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Rapid communication

Brain biomarkers for identifying excited delirium as a cause of sudden death

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ABSTRACT

Excited delirium (ED) syndrome is a serious medical condition associated with acute onset of agitated violent behavior that often culminates in a sudden unexplained death. While the contribution of restraint, struggle and the use of conductive energy devices (CED) to the cause and manner of death raise controversy, a CNS dysfunction of dopamine signaling may underlie the delirium and fatal autonomic dysfunction. We conducted a mortality review for a case series of ninety excited delirium deaths and present results on the association of a 2-protein biomarker signature. We conducted quantitative analyses of the dopamine transporter and heat shock protein 70 validated for specificity and degree of interindividual variation. Incident circumstances, force measures, autopsy and toxicology results were determined for all subjects. A majority of the victims in this case series tested positive for cocaine in blood and brain, although four had no licit or illicit drugs or alcohol measured at autopsy. Mean core body temperature where recorded was 40.7 °C. The expression of the heat shock protein HSPA1B transcript was elevated 1.8–4-fold in postmortem brain. The elevation of Hsp70 in autopsy brain specimens confirms that hyperthermia is an associated symptom and often a harbinger of death in these cases. Dopamine transporter levels were below the range of values measured in age-matched controls, providing pathologic evidence for increased risk of chaotic dopamine signaling in excited delirium. When combined with descriptions of the decedents' behavior prior to death, a 2-protein biomarker signature can serve as a reliable forensic tool for identifying the excited delirium syndrome at autopsy.

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1. Introduction

Victims of excited delirium syndrome who present in a highly agitated state often die in police custody, while being restrained or incapacitated by deployment of conductive energy devices (CED) [1–3]. Excited delirium is one of several terms that describe a syndrome characterized by delirium and agitation, combativeness, unexpected strength and elevated body temperature. Although there is no anatomic cause of death in excited delirium, catecholamine-induced cardiac arrhythmias, restraint or positional asphyxia, or adverse cardiorespiratory effects of CED (e.g. TASER[®]) are often cited [3–5]. However, case reviews demonstrate that the individual is medically unstable and in a rapidly declining state that has a high risk of mortality even with medical

intervention or in the absence of restraint stress or CED deployment [5,6].

Delirium is a syndrome, or group of symptoms, caused by a disturbance of consciousness in the normal functioning of the brain [7]. In hyperactive delirium, there is a change in awareness and response to the environment, which manifests as agitation, hallucinations, delusions, and psychosis. Over 150 years ago, Dr. Luther Bell described a disease in institutionalized psychiatric patients resembling some advanced stage of mania and fever as an overlooked and often unrecorded malady [8]. Fishbain and Wetli [9] recognized the same syndrome in a cocaine body packer, and their report was followed by a series of case reports of excited delirium most often associated with chronic stimulant abuse [10–16]. Although there was no single causal factor cited, long-term psychostimulant abuse appears to increase risk for excited delirium.

We present a retrospective analysis and mortality review of factors associated with sudden unexpected deaths of individuals in states of excited delirium. Scene investigation, autopsy and toxicology results were reviewed for a case series of 90 excited

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