### Excited delirium: A psychiatric review

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#### **Abstract**

The term 'excited delirium' (ED) is used to explain sudden and unexpected restraint-related deaths. Since the 1990s, ED has often been identified as the principal cause of death in restrained individuals, rather than the restraint procedure itself. Forensic pathologists and psychiatrists attach different meanings to the term delirium. For psychiatrists, delirium is a specific technical term, which implies a grave and potentially life-threatening underlying physical illness. If a patient dies during a bout of delirium, psychiatrists assume that there will be autopsy evidence to demonstrate the primary underlying organic cause. Conversely, pathologists appear to be using the term ED to refer to restraint-related deaths in either highly disturbed cocaine users or psychiatric patients in a state of extreme agitation. In these cases, there is no underlying physical disorder other than a terminal cardiac arrhythmia. As the term ED has different meanings for psychiatrists and for pathologists, it would be helpful for these two professional groups to develop a mutually agreed terminology.

#### **Keywords**

Ambiguity of term, Excited Delirum, restraint-related deaths

#### Introduction

An authoritative review of the medical literature on excited delirium (ED) shows that the term is currently used by forensic pathologists, medical examiners and emergency physicians in North America to refer to the following constellation of events:

- An unexpected death during or following restraint in a public or private place, in a police vehicle, in custody or in a medical institution.
- The reason for the restraint is that the subject, usually male, has been behaving in a violent and uncontrollable manner, which presents a severe threat to the safety of other people and/or to himself.
- The subject's behaviour prior to and during restraint involves extreme physical exertion and manifests profound emotional and psychological disturbance.
- In addition to uncontrollable, violent and destructive behaviour, the subject might shout incoherently, sweat profusely and take off his clothes. He is often hyperthermic. He appears to be impervious to pain.
- The subject may be intoxicated by cocaine, amphetamines or other psychostimulants, with or without alcohol. Alternatively, the subject may have a history of a bipolar or schizophrenia spectrum disorder.

 Autopsy material fails to provide a satisfactory explanation for the cause of the death, which might then be attributed, by a process of exclusion, to ED.<sup>1</sup>

There has been an important divergence of understanding of the term 'delirium', which has developed over the past 30 years or so since Wetli and Fishbain<sup>2</sup> used the term ED specifically to explain deaths during or after restraint in American recreational cocaine users. Since then, ED has been invoked to explain numerous other sudden and unexpected restraint-related deaths. Forensic pathologists, medical examiners and psychiatrists currently use the term to mean very different medical scenarios. The term 'excited' in psychiatry is a non-specific adjective used to describe agitation and frantic hyperactivity. By contrast, 'delirium' is a specific technical term, which by definition implies a grave and potentially life-threatening underlying physical illness.

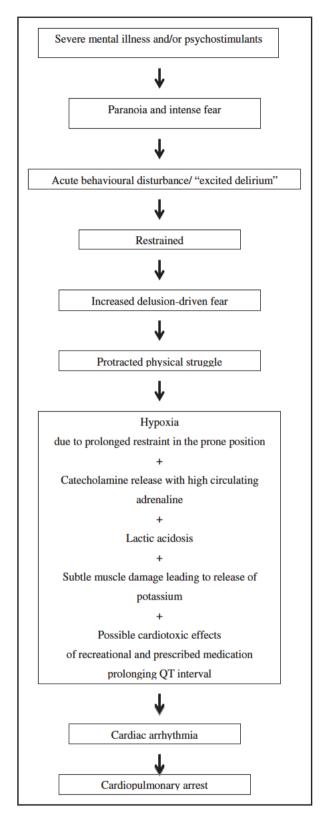
However, the term ED or 'agitated delirium' is often used by North American medical examiners and forensic pathologists to describe any drug- or

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**Figure 1.** The psychophysiological sequence of events in fatal cases of so called excited delirium showing the pivotal role of prolonged restraint in the prone position.

non-drug-induced state of frenetic excitement, which has a fatal outcome following a restraint. For example, Otahbachi et al.<sup>3</sup> describe ED as a 'psychiatric emergency characterised by extreme agitation, hostility and severe mania which can progress to death'.

### The current clinical psychiatric meaning of delirium

The term delirium is synonymous in clinical psychiatric practice with 'acute confusional state', 'acute brain syndrome', 'acute organic reaction' and 'acute psycho-organic syndrome' in which there is by definition an underlying and potentially identifiable medical cause for the disturbed behaviour.

The key clinical feature of delirium is an acute onset of impaired attention, reduced concentration and diminished awareness of the environment. The patient is disorientated in time, place and person, and their short- and long-term memory are impaired. There is a disrupted sleep-wake cycle with daytime somnolence and an exacerbation of symptoms at night. Thinking is disorganised, and speech tends to be irrelevant, unfocused or illogical. There can be hyperactivity, and psychotic symptoms occur in about 50% of cases. Patients experience agitation and delusions and an intense fear of being in danger from others, and are often hypervigilant. There can also be visual hallucinations and illusions, and there may be paranoid delusions. The patients may become combative and defend themselves against imaginary threats or enemies.

These symptoms develop over a period of hours, and they tend to fluctuate in intensity. In delirium, the clinical picture may be predominantly hyperactive, but in a proportion of cases, the patient may be almost stuporose. Delirium is far more common in medical or surgical intensive care units, in hospices and in nursing homes for the elderly than in young adults.

For psychiatrists, delirium, by definition, is the neuropsychiatric manifestation of either intoxication by, or withdrawal from, a psychoactive substance, or of one or more underlying serious and potentially fatal medical conditions which might be infective, inflammatory, metabolic, vascular, neoplastic or traumatic. It can also be caused by the acute withdrawal of alcohol or by the administration of recreational or prescribed drugs.

Some symptoms of delirium overlap with the symptoms of primary psychiatric disorders. However, there is, by definition, no identifiable underlying organic pathological disorder in primary psychiatric conditions. In acute schizophrenia and in brief psychotic disorder, there are delusions and mainly auditory hallucinations. Furthermore, in contrast to delirium, inattention is less prominent, and orientation and memory are generally intact in these acute psychotic states.

From a psychiatric perspective, if a patient dies during a bout of delirium, there will be autopsy evidence to confirm the underlying organic cause (e.g. septicaemia). Thus, the cause of the patient's death is not their psychiatric disorder or their agitated behaviour, but a grave underlying medical condition, property of Statement 17, 2015

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which will be revealed at autopsy. In the absence of an underlying physical cause for an acute behavioural disturbance, the use of the term 'delirium' in this way is self-contradictory.

The implication of the forensic pathologists' use of the term is that ED itself could be the cause of death (as in most of Bell's original cases; see below<sup>5</sup>) or that it renders the patient more vulnerable to cardiac arrest when restrained. For Karch, ED itself is a lethal condition, regardless of whether or how the subject is restrained.<sup>6</sup>

### Potentially lethal acute psychiatric disorders

As already indicated, delirium is the neuropsychiatric manifestation of a grave and life-threatening underlying physical disorder. There are only two acute primary psychiatric disorders which can be life threatening: Bell's mania and malignant catatonia. <sup>5,8</sup> (Anorexia nervosa can also be life threatening, but it is a chronic rather than an acute condition).

#### Bell's mania

Prior to the onset of the widespread recreational use of cocaine and other psychostimulants in the USA in the 1970s and 1980s, acute excited states were generally attributed to severe mental illness. The first systematic description of a rare, grave form of mania characterised by severe clouding of consciousness and rapidly evolving acute excitement that terminated in death in a high proportion of cases was published by Dr Luther Bell in 1849 in the American Journal of Insanity. 5 Bell described 11 cases of 'delirious exhaustive mania' characterised by uncontrollable behavioural excitement combined with some features of delirium, especially disorientation, for which no organic cause could be determined clinically. The duration of 'delirious mania' in the six patients who died ranged from 12 days to 8 weeks with an average overall duration of severe behavioural disturbance of 25 and a half days. At autopsy, there were no specific pathological findings in fatal cases of delirious exhaustive mania.

Nowadays, patients with delirious mania respond to standard treatments for mania. In one series of three patients with Bell's mania treated with electroconvulsive therapy, all recovered. In

#### Malignant catatonia

There have been reports in the psychiatric literature of the similarities between Bell's mania and malignant catatonia. This is a rare life-threatening febrile neuropsychiatric syndrome, which may develop in association with both 'functional' (i.e. non-organic psychotic) and organic illnesses. Malignant catatonia is characterised by mounting fever and extreme hyperactivity that progresses to stuporous, exhaustion.

With medical intervention, there is a reported survival rate of nearly 40%.

#### Neuroleptic malignant syndrome

There are important similarities between the late stages of the malignant catatonia syndrome and the neuroleptic malignant syndrome, which is an acute febrile disorder with a high mortality rate. In addition to hyperpyrexia, the clinical features include catatonic stupor with muscular rigidity which can develop after the administration of neuroleptics.<sup>8</sup>

### Acute behavioural disturbance and the risk of fatal outcome

In general, severely disturbed behaviour which requires restraint might have: (a) a medical cause, (b) a primary psychiatric aetiology, or (c) be due to recreational drug use (Figure 1, page 2)

Medical causes include those numerous organic conditions which cause delirium as defined in both DSM-IV and DSM-5 as well as in ICD-10 and in standard medical and psychiatric textbooks. There is an obvious mortality associated with the underlying organic condition. Neuroleptic malignant syndrome would be included in this section. Most antipsychotic drugs can also be associated with sudden, unexplained and unexpected deaths.<sup>11</sup>

The primary psychiatric causes of severely disturbed behaviour include mania, acute schizophrenia and brief psychotic disorders. Excluding suicide, these disorders do not generally in and of themselves carry the risk of a fatal outcome from physiological causes, although obviously these individuals might be involved in fatal accidents.

A manic state lasting for weeks might have a fatal outcome arising from a physiological cause (e.g. dehydration), but not as a direct result of the psychiatric disorder itself. (Malignant catatonia is an extremely rare condition, and the cause of death in these cases is unclear.)

In a cocaine- or amphetamine-induced psychotic state, a death during restraint might be due to the combination of physical asphyxia and cardiac toxicity or to either one of these causes, taken separately.

#### Fatal ED and psychostimulants

Since the extensive use of cocaine and other psychostimulants in the USA from the 1970s, the term ED has become widely used to account for deaths during restraint where no other underlying medical cause has been established, especially if there is evidence of current or past use of cocaine or amphetamines. <sup>12</sup>

An influential paper published in 1985 by a Florida medical examiner and a psychiatrist first used the term ED to describe seven recreational cocaine users, five

of whom died in police custody.<sup>2</sup> At autopsy, a definite cause of death was not established.

These subjects had presented with intense paranoia of sudden onset, followed by bizarre and violent behaviour which required forcible restraint. They engaged in extreme exertion while trying to escape or resisting arrest or during the attempts to subdue them. They showed unexpected strength and hyperthermia. They all suffered a sudden and unexpected fatal respiratory collapse within a few minutes to an hour after the restraint. Their blood concentration of cocaine was about 10 times lower than that seen in fatal cocaine overdoses. Their deaths were attributed to 'autonomic reflexes', arrhythmias and 'restraint stress'.

Wetli and Fishbain<sup>2</sup> explicitly derived the term ED from a chapter by Lipowsky in Kaplan's standard American textbook of psychiatry, published in 1979.<sup>4</sup> Liposwky had described two clinical variants of delirium, the hyperalert-hyperactive and the hypoalerthypoactive type. By definition, delirium, in its 20th century and current usage, is a clinical condition caused by one or more identifiable underlying organic causes. Wetli and Fishbain's cocaine-intoxicated subjects were certainly hyperactive, but the defining features of delirium (i.e. a fluctuating disturbance of consciousness with reduced ability to focus, sustain or shift attention, together with altered cognition or perceptual disturbance) were not present. On the contrary, the most prominent symptoms were fear, panic, shouting, physical violence, hyperactivity and violent struggle when restrained. These seven case histories make no mention of the global impairment of cognition with disorientation, memory impairment and attention deficits, which are pathognomonic of delirium.

# Why is the use of the term ED not formally recognised by American or British psychiatrists?

ED does not appear as a separate diagnostic category in DSM-IV or DSM-5, or in ICD-10. The term 'delirium' in the American forensic pathology literature is not used in the restrictive DSM or ICD sense of acute behavioural disorder attributed to an underlying organic condition. Although the term ED is not recognised by the American Medical Association or the American Psychiatric Association as a diagnosis, it is now endorsed as a discrete diagnostic entity by the American College of Emergency Physicians and the National Association of Medical Examiners to refer to those cases of extremely severe agitation and hyperactivity combined with threatened or actual physical violence which are generally attributed to illicit drugs and/or severe mental illness. <sup>1</sup>

While for psychiatrists delirium is a clearly defined syndrome with well-established and specific clinical features and demonstrable underlying organic causes, the generic adjective 'excited' in ED is used to describe any uncontrollable, violent and destructive behaviour which requires restraint and which is generally presumed to be caused by intoxication with recreational drugs, or by a severe psychiatric disorder.

In 2012, the Task Force of the American College of Emergency Physicians reviewed 18 reports on ED in the medical literature to establish if this behaviour is definable as a discrete medical entity. They concluded that ED is a syndrome characterised by delirium, agitation, acidosis and hyperadrenergic autonomic dysfunction. ED was typically encountered in subjects with acute-on-chronic drug abuse, or a psychotic illness, or both. A proportion of these subjects experienced a sudden and fatal cardiac arrest.<sup>1</sup>

The Task Force insisted on retaining delirium as one of these defining characteristics, although the 18 publications which they reviewed made little mention of the altered sensorium and fluctuating cognitive impairment which for psychiatrists are the defining features of delirium.

British psychiatrists prefer the terms 'acute excited state' or 'acute behavioural disturbance' to describe such bouts of alarming, frantic, irrational and potentially dangerous physical activity. In their authoritative handbook *Psychiatric Intensive Care*, Beer et al. 13 give a comprehensive descriptive definition of acute behavioural disturbance requiring urgent intervention: 'It usually manifests with mood, thought or behavioural signs and symptoms and can either be transient, episodic or long-lasting. It can have either a medical or psychological aetiology [emphasis added] and may reflect a person's limited capacity to cope with social, domestic or environmental stressors. The use of illicit substances or alcohol can accompany an episode of acute disturbance, or can be causative. The acute disturbance can involve threatening or actual violence towards others, the destruction of property, emotional upset, physiological distress, active self-harming behaviour, verbal hallucinatory behaviour, disinhibition, disorientated or confused behaviour and extreme physical overactivity - "running amok" (p. 14).

Such aggressive behaviour is often unprovoked and is seemingly random or bizarre. Factors associated with an increased risk of violence in people with mental disorders include substance abuse and the presence of psychotic symptoms such as persecutory delusions, command hallucinations and delusions of being controlled.<sup>14</sup> It is important to emphasise that the term 'acute behavioural disturbance' is definitely not synonymous with excited delirium because delirium, by definition, requires an identifiable organic cause, which will be ascertained at autopsy, if not earlier. Ten years ago, the Metropolitan Police Authority Restraint and Mental Health Review<sup>15</sup> recommended that the term 'excited delirium' should not be used. However, it is still being used in connection with the deaths of severely agitated individuals during or shortly after restraint, despite the absence of an identifiable underlying organic disorder.

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In summary, British and most American psychiatrists do not recognise the term ED because cases of the acute behavioural disturbance which they encounter do not necessarily have an underlying organic cause, which is the defining feature of delirium. Furthermore, the presenting symptoms of acute behavioural disturbance do not necessarily include impaired attention, concentration, memory and orientation, which are the core clinical features of delirium.

### The risk of death in so-called excited delirium

Since the 1990s, acute/excited/agitated delirium has often been identified as the principal cause of death in restrained individuals, rather than the restraint procedure itself. In these cases, the fatal ED is attributed to either cocaine or, less commonly, to an underlying psychotic condition. Karch is one of the major proponents of this view. <sup>6,7</sup> Most cases diagnosed as ED in the USA have been chronic cocaine users. Ruttenber et al. <sup>16</sup> claim that chronic cocaine use may predispose individuals to develop fatal ED 'though the mechanism remains to be elucidated'. A smaller group consists of psychiatric patients in their first episode of psychosis or longer-term patients who have stopped their antipsychotic medication.

Vilke, Payne-James et al.<sup>12</sup> suggest that there is 'a spurious perception' that ED is uniformly fatal. Their review of ED shows that only about 10% have a fatal outcome.

Thus, although fatalities can occur during or shortly after the restraint procedure, most individuals with psychiatric or drug-induced acute behavioural disturbance who require physical restraint do not have bad medical outcomes. A prospective study has shown the rarity of a fatal outcome of the use of restraint by the police in excited and agitated individuals. As the American forensic pathologist James Gill has concluded, only a few of the thousands of emotionally disturbed individuals who are restrained, die suddenly.

The mortality associated with ED is multifactorial. Vilke, Bozeman et al.<sup>20</sup> conclude that the pathophysiology of ED is not well understood and that it is not clear why some cases progress to death. Frequently encountered associated factors include sub-lethal cocaine levels. The combination of sympathomimetic agents such as cocaine and amphetamines and a continued struggle despite physical restraint increases the risk of a fatal outcome.

Mash et al.<sup>21</sup> in a paper entitled 'Brain biomarkers for identifying excited delirium as a cause of sudden death' report that a central nervous system dysfunction of dopamine signalling may underlie both ED and fatal autonomic dysfunction. They describe a two-protein biomarker signature in a series of 90 ED deaths, which they propose as a reliable tool for

identifying ED at autopsy. Takeuchi et al.<sup>22</sup> conclude that there may be 'central neuronal system dysfunction of dopamine signalling as a cause of the delirium and fatal autonomic dysfunction' (p. 83).

Other associations include severe metabolic acidosis and copious adrenaline release during or after a violent struggle, in a restrained position causing cardiovascular collapse.<sup>23</sup> Otahbachi et al.<sup>3</sup> have speculated that there may be a fatal stress cardiomyopathy in these cases. It has also been suggested that there may be a genetic basis for fatal ED.<sup>24</sup>

## The causative role of the restraint procedure

Restraint is defined as being held against active resistance by physical or mechanical means. In restraint-related deaths, there are often minimal physical findings at autopsy, and in many cases it is not possible to delineate a single causal factor for the death of a restrained individual. Sudden unexplained deaths during or shortly after restraint have been attributed to a variety of factors which may work synergistically.

## The psychophysiological sequence of events in fatal cases of so-called ED showing the pivotal role of prolonged restraint in the prone position (Figure 1)

The conclusion reached by Reay et al.<sup>25</sup> that the deaths of three men who were being transported in police vehicles in the prone position were caused by positional asphyxia has been challenged by a study of normal volunteers who did not develop hypoxia or hypercapnea while held in the restrained prone position after a period of supervised controlled exercise.<sup>26</sup> However, this experiment, carried out under carefully supervised laboratory conditions in healthy volunteers, fails to replicate the massive autonomic nervous system response to the combination of a grossly disturbed mental state, frantic combative behaviour and the physical struggle associated with being restrained.

Ross<sup>27</sup> reviewed 61 cases of ED deaths associated with restraint in police custody. The subjects tended to have a very high body temperature. Sixty per cent of these individuals were intoxicated with cocaine. Ruttenber et al.<sup>16</sup> concluded that chronic cocaine use causes impaired dopamine function and may predispose victims to ED with acute cocaine toxicity associated with extreme physical exertion and/or restraint.

Stratton et al.<sup>28</sup> reviewed the records of more than 200 subjects in Los Angeles who had been involved in a forceful struggle and were 'hogtied' in the prone position (i.e. their wrists and ankles were bound together behind their backs). About 10% of these individuals died suddenly during or shortly after the restraint. More than three-quarters of the subjects who died had been using psychostimulant drugs, and more than half were obese. Fifty-six per cent

had atherosclerosis, and 12% had a history of mental illness.

Pollanen et al.<sup>29</sup> described 21 cases of sudden unexpected death in people with ED who were restrained by the police in the prone position. Twelve of the subjects had an unspecified psychiatric disorder. Eight had abused cocaine. The authors concluded that positional asphyxia during restraint in the prone position might have contributed to the fatal outcome. By contrast, Otahbachi et al.<sup>3</sup> conclude from this study that 'psychiatric disorder without current recreational drug use predisposes to excited delirium-related deaths'.

In most of these cases, the cause of death is not identified at autopsy. In their review, Otahbachi et al.<sup>3</sup> also conclude that the pathogenesis is probably multifactorial. Furthermore, the restraint deaths were not always immediate but could be delayed.

In summary, many of the published reports on restraint deaths which are attributed to ED show that a high proportion of the victims had taken cocaine, which sensitises the heart to adrenaline and noradrenaline. Cocaine can also cause paranoia and delirium, which leads to fear, suspiciousness, excitement and hyperactivity.

One hypothesised mechanism is the toxic effect of high levels of catecholamines on either cardiac myocytes or on the coronary microvasculature. The autopsy evidence to support this hypothesis would be the presence of contraction bands in the myocardium with normal coronary arteries.<sup>3</sup> Michaud<sup>30</sup> has proposed that the cardiovascular consequences of the prone restraint technique should receive more emphasis. He has also drawn attention to possible mitochondrial dysfunction induced by drugs and extreme physical exertion.

#### **Conclusions**

There is no evidence that acute behavioural disturbance alone is other than a rare cause of death. There is also no evidence that correctly restrained behaviourally disturbed patients are commonly at risk of death. Since the majority of cases will survive arrest, restraint and being transported to custody or to hospital, it appears to me that there is a distinct need for statistics on the frequency of restraint-related deaths in acute behavioural disturbance in all those cases where the restraint procedure has been *correctly* performed.

As the term ED has different meanings for psychiatrists and for pathologists, it would be helpful to have a dialogue between coroners, forensic pathologists and psychiatrists in this country to elucidate the precise meaning of ED and to work out a mutually agreed terminology.

At present, the term ED might imply that an acute behavioural disturbance can, in and of itself, be the main cause of death, even in the absence of an underlying demonstrable organic cause. However, it is debatable whether ED as defined clinically and pathologically can be conclusively regarded as the main cause of death as opposed to the cardiotoxic effects of psychostimulants and/or aspects of the restraint procedure itself.

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#### **Conflict of interests**

The author has served as a paid expert witness at inquests in England regarding sudden deaths in custody.

#### Note

a. This simple scheme excludes deaths during restraint where the individual does not actually present with an acute behavioural disturbance (e.g. a suspected offender who is apprehended and restrained with excessive force and without standard precautions to prevent accidental death by asphyxia).

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