are scanned, the incidence of abnormal findings is about 15%, increasing to 50% when a CT scan is done in only those patients with neurological symptoms.29 However, absence of focal neurological abnormalities on physical examination does not rule out...
CT abnormalities. Since the introduction of the UK National Institute for Health and Clinical Excellence guidelines for management of head injury, the use of CT has substantially increased, and the reported incidence of intracranial abnormalities is about 10%. A low Glasgow coma scale, the presence of a skull fracture, old age, and focal neurological signs are associated with a higher incidence of abnormal CT findings in patients with mild head injury. The overall sensitivity of CT to abnormalities in acute head trauma is 63–75%. In patients with mild-to-moderate head injury, oedema or lesions on CT are related to problems with resumption of work. Also, the presence of subarachnoid blood on CT is a significant predictor of outcome. Contusions in frontal and temporal lobes, when present on CT, result in relevant deficits in outcome caused by behavioural and cognitive problems. Lesion size is inversely associated with outcome. Furthermore, about 20% of patients who sustain mild-to-moderate head injury without abnormalities on the admission CT have problems with resuming work, suggesting that the conventional CT scan has limited ability in detecting structural and functional abnormalities.

MRI

T1, T2, FLAIR, and T2*-weighted gradient recalled echo MRI is the technique of choice in the subacute phase of head injury and during follow-up. The difficulty of using MRI to evaluate skull fractures, the limitations in monitoring patients during MRI, and the susceptibility to motion artefacts related to the relatively long exposure time discourage the use of this technique in the acute phase of head injury. Although in earlier studies MRI was inferior to CT in the detection of parenchymal and subarachnoid haemorrhages, MRI is now as reliable as CT in detecting these haemorrhages in the acute phase because of improvements in MRI techniques. Moreover, MRI is more sensitive than CT in detecting diffuse axonal injury and non-haemorrhagic contusions, especially in the frontal and temporal regions at the base of the skull. MRI is also more sensitive in detecting small subdural haematomas (figure 1) and brainstem injury. A third of patients with mild-to-moderate head injury have focal atrophy in the frontal and temporal regions on MRI in the chronic phase, which is predictive of outcome. In addition to whole brain atrophy, the number, size, and depth of lesions are also associated with the degree of unconsciousness and outcome. Serial MRI scanning showed a resolution of lesions as well as simultaneous improvement on neuropsychological testing. In one of four patients good recovery is observed despite the presence of lesions on MRI scanning. However, about 15% of patients with a normal MRI have a suboptimal outcome and problems with resumption of work. Because there are some inconsistencies about lesions and outcome, consideration of whether the appropriate imaging sequences have been selected is important.

For years, T1-weighted and T2-weighted spin-echo and fluid-attenuated inversion recovery (FLAIR)-weighted sequences were the most commonly used MRI sequences in head injury. T2-weighted spin-echo sequences seem to be more sensitive in detecting contusions compared with T1-weighted spin-echo sequences. The sensitivity of

Figure 1: Subacute subdural haematoma
A 33-year-old woman who was involved in a car accident. Her initial Glasgow coma score was 11. Non-contrast CT on admission showed a doubtful hyperdense ridge over the right frontal lobe (A). FLAIR-weighted MRI sequences on day 15 after trauma revealed a subdural haematoma in this area (B). Her clinical condition remained stable.

Figure 2: Diffuse axonal injury on MRI during follow-up
Top: a 31-year-old man who was involved in a motor cycle accident. His initial Glasgow coma score was 13. Non-contrast CT on admission showed no abnormalities (A). MRI was obtained 6 weeks after trauma. MRI T2-weighted spin-echo sequences revealed no obvious abnormalities (B), whereas T2*-weighted gradient-recalled echo (GRE) images showed a hypointense lesion in the corpus callosum suggestive of diffuse axonal injury (C). Bottom: a 23-year-old woman after a bicycle accident. Her initial Glasgow coma score was 12. Non-contrast CT on admission showed one small haemorrhagic lesion in the right frontal lobe (D). MRI was obtained 7 weeks after trauma. T2-weighted spin-echo sequences (E) revealed no lesions, whereas T2*-GRE-weighted sequences (F) revealed multiple hypointense lesions in the frontal lobes extending into the corpus callosum, suggestive of diffuse axonal injury.
FLAIR-weighted sequences is the same as or better than T2-weighted spin-echo sequences in the assessment of traumatic lesions.64 In the acute stage, FLAIR-weighted sequences are used for the detection of diffuse axonal injury, oedema, and haemorrhage whereas in the subacute and chronic stages FLAIR-weighted sequences are mainly used for the detection of gliosis.65 Although about 80% of diffuse axonal injury lesions were thought to be non-haemorrhagic in nature, improved MRI techniques indicate that the proportion of haemorrhagic diffuse axonal injury lesions is in fact much greater than previously thought.

T2-weighted gradient-recalled echo sequences enable visualisation of haemosiderin deposits as a result of haemorrhage, possibly due to diffuse axonal injury.55,56 T2-weighted gradient-recalled echo imaging is better than T1-weighted and T2-weighted spin-echo sequences in the detection of traumatic lesions (figure 2).56,57 In a study of patients with head injury of varying severity, the number of lesions on T2-weighted gradient-recalled echo sequences was positively correlated with outcome, whereas on T2-weighted imaging it was not.56 In patients with mild head injury, there is a relation between MRI abnormalities detected within 72 h of injury and neuropsychological deficits.58,59 However, there was no relation between these imaging findings and return to work or postconcussive symptoms,58 although slower reaction times were detected.60

Susceptibility-weighted imaging is the most recently developed MRI technique and has high sensitivity for haemosiderin.61 Although further research is needed, the sensitivity of susceptibility-weighted imaging for the detection of haemorrhagic lesions in patients with traumatic head injury is probably higher than that of T2-weighted gradient-recalled echo sequences (figure 3).62

In general, for the detection of post-traumatic abnormalities within 1–3 months of injury, MRI is preferred, on the condition that appropriate MRI imaging sequences are used.63

**Diffusion-weighted imaging**

Diffusion-weighted imaging is another MRI modality that is primarily used to detect vasogenic or cytotoxic oedema. This technique is sensitive to the random movement of water molecules and can distinguish between lesions with increased and restricted diffusion in patients with head injury. The apparent diffusion coefficient can be calculated and used to quantify the degree of restriction of water molecules caused by head injury. Diffusion-weighted imaging is widely used in cerebral ischaemic stroke, showing changes before the onset of visible abnormalities seen on conventional imaging.64-66 In a few studies comprising mild head injury, diffusion abnormalities were seen within days of injury.67-69 In severe head injury, diffusion-weighted imaging can be used to identify diffuse axonal injury as hyperintense lesions that are not visible on T2-weighted spin-echo, T2*-weighted gradient-recalled echo, or FLAIR sequences. Most of these diffuse axonal injury lesions show decreased diffusion probably due to cytotoxic oedema within days67 to weeks of injury.68,69 Although cytotoxic oedema predominates in head injury, there is high diffusion in the acute phase, probably due to vasogenic oedema.64,65 Diffusion-weighted imaging is less sensitive than T2-weighted gradient-recalled echo images for detecting haemorrhagic diffuse axonal injury lesions.67 However, the volume of lesions depicted with diffusion-weighted imaging shows a stronger correlation with clinical outcome in patients with head injury than FLAIR, T2-weighted spin-echo, or T2*-weighted gradient-recalled-echo sequences.70

**Diffusion tensor imaging**

A relatively new MRI technique, diffusion tensor imaging is an extension of diffusion-weighted imaging that allows the reconstruction of white matter tracts in the CNS.71-75 The advantage of diffusion tensor imaging is that it can be used to visualise axonal injury, the major pathological substrate of traumatic brain injury. This technique measures the degree and directionality of water diffusion. Water diffusion in tissue is modified by its structural environment, and in white matter, diffusion is greatest along fibre tracts parallel to the myelin sheaths. With diffusion tensor imaging, the mean diffusivity and fractional anisotropy can be determined; both parameters are measures of axonal integrity. Diffusion tensor imaging allows the reconstruction of the diffusion direction, generating colour maps that reveal the location and orientation of major white matter fibre tracts in the CNS.75-77

In patients with mild head injury, diffusion tensor imaging in the acute phase showed reduced fractional anisotropy in the normal appearing white matter, predominantly in the internal capsule and corpus callosum, most likely as a consequence of diffuse axonal injury.78 This pattern was also seen days to years after...
mild head injury. Of interest here is that the brains of asymptomatic professional boxers revealed comparable changes. The degree of these water diffusion abnormalities is correlated with the acute Glasgow coma score and the Rankin score at discharge. Moreover, reduced fractional anisotropy in the splenium is related to cognitive dysfunction more than 1 year after injury. Thus far, there have been inconsistent findings about diffusivity in head injury, probably related to differing pathophysiological processes that are thought to evolve over time. Restricted diffusivity was observed within the splenium and in the periphery of focal lesions, without any associated increase in T2-weighted signal intensity. In chronic head injury survivors, however, there was a positive correlation between increased diffusivity in widespread areas of the cerebral cortex and learning and memory problems. Diffusion tensor imaging provides a powerful non-invasive tool to study complex brain tissue architecture. With recent improvements in hardware, diffusion tensor imaging acquisition and calculation times have been reduced to allow complete brain coverage and visualisation in colour maps of white matter tracts in a clinically acceptable period. More experience in diffusion tensor imaging is needed, both for research and clinical applications.

In summary, structural imaging techniques, such as conventional CT and MRI, depict primary traumatic brain injury. The timing of imaging is important as information provided by CT imaging is most appropriate early in the course of injury and MRI methods are more helpful in the recovery phase. However, conventional CT and MRI have a limited negative predictive value, as the absence of abnormalities is no guarantee of optimum outcome. The first results of MRI modalities based on diffusion methods, such as diffusion-weighted imaging and diffusion tensor imaging, in head injury are promising. As diffusion-based methods indirectly rely on the energy status of the cells, these techniques could provide information on secondary injury. Further investigation is needed, especially in patients with mild-to-moderate head injury. Because conventional CT and MRI cannot show functional cerebral changes and therefore secondary brain injury, functional imaging techniques might be of more value in predicting outcome.

Functional imaging

Functional imaging techniques are used to measure haemodynamic or metabolic changes in the brain, mainly in the subacute phase of injury when secondary injury is developing. Secondary brain damage mainly consists of ischaemia and is present in more than 80% of fatal cases of head injury. Even in monitored patients, ischaemic damage occurs. In a series of patients with differing severity of head injury, 92% had one or more ischaemic insults lasting for at least 5 min, despite being monitored in a well equipped intensive-care unit.

Functional imaging studies include haemodynamic imaging such as single photon emission computed tomography (SPECT) and PET, although the latter technique also provides information on the metabolic status of the brain. Although xenon-CT was one of the first techniques used to examine perfusion in patients with head injury, information is available mainly on severe head injury and as such is not relevant to this review. Imaging techniques such as perfusion MRI and perfusion CT are described, in which haemodynamic imaging is added to a modality originally used for structural imaging, thereby expanding the possibilities for the visualisation of brain abnormalities. Advanced MRI techniques such as functional MRI and magnetic resonance spectroscopy (MRS) provide information on the metabolic state of the brain with the former combining the accuracy of MRI with information on activation patterns of localised brain functions and the latter providing information on the metabolic state of the brain.

SPECT

SPECT is a procedure that provides an indirect indicator of brain metabolism by measuring cerebral blood flow. Several radiotracers are available, with 99mTc-hexamethylpropyleneamine oxide (HMPAO) being the most common. In 40–70% of patients with mild-to-moderate head injury, abnormal SPECT findings are observed, especially within the first 3 months of injury. Most of these patients have areas of hypoperfusion, predominantly located in their frontal and temporal lobes, basal ganglia, and thalami. Hypoperfusion seen on SPECT imaging correlates with...
the duration of post-traumatic amnesia after mild head injury (figure 4). Also, hypoperfusion on SPECT imaging is shown to be correlated with loss of consciousness and postconcussional syndrome. In symptomatic patients with long-standing mild traumatic head injury and unremarkable structural brain imaging, reduced CBF is seen on SPECT imaging, concordant with neuropsychological testing. A negative initial SPECT study is a reliable predictor of a favourable clinical outcome at 3 months after mild head injury.

In general, HMPAO SPECT seems to be more sensitive than CT or MRI in the detection of brain abnormalities in patients with mild-to-moderate head injury, with a larger area of involvement on SPECT than on CT. However, the greater number of articles describing the use of SPECT than any other technique in mild traumatic brain injury does not indicate that it is more sensitive, because its application is still limited by its poor resolution, radiation exposure, and difficulty in obtaining quantitative data.

**Perfusion MRI**

Perfusion-weighted imaging, in which haemodynamically weighted MRI sequences are based on the passage of a contrast agent through the brain, is sensitive to microscopic tissue-level changes in cerebral blood volume, and parameters like cerebral blood volume, mean transit time, and cerebral blood flow can also be obtained. Garnett and colleagues did a perfusion MRI study in the subacute phase of head injury and found low cerebral blood volume in regions of focal pathology in patients with contusions and oedema visible on conventional MRI. In addition, there was one group of patients who had reduced cerebral blood volume in a normal-appearing brain. These patients had a significantly worse clinical outcome than patients without abnormalities on perfusion MRI. Furthermore, these measurements were present on average 10 days after the injury, implying that delayed changes in haemodynamic parameters, and not just acute changes, may be involved in determining clinical outcome.

An important limitation of this technique is that quantification remains difficult, together with limited application in the emergency setting. Furthermore, the use of a contrast agent is needed, unless the more recently developed spin-labelling technique is used.

**Perfusion CT**

Perfusion CT data are obtained by monitoring the first pass of an iodinated contrast agent bolus through cerebral vasculature. Investigators can then parameter maps of cerebral blood volume, mean transit time, and cerebral blood flow (figure 5), and the use of regions of interest allows quantification of perfusion in the brain. In recent years, the broad introduction of fast multidetector CT systems and the development of commercially available software for perfusion analysis have facilitated the application of cerebral perfusion imaging in the clinical setting.

After first being used in patients with stroke, this technique is gradually being used in those with head injury. Perfusion CT features specific patterns in the acute phase related to outcome in patients with severe head injury. Normal brain perfusion or hyperaemia is seen in patients with favourable outcome and oligaemia is seen in patients with unfavourable outcome. Perfusion CT is more sensitive than conventional unenhanced CT in the detection of cerebral contusions, featured as areas with lowered cerebral blood flow and cerebral blood volume and increased mean transit time. Also, in the first study of head injury in children and in patients with mild-to-moderate head injury, there were comparable abnormalities. Perfusion CT values of cerebral blood volume were lower in the immediate vicinity of epidural or subdural haematoma. Apart from advantages such as low exposure time and 24 h availability in most hospitals, use is limited by partial brain coverage and radiation exposure. The promising potential of perfusion CT in the detection of secondary ischaemic changes in the acute phase of head injury is unproven in mild-to-moderate head injury.

**PET**

Several studies have investigated the use of PET for the assessment of patients with head trauma. PET provides tomographic images of quantitative parameters describing various features of brain haemodynamics, including cerebral blood flow, cerebral blood volume, oxygen extraction fraction, and cerebral metabolic rate of oxygen. The most frequently used PET tracer is fluorine-18 labelled fluorodeoxyglucose (FDG) for the detection of regional glucose consumption.

PET studies generally show cerebral dysfunction beyond the structural abnormalities demonstrated by CT and MRI. About a third of these anatomical lesions are associated with more widespread metabolic abnormalities,
and as much as 42% of PET abnormalities were not associated with any anatomical lesions.\textsuperscript{107} Epidural and acute subdural haematomas cause extensive reduction in metabolism in both the involved adjacent cortex and the corresponding contralateral cortex. Diffuse axonal injury causes widespread hypometabolism, predominantly in the parieto-occipital cortex.\textsuperscript{104,107} The period of metabolic reduction typically persists for several weeks regardless of injury severity.\textsuperscript{108}

In the chronic phase after mild head injury, there are inconsistencies in PET findings varying from regional hypometabolism to global hypermetabolism.\textsuperscript{105,111} Chen and colleagues\textsuperscript{112} found no difference in cerebral FDG uptake between patients with mild head injury and controls in the resting state.\textsuperscript{102} In patients with mild-to-moderate head injury with postconcussive symptoms there is a correlation between complaints and the number of PET metabolic abnormalities, although both hypometabolism and hypermetabolism were seen in the same regions across different patients with mild head injury.\textsuperscript{101} In patients with mild head injury and postconcussive symptoms, a high incidence of temporal lobe injury is visible on FDG-PET,\textsuperscript{111} with a good association between PET abnormalities and neuropsychological assessment.\textsuperscript{104,105,114} Global and regional metabolic rates improve as patients clinically recover from head trauma.\textsuperscript{104,106,107}

Besides glucose metabolism, information from PET imaging of cerebral blood flow in patients with head injury is also obtained with oxygen-15 labelled $H_2O$, CO, and $O_2$ tracers. Information on patients with mild or moderate head injury is scarce. Coles and colleagues\textsuperscript{115} showed that a large ischaemic brain volume was associated with a poor outcome as measured with the Glasgow outcome score 6 months after injury. In addition, a PET study of patients with moderate-to-severe head injury revealed the use of altered functional neuroanatomical networks when performing memory tasks,\textsuperscript{116} whereas patients with mild head injury had a small increase in cerebral blood flow in the right prefrontal cortex, compared with that in healthy people, during a memory task.\textsuperscript{112}

Although quantitative data can be obtained with PET and it offers a better resolution than SPECT, the application of this technique is limited by radiation exposure and scarce availability due to high costs. It is mainly used as a research tool in a non-emergency setting.

MRS

MRS offers a unique approach for assessing the metabolic status of the brain in vivo. In particular, this technique provides a non-invasive means for quantifying numerous metabolites such as N-acetyl aspartate, creatine, choline, and lactate.\textsuperscript{111} Of particular importance is N-acetyl aspartate, because it is considered a marker of neuronal injury or loss. N-acetyl aspartate is found to be decreased in cerebral contusions\textsuperscript{118} and in the corpus callosum.\textsuperscript{119} N-acetyl aspartate concentrations in grey matter were predictive of overall neuropsychological ability in patients with moderate-to-severe head injury.\textsuperscript{101} Moreover, a N-acetyl aspartate/choline ratio is related to injury severity and outcome even when white matter appears normal on MRI (figure 6).\textsuperscript{121,122} Son and colleagues\textsuperscript{123} showed that in patients with mild head injury the N-acetyl aspartate/creatine ratio was low in areas of pericontusional oedema. Moreover, the lactate/creatine ratios were high.

Figure 6: Magnetic resonance spectroscopy

A 19-year-old female who was involved in a motor vehicle accident. Her initial Glasgow coma score was 11. Early MRI (ie, 18 days after injury) showed no abnormalities, whereas magnetic resonance spectroscopy showed a low N-acetyl aspartate/creatine ratio and a high choline/creatine ratio compared with a healthy person. At the late study (ie, 8.1 months after injury), conventional MRI remained unremarkable with a further decrease in the N-acetyl aspartate/creatine ratio compared with that in the early study. Reproduced with permission from Oxford Journals.\textsuperscript{111}
in these areas, suggestive of ischaemic damage.\textsuperscript{121} Patients with good recovery, as measured with the Glasgow outcome score, have high N-acetyl aspartate/creatinine ratios.\textsuperscript{124} Despite these positive results, other researchers have found no associations between metabolic ratios and outcome at 6 months in individuals with mild head injury.\textsuperscript{131}

Choline, a marker for cell membrane disruption and inflammation, was high in the normal-appearing frontal white matter,\textsuperscript{121,122} grey matter,\textsuperscript{120,122} and parieto-occipital white matter.\textsuperscript{124} Friedman and colleagues\textsuperscript{126} showed that increased choline concentrations in grey matter were not related to neuropsychological outcome at 6 months postinjury,\textsuperscript{125} contrary to another MRS study that revealed that a high choline concentration in both white and grey matter at 3 months after injury was significantly related to poorer outcome.\textsuperscript{127}

Although MRS provides a rapid way to assess in vivo brain composition, the interpretation of results is hindered by reliance upon ratios in various brain regions. Furthermore, the technique has a poor resolution and only partial brain coverage, and its use is limited in the acute phase of head injury.

**Functional MRI**

Functional MRI is a non-invasive technique in which blood-oxygen changes serve as an endogenous contrast agent. Most current functional MRI studies are based on the blood-oxygen-level-dependent (BOLD) method, in which the signal is derived from local changes in the ratio of deoxygenated to oxygenated haemoglobin that accompany neuronal events. Deoxyhaemoglobin and oxyhaemoglobin differ in their magnetic properties, so the changes in their relative proportions result in a temporary change in the magnetic resonance signal of the target region relative to surrounding tissue.\textsuperscript{128}

Functional MRI is a promising technique because it combines the anatomical precision of MRI with functional information. Activation of brain regions involved in a particular language or cognitive task can be mapped, thereby increasing our knowledge of neuropsychological dysfunction. To date, standardised imaging protocols for functional MRI have been developed mainly for the assessment and visualisation of brain regions involved in cognition and behaviour. In severe head injury, functional MRI displays a more regionally dispersed pattern of cerebral activation, lateralised to the right hemisphere.\textsuperscript{122,125}

In a study on head injuries of varying severity, there were changes in brain activation, suggesting that altered neural networks mediate cognitive control after head injury, possibly as a result of diffuse axonal injury.\textsuperscript{129} In patients with pure diffuse axonal injury, compensatory activation of the prefrontal region was seen in comparison to healthy controls.\textsuperscript{122}

McAllister and colleagues\textsuperscript{133} used functional MRI in patients with mild-to-moderate head injury to probe working memory function (ie, the ability to retain information and to manipulate it in reaction to newly incoming material) within about 1 month of injury\textsuperscript{135} and in some cases 1 year later.\textsuperscript{134} Patients with head injury differed from control individuals in the activation pattern of working memory circuitry, with significantly higher activation on functional MRI during moderate working memory load conditions, especially in the parietal and prefrontal regions. Task performance did not differ between patients and controls, suggesting that injury-related changes to modulating working memory might underlie some of the memory complaints after mild head injury.\textsuperscript{128,133,134} In a study of concussed athletes with mild head injury, patients had low activation in the right prefrontal cortex compared with healthy controls on a memory task.\textsuperscript{135} However, football players have larger amplitude and more extensive activation patterns, predominantly in parietal, lateral frontal, and cerebellar regions, after a motor sequencing task in the absence of a decline in neurobehavioural performance.\textsuperscript{136}

Functional MRI is a promising diagnostic imaging method for the assessment of cognitive, task-related dysfunction in the chronic phase after head injury. Functional MRI has the advantage over imaging techniques such as PET and SPECT because multiple sessions can be done on a single patient in a short period of time. These features promote prospective studies with baseline measures of neurological function. Furthermore, functional MRI holds great potential for widespread research and clinical use because it does not require exposure to ionising radiation. Application of this technique is best in the chronic phase when the patient is cooperative and able to comprehend test instructions.

**New techniques**

Magnetoencephalography is a new technology that is based on the detection of magnetic field potentials and permits real-time direct assessment of brain electrophysiology. Magnetoencephalography is superior to standard electroencephalography as it provides more precise temporal and spatial patterns that are free from artefacts. The source of the electroencephalography abnormality can be localised by magnetoencephalography and registered on a standard MRI. As such, this technique is not a common imaging technique but provides a combination of a measure of electrophysiological dysfunction with anatomical information.\textsuperscript{137}

Magnetoencephalography technology is used as a clinical diagnostic procedure for epilepsy and experimental research on sensimotor and language function.\textsuperscript{138,139} It also provides useful information for the assessment of cognitive complaints.\textsuperscript{140} In a study of head injury patients with postconcussive symptoms, the combined use of magnetoencephalography and MRI resulted in the detection of abnormal activity in 65% of patients compared with 10% in asymptomatic patients.\textsuperscript{141} The level of
functional damage in patients with head injuries far exceeds the area of focal damage depicted with structural imaging. To date, clinical studies with magnetoencephalography are limited and it is too early to draw any conclusions relating to its potential use in head injury.

Additional limitations for its use in a routine setting include costs and specialised requirements for housing these systems as a result of the need to shield the magnetic noise.

In summary, functional imaging techniques depict more and larger areas of abnormalities than do structural imaging techniques in patients with head injury. Although functional imaging in patients with severe head injury is of prognostic value, there are few data from patients with mild-to-moderate head injury.

**Conclusions**

We have assessed various structural and functional imaging techniques in a clinical setting to guide management and to provide prognostic information on mild-to-moderate head injury (tables 1 and 2). General problems that apply to imaging in patients with mild-to-moderate head injury are the heterogeneity of the population in terms of the extent, type, and location of injury. Distinction has to be made between management in the acute phase after injury when the varying cooperation in agitated or confused patients interferes...
with rapid assessment and the investigation of symptoms and abnormalities in the chronic phase.

In the management of head injury, conventional CT is the imaging modality of first choice in the acute phase. CT is the most relevant imaging procedure for the detection of lesions eligible for surgical intervention, and it is rapidly and easily done. However, a normal CT on admission does not preclude brain injury and is of limited prognostic value. Although MRI is superior to CT in detecting diffuse axonal injury and non-haemorrhagic contusions, this technique is not easily applicable in the acute phase of head injury owing to the limitations in the monitoring of patients during MRI and the susceptibility to motion artefacts related to the long exposure time. Furthermore, there is no evidence that additional MRI affects neurosurgical management in patients with head injury. In general, within 1–3 months after injury, MRI assessment is preferable to other approaches if the appropriate sequences are used for the detection of post-traumatic abnormalities. Recently developed MRI techniques such as diffusion-weighted imaging and diffusion tensor imaging are promising as they provide more insight into the pathophysiological mechanisms of head injury. However, their prognostic value is unknown.

Functional imaging can provide useful information for determining the extent of ischaemic and metabolic injury in patients with head injury. The main imaging techniques dedicated to brain haemodynamics and metabolism in head injury are MRS, functional MRI, SPECT, and PET. In general, SPECT and PET seem to be more sensitive in lesion detection compared with structural imaging techniques such as CT and MRI. Both imaging techniques have limited availability and are mainly used in a research setting, MRS and functional MRI combine the accuracy of MRI with information on brain function and the metabolic state of the brain and are preferably used in the chronic phase after injury. The use of perfusion MRI and perfusion CT is not extensively investigated in traumatic head injury. Perfusion MRI provides better brain coverage than does perfusion CT, although this latter technique has some promising qualities, despite its radiation exposure, as it has a low exposure time and is readily available in most emergency departments. If it becomes more ready available, magneto-encephalography might be a promising neuroimaging technique in the future. This new technique provides anatomical information that can be related to neuropsychological and neurobehavioural outcome.

New technologies adding a functional dimension to structural imaging are likely to improve the relation between neuroimaging and outcome as they provide an index of haemodynamic and metabolic function in addition to anatomy. Additional studies are needed to assess the extent and duration of abnormalities found in symptomatic and asymptomatic patients. The potential ability of new MRI techniques to visualise axonal injury as the major pathological substrate of traumatic brain injury is promising. The ability of functional neuroimaging to depict brain activity during cognitive tasks will enable the possibility to determine the efficacy of various rehabilitation programmes.

Further studies of mild-to-moderate head injury are necessary to prove the feasibility of neuroimaging for this patient group, as management is increasingly directed by the demand for imaging techniques that provide information to guide clinical management and help to determine prognosis.

Contributors
ZM wrote the first draft. All authors critically revised the paper and contributed to the final version.

Conflicts of interest
We have no conflict of interest.

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