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Diagnostic approach to children with minor traumatic brain injury and children with headaches in Germany: The role and limitations of the electroencephalogram and imaging studies (MRI)

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List of abbreviations

cCT/CT	(cranial) Computer tomography
EEG	Electroencephalogram
cMRI/MRI	(cranial) Magnetic resonance imaging
MTBI/TBI	(Mild) traumatic brain injury
GCS	Glasgow coma scale
PTA	Posttraumatic amnesia
LOC	Loss of consciousness
PCS	Post-concussion syndrome
CDR	Clinical decision rules
qEEG	Quantitative EEG
cEEG	Continuous EEG

Introduction

Traumatic brain injury (TBI) from unintentional blunt trauma is a leading cause of death and disability among children and teenagers in western countries [1]. The majority (approximately 50-80%) of children presenting to the emergency department with head trauma have minor head trauma [2], including those with a Glasgow coma scale of 13-15. Recent studies have tried to identify children at low or high risk to develop brain injuries after blunt head trauma [3]. The lack of a consensus on the definition and terminology of mild head injury, TBI and concussion contributes to the misunderstanding and underestimation of this disease entity [4].
In addition to imaging studies the use of protein biomarkers for detection of injury and/or as a prognostic marker have emerged as an area of clinical and research interest [5]. However, despite these advances, there is valid concern that CT scans are overused and that they may be detecting a number of clinically inconsequential findings that require no intervention [3; 6; 7].
Over the last decade the number of CT scans in children with MTBI has increased while its diagnostic yield has remained low. In Canadian paediatric emergency departments the use of CT has increased from 15% in 1995 to 53% in 2005 [8; 9].
In addition to imaging studies, clinicians and researchers have used EEG to evaluate changes in the electrical activity of the brain following Mild traumatic brain injury (MTBI). Standard clinical EEG analyses are often provided in acute care facilities to detect the presence of focal or generalized slowing as well as to detect the presence of epileptiform activity related to brain injury.
The aim of the first study was to evaluate whether MTBI causes *pathological* electroencephalographic alterations (fig.1: Panel 1a) – c))

(a) focal slowing *(corresponding to a focal anatomic lesion)*
(b) generalized slowing or *(corresponding to generalised cerebral dysfunction)*
(c) epileptiform discharges *(usually localised or multifocal cerebral dysfunction with occurrence of spike-wave complexes secondary to localised lesions)*

Moreover, we examined whether these EEG changes led to further imaging studies (cerebral sonography, computed tomography, or MRI), and if subsequent neurosurgical interventions were required.
Following this first study by our group on the use of EEG in children with MTBI [10], the aim of the second study was to evaluate the diagnostic approach in children with MTBI in Germany, using a standardised electronic survey (see appendix).

After all decision making in the initial management of MTBI in children is also influenced by certain circumstances like regional factors, ethnicity and parental anxiety [11].

In addition to pediatric MTBI, children with headache encompass another large patient cohort that is commonly seen in paediatrics. Headache is a very common problem in children and adolescents affecting some 69% of boys and 84% of girls within the age group of 13–19 years [12]. Previous reports have stressed the importance of a carefully taken history, and a thorough physical examination rather than any testing in the initial assessment of children with headaches [13]. Nevertheless, imaging studies (cMRI and cCT) as well as neurophysiological studies (EEG) are commonly requested diagnostic tests when children and adolescents present with headaches [14; 15]. Thus, the aim of the third study of our research group (DM, IO, SM) was to generate up-to-date data on the role of cMRI and EEG studies in the initial evaluation of children and adolescents with headaches. We also correlated risk factors as described by *the Subcommittee of the American Academy of Neurology and the Pediatric Committee of Child Neurology Society* with abnormal findings (space-occupying lesions) with findings of cMRI studies [16].

Moreover, by performing these studies/audits, it was also our aim to critically evaluate our own diagnostic approach, thus defining areas for potential improvement in our diagnostic strategy.

Summary I

Background: Mild traumatic brain injury (MTBI) is one of the most frequent causes for hospitalization in childhood. Because of different guidelines in the management the diagnostic approach varies substantially. Apart from neuro-imaging studies (CT, MRI, sonography) an electroencephalogram (EEG) is often performed without any evidence-based data supporting its use. **Methods:** Retrospective analysis of 150 children with MTBI (age 0-16 years), who were admitted to the Children's Hospital of the University of Saarland from 01/2006 to 12/2007. **Results:** Mean age was 4.3 (SD 3.6) years: 55.3% were boys. The most common mechanisms of injury were: Minor fall <1m of height (60%) and fall >1.5m of height (10%). The most common symptoms were: one or more episodes of vomiting (60%), somnolence (26.7%) and headache (12.7%). On 118 patients an EEG was performed; 106 (89.8%) were normal, 11 (9.3%) pathological and 1 (0.9%) invalid because of artefacts. The pathological EEGs showed focal findings with localized slowing in 9 cases, spike-wave complexes in 1 case and general slowing in 1 case. Of the 11 patients with pathological EEG 2 had a cCT scan, 2 a cMRI and 2 a cranial sonography; all neuro-imaging procedures were normal. None of the children required neurosurgical intervention, had a negative outcome or showed persistent symptoms. **Conclusion:** The routine performance of an EEG after MTBI in children is not indicated because in most of the cases it is unrevealing, and may lead to unnecessary diagnostic procedures. Instead, children with MTBI should be closely monitored for possible clinical complications and neurological deterioration.

Summary II

Introduction: The diagnostic approach in children with minor traumatic brain injury (MTBI) varies substantially. The aim of this survey was to analyse the management of MTBI in paediatric hospitals in Germany. **Materials and methods:** An electronic survey was sent to 72 representative children hospitals in Germany using a standardised questionnaire. **Results:** 45/72 (62.5%) hospitals replied to our questionnaire. All participating hospitals had facilities to perform an electroencephalogram (EEG), 98% a cranial ultrasonography, 94% MRI studies, and 87% a CT scan. Forty per cent of all hospitals used the initial Glasgow Coma Scale (GCS), the clinical presentation (neurological deficits, recurrent episodes of vomiting, amnesia, initial loss of consciousness), the intensity of the trauma and external/visible injuries for initial assessment while in 22% of hospitals trauma classification was based on only GCS and clinical presentation. The main singular reason for in-patient monitoring was initial clinical neurologic presentation (44%). X-ray scans were used routinely in only 2%, cerebral MRI scans in 7% and cerebral CT scans in 13% of the responding hospitals. Approximately one third of the hospitals employed ultrasonography. In only 6.6% of hospitals was an EEG part of the routine diagnostic work-up of MTBI in children. EEG was considered most useful in case of suspected seizure activity (44%), and deteriorating neurology (37%). In-patient monitoring for 24 to 48 hours was done in 80% of the participating hospitals; children less than 6 months of age were commonly monitored for at least 48 hours. **Conclusion:** Our study provides current data on the diagnostic and therapeutic approach in children with MTBI. In Germany, children with MTBI are often monitored clinically without resorting to potentially harmful and expensive diagnostic procedures (cCT scans). Neurophysiologic studies (EEG) are only used under defined circumstances.

Summary III

Background and study purpose: High resolution imaging modalities and electroencephalographic studies (EEG) are used in the assessment of children with headaches. We evaluated the role of cerebral MRI (cMRI) and EEG in the initial assessment of children with headache as the chief complaint of initial presentation. **Methods:** A retrospective chart analysis was performed at a tertiary University Hospital. **Results:** 209 patients were included in this study [mean age 11.3 years; male 91 (43.5%); female 118 (56.5%)]. The following types of headaches were seen: Unclassified headache: 23.4%; probable migraine 17.2%, migraine without aura 13.4%, complicated migraine 12.4%, migraine with aura 1.0%; tension-type 15.3%, and cluster headaches 0.5%, and secondary headaches 16.7%. In 93 children (44.5%) abnormal physical/neurological findings were noted (multiple entries possible). On cMRI studies the following findings were seen: Infection of sinuses (7.2%), pineal cysts (2.4%), arachnoidial cyst and Chiari malformation (1.9%), unspecified signal enhancement (1.0%), and pituitary enlargement, inflammatory lesion, angioma, cerebral ischaemia, and intra-cerebral cyst (each 0.5%). Electroencephalographic findings included both focal and generalised abnormal slowing (5.3%) and spike-wave complexes (3.3%). **Conclusion:** Despite abnormal findings on neurological/physical examination in a substantial number of children with headaches, the yield of pathological cMRIs was low. The use of EEG recordings was not contributory to the diagnostic and therapeutic approach. More research is needed to better define those patients who are likely to have an intracranial pathology.

Study I

Materials and Methods

This retrospective study was done in accordance with the policy of the Institutional Review Board and Ethics Committee of the University Hospital of Saarland, Homburg, Germany.

Enrolment criteria

Patients (aged 0-16 years) admitted to our hospital with MTBI were included in this study. One of the problems we faced in this study was the lack of a universal definition for MTBI. Different definitions exist for mild head injury and concussion. MTBI in this study was defined as outlined by the *Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitative Medicine*: period of posttraumatic amnesia (PTA) not greater than 24 hours, an initial Glasgow Coma Scale (GCS) of 13-15, and the loss of consciousness of less than 30 minutes (Table 1) [17]. These criteria are in line with the recommended definitions of the *Report to Congress on Mild Traumatic Brain Injury in the United States* of the National Centre for Injury Prevention and Control [18].Exclusion criteria were moderate and severe head injury requiring intensive care medicine treatment or neurosurgical interventions and inflicted brain injuries.

Mechanisms of injury

Minor fall (e.g. soccer, ice-skating), fall < 1m of height (e.g. bed, couch, swing, perambulator), fall from 1-1.5m height (e.g. see-saw, changing table, supermarket trolly, baby´s high chair) fall > 1.5m of height (e.g. horse-riding, slide, climbing pole) with minor head collision, and others.

EEG recordings

Routine clinical protocol mandated the realization of an EEG within 48 h after admission, prior to discharge. The follow-up examinations were reviewed until 12/2008, which means a minimal review period of 12 month and a maximal period of 36 month.

Twenty silver cup electrodes were placed according to the 10–20 international system. Electrode impedances measured less than 5 kOhm. An IT med® (IT Medical, Usingen, Germany) model EEG Neurofile NT/XP machine was used to record 12 channels. A high-frequency channel was set at 70 Hz; bipolar longitudinal and transversal montages were used. Each EEG recording lasted 15–20 min. All EEGs were evaluated by the same experienced

neuropediatricians (GS and SM), based on conventional EEG criteria. Age-dependent EEG differences were taken into account [19].

Results

Population Characteristics

In this study, 150 patients admitted to the Children's Hospital of the University of Saarland with a minor head trauma between 01/2006 and 12/2007, were included. Mean age was 4.3(SD 3.6) years and 55.3% were boys. Patients´ demographics are detailed in fig.2.

Mechanisms of injury and place of accident

The five most common mechanisms of injury were minor fall < 1m of height (60%), fall > 1.5m of height (10%), fall 1- 1.5m of height (7.3%), minor head collision (6%), and others (16.7%). In 60% of the cases accidents happened at home, in 23.3 % during free-time activities in swimming pools, playgrounds and sports, in 12.7% at school or kindergarten and in 2.7% on the road.

Symptoms

The clinical presentation of the paediatric patients was very variable. The most common symptoms were one or more episodes of vomiting (60%), somnolence (26.7%), headache (12.7%) and transient loss of consciousness (9%). Less frequent symptoms were nausea (5.3%), transient visual (4.7%) and speech deficit (1.3%), seizure (4%), vertigo (3.3%), motor deficit (2%) and retrograde amnesia (1.3%). In none of the patients symptoms were persistent. Apart from the neurological symptoms 34% had frontal or facial haematoma, and 16% temporal or occipital haematoma. In 6.1% of MTBI occurred secondary to syncope. In those cases, an electrocardiogram and an echocardiogram were performed. Ophthalmological or otorhinolaryngological work-up was done because of visual alterations, periorbital soft tissue haematoma, epistaxis or trauma to the ear. In case of lacerations or to detect fractures or an intra-abdominal haemorrhage after fall from significant height (4.8%) trauma service was consulted. In 1.3 % oral and maxillofacial surgery was consulted because of dental trauma.
Most patients stayed in hospital for either 2 (25.3%) or 3 days (65. 3%).

EEG

One hundred and eighteen of the 150 patients had an EEG; 106 (89.8%) did not show any abnormalities; in 11 (9.3%) pathological changes were noted, and one EEG could not be formally assessed because of artefacts (0.9%).

In 59% EEGs were performed approximately 48 h after injury; in 20% 24 h after injury; 21% were performed between 3 and 6 days after the injury occurred. Of the 106 children with an initially normal EEG five children had an EEG control which was done because of seizures, a skull fracture and excessive artefacts in the first EEG. Of the 11 pathological EEG´s two had no control, 6 had a normal EEG control and three a pathological control. The child with the invalid EEG had a normal EEG control one week later.

The pathological EEGs showed in 9 cases focal findings with focal slowing (increased underlying Delta wave activity); in one case general slowing (generalized underlying Theta wave activity), and in one patient spike-wave complexes (fig. 1: panel 1a)-c)). The epileptiform discharges we found in one of our patients persisted in the follow-up EEG four weeks later. This finding was compatible with benign epilepsy of childhood with central temporal spikes ("Rolando focus"), unrelated to the MTBI.

Imaging studies following pathological EEG

In all patients with initially pathological EEGs imaging studies were recommended, but only two of them had a cCT scan, two a cMRI and two a cerebral sonography; in the others, imaging studies were not performed because of lack of parental consent. Cerebral MRI was preferred to cCT because of the significant radiation exposure caused by computed tomography.

Five children with a normal EEG who developed neurological symptoms (transient paraesthesias, transient visual alterations) during their hospital stay had imaging studies. All imaging studies were normal. None of the children required neurosurgical intervention, and none of them had a negative outcome (i.e. trauma-related persistent symptoms).

Patient follow-up

Of the 11 children with a pathological EEG 7 had a normal on follow-up, two a pathological and in two no EEG control was performed. Follow-up period was 12 to 36 month. None of the children included in this study presented again with trauma related neurological symptoms or sequelae after discharge.

Discussion

Electrophysiological techniques are among the most frequently used methods to provide information about the functioning of the human brain [22]. These techniques are useful in that they are non-invasive and relatively inexpensive. Until today, clinicians and researchers have used EEG to evaluate changes in the electrical activity of the brain following MTBI.

In this retrospective study, we demonstrated that routine EEG examination is of little value in children with minor head injury as in most of the cases it is unrevealing, and may lead to unnecessary diagnostic procedures. Moreover, we did not see any association between abnormal EEG findings and clinical symptoms (eg, period of posttraumatic amnesia, initial GCS score, loss of consciousness, and neurological deficit) or prolonged recovery or hospital stay in our study cohort. This is in line with previous studies using standard EEG techniques that have not provided a clear depiction of functional change following MTBI [23]. Liguori et al. suggested that EEG findings can play a major role in the diagnostic work-up of children with minor head trauma, specifically in asymptomatic patients with normal EEG it is likely that the CT scan will also be normal [24]. Contrary to our results, in the study by Liguori et al. a significant percentage of children with MTBI had pathological EEGs, and all children with abnormal CT findings had pathological EEG studies [24]. The most common pathological EEG finding in our study consisted in focal slowing, possibly corresponding to a localized brain “injury”. However, the functional EEG changes did not go along with sufficient tissue damage to be detected on imaging studies (sonography, CT, MRI), or to warrant neurosurgical interventions of any kind in our cohort.

Early studies reported higher rates of EEG abnormality in subjects with post-concussion syndrome (PCS) [25]; however, these studies were often qualitative, had no modern radiologic information, lacked detailed analysis of paroxysmal activity (epileptic spike activity not associated with a major seizure), and included individuals outside the current definition of MTBI [26; 27; 28]. Other early studies did not demonstrate a higher incidence of abnormalities in the EEGs of MTBI patients than in the general population [29]. Similarly, in a sample of 54 primarily MTBI subjects who were symptomatic for PCS at the time of investigation [30] observed no concurrent EEG abnormalities in 24-hour ambulatory monitoring alone. However, 9.2% of patients had either specific or nonspecific paroxysmal activity. In a more recent study, 12 patients with MTBI underwent a clinical examination within 24 hours after injury that included a standard clinical EEG assessment based on

“current EEG criteria.” No EEG abnormalities were recorded in these patients. Even in patients with structural lesions no focal changes or generalized slow activity have been found [31]. Therefore, *LeBlanc's* negative characterization of standard clinical EEG for the assessment of MTBI, when compared with CT or MRI, may be somewhat warranted [32]. *Korinthenberg et al.* demonstrated that post-traumatic syndrome after minor head injury cannot be predicted by serial EEG examinations in children [33]. As a consequence, the authors of this study discourage routine EEG examinations in children with very slight head injury and instead recommend parent and patient counselling. They are recommended to observe symptoms like headache, fatigue, sleep disturbances, anxiety and affect instability [33].

The standard clinical techniques currently used in most acute care facilities were initially designed to detect seizure activity or abnormal activity associated with large focal lesions. As such, these techniques may be less useful for the detection of mild diffuse damage believed to occur with MTBI as in our study. However, there is a considerable body of experimental work suggesting that more complex EEG paradigms may one day be used to assess changes in brain function after injury (discriminating functions based on patterns of coherence, phase, and amplitude) [34]. Because standard techniques are often used in hospitals, their lack of sensitivity may mislead some to conclude that EEG is generally insensitive to damage. On the basis of the experimental studies, this does not seem to be the case. With continued progress, newer paradigms may eventually be integrated into a standard battery for assessment, thus supplanting standard clinical techniques. This position is consistent with the American Academy of Neurology and American Clinical Neurophysiology Society Guidelines by Nuwer [35]. These guidelines stated that EEG studies on MTBI have resulted in “very interesting changes”; however, they were not recommended at that time as diagnostic procedures for MTBI. Using the identical rating procedures as these published guidelines, a more recent medical position paper has suggested a limited “positive recommendation” for the use of quantitative EEG in the assessment of MTBI [36].

Another important field of research in the initial management of MTBI is the relevance of the S-100-B protein. Different groups showed that patients with pathologies in the CT scan had a significant higher serum level of S100B protein with a sensitivity of 100%. But those studies lacked specificity which could be explained by the low sensitivity of CT scans for small intracerebral lesions. Instead of CT scans a MRI study should be performed [37; 38]. All patients with a normal S100B serum level didn´t show any abnormalities in the CT. Thus the

implementation to the clinical routine management could reduce the number of unnecessary CT scans [38].

Limitations of our study include the retrospective nature of our study design; moreover, the number of children included in our study was too small (inadequately powered) to definitely rule out a positive correlation between an abnormal EEG and a substantial intracranial pathology, given the overall low incidence of significant intracranial and cerebral tissue damage. Moreover, since only in a small proportion of our patients imaging studies were performed, the occurrence of small intracerebral lesions cannot be ruled out with certainty. However, it is ethically questionable to perform imaging studies in this patient cohort as it would expose the child to substantial radiation (cCT), or would mandate the administration of sedatives (cMRI).

In summary, our data suggest that the routine performance of an EEG after minor head trauma in children is not indicated because in most of the cases as it is unrevealing and may lead to unnecessary diagnostic procedures. Of note, none of our patients required neurosurgical interventions. Possibly, the recording of an EEG based on individual findings and risk factors may be helpful in detecting patients at risk for neurological complications. This hypothesis should be ideally assessed in a prospective, adequately powered study. Moreover, in the future more elaborate EEG techniques and other neurophysiological studies may have the potential to detect pathological changes that may have long-term implications more effectively. Of importance, close clinical and parental observation of the affected child with MTBI may be more effective in defining children at risk of developing severe complications.

Study II

Materials and Methods

This survey was done in accordance with the policy of the Institutional Review Board and Ethics Committee of the University Hospital of Saarland, Homburg, Germany. The complete survey can be found as a supplemental file on the journal´s homepage (www.elsevier.com/locate/pedneu). Based on a list of hospitals provided by the *Deutsche Gesellschaft für Kinderheilkunde und Jugendmedizin (DGKJ: http://www.dgkj.de)* a total of 72 representative children´s hospital in Germany were contacted and asked to provide data with regard to their management of children with MTBI. Among others, the electronic survey/questionnaire included the following main items:

a) Facility equipment (i.e. availability of cerebral sonography, cCT scan, cMRI, and EEG laboratory) of the admitting hospital
b) Diagnostic approach in children with MTBI: Clinical approach and choice of diagnostic procedures
c) Type and length of monitoring of patients

The electronic survey was subsequently sent by protected e-mail to the hospitals. Hospitals that did not provide complete data sets were excluded from further data analysis. We then performed a comparison between large (> 80 beds and smaller hospitals (80 ≤ beds) with regard to our main outcome variables. Mild traumatic brain injury was defined according to the EFNS and WHO TBI task force operational definition of MTBI [20].

Statistical analysis was performed using standard tests. Data were stored using SPSS.18.0 package (SPSS, Chicago, IL, USA). A p-value < .05 was considered significant.

Results

45 of 72 hospitals that were contacted (62.5%) provided complete sets of data with regard to our electronic survey, and were subsequently used for data analysis. All participating hospitals had facilities to perform an electroencephalogram (EEG), 98% a cranial

ultrasonography, 94% MRI studies, and 87% a CT scan. The mean number of hospital beds was 93.3±53.1.

Forty percent of all hospitals used the initial GCS, the clinical presentation (neurological deficits, recurrent episodes of vomiting, post-traumatic amnesia (PTA), initial loss of consciousness (LOC)), the intensity of the trauma and external/visible injuries for initial assessment and further decision making, while in 22% of hospitals trauma classification and assessment was only based on GCS and clinical presentation (fig. 3).

The main singular reason for hospital admission and in-patient monitoring was the initial clinical neurologic presentation (44%); other reasons are depicted in figure 4.

Conventional X-ray scans were used in only 2%, cerebral MRI scans in 7% and cerebral CT scans in 13% of the responding hospitals. Approximately one third of the hospitals employed ultrasonography if feasible. 80% of hospitals considered blood tests of little help in the diagnostic evaluation of children with MTBI. In only 6.6% of hospitals was an EEG part of the routine diagnostic work-up of MTBI in children. EEG was considered most useful in case of suspected seizure activity (44%), and in case of deteriorating neurology (37%) (fig. 5).

In-patient monitoring for 24 to 48 hours was done in 80% of the participating hospitals; children less than 6 months of age were commonly monitored for 48 hours.

When comparing smaller (≤ 80 beds; n=23) to larger hospitals (beds > 80; n=22) no significant differences were seen with regard to the diagnostic approach and the main outcome variables. Also no significant differences existed between responding and non-responding hospital with regard to geographic location, size of hospital, and type of hospital (e.g. tertiary hospital).

Discussion

This is one of only a few studies that systematically assessed the initial diagnostic and therapeutic approach of patients/children with MTBI (in Germany) [39].
To optimise the balance between identifying significant injury and minimizing exposure to radiation several clinical decision rules (CDR) have been derived. There are three high quality

CDRs for pediatric head injuries: CATCH (Canadian Assessment of Tomography for Childhood Head Injury), CHALICE (Children´s Head Injury Algorithm for the Prediction of Important clinical events) and PECARN (Pediatric emergency care applied research network) [40].

The PECARN study evaluates a prediction about the important question what does the rule mean for the child. It correctly identifies children as not having an intracranial injury when certain symptoms are missing. Though 25 % of the CT scans can be avoided. Additionally it has got a separate algorithm for children < 2 years [40].

Following the publication of a number of national and international reports and guidelines on the management of children with MTBI [41]; our study demonstrates a somewhat homogeneous approach to children with MTBI, albeit some variability in the initial management was noted. Of importance, the data of our survey demonstrate that both imaging and electrophysiological studies are not performed on a routine basis in children with MTBI. This is in contrast to the results from a study that evaluated the initial management of MTBI by neurosurgeons in Germany [39]. The authors of that study demonstrated that various definitions were used in the assessment of patients with minor head trauma: while the diagnosis 'mild brain injury' was used by 63%, 'commotio cerebri' by 49%, and 'brain concussion' by 4% of the institutions. In their study both the GCS and clinical parameters were used for classification (GCS by 60%, post-traumatic amnesia (PTA) 48%, retrograde amnesia by 50%, and loss of consciousness (LOC) by 63% of institutions). This is somewhat similar to our data. Of note, diagnostic imaging studies were much more commonly used than in our report (x-ray of the skull is used in 77%, x-ray of the cervical spine in 62%, cCT in 66%, cMRT in 7%). Conversely, the results of our study suggest that close clinical monitoring is favoured over the utilisation of costly and potentially harmful procedures (eg, cerebral CT scans with substantial radiation exposure) in children with MTBI.

CCT in children is associated with exposure to ionizing radiation and sedation. In recent years an increased awareness of radiation risk involved in cCT in children has lead to a decreased rate of neuroimaging. But the rate of cCT is still around 30% [42]. Practitioners will increasingly need to weigh the undoubted benefits of CT scans in the initial management of MTBI in the emergency department against the potential risks of radiation to justify the performance of CT scans in children [43]. Mathews et al. showed in a retrospective study of 11 million Australians, 680000 of them exposed to CT scans, a significant increased cancer incidence rate in individuals exposed to ionising radiation from diagnostic CT scans. The

incidence of cancer was 24% greater for exposed than for unexposed patients. After all the incidence rate ratio was greater after exposure at younger ages, especially under the age of 5 years [43]. Brenner and colleagues estimated that lifetime cancer mortality risk caused by the ionizing radiation to which a one year old child would be exposed through a single cranial CT scan was about 1:1500. For a 10 year old child it would be 1:5000 [44]. Osmold et al. developed in a recent study a decision rule for the use of CT scans in children with minor head trauma. They indentified four high – risk factors which are significant for the requirement of a neurosurgical intervention. Those are: failure to reach a score of 15 in the GCS within two hours, suspicion of open skull fracture, worsening headache and irritability. Those factors were 100% sensitive for predicting the need for neurosurgical intervention. Fifty three per cent of the children included in the study underwent CT scan but in only 4.1% of them CT scan revealed an acute brain lesion and 0.6% a neurosurgical intervention. The variables with the highest associations with brain injury were those found on physical examination. Among the decision rule 30.2% of the patients should undergo CT. The second outcome measurement was the presence of brain injury as determined by CT. Therefore three medium risk factors were ruled out: large hematoma of scalp, signs of basal skull fracture, dangerous mechanism of injury. Those would require that 52% of patients undergo CT. Besides the increased cancer risk, Hall recently reported that low doses of ionizing radiation to the brain may also influence cognitive abilities in adulthood [45]. An accurate decision rule for the management of minor head trauma is important to minimize the use of CT scans which means to reduce the harmful effects of ionizing radiation [46].

The long-term prognosis of children with MTBI is still under debate. A recent study demonstrated that - when controlling for pre-injury factors - there is no evidence of *long-term* neurocognitive impairment in MTBI children [47]. Conversely, another study confirms that children with MTBI, particularly those characterized by LOC, demonstrate significant post-concussive symptoms as compared to children with orthopaedic injury, even when pre-morbid child and family adjustment variables are taken into account. Children with mild TBI showed significant post-injury increases in both somatic and cognitive symptoms, although somatic symptoms tended to resolve over time, while cognitive symptoms persisted as much as 12 months post-injury [48].

In our second study, we also looked specifically whether hospitals and emergency departments employed EEG studies in the initial management of children with MTBI. The results of our survey showed that routine EEG studies are only rarely performed.

A survey among neurosurgeons in Germany demonstrated that 35% of institutions with neurosurgical service still employ routine EEG recordings [39].

Our study has some limitations. First, a little less than 2/3 of all hospital provided full data sets that were included in the final analysis. Although this is generally considered a good response rate, our data may not be fully representative and accurate interpretation may be impeded, although no significant differences were seen between responding and non-responding hospital were seen (geographic location, size of hospital, tertiary hospital).

Second, our survey did not relate the initial approach to outcome variables. Recently, the *Pediatric Emergency Care Applied Research Network group* prospectively evaluated a large cohort of children (some 42.412) with MTBI (GCS 14-15) [49]. Looking at clinical history, a prediction tree for clinically important TBI (death from TBI, neurosurgery, intubation >24 h, or hospital admission ≥2 nights) for children younger than 2 years of age and for children 2 years or older was developed. This algorithm had a negative predictive value of 99.95% (95% CI: 99.9-99.98) and a sensitivity of 96.7% (95% CI: 93.4-98.7) for children 2 years old and older and 99.9% (95% CI: 99.88-99.999) negative predictive value and 98.6% (95% CI: 92.6-99.97) sensitivity for children younger than 2 years [49]. Based on these findings, one possible approach to further improving the diagnosis and management of MTBI may be the use of computerized decision support systems, particularly in deciding when a cranial CT scan should be obtained [50].

Summary and future implications

In summary, probably the most interesting finding of our survey was the fact that most hospitals used imaging studies, laboratory diagnostic work-up, and electrophysiological studies (EEG) rather restrictively. Instead, children were commonly admitted to the hospital as in-patients, and were monitored clinically. The use of diagnostic procedures was then dependent on the clinical status and later deterioration. While this approach is cost-intensive, it has the advantage of not exposing the child with MTBI to unnecessary and potentially harmful diagnostic procedures. Moreover, by clinical observation changes in the clinical status after admission can be readily detected and adequate diagnostic and therapeutic steps can be taken.

Study III

Materials and Methods

This retrospective study was done in accordance with the policy of the Institutional Review Board and Ethics Committee of the University Hospital of Saarland, Homburg, Germany. Relevant data were retrieved from an electronic hospital database (SAP, Germany). In case of missing data, patients' hospital charts were hand-searched individually. We included all children who presented to our neuropediatric outpatient clinics with "headache" as the main presenting symptom between January 2006 and December 2009. A detailed history was taken and a complete neurological examination was performed. We entered all relevant information into an electronic database (SPSS 18.0, Chicago, IL, USA). Statistical analysis was performed using SPSS 18.0. For data interpretation we used frequencies and cross-tables. For further statistical analysis the Pearson Chi-Square Test and Fischer's exact test was employed. A p-value of ≤ 0.05 was considered significant. Headaches were classified according to the second edition of the International Headache Society (IHS) classification, and its modification for the paediatric population [21]. Diagnostic work-up in children with headaches included cerebral MRI studies and EEG recordings as per our hospital protocol. Cerebral MRI studies were performed by a 1.5-T MRI system (Siemens Magnetom Sonata; Siemens; Erlangen, Germany). Electroencephalographic studies were performed using as a standardised protocol as described previously. Electroencephalographic recordings were analysed by experienced neuropediatricians (SM and GS), who was blinded to the findings of cMRI studies.

Results

During the time period 1 January 2001 to 31 December 2009 a total of 818 patients seen in our hospital with a history of headache were entered in our hospital database. These patients were screened for possible study enrolment. Six-hundred and nine of these patients were excluded from study enrolment for one or several of the following reasons: Previous history of headaches (including previous imaging studies), head trauma, age (patients younger than three years of age or older than seventeen years of age), a history of neurosurgery (including obstructive hydrocephalus with ventriculo-peritoneal shunting), other medical conditions with acute onset (most importantly infectious diseases), inadequate/incorrect documentation and

data entry, and lack of parental consent to perform cMRI studies. Thus, a total of 609 patients were excluded from the study enrolment.

Two-hundred and nine patients were included in this study (age 3 to 17 years, mean age 11.3 years; male 91 (43.5%); female 118 (56.5%)). The following types of headaches were seen: Unclassified headache 49 (23.4%); probable migraine 17.2%, migraine without aura 13.4%, complicated migraine 12.4%, migraine with aura 1.0%; tension-type 15.3%, and cluster headaches 0.5%, and secondary headaches 16.7%.

In 44.5% (93) of all children, abnormal findings on physical and neurological examination were noted: Physical and neurologic examination findings (multiple entries possible) included the following in order of frequency: Vomiting (55; 26.2%), syncope (18; 8.6%), speech impediment (13; 6.2%), fever (9; 4.3%), papilloedema 6 (2.9%), gait abnormalities (5; 2.4%), and facial palsy (4; 1.9%). Less common symptoms and clinical signs on neurological examination were: hearing disorder (4; 1.9%), hemiplegic symptoms (2, 1.0%), aphasia, hearing disorder, miosis, amnesia, paralysis and muscle spasms (each 1; 0.5%). In 55.5% (116) of all children, no physical or neurological signs/abnormalities were seen. All 6 children (n = 6) with papilloedema presented with true papilloedema.

The duration and history of headaches lasted: <1 day (49), 1–7 days (23), 1–4 weeks (31), or longer (56); no data for the duration of headaches could be elicited in 50 patients.

On cMRI studies the following findings were seen: no pathological findings 157 (75.1%), infection of sinuses 15 (7.2%), pineal cysts 5 (2.4%), arachnoidic cyst and Chiari malformation (each 4; 1.9%), unspecified signal enhancement 2 (1.0%), pituitary enlargement, cerebral ischaemia, inflammatory lesion, angioma, and intra-cerebral cyst (each 1; 0.5%).

Electroencephalographic findings included: no pathological findings 173 (82.8%), Spike-wave complexes (7; 3.3%), both focal and generalised abnormal slowing (increased delta waves) (11; 5.3%). In 9 EEG recordings (4.3%) artefacts were noted, and unspecific findings were seen in (3; 1.4%). Abnormal findings on EEG studies were not linked to abnormal cMRI results.

Consequences that were taken – depending both on clinical grounds and results of imaging studies – included: conservative medical treatment (10; 4.8%; e.g., anticoagulation for cerebral ischaemia, preventive measures for migraine, and analgesia). In patients with intra-

cerebral cysts follow-up cMRI studies were recommended in 11 children (5.3%), antibiotic treatment in 8 patients with symptoms consistent with a sinusitis (3.8%), further diagnostic investigation in 4 (1.9%) (e.g. lumbar puncture and spinal MRI), interventional embolisation (1; 0.5%), surgery in 1 (0.5%). Table 2 gives common findings on cMRI and physical/neurological abnormalities. No single factor (age, length or type of headache, gender) was significantly associated with pathological cMRI results.

Discussion

In our third study, we examined the role of cMRI and EEG studies in the initial evaluation of children and adolescents with headaches. It is generally assumed that recurrent headaches occur commonly in children and are diagnosed on a clinical basis rather than by any testing. According to current guidelines obtaining a neuroimaging study on a routine basis is not indicated in children with recurrent headaches and a normal neurologic examination [16]. However, in clinical practice, cCT scans or cMRI studies are often performed to rule out an intracranial pathology and for parental re-assurance. In the study by *Rho and colleagues* neuroimaging procedures were performed in 77.1% of the patients. Overall, 9.3% of these studies yielded abnormal findings with the highest yield in patients with an abnormal neurological examination. Conversely, the rate of pathological findings was low when imaging was carried out in view of changes in the type of headache (12.9%), neurologic dysfunction (10.8%), demands of parent and physicians (10.1%), and recent onset of severe headaches (7.0%). No significant association was seen between abnormality on neuroimaging and age, sex, headache type, age of onset of headache, duration of symptoms before presentation, duration, frequency, location and intensity of headache. Based on their findings the authors conclude that stricter guidelines for rational use of neuroimaging are needed for paediatric headache patients and should be employed. According to the current practice parameters, neuroimaging should be considered in children with an abnormal neurologic examination or other physical findings that suggest central nervous system (CNS) disease. Variables that predicted the presence of a space-occupying lesion included 1) headache of less than 1-month duration; 2) absence of family history of migraine; 3) abnormal neurologic findings on examination; 4) gait abnormalities; and 5) occurrence of seizures [16].

Cerebral CT scanning is a useful diagnostic tool, especially under emergency circumstances, and should be used to identify subarachnoid haemorrhage, ventricular enlargement (e.g., shunt blockage), mass lesion, and haemorrhage secondary to trauma [51]. If, however, the diagnosis

of CNS pathology is suspected and the situation is not urgent, MRI at times coupled with angiography (MRA) should be considered. It should be noted that as many as 40% of individuals imaged for headache may have non-specific abnormalities, including abnormalities of the sinuses, non-specific white matter abnormalities, arachnoid cysts, pineal cysts, venous angiomas, and Chiari malformation [52; 53]. Of note, a recent report demonstrated a higher incidence of abnormal findings compared to previous reports when using modern sequences in children with headache; however, there was only limited clinical gain of information using this sequences [54]. This is in line with our results. Conversely, in the series of *Chu and Shinnar* [55] some 30% of 104 children younger than the age of 7 years who presented with headache underwent imaging. On only one instance, a child with Chiari I malformation, did these studies uncover a previously unknown finding [55]. In the series of *Maytal and coworkers*, neuroimaging studies disclosed cerebral abnormalities in 3% of paediatric headache patients [56]. All abnormalities were deemed to be unrelated to the presenting complaint [56]. These findings are corroborated by another report that demonstrated that approximately 20% of paediatric headache patients with brain imaging had benign abnormalities that did not result in a change in headache management [57]. Imaging findings that required a change in management were rare in patients with an absence of abnormal neurologic symptoms and signs, occurring only in 1.2% of patients imaged in this study [57]. This is somewhat in contrast to the results of our study where further treatment was at least in part dependent on the results of cMRI studies in 16.8% of patients; however, in only 2 patients (1%) were intervention or surgery deemed necessary based non cMRI studies. The findings on cMRI in both patients with subsequent intervention/surgery could be well correlated to their physical/neurological complaints, and thus cannot be considered ‘incidentaloma’.

Electroencephalographic studies are not recommended in the routine evaluation, as it is unlikely to define or determine the aetiology or distinguish migraine from other types of headaches. Moreover, previous studies have shown that EEG studies are of limited value in the routine evaluation of children with headaches [53; 58]. Non-specific abnormalities are frequently found in normal children as well as in children who are ill. This is in line with our findings where we did not find specific findings in a substantial percentage of children on EEG recordings. Moreover, no association between abnormal EEG studies and pathological findings on cMRI could be demonstrated in our trial. Children undergoing evaluation for recurrent headaches were found to have a paroxysmal EEG, the risk for future seizures is

considered negligible; therefore, further investigation for epilepsy or treatments aimed at preventing future seizures is not indicated.

In summary, our results have shown that the rate of pathological findings on cMRI studies in children with headaches of different aetiology is low despite the occurrence of abnormal findings on both physical and neurological examination in a substantial number of children. In the future it will be important to better define those patients who are likely to have an intracranial pathology, and who will benefit from early imaging studies. The additional routine use of EEG studies in the initial diagnostic work-up of children with first-episode headaches is non-contributory to the diagnosis.

Concluding Discussion

In the future special techniques like qEEG (quantitative EEG) and TBI – indices which are still very uncommon in the paediatric emergency department might be used in the diagnosis of mild traumatic brain injury (mTBI) and headaches. Quantitative EEG makes use of quantitative techniques to analyze EEG characteristics such as frequency, amplitude, coherence, power, phase and symmetry over time independently or in combination. It refers to software assisted interpretation of EEG recordings that can be used to demonstrate quantitative trends in EEG not visualized by routine EEG measurements. There are different techniques like spectral analysis which is used to demonstrate the frequency composition over a given period or coherence measurements which correlate the EEG frequency between two channels to see how similar or coherent the underlying brain activity is [59].

Conventional EEG is appropriately applied to the evaluation of posttraumatic epilepsy but it´s not recommended as a routine element of mTBI. By contrast quantitative EEG interpretation with its computer assisted EEG analysis and interpretation offers multiple advantages over visual inspection of raw EEG tracings. Including the ability to derive measures, perform data transforms and identify subtle shifts in the types and patterns of EEG activity. Common findings among persons with mTBI are reduction in mean alpha frequency, increased theta activity or increased theta alpha ratios. However additional research is needed in order to better define and guide its application to the clinical and forensic evaluation of this population [60]. There is also criticism regarding the use of qEEG like the predisposition to be contaminated by artifacts such as drowsiness, eye movements, muscle activity, medication, technical issues and their misinterpretation. Apart that the likelihood of normal variation of EEG between persons or even over time within the same person to be marked as abnormal by qEEG panels and the lack of a sufficiently large normative database of the test population for comparison [59].

Quantitative EEG is also useful in general neurological practice and the treatment of headaches. Statistical analysis showed that qEEG analysis contributed in 95% of neurological cases (seizures, headaches, post-concussion syndrome, cognitive problems, and behavioural dysfunctions) to the diagnosis and/or furthered patient's treatment. That indicates great potential for wider application of this modality in general neurology [61]. Walker showed that qEEG-guided neurofeedback appears to be dramatically effective in abolishing or significantly reducing headache frequency in patients with recurrent migraine [62].

A qEEG derived TBI index appears to be a sensitive measure of brain function that may be used in conjunction with other clinical information or determine whether or not a patient has a severe brain injury [63].

In 2001 Thatcher et al. developed an EEG severity index of TBI using EEG spectral analyses. Sixteen variables were entered into a multivariate discriminant analysis. Significant correlations between EEG discriminant scores, emergency admission measures, and post-trauma neuropsychological test scores validated the discriminant function as an index of severity of injury and a classifier of the extremes of severity [64].

Different study groups developed an index of brain electrical activity to identify intracranial hematomas in TBI. Sensitivity to hematomas was found to be 95.7% - 100%. A significant correlation was found between TBI-Index and blood volume. There was no significant relationship between the TBI-Index and type of hematoma, or distance of the bleed from recording sites. A TBI-Index for structural brain injury derived from brain electrical activity submitted to a classification algorithm is a highly sensitive measure for the detection of potentially life-threatening traumatic intracranial hematomas, and could contribute to the rapid, quantitative evaluation and treatment of such patients [65; 66].

In a new high-density EEG brain mapping technique potentials were recorded with 128-channel EEG to investigate spatiotemporal aspects of brain activity in response to muscle pain in patients with chronic tension-type headache (CTTH) [67].

Another technique is the continuous EEG (cEEG) monitoring which significantly improves the detection of early posttraumatic seizures/status epilepticus and is the only way to detect subclinical seizures. cEEG may be indicated after paediatric TBI, particularly in younger children [68]. However further research is needed to apply those techniques appropriately in paediatric neurological diagnostics.

The indiscriminate and routine use of EEG studies in both children with MTBI and headaches is not indicated and not contributory in establishing the correct diagnosis. On the contrary, unspecific findings may warrant further diagnostic procedures that are both potentially harmful and expensive. The decision to employ electrophysiological studies (EEG) in these patient cohorts should be made on an individual basis. Based on the findings of our studies, we have re-evaluated the diagnostic algorithm in our hospital, and have put in place a different diagnostic work-up for these patients. Importantly, we have abandoned the routine use of EEG studies in children with MTBI and headaches. Thus, our studies/audits also demonstrate that the process of critically assessing and evaluating ´traditional´ diagnostic

algorithm has the potential to change and most likely improve the quality of care in the field of child neurology, without exposing these children to unnecessary risks.

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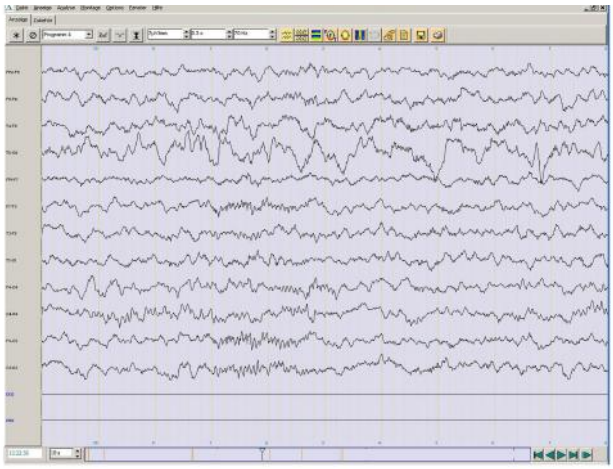
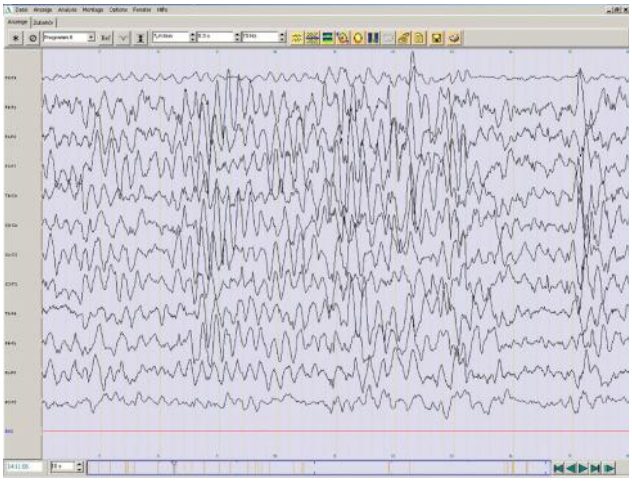
Appendix

Figure 1: Panel 1a)-c): Pathological EEG results

a) Focal slowing in right temporal occipital lead



b) generalised slowing



c) Spikes-and-wave complexes (“Rolando-Focus”)

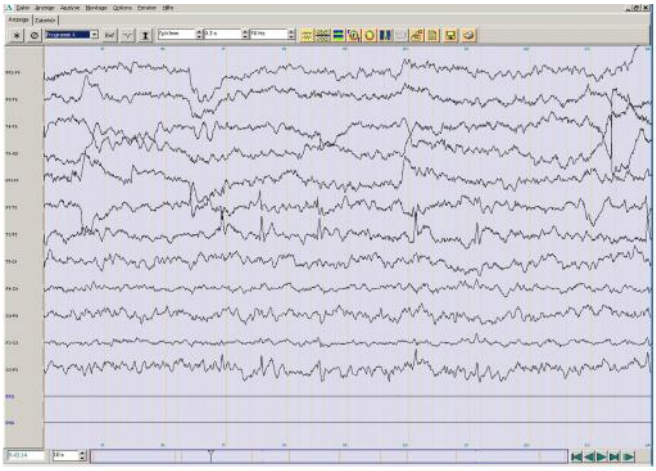


Figure 2: Demographic details

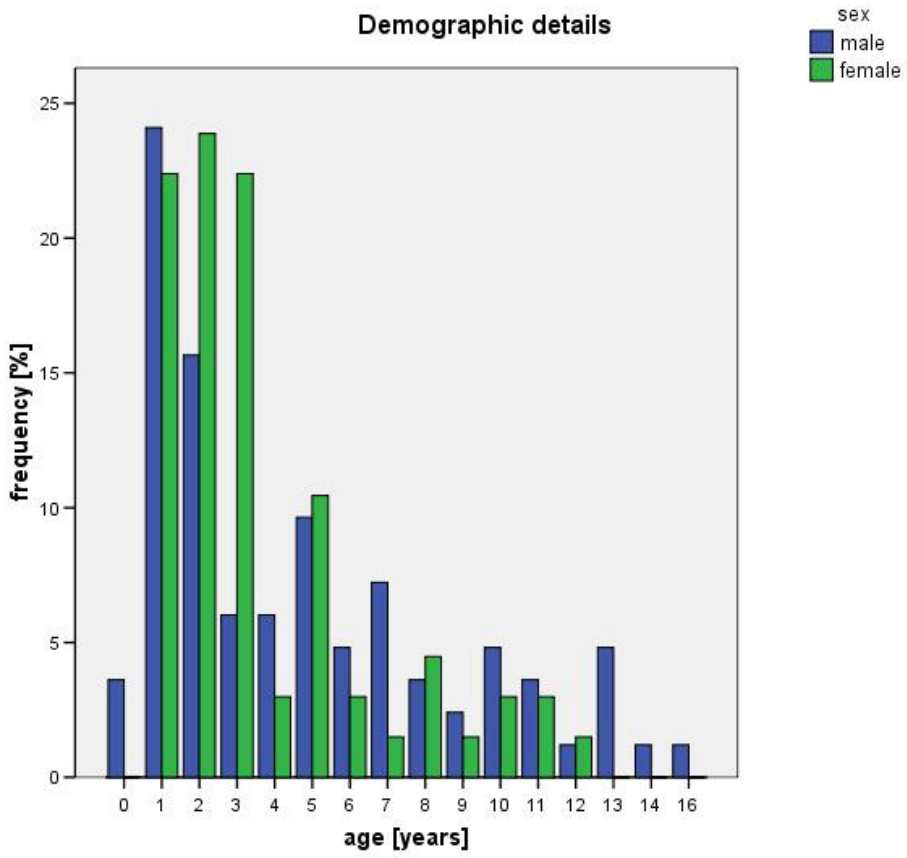


Figure 3: Items used in the initial severity assessment of children with MTBI

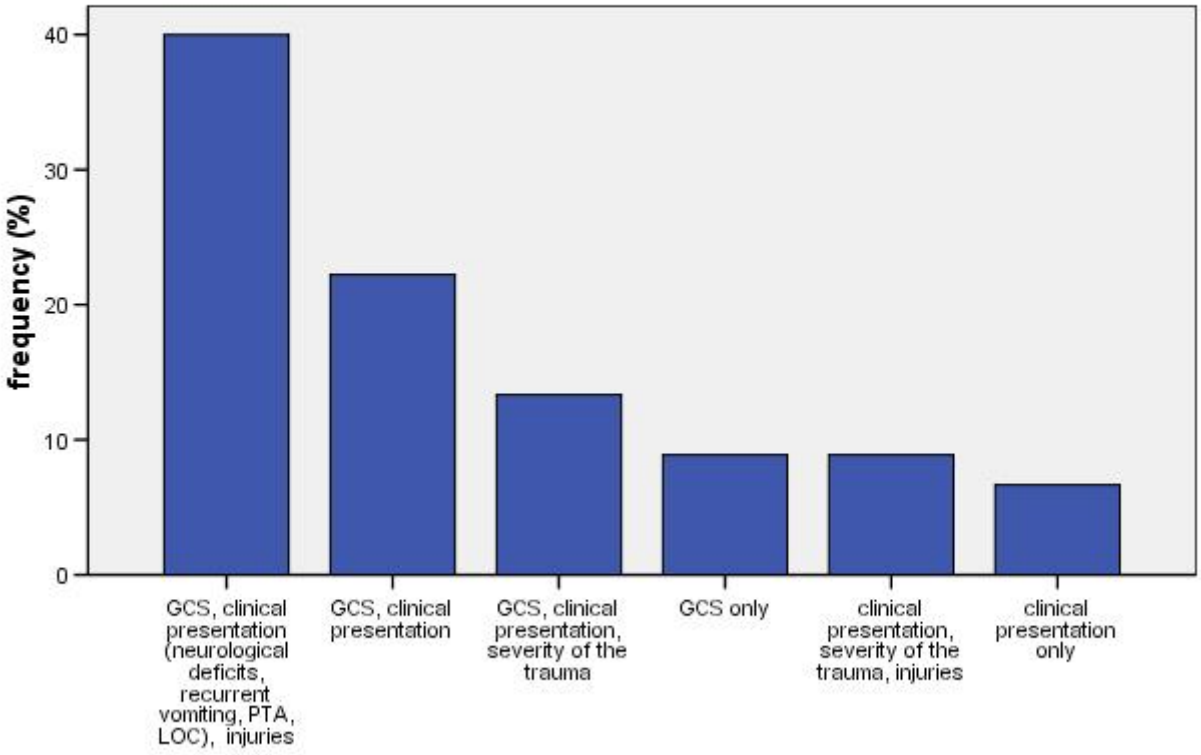


Figure 4: Reasons for admission of children with MTBI as in-patient

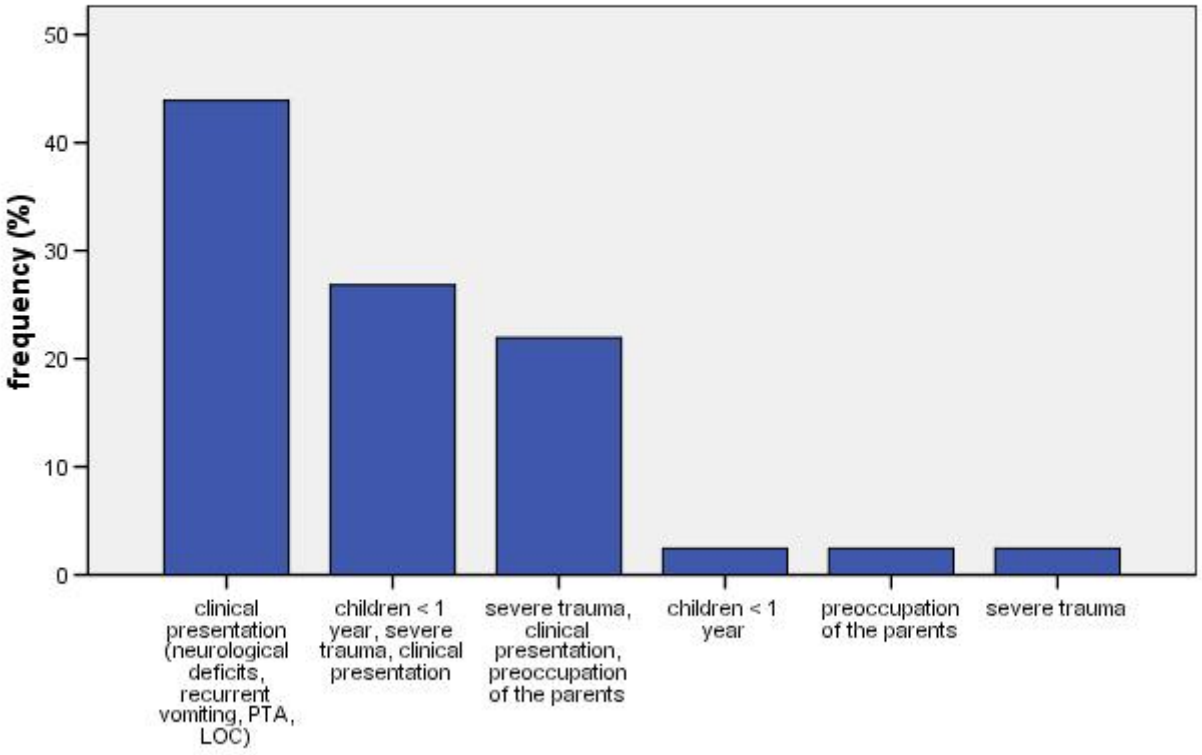


Figure 5: Reasons for performing an EEG study in children with MTBI

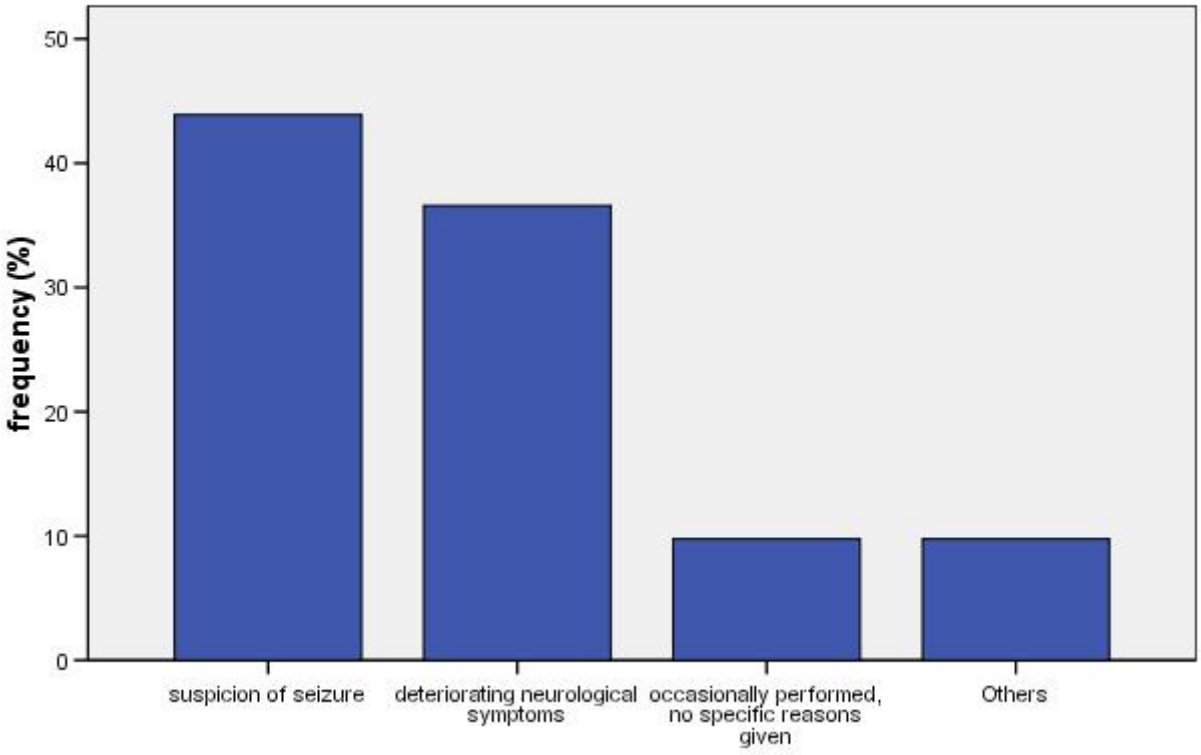


Table 1. Definition of MTBI (according to [17])

WHO TBI task force operational definition of MTBI

WHO, World Health Organisation; MTBI, mild traumatic brain injury; LOC, loss of consciousness; PTA, post-traumatic amnesia; GCS, Glasgow Coma Scale.

One or more of the following:

Confusion or disorientation

LOC •</= 30 min

PTA • <24 h

Transient neurological abnormalities such as focal signs, seizure, and intracranial lesion

And:

GCS 13–15

Manifestations of TBI are not due to drugs, alcohol, or medications, are not caused by other injuries or treatment for other injuries, and are not caused by other problems (e.g. psychological trauma, language barrier, or coexisting medical conditions) or penetrating craniocerebral injury.

Table 2: Cranial MRI results and most common symptoms in five most common conditions on imaging studies.

MRI results	**Symptoms**
Pineal cyct (5)	Headache, phonophobia, vertigo, paraesthesia, syncope
Arachnoid cyct (4)	Headache, vision disturbance, phonophobia, photophobia, vomiting
Chiari-malformation (4)	Severe headache, vomiting, nausea, vertigo, photophobia, vision disturbance
Unspecific contrast media enhancement (2)	Headache, vertigo, photophobia, phonophobia

Electronic Survey

1.) Allgemeine Informationen
Anzahl der Betten:

Apparative Diagnostik im Haus:
□ EEG
□ Sonographie
□ CT
□ MRT

2.) Nach welchen Kriterien erfolgt die Schweregradeinteilung der Schädelhirntraumata an Ihrer Klinik?

Glasgow Coma Scale
Klinische Kriterien (Schweregrad der Symptome: z.B. rezidivierendes Erbrechen, Somnolenz, Dauer der initialen Bewusstlosigkeit/Amnesie)
Schweregrad des Unfallereignisses (z.B. Sturzhöhe, Verkehrsunfall)
Verletzungen (Schädelfraktur, Platzwunde, Prellmarke, etc.)

3.) Wie ist das diagnostische Vorgehen beim leichten SHT bei Kindern? (Mehrfachnennungen möglich)

Überwachung der Vigilanz/neurologischer Status	Immer (90%-100%)	Manchmal (50%-90%)	selten (10%-50%)	nie (<10%)
Für < 24 Stunden				
Für 24-48 Stunden				
Für > 48h				
Apparative Diagnostik				
Schädel-Sonographie				
CT				
MRT				
EEG				
Röntgen				
Labordiagnostik				

4.) In welchen Fällen wird ein EEG nach leichtem SHT (GCS 13-15 oder nach klinischer Einschätzung) durchgeführt?
□ routinemäßig
□ selektiv
Falls selektiv, in welchen Fällen?

5.) Anhand welcher Kriterien erfolgt die stationäre Aufnahme? Wenn ja wie lange?

Publications

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3. Martens D, Oster I, Gottschling S, Papanagiotou P, Ziegler K, Eymann R, Ong MF, Gortner L, Meyer S. **Cerebral MRI and EEG studies in the initial management of pediatric headaches.** Swiss Med Wkly. 2012 Jul 10; 142:w13625.
4. Martens D, Oster I, Papanagiotou P, Gortner L, Meyer S. **Role of MRI and EEG in the initial evaluation of children with headaches.** Pediatr Int.2012 Aug;54(4):580-1.

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