

## EPILEPSY AND ACTIVITY OF THE AUTONOMIC NERVOUS SYSTEM

### Decrease of Sympathetic Cardiovascular Modulation after Temporal Lobe Epilepsy Surgery

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In temporal lobe epilepsy (TLE), there is evidence of ictal and interictal autonomic dysregulation, predominantly with sympathetic overactivity. The effects of TLE surgery on autonomic cardiovascular control and on baroreflex sensitivity (BRS) have not been studied. To evaluate such effects, we monitored heart rate (HR), systolic blood pressure [BP(sys)], and respiration in 18 TLE patients 3–4 months before and after TLE surgery. We used Blackman–Tukey spectral analysis to assess sympathetic and parasympathetic modulation as powers of HR and BP(sys) oscillations in the low-frequency (LF, 0.04–0.15 Hz) and high-frequency (HF, 0.15–0.5 Hz) bands. BRS was determined as the LF transfer function gain between BP and HR. After surgery, HR, BP(sys), respiration, and HF powers remained unchanged, whereas LF powers of HR [ $1.57 \pm 1.54$  beats/min(2)] and BP(sys) [ $2.19 \pm 1.34$  mm Hg(2)] and BRS ( $0.68 \pm 0.31$  beats/min/mm Hg) were smaller than presurgical LF powers of HR [ $3.87 \pm 3.26$  beats/min(2)] and BP(sys) [ $4.80 \pm 3.84$  mm Hg(2)] and BRS ( $1.12 \pm 0.39$  beats/min/mm Hg;  $P < 0.05$ ). After TLE surgery, there is a reduction of sympathetic cardiovascular modulation and BRS that might result from decreased influences of interictal epileptogenic discharges on brain areas involved in cardiovascular autonomic control. TLE surgery seems to stabilize the cardiovascular control in epilepsy patients by reducing the risk of sympathetically mediated tachyarrhythmias and excessive bradycardiac counterregulation, both of which might be relevant for the pathophysiology of sudden unexpected death in epilepsy patients (SUDEP). Thus TLE surgery might contribute to reducing the risk of SUDEP.

### COMMENTARY

Sudden unexplained death in epilepsy (SUDEP) has been reported to be 24 to 40 times higher than that in the general population, with estimates ranging between 1 in 200 and 1 in 1,000. SUDEP accounts for 7% to 17% of deaths in the general population of patients with epilepsy, and for up to 50% of deaths in patients with refractory epilepsy (1–4). Between 5% and 15% of SUDEPs have been attributed to autonomic dysfunction that led to tachyarrhythmias in most cases, although bradyarrhythmias and episodes of cardiac asystole also have been reported (5,6).

In this study, Hilz et al. demonstrate a reduction of sympathetic cardiovascular modulation and baroreflex sensitivity after anterotemporal lobectomies in 18 patients with pharmacoresistant temporal lobe epilepsy (TLE). Such changes in sympathetic autonomic function are thought to minimize the risk of sympathetic-mediated cardiac arrhythmias as well as extreme bradycardiac counterregulations, two pathogenic mechanisms thought to be operant in SUDEP. Most of these cardiac arrhythmias have been directly attributed to ictal activity (more often during generalized tonic–clonic seizures). Hilz et al., however, citing data from experimental studies done in animals, also suggest a pathogenic role of interictal epileptic discharges through an enhancement of the sympathetic tone. Other authors have suggested that intense sympathetic stimulation after recurrent seizures can cause a nidus of myocardial irritability during periods of prolonged cardiac repolarization (evidenced by long QT intervals) (7). Such processes eventually result in “cardiac electrical instability” that can be reversed after surgical treatment. For example, in a study of 15 patients with refractory TLE who underwent an anterotemporal lobectomy, Frysinger et al. (8) found wider variations in heart rate (measured with spectral plots of the RR interval) among patients with persistent seizures after surgery than in seizure-free patients and controls. Eventually, pathologic evidence of these disturbances can be identified in the myocardium of victims of SUDEP. Falconer and Rajs (9) described minor areas of fibrosis and scarring in the myocardium of nine victims of “epilepsy deaths.” It is clear, therefore, that the impact of epilepsy surgery reaches beyond seizure remission. It reduces the risk of SUDEP in a patient population where its prevalence is not insignificant.



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## References

1. Hirsch R, Martin D. Unexpected death in young epileptics. *Neurology* 1971;21:678–690.
2. Terrence DR, Wisotskey HM, Perper JA. Unexpected, unexplained death in young epileptics. *Neurology* 1975;25:594–598.
3. Leetsma JE, Annegers JF, Brodie MJ, et al. Sudden unexplained death in epilepsy: observations from a large clinical development program. *Epilepsia* 1997;38:47–55.
4. Sperling MR, Feldman H, Kinman J, et al. Seizure control and mortality in epilepsy. *Ann Neurol* 1999;46:45–50.
5. Hauser WA, Annegers JF, Elveback LR. Mortality in patients with epilepsy. *Epilepsia* 1980;21:399–412.
6. Burgess R. Autonomic signs associated with seizures. In: Luders HO, Noachtar S, eds. *Epileptic seizures: pathophysiology and clinical semiology*. New York: Churchill Livingstone, 2000:631–641.
7. DeSilva RA, Lown B. Ventricular premature beats, stress and sudden death. *Psychosomatics* 1978;19:649–661.
8. Falconer B, Rajs J. Post-mortem findings of cardiac lesions in epileptics: a preliminary report. *J Forens Sci* 1976;8:63–71.
9. Frysinger R, Harper R, Kackel R. State-dependent cardiac and respiratory changes associated with complex partial epilepsy. In: Engel J, Ojemann G, Luders H, eds. *Fundamental mechanisms of human brain function*. New York: Raven Press, 1987:219–225.