

Altered mental status (confusion, delirium, agitation)

Mechanism: Confusion and behavioral changes are in most cases the clinical picture of delirium (fluctuating confusion over time). Most commonly they arise on the basis of neurotransmitter imbalance, neuroinflammation (including autoimmune), metabolic failure, multifactorially, during intoxication and within withdrawal, or psychological causes. The main clinical principle is that a sudden change in mental status is a symptom of physical illness until proven otherwise.

Syndromes:

Hyperactive delirium: agitation, hallucinations, delusions, sometimes combative behavior

Hypoactive delirium: lethargy, depression, apathy

Mixed delirium: fluctuation between hyper- and hypoactive states

Withdrawal syndromes and intoxications: most often alcohol, CAVE often after medication (opioids, BZD)

Metabolic/toxic encephalopathy: diffuse cerebral dysfunction without focal signs

Encephalitis: fever, focal deficit (including epileptiforms); e.g. autoimmune anti-NMDA receptor encephalitis

Nonconvulsive status epilepticus: fluctuating confusion with subtle motor signs (automatisms)

Organic psychosyndrome / psychosis: structural cause (e.g. craniotrauma)

Acute psychosis or manic episode: with preserved consciousness and typically auditory (not visual) hallucinations.

Red flags:

- Fever + confusion + meningeal signs/epileptic seizures / focal deficits → bacterial meningitis or encephalitis
- Focal neurological deficit + acute onset → stroke or intracranial hemorrhage
- Hypoglycemia, severe hyponatremia, hypoxia, or hypercapnia → immediate correction
- Prolonged/fluctuating impairment of consciousness with subtle twitches/automatisms → nonconvulsive status epilepticus
- Ophthalmoplegia + ataxia + nystagmus → Wernicke encephalopathy (give thiamine before glucose!)
- Autonomic instability with rigidity and hyperthermia → neuroleptic malignant syndrome or serotonin syndrome
- Signs of withdrawal syndrome (tremor, restlessness, craving...).

Examination:

- 1) Determination of the time course and fluctuation of the state + basic vital signs
- 2) Blood count, electrolytes (ions), glycemia, liver tests, toxicological screening, urinalysis and culture
- 3) Noncontrast CT of the brain for suspected trauma, possibly perfusion and CTag for focal symptoms and suspected stroke
- 4) Lumbar puncture for suspected neuroinfection
- 5) EEG for suspected nonconvulsive status epilepticus.

Treatment: Treatment of the provoking cause + nonpharmacological care (first choice for all patients): reorientation (reminding them where they are, what day it is), presence of family, aids (glasses, hearing aids), early mobilization, normalization of the sleep cycle, ensuring hydration and nutrition; if insufficiently effective, pharmacological treatment (reserved for severe agitation)

- low doses of antipsychotics); BZDs only for withdrawal syndromes!; acute severe behavioral disturbances: attempt to calm the situation and ensure safety; if necessary, parenteral sedation.

Onset	Children	Adults
Acute	acute infections, drug or toxin intoxication, acute metabolic disorders (hypoglycemia), acute CNS infections and nonconvulsive seizures, craniotrauma	delirium (up to 95% of hospitalized!), acute intoxication or withdrawal syndromes (alcohol, drugs), acute metabolic encephalopathies (hypoglycemia, hyponatremia, dehydration, hypoxia), stroke or intracranial hemorrhage, craniotrauma
Subacute	subacute CNS infections / encephalitides	meningitis, encephalitis, nonconvulsive status epilepticus (often underdiagnosed), adverse effects of medications (anticholinergics, BZD, opioids~31%)
Chronic	developmental delay and autism spectrum disorders, primary psychiatric diseases and agitation in ASD	dementia, primary psychiatric disorders (psychosis, mania), advanced organ failures

Explanatory notes: BZD - benzodiazepines, CNS - central nervous system, ASD (PAS) - autism spectrum disorders.