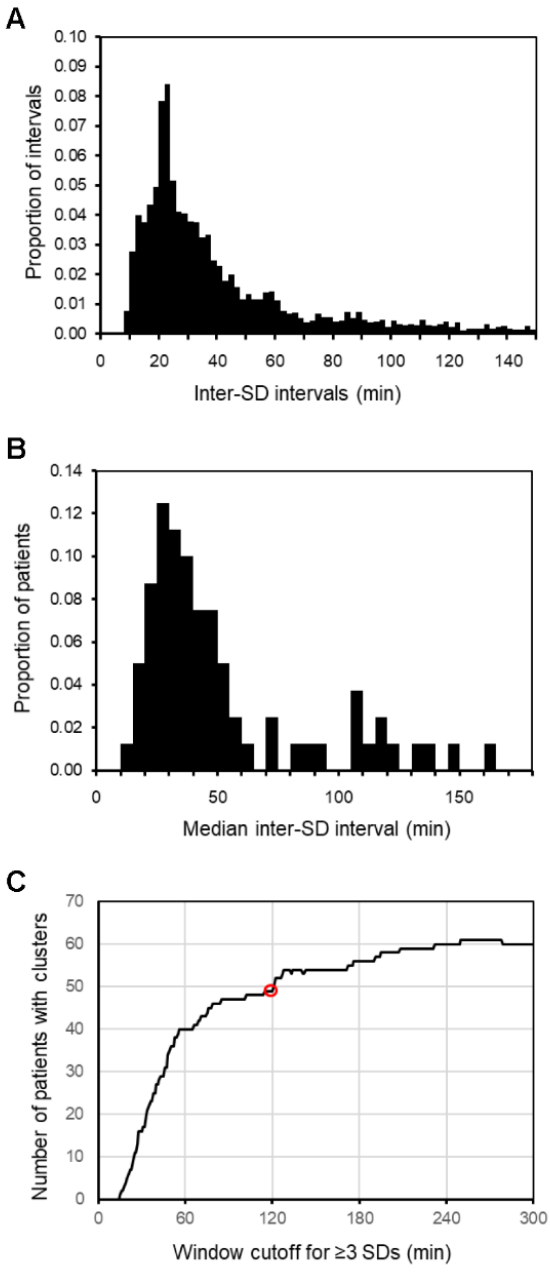
Supplementary Online Content

Hartings JA, Andaluz N, Bullock MR, et al. Prognostic value of spreading depolarizations in patients with severe traumatic brain injury. *JAMA Neurol*. Published online December 30, 2019. doi:10.1001/jamaneurol.2019.4476

This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1. Definition of spreading depolarization clustering.

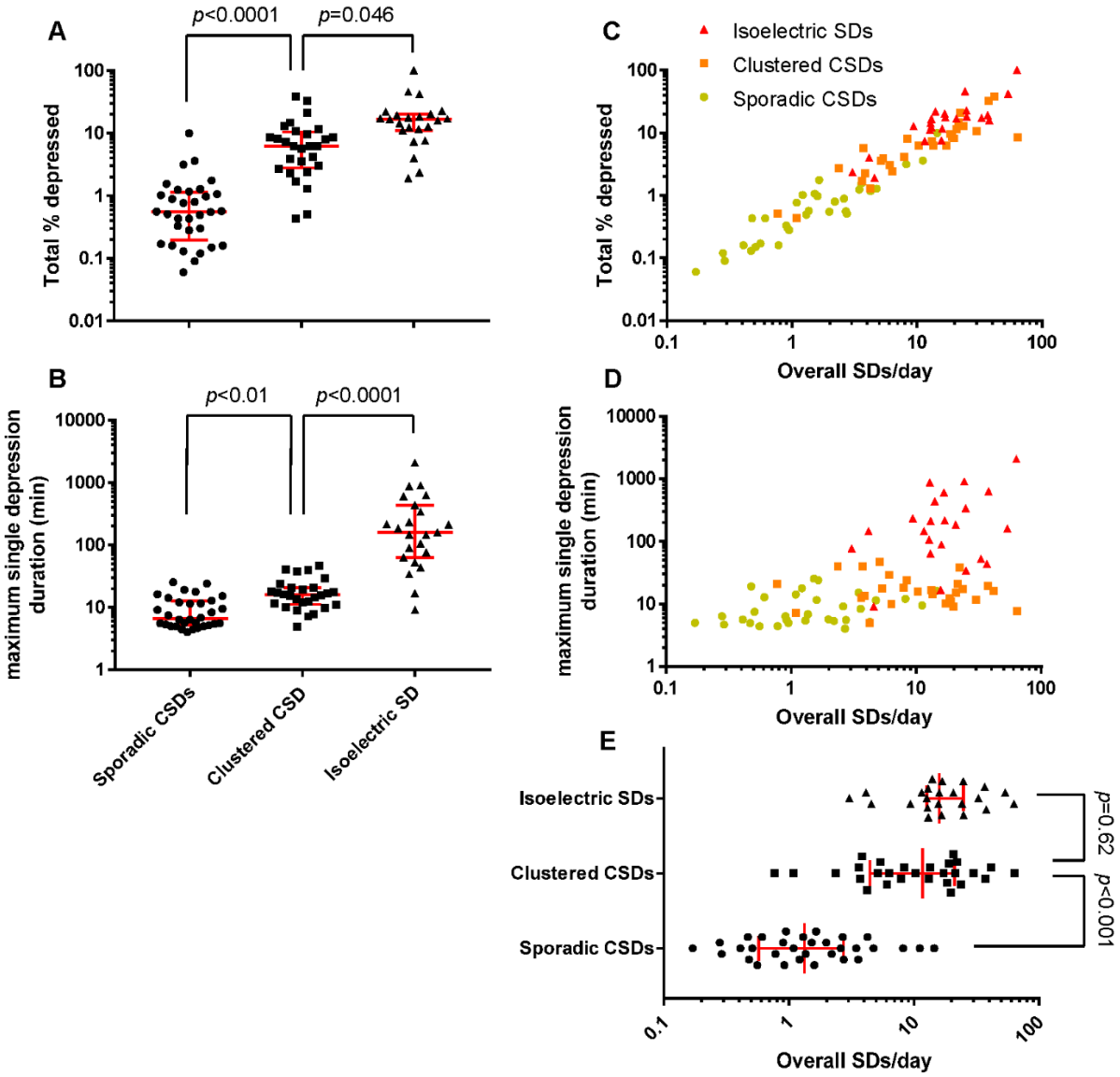
The working definition of a cluster was based on analysis of depolarization patterns in 181 brain trauma patients from the present study and the preceding pilot study.[1] A total of 3,224 spreading depolarizations (SDs) occurred in 105 of these patients. **(A)** shows a histogram of 2,673 inter-SD intervals (ISIs) recorded during uninterrupted monitoring epochs, and **(B)** shows the distribution of median ISI values observed in each patient (n=80 with ≥3 ISIs). These data suggest 60 min as a rational threshold interval to distinguish patterns of sporadic events from temporal clustering. Clusters were therefore defined as the occurrence of two consecutive ISIs with values ≤ 60 min (three SDs within ≤120 min). **(C)** shows the effects of varying the window duration criterion for three depolarizations on the number of patients identified as having clusters.



eFigure 2. Continuous measures of spreading depolarizations.

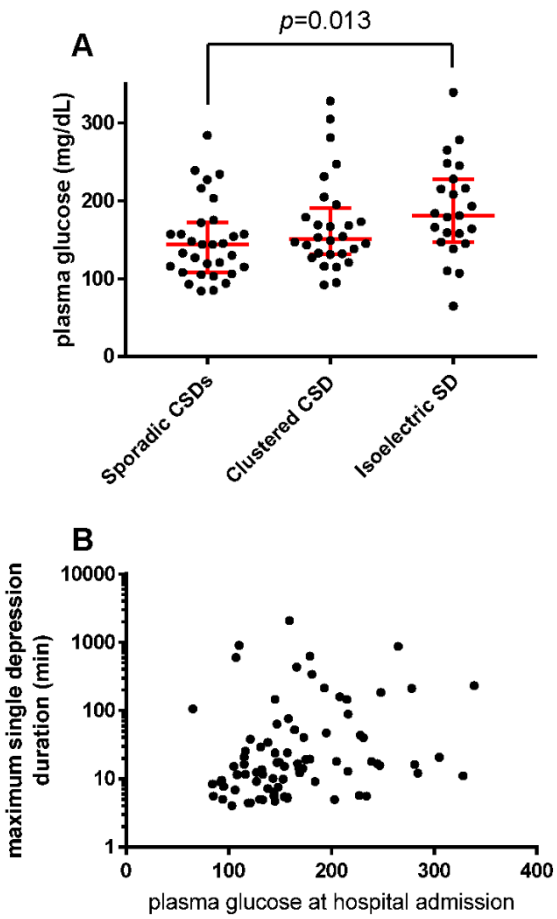
Scatter plots show values of various continuous measures of depolarization burden for the three different patient categories (total n=83). P-values are shown for Dunn's multiple comparisons tests. Continuous measures are summarized by depolarization

category in Table 2.



eFigure 3. Plasma glucose at hospital admission.

(A) There was no difference in plasma glucose at hospital admission between patients with and without depolarizations (M-W, p=0.502). However, among patients with depolarizations, plasma glucose differed by depolarization category (Kruskal-Wallis, p=0.017). Values are shown for each patient, and bars shows medians and interquartile ranges [144 mg/dL (112,165), 151 (132,183), and 181(153,222)]. P-value reflects Dunn's multiple comparison. **(B)** Plasma glucose at hospital admission significantly correlated with the maximal single depression duration observed for the patient during subsequent electrocorticography (SROC, r=0.348, p<0.01).



eTable 1. Surgical procedures and indications

		No. (%)*	Diameter, cm (Median, IQR)
Cause of trauma	Fall	58 (42)	
	MVA	19 (14)	
	Motorcycle	17 (12)	
	GSW	11 (8)	
	MVA-P	10 (7)	
	Assault	9 (7)	
	All-terrain vehicle	4 (3)	
	Other	7 (5)	
	Unknown	3 (2)	
Indications for surgery[A]	Initial CT findings	94 (68)	
	Neuroworsening	43 (31)	
	Expanding hematoma	26 (19)	
	Refractory ICP	19 (14)	
Type of surgery	Bone flap replaced	29 (21)	11.0, 10.0-13.8
	Lateralized decompressive craniectomy	95 (69)	14.0, 12.0-15.0
	Bifrontal decompressive craniectomy	14 (10)	14.5, 11.3-19.5
Location	Left	72 (52)	
	Right	51 (37)	
	Bifrontal	14 (10)	
	Bilateral	1 (1)	
Time to Surgery[B]	<8 hr	103 (75)	
	8-24 hr	19 (14)	
	>24 hr	16 (12)	
Procedures performed[A]	Evacuate subdural hematoma	110 (80)	
	Contusion resection	41 (30)	
	Lobectomy	14 (10)	
	Evacuate intracerebral hematoma	20 (14)	
	Evacuate epidural hematoma	12 (9)	
	Placement of EVD	22 (16)	
	Elevate depressed skull	9 (7)	
	Removal of foreign body	6 (4)	
	Anterior fossa repair for CSF leak	4 (3)	

*Values represent number of patients and percentages based on 138 study patients. [A]More than one selection was possible for each patient. [B]Time of surgery after admission to study hospital. CSF = cerebrospinal fluid; CT = computed tomography; EVD = extraventricular drain; GSW = gunshot wound; ICP = intracranial pressure; MVA = Motor vehicle accident, MVA-P = pedestrian involved in motor vehicle accident.

REFERENCES

1. Hartings JA, Bullock MR, Okonkwo DO, et al. Spreading depolarizations and outcome after traumatic brain injury: a prospective observational study. *Lancet Neurol.* 2011;10(12):1058-1064.