# Differential diagnosis and management of non-psychiatric acute confusional states

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**Summary**

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Acute confusional states (ACS, syn. delirium) represent a medical emergency with significant morbidity, mortality and socio-economic consequences. This paper offers an overview on non-psychiatric causes of acute confusional states and their management. Identification of risk and precipitating factors for acute confusional states, neurological (stroke, traumatic brain injury, encephalitis, non-convulsive status epilepticus, etc.) and non-neurological causes (metabolic-septic encephalopathies, intoxications/poisonings, etc.) of acute confusional states and occurrence of acute confusional states in special settings (intensive care unit, postoperative situation, advanced cancer) are discussed first. Differential diagnosis, diagnostic work-up and treatment strategies of non-psychiatric acute confusional states are then presented. The review is completed with six clinical vignettes.

*Keywords: acute confusional state; non-psychiatric; delirium; diagnosis; treatment*

## Introduction

The acute confusional state (ACS, syn. delirium) is a frequent emergency which is associated with a significant morbidity/mortality and an important burden to health care. The frequency of acute confusional states has been estimated to be as high as 11–42% in medical in-patients [1] and to cause additional costs of about 2500 USD per patient [2]. The frequency of acute confusional states is higher in older patients, postoperatively and in intensive care. The frequency of neurological (intracerebral) and non-neurological (extracerebral) causes of acute confusional states depends upon the age and selection of patients (ambulatory versus hospitalised, medical/neurological/psychiatric/intensive care wards, etc.) [1, 3–5].

The diagnosis of acute confusional states is based on bedside clinical criteria including (1) a disturbance of attention (detectable for example with forward digit span test), (2) acute onset/fluctuating course and (3) incoherent/disorganised thinking with nonsense speech (amphigory [6]) (table 1 and 2). Altered level of consciousness with hypervigilance/insomnia/hyperactivity or hypovigilance/somnolence/hypoactivity ("quiet delirium", German "Dämmerzustand"), global/multiple cognitive deficits (detectable for example with the mini mental state examination), perceptual disturbances (illusions, hallucinations), psychomotor disturbances (hyperactive, hypoactive) and sleep-wake abnormalities are also frequently seen.

Prevention, evaluation and management of acute confusional states include the following steps:

- identification of patients at risk,
- evaluation of potential causes (primary neurological vs primary non-neurological causes),
- differentiation of acute confusional states from other conditions.

These three steps will be discussed in the following paragraphs in more detail.

## Risks and non-specific precipitating factors

Several predisposing (risk) factors for acute confusional states have been identified ("baseline vulnerability") [7]. The *main risk factors* are: (1) age >65, (2) pre-existing dementia ("delirium on dementia") or depression, (3) sensory impairments (vision, hearing), (4) malnutrition/dehydration, (5) alcohol abuse, (6) pre- and coexisting medical conditions and (7) multiple (particularly psychoactive) drugs.

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Particularly in older patients the presence of multiple risk factors may predispose them, in presence of non-specific or unobvious precipitating factors, to acute confusional states. Typical *non-specific precipitating factors* that can trigger acute confusional states include: (1) surgery, (2) intercurrent illnesses (infections, shock, hypoxia, anaemia, dehydration, bladder retention), (3) environmental factors (admission to intensive care unit, hospitalisation), (4) pain, (5) sleep deprivation, (6) emotional stress and (7) new psychoactive (particularly analgesic and sedating) drugs. Some of these factors are iatrogenic or preventable.

**Table 1** Differential diagnosis of acute confusional state / delirium.

| |
|---|
| **neurological causes** |
| stroke |
| traumatic brain injury, subdural haematoma |
| infectious encephalitis/meningoencephalitis |
| CNS vasculitis (Lupus, ...), limbic encephalitis |
| granulomatous meningoencephalitis (Tbc, sarcoidosis) |
| non-convulsive status epilepticus |
| migraine |
| **non-neurological causes** |
| hypoxia |
| hypoglycaemia, hyperglycaemia |
| hyponatraemia ("dilution delirium"), hypernatraemia |
| hypocalcaemia, hypercalcaemia |
| hepatic, uraemic encephalopathy |
| vitamin $B_1$ deficiency (Wernicke's encephalopathy) |
| vitamin $B_{12}$ deficiency |
| systemic colagenoses, chrondrocalcinosis |
| hyperviscosity syndrome |
| acute porphyria |
| endocrine disturbances (hyperthyroidism, hypothyroidism, Cushing's disease, adrenal/pituitary insufficiency) |
| drugs: levodopa, dopamin agonists, anticholinergics, antidepressants, antibiotics, chemotherapeutics, intrathecal medications, steroids, etc. |
| malignant neuroleptic syndrome |
| serotonin syndrome |
| alcohol withdrawal ("delirium tremens"), benzodiazepine/ barbiturates withdrawal |
| poisonings |
| **often multifactorial origin** |
| intensive care ("ICU delirium") |
| postoperative |
| advanced cancer |
| older patients |

Case 1

This 84-year-old man (E. H.) is hospitalised for evaluation of a subacute right lombosciatalgia in October 2007. On admission he is alert, oriented in space but only partially in time. His attention and his mini mental state score (28/30) appear to be within normal limits. A sensory deficit in the dermatome L5 and a positive Lasègue's sign on the right side are found. Symptomatic treatment with increasing doses of non-steroidal analgesics and subsequently, because of persisting pain even at rest/night, with steroids and opioid derivates is installed. Within a few days the patient develops a hypovigilant acute confusional state ("quiet delirium") in association with a status febrilis (temperature >38, C-reactive protein levels >100) and a urinary infection with *E. coli.* His attention (forward digit span of 2–3) and his mini mental state score (16/30) are reduced. The acute confusional state resolves progressively under antibiotic treatment and reduction of the opioid medication.

This case illustrates the occasional presence in an older patient of multiple precipitating factors (pain, sleep deprivation, medication, infection) of an acute confusional state.

**Table 2**
Diagnostic work-up of patients with acute confusional state / delirium.

| | |
|---|---|
| **history** | |
| 1 | vulnerability profile |
| 2 | triggering factors |
| 3 | known medical, neurological, psychiatric disorders |
| **clinical examination** | |
| 1 | mental status |
| 2 | focal neurological signs |
| 3 | other neurological symptoms/signs |
| 4 | other medical findings |
| **investigations** | |
| 1 | laboratory (see table 1) |
| 2 | neuroimaging (stroke?, subdural haematoma?, encephalitis?, etc.) |
| 3 | cerebrospinal fluid (infection?, autoimmune disorder?, paraneoplastic disorder?) |
| 4 | EEG (status epilepticus?, metabolic/toxic encephalopathy?, etc.) |
| 5 | others (toxicological screening, etc.) |

## Potential causes of an acute confusional state

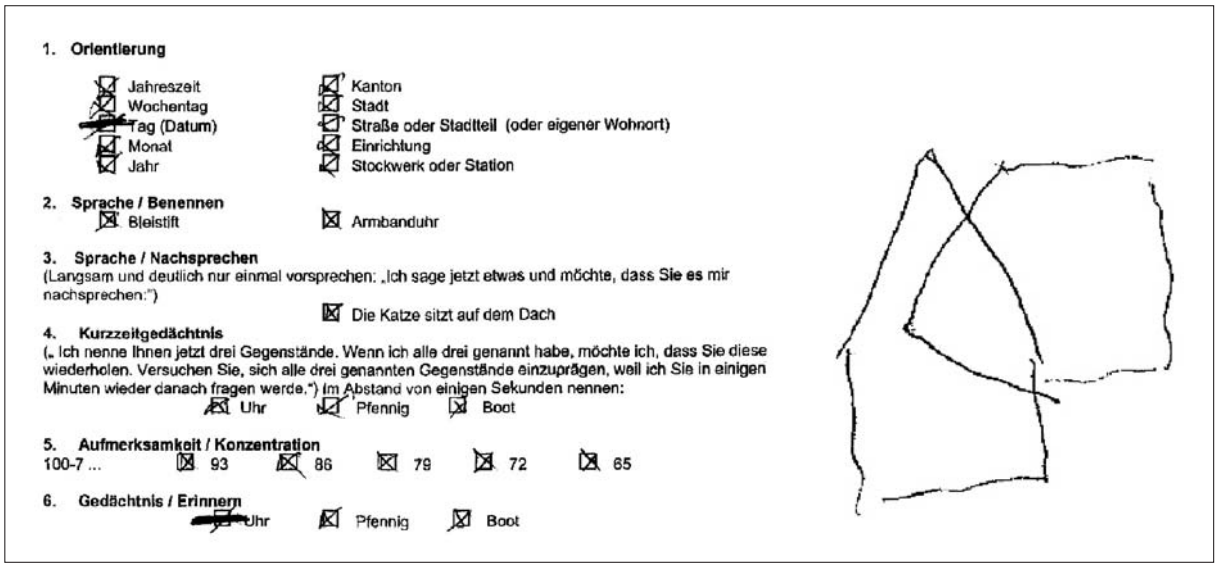
### Neurological causes

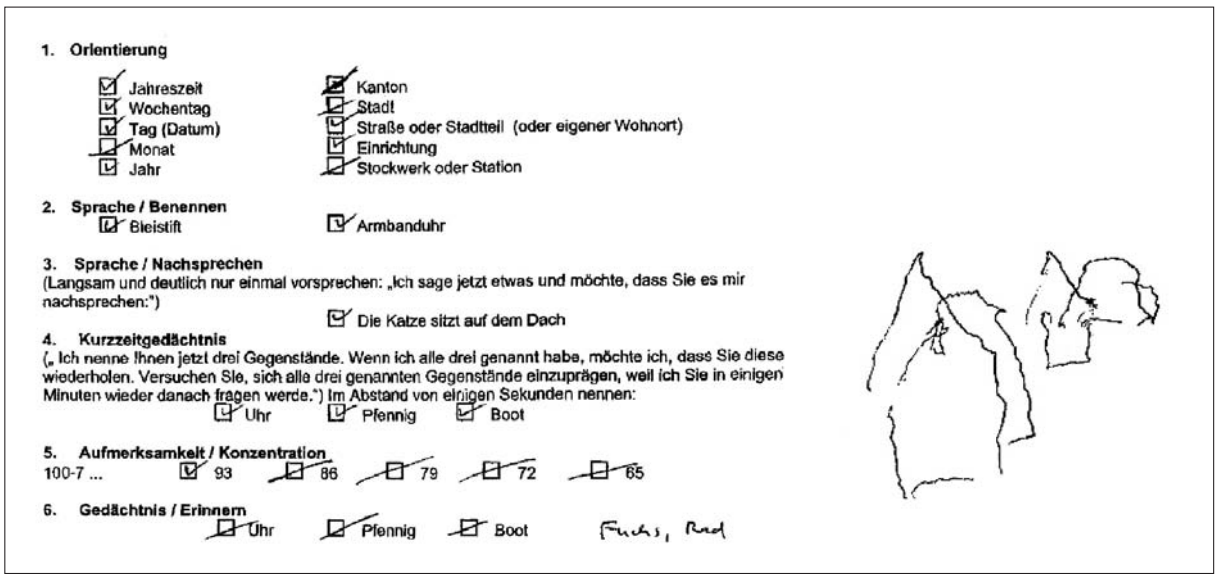
*Stroke*

An acute confusional state is found in about 10–20% of stroke patients. Both hypovigilant/hypoactive and hypervigilant/hyperactive forms of acute confusional states are possible. In some patients hallucinations, behavioural changes (fig. 1), neuropsychiatric symptoms may additionally be observed [8, 9]. Focal neurological findings can be minor and easily overlooked on a superficial/cursory clinical examination (vertical gaze palsy in thalamo-mesencephalic strokes [fig. 2], visual field deficits in temporal and parieto-occipital strokes). The presence of an acute confusional state with visual hallucinations (Lilliputian) has been observed first with tegmental midbrain stroke *peduncular hallucinosis* [10, 11]. Lesions in the thalamus, stratum and occipital lobes can lead to the same clinical picture [12, 13].

Advanced age, severe stroke, specific topographies (frontal, temporo-parietal, occipital, thalamo-mesencephalic, right-sided) are more often associated with acute confusional states [9, 14–17]. Associated metabolic disturbances, fever, sleep-wake disturbances, emotional distress and epileptic seizures may also play a role.

**Figure 1** An 84-year-old man (E. H.) with acute confusional state of multifactorial origin (age, pre-existing mild memory impairment, analgesics, pain, medication, see text) in October 2007.
*The upper picture shows* extracts of his mini mental state score (MMS 28/30) with practically normal orientation, unremarkable 100-7 test (5x), recall within minutes of 3 out of 3 names and satisfactory copy of intersecting figures the day of admission. *The lower picture shows* extracts of his mini mental state score (MMS 16/30) with partial disorientation, abnormal 100-7 test (1x), recall within minutes of 0 out of 3 names and unsatisfactory copy of intersecting figures 20 days later when he, while still confused, was already recuperating from severe acute confusional state.



Case 2

This 54-year-old man (U. T.) presents an acute confusional state in September 2002 in the course of a bilateral acute ischaemic stroke in the paramedian thalamus.

Case 3

This 67-year-old man (J. A.) presents an acute confusional state in November 2006 in the course of an acute ischaemic stroke in the right occipital lobe (fig. 3). In the acute phase disorientation difficulty in using the cellular phone and mild headaches occur. On examination left upper homonymous quadrantanopsia is found. The patient makes a recovery from the acute confusional state within hours.

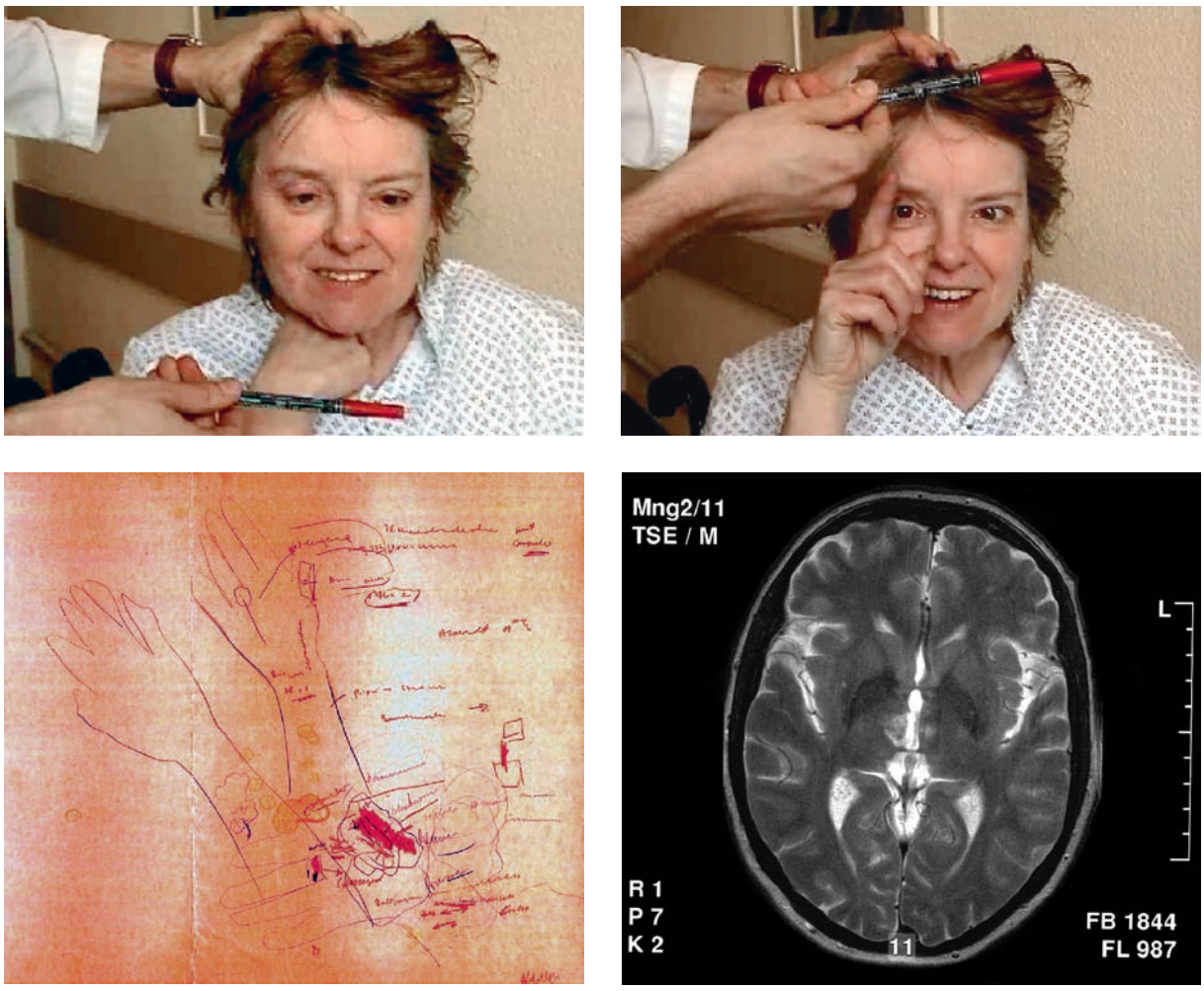
Case 4

This 79-year-old woman (R. S.) presents an acute confusional state in March 2006 in the course of an acute ischaemic stroke in the left parietal lobe (fig. 4). In the acute phase disorientation and speech difficulties occur. On examination mild sensory aphasia, abnormal forward digit span [3] and a mini mental test score (MMS) of 16/30 are found. The patient makes a recovery from the acute confusional state within several days. At a follow-up examination a few months later digit span is 5 and MMS 30/30.

*Traumatic brain injury*

Brain lesions after trauma are classified according to localisation (diffuse, focal, multifocal), time course (acute, subacute, chronic) and severity. A variety of cognitive and behavioural disturbances

**Figure 2** A 54-year-old woman (U. T.) with acute confusional state in the course of a bilateral acute ischaemic stroke in the paramedian thalamus in September 2002.
The first two pictures show downgaze and upgaze palsy which – together with neuropsychiatric changes (childish behaviour with "high-pitched voice", hyperorality with craving for chocolate, perseverations, hallucinations), amnesia and hypersomnia – was the leading clinical sign. The third picture shows a drawing of the patient during the acute confusional state where she depicted (and made written comments about her) hallucinations on injuries/bleeding of both her arms.

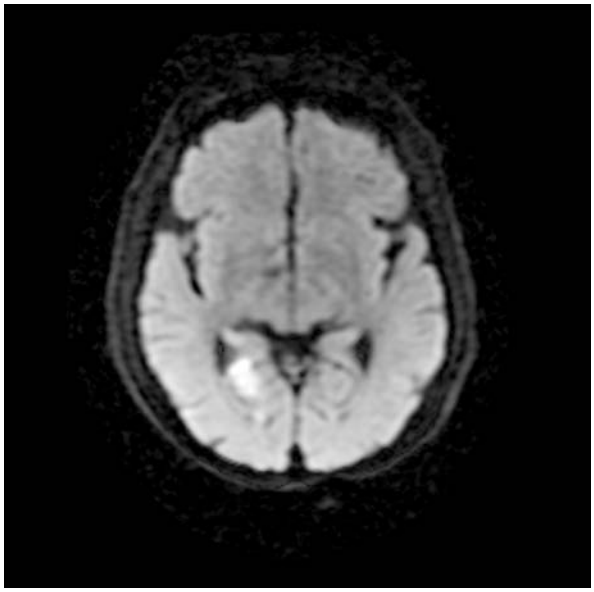



(Brain MRI: courtesy of Prof. A. Valavanis, Neuroradiology Department, University Hospital, Zurich, Switzerland.)

including acute confusional states and posttraumatic amnesia can be observed in patients with acute traumatic brain injuries [18, 19].

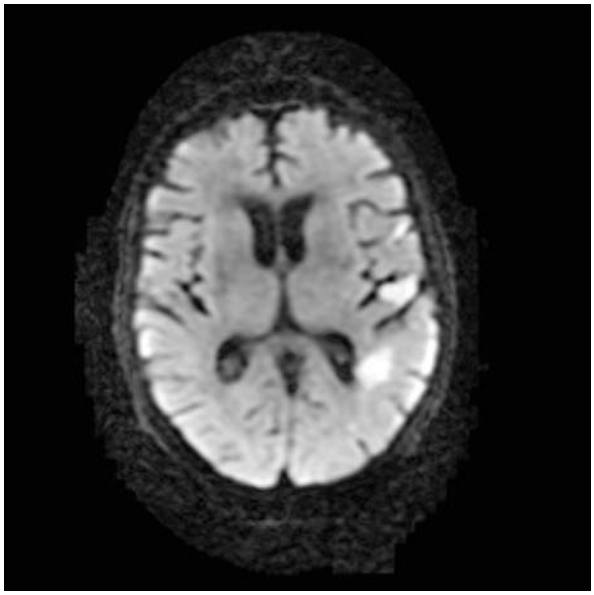
The presence of acute confusional states is predictive of a poorer outcome after *acute traumatic brain injury* [20]. Headaches, fluctuating hypovigilant acute confusional states and focal epileptic seizures are typical of *chronic subdural haematomas* [18]. The latter can occur in older patients after mild traumas, in particular in alcoholics and people using anticoagulants.

**Figure 3** A 67-year-old man (J. A., see text) with acute confusional state and acute ischaemic stroke in the right occipital lobe (cuneus, shown in a diffusion-weighted brain MRI).



(Brain MRI: courtesy of Prof. A. Valavanis, Neuroradiology Department, University Hospital, Zurich, Switzerland.)

**Figure 4** A 79-year-old woman (R. S., see text) with acute confusional state and acute ischaemic stroke in the left parietal lobe (shown in a diffusion-weighted brain MRI).



(Brain MRI: courtesy of Prof. A. Valavanis, Neuroradiology Department, University Hospital, Zurich, Switzerland.)

Case 5

This 78-year-old man (W. S.-H.) presents an acute confusional state in November 2006 in the course of a bilateral chronic subdural haematoma (probably consequence of a fall in June 2006), complicated by a focal convulsive status epilepticus (fig. 5). In the acute phase disorientation in time and space and decreased level of consciousness ("quiet delirium") occur. On examination somnolence, repetitive clonic activity of the right face and arm, paraphasias, perseverations and echolalia are found. The patient makes an incomplete recovery from the acute confusional state at discharge (three weeks later).

*Encephalitis/meningoencephalitis*

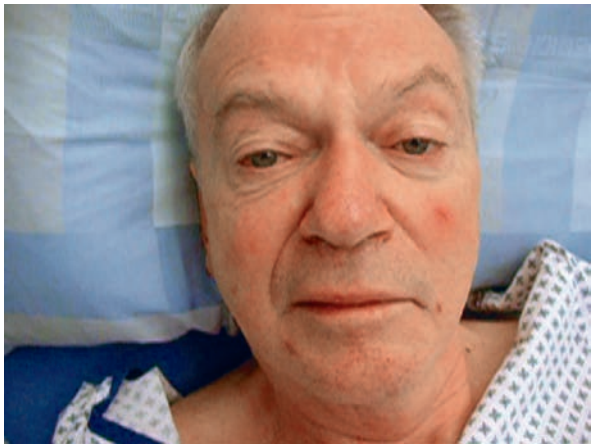
*Herpes simplex encephalitis,* the most frequent sporadic encephalitis, typically presents with acute-onset fever, headache, acute confusional states with hallucinations (olfactory, gustatory), personality/behavioural/psychiatric changes, seizures (and occasionally status epilepticus [fig. 6]) and focal neurological deficits (hemiparesis, aphasia, ataxia). Lymphocytic pleocytosis, asymmetric and enhancing MRI abnormalities in the frontal and temporal lobes (in 90% of cases) and focal EEG changes (including periodic lateralised epileptiform discharges [PLEDs]) are typically associated. The cerebrospinal fluid herpes simplex polymerase chain reaction has a sensitivity/specificity >95% for the diagnosis [21].

The differential diagnosis of herpes simplex encephalitis includes other herpetic (for example varicella), viral (for example HIV [22, 23]) and non-viral (for example bacterial or fungal) forms of encephalitis and meningoencephalitis as well as *autoimmune disorders* of the central nervous system (limbic encephalitis, neurolupus, antiphospholipid syndrome, Hashimoto thyroiditis and primary CNS angiitis, see also below) [24]. Granulomatous disorders such as *tuberculosis* and *sarcoidosis* can also rarely present with an acute confusional state [25, 26].

In susceptible and/or older patients also *non-cerebral, systemic infections* such as pneumonia, urinary tract infections *("cystocerebral delirium")* and septicaemia can lead to acute confusional states.

*Limbic encephalitis* is an autoimmune disorder, often (but not invariably) related to cancer, which is in about 50% of cases associated with serum antibodies against intracellular antigens (Hu, Ma2, amphiphysin, etc.) or cell membrane-antigens (voltage-gated potassium channels [VGKC], etc.). Classical limbic encephalitis presents with

**Figure 5** A 78-year-old man (W. S.-H.) with acute confusional state and bilateral chronic subdural haematoma. The picture demonstrates the mild contraction of the right frontal, periocular and nasolabial musculature in the course of the right-sided, focal, convulsive status epilepticus.



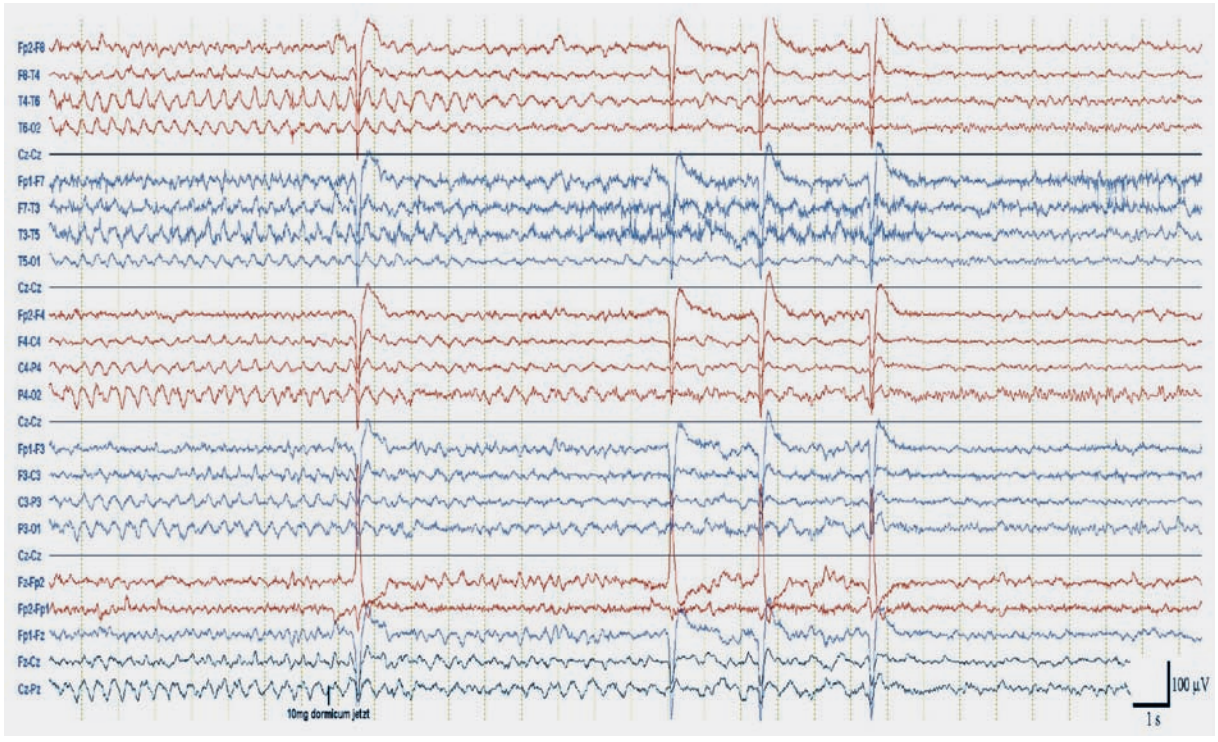
the subacute onset of attention and/or memory disturbances, personality/behavioural/psychiatric changes and seizures [27, 28]. It is typically associated with anti-Hu antibodies and lung cancer. Variants of limbic encephalitis may present with hypersomnia ("diencephalic encephalitis", often associated with anti-Ma antibodies and testis tumour), movement disorders ("basal ganglia encephalitis" and "stiff person syndrome") or brain-stem symptoms/signs ("brain-stem encephalitis"). Liquor pleocytosis, brain MRI changes in the limbic (and/or other specific brain) areas and auto-antibodies are necessary for the diagnosis [29].

*Non-convulsive status epilepticus*

A non-convulsive status epilepticus (NCSE) can be defined as a change in behaviour/cognition associated with continuous epileptiform discharges in the EEG [30].

The so-called *"absence status"* (non-convulsive generalised status epilepticus) typically presents with a fluctuating, hypovigilant/hypoactive acute confusional state (with decreased spontaneity, slow speech, hallucinations) which can continue for days to weeks [31, 32]. Multifocal myoclonic jerks and rhythmic blinking can be observed. The EEG reveals a generalised epileptiform activity. The aetiology may be a petit mal epilepsy (since childhood) or a "de novo" epilepsy (in adulthood). In the latter case, benzodiazepine/alcohol with-

**Figure 6** A 27-year-old woman (A. F.-S.) with an agitated acute confusional state. During a trip to Italy the patient becomes progressively agitated, hallucinating and violent. Three days after onset of the acute confusional state a brain CT is normal, the patient is referred to a psychiatric institution. Because of subfebrile temperature, ataxia, dysarthria and fluctuating acute confusional states with visual hallucinations the patient is referred to our institution. Liquor analysis reveals a lymphocytic pleocytosis (14–44 cells/ml). All microbiological and serological tests are negative (viral encephalitis of unknown origin). The EEG demonstrates the presence of a focal, non-convulsive status epilepticus (in form of rhythmic, high amplitude waves over the left fronto-opercular region) which is interrupted by 10 mg of Dormicum® intravenously.




(Courtesy: PD D. Zunsteg and Prof. H. G. Wieser, Epileptology Division, Neurology Department, University Hospital, Zurich, Switzerland.)

drawal, metabolic disturbances, (herpes) encephalitis [21] (fig. 6), stroke and brain trauma may be involved [33].

The so-called *"complex partial status"* (non-convulsive focal status epilepticus) may appear similar to the "absence status", except for the presence of automatisms, a more fluctuating course and a focal EEG epileptiform activity [34–36].

The differential diagnosis of NCSE in patients with known epilepsy includes a prolonged postictal confusion, a metabolic-toxic encephalopathy (related to antiepileptic therapy), a structural brain damage (including encephalitis, which can also be the cause of epilepsy [fig. 6]) and an (associated) psychiatric disorder.

*Migraine*

The presence of an acute confusional state has been reported as *"confusional migraine"* in patients with basilar migraine and with familial hemiplegic migraine, conditions that are today considered as belonging to the same spectrum of disorders [37–39].

## Non-neurological causes

*Metabolic/septic encephalopathies*

Metabolic/septic encephalopathies are probably the most common cause of acute confusional states.

*Hypoxia* (due to low cardiac output, respiratory insufficiency, pulmonary embolism or fat embolism) can lead to acute confusional states. The trias tachypnoea/dyspnoea, cerebral symptoms (including acute confusional states) and petechiae suggests the presence of a *fat embolism syndrome,* which is often (but not invariably) due to trauma (and fractures) [40].

Neuroglycopenic symptoms of *hypoglycaemia* include headache, blurred vision, diplopia, transient hemiparesis, acute confusional states and coma. Hypoglycaemia can arise in the fasting state or as a reactive phenomenon (after eating, alcohol, etc.). Patients with insulinoma presenting with an acute confusional state (occasionally at night) are well described in the literature [41]. *Hyperglycaemia* usually presents with polyuria, thirst, fatigue, rapid (Kussmaul) breathing (if ketoacidotic) and mental changes including acute confusional states and coma.

Dehydration and rapid changes in electrolyte levels (natrium, magnesium) may also lead to acute confusional states. *Hyponatraemia* due to water intoxication *("diluting delirium")* may present with acute confusional states and is seen as paraneoplastic syndrome (due to SIADH), after head trauma, or secondary to drugs (antiepileptics, antidepressants, etc.) [42]. Rapid correction of hyponatraemia with mental changes, pseudobulbar palsy and spastic tetraparesis suggest *pontine myelinolysis* [43]. An extrapontine (supratentorial) variant of this syndrome presents with mental changes (including acute confusional states) and movement disorders. *Hypernatraemia* can lead to seizures and mental changes including acute confusional states [44].

*Hypercalcaemia,* often as paraneoplastic manifestation, presents with mental changes including acute confusional states, fatigue, nausea and polydipsia/polyuria [45]. *Hypocalcaemia* due to hypoparathyroidism can also lead to acute confusional states, sometimes in association with papilloedema [46].

*Hepatic encephalopathy* presents with a wide spectrum of symptoms including asterixis, slurred speech, somnolence and such mental changes as acute confusional states and coma [47, 48].

*Uraemic encephalopathy* can present with a similar, typically fluctuating clinical picture [49]. Seizures and restless legs syndrome may also be present. Acute confusional states in the course of *dialysis* may be caused by different mechanisms (cyclosporine and other drugs, vitamin $B_1$ deficiency, etc.) [50].

*Wernicke's encephalopathy* (pseudoencephalitis haemorrhagica superior) is due to thiamine (vitamin $B_1$) deficiency with perivascular haemorrhages in midbrain, hypothalamus and corpora mamillaria. The complete classical triad of acute confusional states (82–90% of cases), ataxia and ocular signs (gaze plasies, nystagmus) is only observed in a minority of patients [51]. In clinical situations known to be associated with vitamin $B_1$ deficiency (see below) even the presence of an isolated acute confusional state should make one considering the diagnosis of Wernicke's encephalopathy. Amnesia with confabulations is also often seen (Korsakoff's syndrome) [52]. Vitamin $B_1$ deficiency is usually related to chronic alcoholism, can, however, also arise from chronic dialysis, hyperemesis gravidarum, poor nutrition and wasting (terminal) illnesses [51].

Vasculitis, collagenoses and autoimmune disorders with involvement of the central nervous system, such as *neuro-lupus, neuro-behçet,* acute demyelinating encephalomyelitis *(ADEM)* and *Hashimoto's encephalopathy* can also present with acute mental changes including acute confusional states [53–55].

*Vitamin $B_{12}$ deficiency* can also manifest with acute confusional states, occasionally even in the

absence of blood changes and other (spinal cord, peripheral nervous) symptoms/signs [56].

Older subjects can develop an acute confusional state with fever and painful proximal limb weakness in the course of acute attacks of systemic *chondrocalcinosis* (pseudogout) [57].

Mental changes including acute confusional states can be seen with hyperviscosity syndrome *("paraproteinaemic delirium").*

*Acute porphyria* presents with abdominal pain, nausea-vomiting, (occasionally ascending) motor paralysis and cerebral symptoms including acute confusional states and seizures. Attacks are typically triggered by barbiturates or other drugs.

Endocrine disturbances such as *hyperthyroidism, hypothyroidism* [58], Cushing's syndrome, adrenal and pituitary ("lethargia pituitaria") insufficiency are frequently accompanied by mental changes including acute and subacute confusional state and coma.

*Toxic encephalopathies / poisonings*

Dopaminergic drugs *(levodopa and dopaminergic agonists)* can exacerbate or trigger "de novo" an acute confusional state in patients with Parkinson's disease. The presence of an underlying cognitive impairment should always be looked for in these patients. In some patients the neurodegenerative process may play a more important role than medications [59].

*Malignant neuroleptic syndrome* (MNS) is a syndrome characterised by the insidious (rarely fulminant) onset of acute confusional states with fever, muscle rigidity and serum creatine kinase elevation in patients treated with antipsychotic drugs [60]. A similar clinical picture has been observed in patients treated with antiemetics and after abrupt withdrawal from dopaminergic drugs. The differential diagnosis of MNS includes serotonin syndrome, malignant hyperthermia and poisoning with anticholinergics.

*Anticholinergic drugs* and medications with anticholinergic effects (tricyclic antidepressants, antihistaminics, benzodiazepines, codein, digoxine, theophylline, oxybutynin, valproate) can trigger acute confusional states in older subjects [61].

Serotoninergic drugs (tricyclic antidepressants, SSRI, mirtazapine, trazodone, lithium, monoamino oxidase inhibitors, opiod analgesics, valproate, sumatriptan, etc.) can lead, occasionally within hours after starting a new drug in monotherapy [62], to a spectrum of clinical manifestations ranging from mild and non-specific symptoms (tremor, akathisia) to a life-threatening acute confusional state *(serotonin syndrome)* which is typically associated with neuromuscular signs (tremor, hyperreflexia, ataxia) and autonomic instability (fever, tachycardia, sweating, diarrhoea) [63].

*Intrathecal drugs* often lead to acute confusional states.

*Corticosteroids* in high doses can lead to acute confusional states within days even in otherwise mentally healthy subjects.

Antibiotics such as *cephalosporines* and *chemotherapeutics* can lead to encephalopathies with acute confusional states, tremor, myoclonus and seizures [50].

High doses of *salicylates* can lead to respiratory alkalosis, fever, hearing loss, acute confusional states and eventually coma.

The alcohol withdrawal syndrome *("delirium tremens")* is characterised by a hyperactive acute confusional state with restlessness, tremor, hallucinations, seizures and autonomic changes (fever, tachycardia, sweating). A similar clinical picture is seen in patients with *benzodiazepine and barbiturate withdrawal* [64].

Poisoning with different drugs can lead to acute confusional states and eventually coma. Associated symptoms and features of clinical presentation can be of diagnostic help. Mydriasis, tachycardia and ECG changes (poisoning with *anticholinergics*); mydriasis, tachypnoea, tachycardia, arterial hypertension *(amphetamines, cocaine);* and respiratory depression, arterial hypotension *(barbiturates)* are suggestive *"toxidromes".*

Intoxications with lead, organic solvent, manganesy, mercury and heavy metals can also present with an acute confusional state.

## Special situations

*Intensive care unit*

An acute confusional state is observed in 20–50% of ICU patients *("ICU delirium"),* typically 2–3 days after admission, and in up to 60–80% of those receiving mechanical ventilation [65] and leads to longer hospitalisations, threefold higher in-hospital mortality and increased costs [65]. Most patients are somnolent/hypoactive, some patients are hypervigilant/hyperactive ("ICU psychosis").

*Postoperative situations*

An acute confusional state is not infrequently observed in the postoperative setting, particularly after *cardiac surgery* (30–50% of patients after open heart or coronary bypass surgery). Orthopaedic and urogenital surgery is also not infrequently complicated by acute confusional states.

Cataract surgery may lead to visual hallucinations without acute confusional states (Charles Bonnet's syndrome, see below).

*Advanced cancer*
An acute confusional state is observed in at least 30% of patients with advanced cancer and even more frequently in terminally ill cancer patients. The differentiation between a cerebral (for example in the context of leptomenigeal carcinomatosis) and a non-cerebral cause of acute confusional state is not always obvious [66].

Multiple factors including age, hypoxia (low cardiac output, respiratory insufficiency, anaemia), metabolic changes (hypercalcaemia, renal insufficiency, etc.), fever, sleep deprivation, pain, microemboly, fat embolism, medications (psychotropics, antibiotics, etc. [50]), infections, psychological stress/fear/unfamiliarity, poor nutrition (and vitamin $B_1$ deficiency [51]) and sensory deprivation can contribute to the appearance of acute confusional states in the intensive care unit and postoperatively.

*Psychiatric disorders*
Acute confusional states of psychiatric origin can be observed in the course of acute/transient psychotic disorders, severe depression episodes, manic episodes *("delirious mania")* or as toxic effect of pharmacological treatment of these disorders. The contribution of Dr. Bader in this issue of the *Swiss Archives of Neurology and Psychiatry* discusses in detail acute confusional states of psychiatric origin.

## Conditions to be differentiated from an acute confusional state

### Dementia

Dementia is characterised by a progressive change of mental status with often insidious onset, no (or only limited) fluctuations, preserved attention (until late stages), no or only minor changes in sleep-wake cycle and autonomic functions. Patients with dementia are more susceptible, in the presence of triggering/precipitating factors, to develop acute confusional states *("delirium on dementia")*. In patients with *Parkinson's disease* and *Lewy body disease* with hallucinations, fluctuations and sleep-wake disturbances the differentiation between acute confusional states and dementia may be difficult.

### Transient global amnesia

Patients with transient global amnesia (TGA) present the sudden loss of both antero- and retrograde amnesia accompanied by anxiety and repetitive questions concerning their environment. Episodes typically last only a few hours in the absence of attention problems and other mental changes [67]. The origin of transient global amnesia is unknown. Recurrences are rare (about 10% of cases).

Complex partial seizures, migraine and transient limbic ischaemia can mimic transient global amnesia. Drug and alcohol intoxications and head trauma can also cause transient amnesia.

### Wernicke's aphasia

Patients with acute stroke and Wernicke's aphasia are not uncommonly mistaken initially has being confused. These patients exhibit language changes (prominent paraphasias, neologisms, agraphia) but a normal attention and also no other features of acute confusional state. In some stroke patients aphasia and delirium can, however, co-exist (see above).

### Hallucinations without confusional state

Patients with sensory (visual, acoustic) deprivation are prone to develop hallucinations. *Charles Bonnet's syndrome* refers to complex visual hallucinations which, in the presence of a preserved insight, can last for hours to days in the context of acute visual deterioration ("visual hallucinations of the blind", [12]). This syndrome may occur in up to 10% of patients with acute visual loss [68].

## Management of non-psychiatric acute confusional states

The first aim in the management of acute confusional state is to remove its cause and its potential triggering factors. All patients' medications should be reviewed and potentially implicated drugs should be discontinued.

Non-pharmacological treatment approaches include the frequent reorientation and information of the patients; the involvement of family members (for communication and support) and sitters; the use of non-pharmacological relaxation methods (massage); the normalisation of sleep-wake patterns (avoidance of naps, quiet room, low levels lighting); the avoidance of sensory under-

(use of eyeglasses, hearing aids, soft music) and overstimulation (limit noise and visits), unfamiliarity (family pictures, night light) and physical restraints [7]; sufficient hydration and accompanied mobilisation.

*Haloperidol* (starting at 0.25 mg i.v./p.o. up to 50 mg daily) and *quetiapine* (starting at 25 mg twice a day) can be used to control anxiety, agitation, hallucinations and aggression. Quetiapine and *clozapine* should be preferred in patients with Parkinson's disease and acute confusional states.

Benzodiazepines such as *lorazepam* (starting at 1 mg i.v./p.o., up to 20 mg daily) are the drugs of first choice for alcohol- and benzodiazepine-withdrawal delirium and are also often used in malignant neuroleptic and serotonin syndrome. In other forms of acute confusional states benzodiazepines should be avoided.

*Cholinesterase inhibitors* can improve acute confusional states in patients with Parkinson's disease and Lewy body dementia.

*Dopaminergic drugs* are used in malignant neuroleptic syndrome.

The average duration of acute confusional states is days to a few weeks. In some (particularly) older patients the confusional state may persist for months. The 1-year mortality rate associated with acute confusional states in hospitalised patients is 35–40% [7].

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