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ORIGINAL ARTICLE

Electrical weapons and excited delirium: shocks, stress, and serum serotonin

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Abstract

It has been suggested that a CEW (conducted electrical weapon) exposure could elicit a stress response that could cause ExDS (excited delirium syndrome). There are some parallels between the signs of ExDS and serotonin syndrome (SS). Electroconvulsive therapy raises serotonin levels and therefore provides a plausible link between CEW applications and elevated serotonin levels. This study was designed to determine whether a CEW exposure elevates serum serotonin. A total of 31 police academy cadets were exposed to a very broad-spread 5-s CEW stimulus from a TASER brand X26 CEW. Blood was drawn before and after the exposure and at 24 h post exposure to measure serum serotonin levels. Lactic acid and cortisol levels were also compared. Median serum serotonin levels were 30 IQR (21,46), 36 IQR (22,50), and 32 IQR (21,45) ng/mL before exposure, after exposure, and 24 h after exposure (NS by pooled comparisons). The increase from baseline to post-test serotonin (Δ median = +6, Δ mean = +2.7) ng/mL was not significant by a paired T-test ($p = .29$) but was significant by the Wilcoxon signed-rank test ($p = .037$). The increase to post-test *log* serotonin was not significant by a paired T-test ($p = .13$) but was significant by the Wilcoxon test ($p = .049$). All serotonin levels remained within the normal reference range of 0–200 ng/mL. Post-hoc analysis demonstrated that the study was powered to detect a ½ SD change, in *log* serotonin, with a 90% likelihood. With a very-broad electrode spread, CEW exposure did not significantly raise serum serotonin levels.

Keywords Force · TASER · Weapon · CEW · Serotonin · Excited delirium

Introduction

Arrest-related death (ARD) syndrome describes sudden non-firearm death during law-enforcement restraint. While many ARDs are due to well-studied entities such as subclinical cardiomyopathy and drug toxicity, there is significant overlap with excited delirium syndrome ("ExDS"). The American College of Emergency Physicians has recommended the use of the CEW (Conducted Electrical Weapon) in the setting of ExDS to reduce the risk of acidosis from a prolonged physical struggle [1]. However, it has been questioned whether a CEW causes such metabolic or adrenergic derangements that could cause or contribute to sudden death. Lee et al. have suggested that a CEW exposure could elicit a stress response that could actually cause ExDS [2, 3].

The mechanisms by which ExDS is precipitated or how sudden death occurs in the setting of ExDS has still not been fully delineated. Since there are some parallels between the signs of ExDS and other hyperthermic disorders, including serotonin syndrome (SS), it is relevant to explore and consider the similarities and differences between ExDS and SS as clinically distinct syndromes, and whether ExDS may be caused by serotonergic excess. It is also noteworthy that serotonin is a neuro-endocrine stress biomarker. It was therefore decided to test whether a CEW exposure elicits a stress response that elevates serum serotonin.

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Electroconvulsive therapy (ECT), for the treatment of resistant major depressive disorder, provides another plausible link between CEW applications and serotonin levels. The mechanism of ECT action has not been fully elucidated but it appears to down-regulate serotonin receptors in the brain and also cause transient elevations of plasma serotonin and a catecholamine surge (note: typical ECT therapy delivers 20 watts vs. the CEW which delivers less than 2 watts of electrical power) [4–6].

In the Hasani study 36 major depression patients (age: 20–65 years old) were allocated to an ECT group ($n = 21$) and a non-ECT group ($n = 15$) [7]. Serum serotonin levels of the ECT group were measured before ECT, 15 min and 2, 6, and 24 h after the first session, and 24 h and 30 days after the last ECT session. Measurements were performed at the time of admission and 30 days after hospitalization in the non-ECT group. Mean serotonin levels of the 2 groups were elevated at 24 h and 30 days after the last session of ECT ($p = 0.048$ and $p = 0.04$, respectively). Mean serotonin levels in the ECT group were also elevated from baseline 15 min after ($p = 0.044$), 6 h after ($p = 0.015$), 24 h after ($p = 0.007$), and 24 h after the last ECT ($p = 0.002$).

There have been cases of transient serotonin syndrome initiated by ECT [8–10]. Conversely, there have been cases where ECT was thought to have treated serotonin syndrome [11, 12].

There exists a strong positive correlation between serotonin levels in cerebral spinal fluid and blood plasma and serum [13–15]. Thus peripheral serotonin levels might be used as a surrogate for central concentrations. In whole blood, serotonin is mainly stored in platelets and thus free and unbound serum serotonin is more likely to represent the cerebral levels. This study was designed to investigate whether a very-broad electrode spread CEW exposure would raise serum serotonin concentrations.

Methods

Study design Participants were cadets from the Austin (Texas) Police Academy who had previously volunteered to undergo CEW exposure. The CEW exposure was performed by Academy staff per their normal training methods. The study was approved by the Institutional Review Board of Texas A&M University. Consent forms were obtained from all volunteers. The medical monitor of the study interviewed each consenting volunteer to exclude any subjects with recent illness, musculoskeletal injury, pregnancy, lactation or with any known cardiovascular, pulmonary, or hematological condition.

CEW application Each subject was positioned face-down on a narrow, slightly raised padded mat (approximately 60 cm wide × 180 cm long × 30 cm high) such that the torso and legs were supported by the mat but the arms and hands could move easily about the side and front of the mat.

Alligator clips were connected to the CEW on the subject's shoulder (clamped to the shirt in the mid-scapula region of right shoulder) and waist (clamped to the upper edge of pants mid-way from spine to right margin). These locations were chosen to achieve maximal CEW-induced control of the subject's upper and lower extremities by simulating a 45–61 cm CEW-probe spread [16]. The goal was to obtain the highest level of muscle contraction within the training-authorized 5 s in order to increase the likelihood of detecting an increase of serotonin, lactate, and cortisol. The alligator-clipped electrodes were applied manually to ensure consistency of lead placement throughout data collection. A standard X26 CEW was triggered by an instructor. Electrical current delivery lasted for a duration of a standard 5-s cycle (single pull of the trigger), as used in training and in the field.

Serum biomarker protocol A 20 mL venous blood sample was taken before, immediately after, and at 24 h following the CEW exposure. All phlebotomies were performed by certified emergency medical technicians using routine venipuncture practices, wherein a sterilized intravenous catheter was placed in the vein of the anterior forearm for ease and repeatability. All drawn blood specimens were labeled, collected and transported to an off-site facility by an independent laboratory organization (Laboratory Corporation of America, Austin, TX).

The primary endpoint was serotonin shifts. Secondary endpoints were shifts in lactate and cortisol.

Statistical analysis Pooled comparisons were by Student's t-test. Paired comparisons were also done by Student's T-test and the Wilcoxon signed-rank test. Serotonin levels were analyzed by both raw values and after a natural logarithm transformation. Since no one has tested serotonin levels with a CEW exposure, an a priori power estimate could not be made. Due to the non-normally distributed findings, log conversion was necessary for analysis. Post-hoc analysis demonstrated that the study was powered to detect a ½ standard deviation change, in log serotonin levels, with a 90% likelihood.

Results

A total of 31 subjects (28 male and 3 female) participated and provided blood samples before and after the CEW exposure. Subject ages ranged from 21 to 55 years. A single subject (Z990) failed to return at 24 h and thus the long-term values are calculated with $n = 30$. His baseline (pre-test) and post-test serotonin levels were 29 and 20 ng/mL, respectively.

Median serum serotonin levels were 30 IQR (21–46), 36 IQR (22–50), and 32 IQR (21–45) ng/mL before exposure, after exposure, and at 24 h after exposure (NS by pooled

comparisons). The baseline serotonin levels were very non-normal with 3 Tukey outliers for high values (see Fig. 1). We repeated the pooled comparisons for the natural logarithm of serotonin levels but there was still no significant difference.

The increase from baseline to post-test serotonin (Δ median = 6, Δ mean = 2.7, $n = 31$) ng/mL was not significant by a paired T-test ($p = 0.29$) but was significant by the Wilcoxon signed-rank test ($p = 0.037$). The increase from baseline to post-test *log* serotonin (Δ mean = 0.125 equivalent to 13% average increase) was not significant by a paired T-test ($p = .13$) but was significant by the Wilcoxon signed-rank test ($p = 0.049$). The confidence interval for the serotonin increase was (−7.5, 13.0 ng/mL); for the *log* serotonin increase it was (−0.1, 0.3).

The change from baseline to 24-h serotonin (Δ median = + 2.5, Δ mean = −0.9, $n = 30$) ng/mL was not significant by either a paired T-test ($p = 0.54$) or the Wilcoxon signed-rank test ($p = 0.21$). The increase from baseline to 24-h *log* serotonin was not significant by either a paired T-test ($p = 0.42$) or the Wilcoxon signed-rank test ($p = 0.23$). All serotonin levels remained within the normal reference range of 0-200 ng/mL.

Median lactic acid levels were 12 IQR (9–14), 20 IQR (18–24), and 8 IQR (7–11) mg/dL for baseline, post-test, and at 24 h. Mean lactic acid increased immediately following the CEW application from 12.2 ± 4.0 to 21.0 ± 5.8 mg/dL ($p < 0.0001$ by both paired T-test and Wilcoxon signed-rank test). The statistically significant increase in lactic acid demonstrated metabolic stress and was expected based on the full-trunk exposure causing involuntary contraction of most of the skeletal muscles. Lactic acid levels decreased to normal levels within 24 h—probably much sooner but the day after was the next collected sample. The 24-h levels were 9.6 ± 4.2 mg/dL which was slightly lower than baseline ($p = 0.001$ by paired-test and $p = 0.0004$ by Wilcoxon signed-rank test, $n = 30$). There were 2 Tukey outliers (with baseline lactic acid levels of 20.6 and 26.3 mg/dL) included in the above analysis but they had no material effect on statistical comparisons when excluded.

Median cortisol levels were 15 IQR (10–18), 19 IQR (16–25), and 11 IQR (8–14) μg/dL for baseline, post-test and at 24 h. Mean cortisol levels were elevated immediately following the CEW application, rising from 14.6 ± 4.8 to 19.9 ± 5.5 μg/dL ($p < 0.0001$ by both paired T-test and Wilcoxon signed-rank test). Cortisol levels decreased to normal levels within 24 h—probably much sooner. The 24-h levels were 11.4 ± 4.0 μg/dL which was slightly lower than baseline ($p = 0.0008$ by paired-test and $p = 0.0006$ by Wilcoxon signed-rank test, $n = 30$). There were no Tukey outliers in the cortisol levels.

Some of the baseline high-value serotonin Tukey outliers may have been due to anticipatory stress over the upcoming electrical-shock exposure [17]. A similar effect may explain why the 24-h cortisol levels were slightly lower than the baseline levels.

Discussion

The physiological effects of the CEW have been well studied [18–29]. A CEW exposure does result in a stress response, as demonstrated by biomarkers, but at lower levels than those of alternative restraint techniques [17, 30, 31]. Serum serotonin concentrations have not been previously studied after exposure to a CEW. This is important with regard to the hypothesis that CEWs elicit a stress response via the stress biomarker serotonin. There have been parallels in the medical literature between ExDS and the SS so it is also relevant to consider whether ExDS and SS are clinically distinct syndromes and if ExDS might be possibly initiated by serotonergic excess.

Zimmer et al. studied 121 (37F, 84 M) healthy normal young adults (age 18–35) with low (50% maximum HR), medium (65–70% HR_{MAX}) and high intensity (85 = 90% HR_{MAX}) 30-min exercise rates [32]. Serotonin level increases were 35 ± 60, 44 ± 68, and 78 ± 88 ng/mL respectively. In

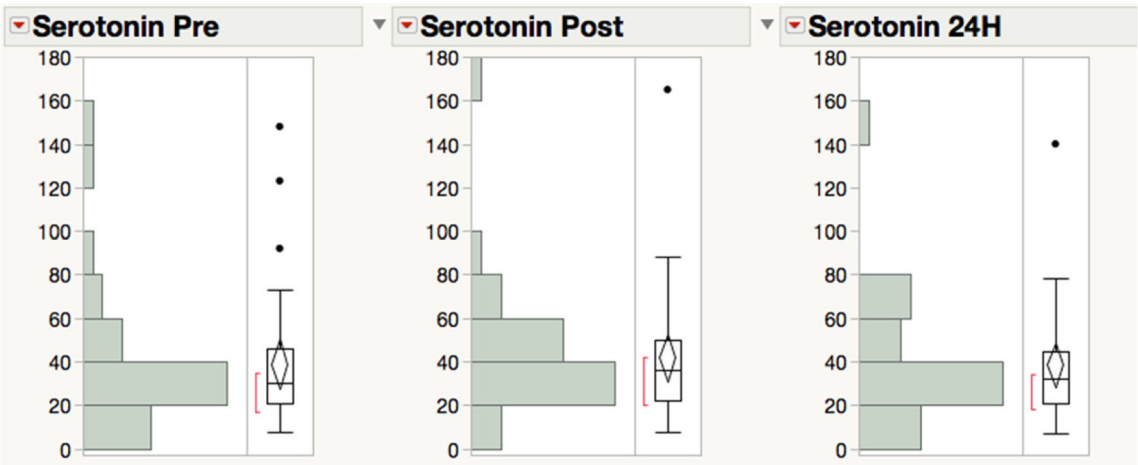

Fig. 1 Serum serotonin levels (ng/mL) with Tukey whisker plots and outliers

contrast, our study found that a full-trunk CEW exposure raised serum serotonin concentrations trivially (2.7 ± 28.0 ng/mL) unlike what Zimmer reported (35 ± 60 ng/mL) after low-intensity exercise [32].

Links to excited delirium Lee and Tseng first suggested that a CEW exposure could trigger or exacerbate excited delirium, and then Lee repeated the hypothesis in a later review article [2, 3]. Both articles used essentially the same words, for framing the hypothesis:

> "We do not know the mechanism of excited delirium but it seems that a surge in adrenergic tone, hyperthermia or acidosis may decrease the threshold for life threatening arrhythmias. Therefore, excited delirium may be another potential mechanism by which TASERs may harm a police suspect. TASER deployment can cause severe pain, which would undoubtedly lead to an increase in adrenergic tone that could be a trigger or contributory factor for excited delirium. In addition, studies in both animal models and in humans have demonstrated that TASER application can cause transient acidosis, that may play a role in the development of excited delirium."

The hypothesis, of an electrical trigger, was novel, as all other reports have focused on stimulant or schizophrenic triggers [33–49]. Multiple human studies have demonstrated that the CEW does not cause an adrenergic surge, hyperthermia, or acidosis [17, 22, 28, 30, 31, 50, 51]. Increases in epinephrine, norepinephrine, cortisol, and alpha-amylase are minor and less than those seen with other control techniques [17, 30, 31, 52, 53]. We have shown that any increase in serum serotonin with CEW exposure is far less than the increase seen with exercise. With the instant findings, we believe that the speculated link, between a CEW and excited delirium, is lacking in support.

Although the physiologic mechanism precipitating ExDS has not been fully elucidated, it is believed that one potential mechanism involves neurotransmitters that alter body temperature regulation since hyperthermia is a frequent feature of ExDS. Norepinephrine, serotonin, and dopamine are neurotransmitters thought to play a role in hypothalamic control of body temperature.

Serotonin is an independent modulator of dopaminergic neurotransmission. Mash et al. compared serotonin transporter density in brain tissue from cocaine overdose victims and cocaine-associated ExDS victims, finding that the transporters localized to the dopamine-rich substantia nigra and striatum in response to chronic cocaine use [54]. ExDS victims failed to display an up-regulation of serotonin transporters within these brain regions. In addition to altering dopamine reuptake directly, cocaine strongly inhibits serotonin reuptake, thus elevating synaptic levels of the neurotransmitter [55].

Labotz et al. presented a case series of patients on selective serotonin reuptake inhibitors that developed rhabdomyolysis after eccentric exercise [56]. This is an interesting finding since ExDS cases often present with rhabdomyolysis.

Symptoms of SS include altered mental status, agitation, myoclonus, hyperreflexia, diaphoresis, tremor, diarrhea, incoordination, muscle rigidity (especially of the lower extremities), and hyperthermia. Note that ExDS symptoms often include altered mental status, agitation, hyperreflexia, diaphoresis, and hyperthermia. Although ExDS may share some clinical characteristics with SS, individuals with SS do not share the aggressive violent behavior displayed by patients with ExDS [57]. While dysregulation of catecholamines and serotonin can be responsible for the symptoms of excessive sweating, hyperthermia and blood pressure abnormalities, myoclonus, tremor, muscle rigidity and hyperreflexia are strongly considered hallmarks of serotonergic toxicity in clinical practice. Myoclonus, tremor, and muscle rigidity are not typical features of ExDS.

Although CEW exposure has been implicated in causing stress, this study represents the first report addressing serotonin levels after a worst-case (very broad-spread probe) CEW exposure. Elevated serum serotonin concentrations have been reported after stress from acute exercise but were negligibly increased in this study after exposure to a CEW.

There are many reports of CEW exposure effects on lactic acid. A recently published meta-analysis found a mean increase of 1.31 mmol/L which is equivalent to 11.8 mg/dL and very close to the change of 21 ± 5.8 mg/dL that we found [17]. Dawes et al. reported a median cortisol increase of 0.38 μg/dL compared to the median increase of 5.3 IQR (2.9–8.2) μg/dL in this study [30]. We have suggested to the authors of that study that their paper had a 10× units error so that their median increase was actually 3.8 IQR (1.5–4.6) μg/dL which is close to our finding.

Limitations

In addition to being volunteers, police academy cadets undergo extensive physical training and are prescreened to eliminate health problems and drug use. A longer exposure-duration, such as 15 s, might have provided greater changes in serotonin levels. However, even a tripling (3×) of the Δ mean of 2.7 μg/dL would not have been clinically significant compared to the shifts seen with exercise.

Conclusions

A full-trunk 5-s CEW exposure caused no clinically significant increase in serum serotonin. The small increase was far less than that seen with exercise. The hypothesis of CEW-

induced excited delirium, through increased serotonin release, was not supported by the findings of this study.

Key points

1. A full-trunk electrical weapon exposure slightly raises serum serotonin levels.
2. The increase is less than that seen with exercise.
3. The resulting serotonin levels are within clinically normal limits.

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Compliance with ethical standards

Conflict of interest Authors 1, 2, and 4 have been expert witnesses in use-of-force litigation. Author 1 is a member of the scientific advisory and corporate boards of Axon Enterprises, Inc. (fka TASER Intl, Inc.).

Ethical approval Institutional Review Board of Texas A&M University.

Informed consent Consent forms were obtained from all subjects before inclusion in this study. Participants were cadets from the Austin (Texas) Police Academy who had previously volunteered to undergo a CEW exposure as part of their training.

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