Clin Epileptol 2023 · 36 (Suppl 2):S120–S124
https://doi.org/10.1007/s10309-023-00586-0
Accepted: 27 March 2023
Published online: 7 June 2023

Impaired consciousness in the pediatric intensive care unit: etiology and diagnostics—English version

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Abstract

This article provides an overview of the management of children with disorders of consciousness. Rapid diagnostics are necessary to identify treatable etiologies and minimize neurological sequelae. The differential diagnosis is extensive. Brief neurological findings include quantification of impaired consciousness using the Glasgow Coma Scale (GCS), testing of the eyes, motor function, and the presence of meningism. Laboratory tests include rapid exclusion of hypoglycemia and, if CNS infection is suspected, CSF examination. An emergency head CT is mandatory in cases of nonreactive unilateral or bilateral pupils before further diagnostic work-up is carried out. We recommend head MRI, especially if encephalitis, vasculitis, ischemic stroke, and sinus vein thrombosis are suspected. An EEG rarely provides clues to the cause of coma but it serves primarily as an objective measure of the severity of encephalopathy, the prognosis, and the effectiveness of therapy.

Keywords
Glasgow-Coma-Scale (GSC) · Encephalopathy · Coma · Nonreactive pupil · ICP

Disorders of consciousness are an expression of impaired brain function and represent a major challenge. Rapid diagnosis is essential in order to identify treatable etiologies and minimize neurological sequelae. This review presents a structured approach to the clinical examination and diagnosis of acute pediatric disorders of consciousness beyond the neonatal age. Status epilepticus is not addressed in this article. The guidelines of the Association of the Scientific Medical Societies in Germany (*Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften*, AWMF) "*Akute Bewusstseinsstörung jenseits der Neugeborenenperiode*" ("Acute disturbance of consciousness beyond the neonatal period"; [1]) and "*Das Schädel-Hirn-Trauma im Kindes- und Jugendalter*" (Traumatic brain injury in childhood and adolescence; [2]) are highly recommended for a more in-depth study of the topic.

Etiology

The differential diagnosis is extensive. The most important differential diagnoses are listed below and can be summarized under the acronym I WATCH DEATH [3]:

- ***I****nfection*: meningitis/encephalitis, sepsis, abscess
- ***W****ithdrawal*: barbiturates, benzodiazepines, sedatives, hypnotics, alcohol
- ***A****cute metabolic*: liver damage, kidney damage, electrolyte imbalance, metabolic disturbance
- ***T****rauma:* intracranial injury, postoperative delirium, heat stroke
- ***C****NS pathology*: CNS inflammation (acute disseminated encephalomyelitis [ADEM], antibody-mediated encephalitis), ictal/postictal states, hydrocephalus, tumors

The German version of this article can be found under https://doi.org/10.1007/s10309-022-00535-3.

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Table 1 Pediatric Glasgow Coma Scale		
Eye opening	Spontaneous	4
	In response to verbal stimuli	3
	In response to pain	2
	No reaction	1
Communication	Babbling, cooing	5
	Crying, consolable	4
	Crying, inconsolable	3
	Moaning, unintelligible sounds	2
	No verbal reaction	1
Motor response	Spontaneous movements	6
	Targeted movement to pain stimulus	5
	Untargeted movement to pain stimulus	4
	Decorticate posturing	3
	Decerebrate posturing	2
	No motor response	1
Maximum score		15

- ***H**ypoxia:* pulmonary/cardiac failure, drowning accident
- ***D**eficiencies*: vitamin B_{12}, thiamine
- ***E**ndocrinopathies*: hypo-/hyperglycemia, diabetic ketoacidosis, hypothyroidism
- ***A**cute vascular*: stroke including sinus vein thrombosis, hemorrhage, vasculitis, posterior reversible hypertensive encephalopathy syndrome (PRES)
- ***T**oxins* or drugs: medications, drugs, carbon monoxide poisoning (e.g., due to shisha use)
- ***H**eavy metals*: lead, manganese, mercury

Clinical examination

In all children with impaired consciousness, the preservation of vital functions according to ABC guidelines (airway, breathing, circulation) has absolute priority. The diagnosis and treatment must be performed simultaneously. A quantitative assessment of the disorder of consciousness has to be rapidly carried out. The standard instrument for this is the Glasgow Coma Scale (GCS; [4]), which is scored between 3 and 15, with 3 being the worst and 15 the best. It is composed of three parameters: best eye response (A), best verbal response (V), and best motor response (M). The components of the GCS should be recorded individually; for example, A4V3M3 yields a GCS score of 10. The Pediatric Glasgow Coma Scale (PGCS) has been validated for children under 2 years of age ([5]; ◘ **Table 1**). Brainstem reflexes are not considered in the GCS.

Brief neurological examination

A brief neurological examination includes testing of the eyes and motor function as well as for the presence of meningism.

Eyes. A brief examination includes testing of eyeball position and pupillomotor function. Non-convulsive status epilepticus should not be overlooked. Open eyes with gaze deviation to the side are highly suggestive of an ictal state. The pupils are usually wide in this case.

Unilateral pupillary areflexia to light indicates transtentorial herniation into the supratentorial space or increased intracranial pressure.

Bilaterally dilated pupils are found in cerebral anoxia or ischemia. However, catecholamine administration or intoxication by anticholinergics, amphetamines, cocaine, and carbon monoxide can mimic similar pupillary findings. Intoxication by cholinergics, barbiturates, or opiates is possible in the case of equally narrow pupils on both sides.

In cases of impaired consciousness with unilaterally/bilaterally nonreactive dilated pupil(s), an emergency CT of the skull must be performed prior to further diagnostic workup [1, 2].

Motor skills. The most common cause of acute hemiparesis in children is postictal paresis (Todd's paresis), but stroke or encephalitis is also possible. Symmetrical decorticate posturing or decerebrate posturing indicates brainstem dysfunction (herniation, trauma, hemorrhage).

Meningism in childhood is mainly due to meningitis, while subarachnoid hemorrhage is much less common. In young children, meningism is not obligatory in meningitis. Attention should be paid to the tension or bulging of the fontanel.

Physical examination

In particular, attention must be paid to the respiratory pattern, skin findings, halitosis, and evidence of trauma. Hematomas at atypical sites are found in child abuse.

Kussmaul breathing is indicative of (diabetic) ketoacidosis, while periodic (Cheyne–Stokes) or apneic respiration indicates diencephalic or brainstem involvement. The combination of bradypnea, arterial hypertension, and bradycardia is referred to as *Cushing's triad*. It is a late sign of increased intracranial pressure and is usually indicative of impending herniation of the medulla oblongata.

Prolonged recapillarization time of >3 s, petechiae, or exanthema is suggestive of infection or shock. Jaundice beyond the neonatal age suggests liver failure.

Laboratory

Blood glucose must be determined rapidly. Hypoglycemia is defined as blood glucose level of ≤ 50 mg/dl (2.8 mmol/l). In hypoglycemia, in addition to blood glucose determination, a critical sample should be taken before administration of glucose 2 ml/kg 10% ml/kg body weight (BW) intravenously followed by continuous infusion (caveat: rebound hypoglycemia; [6]).

In cases of unexplained loss of consciousness, laboratory tests should be performed with regard to infections, organ dysfunction, electrolyte imbalances, metabolic disorders, and intoxications:

- Blood count, ESR, CRP, blood gas analysis (with acid–base balance, electrolytes including calcium and magnesium, glucose and lactate),

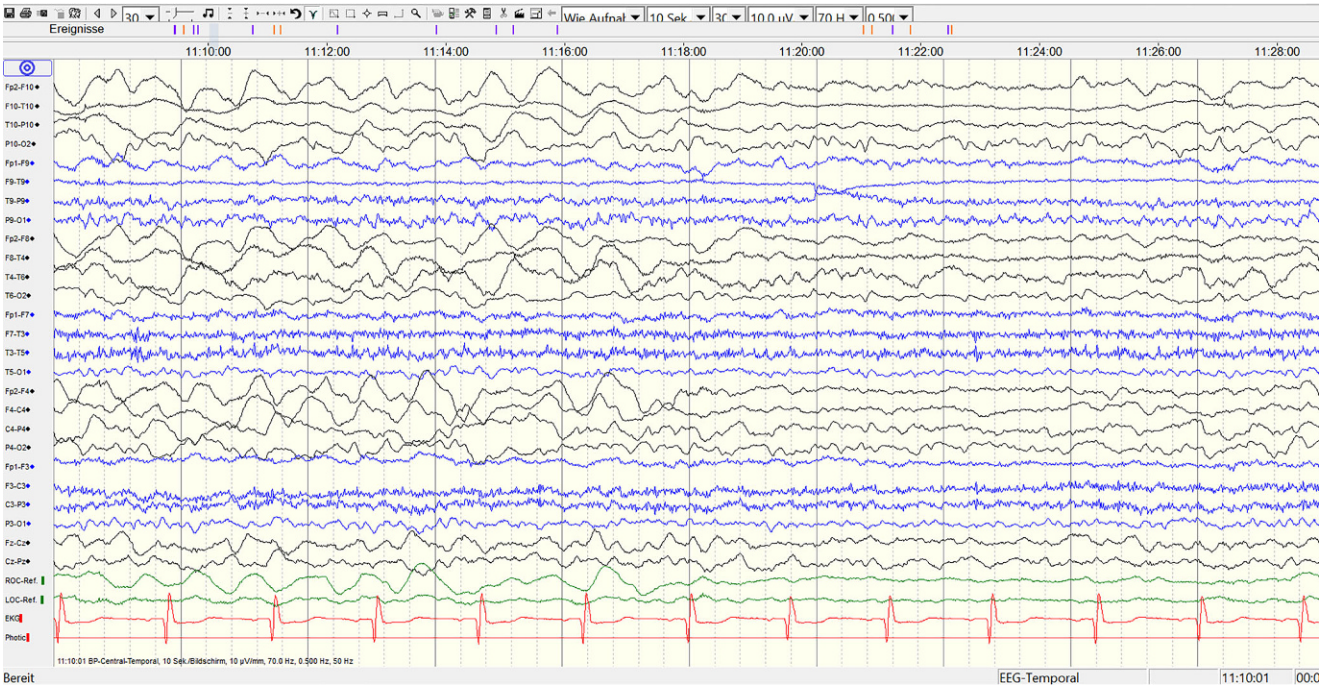

Fig. 1 ▲ Electroencephalogram of a 15-year-old boy with herpes encephalitis: temporal slowing accentuated in the right hemispheric frontotemporal region

coagulation including D-dimers, ALAT, ASAT, γGT, ammonia, creatinine, urea, TSH, fT3, fT4, CK
- Toxicological screening including ethanol, drugs, and heavy metals where appropriate, carboxyhemoglobin in the case of fire
- If infection is suspected: virus serology, in the case of fever, blood culture
- Metabolic screening: acylcarnitine profile, amino acids in plasma, ketone bodies and organic acids in urine
- Cortisol in suspected Addisonian crisis

Lumbar puncture

Lumbar puncture (LP) should be performed rapidly if CNS infection is suspected. Patients with unexplained loss of consciousness should undergo imaging before LP, especially if there is focal neurology or evidence of increased intracranial pressure (see "Brief neurological examination" above). However, LP is contraindicated in suspected sepsis with coagulopathy, unstable patients, full heparinization, and severe thrombocytopenia. In these cases, the platelet limit is unclear. In a study of patients with acute lymphoblastic leukemia, no severe complications occurred regardless of platelet count. In patients with platelets < 10,000/µl, platelet transfusion is recommended before LP, especially since the small number of patients did not allow any conclusions to be drawn for this subgroup [7]. The following values should be measured:
- Cerebrospinal fluid opening pressure
- Cell count, glucose, lactate, protein
- Bacteriological culture, Gram stain, viral PCR: herpes simplex 1 and 2, varicella-zoster virus, enteroviruses, in infants, possibly human parechovirus (hPeV; [8])
- Where appropriate, *Borrelia* IgG/IgM, mycoplasma IgA/IgG/IgM each from CSF and serum
- Where appropriate, determination of intrathecal antibodies, oligoclonal bands

Imaging

In cases of focal neurology, persistent and progressive loss of consciousness, clinical suspicion of elevated intracranial pressure, and/or evidence of traumatic brain injury, emergency cerebral imaging is necessary to assess the indication for neurosurgical intervention. In unstable children, CT is sufficient for this specific question [18].

In infants with an open fontanel, bedside cranial sonography provides rapid guidance. Unfortunately, processes of the posterior fossa and calvarial hemorrhage are poorly visualized on cranial ultrasonography. Magnetic resonance imaging of the skull has much greater validity and should be sought, especially in cases of suspected encephalitis, vasculitis, ischemic stroke, and sinus vein thrombosis [9].

Electroencephalography

The most important indication is the detection of a nonconvulsive status epilepticus. The main finding in the EEG is the detection of rhythmic activity with temporal and spatial trends. Epilepsy-typical potentials may still be detectable even after a prolonged course of status epilepticus. Status epilepticus is not discussed in this article.

Differentiating periodic patterns such as lateralized periodic discharges (LPDs) from a seizure pattern can be difficult. When in doubt, treatment with antiseizure medication can be attempted in both cases. These LPDs occur in herpes encephalitis and stroke, but also in tumors or anoxia. Herpes encephalitis has a predilection for the temporal lobe,

where temporal slowing is found in early stages ([10]; ◘ **Fig. 1**).

Nonepileptiform EEG abnormalities are rarely suggestive of etiology. Thus, Radermecker complexes are highly suggestive of subacute sclerosing panencephalitis. They are repetitive, generalized, bilateral, polymorphic complexes of predominantly 0.5–2 s duration occurring at 4- to 14-s intervals. In the same patient, at least for the duration of the EEG, the repetition frequency is relatively constant [6]. Nonepileptiform EEG abnormalities are more nonspecific in other cases, sometimes suggestive of a cause without being sufficient to diagnose the disease in question: for example, extreme delta brushes in anti-NMDA receptor encephalitis [11] and triphasic waves in metabolic encephalopathy [8, 12]. Triphasic waves are rarely found in children [13].

The EEG pattern rarely provides clues as to the cause of coma. Its main purpose is to provide an objective measure of the severity of encephalopathy, prognosis, and effectiveness of treatment. In mild encephalopathy, generalized slowing is seen. In more severe cases, a burst suppression pattern to a flatline (corresponding to electrocerebral inactivity) is observed. A number of different EEG patterns have been associated with coma: alpha coma, beta coma, spindle coma, theta/delta coma. Unlike physiological EEG patterns such as alpha EEG, these forms of coma lack responsiveness to external stimuli, such as (passive) eye opening. Prognosis varies, being better in spindle than in alpha coma. Lack of responsiveness and variability are negative prognostic factors [14].

Another EEG pattern associated with a mild form of encephalopathy is the presence of bursts of "intermittent rhythmic delta activity" (IRDA) superimposed on more or less normal background activity [14].

Continuous EEG monitoring is recommended to manage sedation induced for intracranial pressure therapy [15]. In cases of persistent or fluctuating loss of consciousness, the indication for continuous EEG monitoring should be made generously in order to detect electroencephalographic seizures; this monitoring should be performed for at least 24(up to 48) h [16].

If EEG is unremarkable in the presence of a disorder of consciousness that is high-grade according to clinical criteria, encephalopathy as a cause is very unlikely. In these cases, other causes such as locked-in syndrome (e.g., in lesions to the brainstem), acute neuromuscular disorders in, for example, botulism and Guillain–Barré syndrome, or psychogenic disorders of consciousness (such as akinetic mutism) must be included in the differential diagnosis [17].

Evoked potentials

In the pediatric intensive care unit, somatosensory evoked potentials (SEPs) and auditory evoked potentials (AEPs) in particular play a role in the prognostic assessment. Compared with EEG, these are less affected by sedating drugs and electrical interference [18].

In children with hypoxic ischemic encephalopathy, the combination of pathological findings on clinical examination (pupillary response and motor function), SEPs (absent N20 waves bilaterally), EEG (flatline or burst suppression pattern), and MRI (restricted diffusion in the cortex and basal ganglia) is highly predictive of poor prognosis. If there is appropriate pathology evident in the EEG, a metabolic or drug cause for the abnormalities should be excluded. These examinations should be performed 24 h after the triggering event [19].

Cardiological examinations

If there is evidence of cardiac etiology, echocardiography and, where appropriate, an electrocardiogram should be performed.

Intracranial pressure measurement

Intracranial pressure (ICP) measurement is indicated in traumatic brain injury with a GCS < 9 [20]. In other etiologies, the data on prognostic relevance are not established.

Optic nerve ultrasonography has been used with a mostly good correlation to ICP for the detection of elevated ICP [21].

Practical conclusion

Rapid diagnosis is essential in children with impaired consciousness. The preservation of vital functions according to ABC guidelines has absolute priority. The diagnosis and treatment must proceed simultaneously. Impaired consciousness is assessed quantitatively using the pediatric Glasgow Coma Scale. A brief neurological examination includes testing of the eyes and motor function as well as testing for meningism. Laboratory diagnostics include rapid exclusion of hypoglycemia and lumbar puncture if CNS infection is suspected. An emergency CT of the skull must be performed if unilateral/bilateral pupillary areflexia to light persists. In other cases, MRI of the skull should be sought, especially if encephalitis, vasculitis, ischemic stroke, and sinus vein thrombosis are suspected. The EEG serves primarily as an objective measure of the severity of encephalopathy, prognosis, and treatment efficacy. In rare cases, it provides indications as to the cause of coma.

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Funding. Open access funding provided by University of Bern

Declarations

Conflict of interest. I. Sanchez-Albisua declares that he has no competing interests.

For this article no studies with human participants or animals were performed by any of the authors. All studies mentioned were in accordance with the ethical standards indicated in each case.

The supplement containing this article is not sponsored by industry.

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