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Abstract 6

Sudden Unexpected Death in Epilepsy: Finding the Missing Cardiac Links

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Sudden unexpected death in epilepsy (SUDEP) is a significant cause of mortality in patients with refractory epilepsy, accounting for up to 17% of all deaths in epilepsy and exceeding the expected rate of sudden death in the general population by nearly 24 times. Most of the identified SUDEP risk factors are unavoidable, and patients with refractory epilepsy currently face a lifelong SUDEP risk as high as 1% per year. Elucidating the mechanisms of this devastating condition might offer an opportunity for preventative measures, and therefore could have significant implications for reducing mortality in this patient population. One commonly postulated mechanism is cardiac arrhythmia precipitated by seizure discharges acting via the autonomic nervous system.

The *specific aims* of our pilot study are as follows:

1. To evaluate the interictal (between seizures) and ictal (during seizures) cardiac rhythm characteristics of patients with SUDEP, as compared to the general population and to other patients with epilepsy
2. To study the cardiac and neurological clinical characteristics of patients with SUDEP, as compared to the general population and to other patients with epilepsy
3. To evaluate the interictal and ictal EEG characteristics of patients with SUDEP in relation to any identified interictal and ictal cardiac rate/rhythm changes.

The long-range goal is to define better the electrophysiological characteristics of patients at risk for SUDEP. The study is a case-control comparison of SUDEP cases identified through death certificate review of mortalities queried from the Social Security Death Index registry with alive matched controls (who have nonepileptic seizures or medically controlled epilepsy).

307 mortalities were identified out of 3,842 patients monitored in our Epilepsy Monitoring Unit during the years 1990–2005. Of those, 237 (77%) had epilepsy (86 had temporal lobe epilepsy, 27 had frontal lobe epilepsy, 14 had parieto-occipital lobe epilepsy, 7 had multifocal epilepsy, 20 had hemispheric epilepsy, 17 had nonlocalizable focal epilepsy, and 36 had generalized epilepsy), 41 (13%) had nonepileptic seizures, and 29 (9%) had both recorded. Mean age at death was 49.9 years (range 18.6–99.6), with a standard deviation (SD) of 17.9 years. Mean epilepsy duration was 16.1 years (range 2 weeks–66 years) (SD = 15.3). Mean overall seizure frequency was 70 seizures per month (median 14 per month), with a mean monthly generalized tonic-clonic seizure frequency of 5.3 (median 1). The cause of death was identified in 211 of the total (including 158 of the 237 patients with epilepsy, 28 of the 41 patients with nonepileptic seizures, and 22 of the 29 patients with both); death certificates need to be obtained for the remainder.

SUDEP accounted for 21% of the deaths in our cohort with epilepsy. Significant differences between SUDEP cases and controls were observed in mean epilepsy duration (22.9 years [± 2.3] in SUDEP cases vs 13.7 years [± 1.5] in controls; $P = 0.005$) and in mean monthly seizure frequency (31.3 seizures per month [± 16.9] in SUDEP cases vs 1.4 [± 0.7] in controls; $P = 0.005$). Patients with SUDEP were more likely to have been discharged on valproic acid (VPA) from the Epilepsy Monitoring Unit. (VPA was only used in controls on admission. In SUDEP cases, it was used 50% of the time on admission only, 33% of the time on admission and discharge, and 17% of the time on discharge only [$P = 0.01$].) The risk for SUDEP was independent of epilepsy type or localization.

Our current data-collection efforts are focused on obtaining the cardiac data elements and obtaining the remaining death certificates to identify the rest of the SUDEP cases.

* BHBI = Bakken Heart-Brain Institute