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Advances in radiofrequency ablation of the cerebral cortex in primates using the venous system: Improvements for treating epilepsy with catheter ablation technology

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Summary
Background: Pharmacology frequently fails for the treatment of epilepsy. Although surgical techniques are effective, these procedures are highly invasive. We describe feasibility and efficacy of minimally invasive mapping and ablation for the treatment of epilepsy.
Methods: Mapping and radiofrequency ablations were performed via the venous system in eleven baboons and three dogs.
Results: Mapping in deep cerebral areas was obtained in all animals. High-frequency pacing was able to induce seizure activity of local cerebral tissue in 72% of our attempts. Cerebral activity

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could be seen during mapping. Ablative lesions were deployed at deep brain sites without steam pops or sudden impedance rise. Histologic analysis showed necrosis at the sites of ablation in all primates.

Conclusion: Navigation through the cerebral venous system to map seizure activity is feasible. Radiofrequency energy can be delivered transvenously or transcortically to successfully ablate cortical tissue in this animal model using this innovative approach.

Introduction

Epilepsy affects 0.5—1% of the world's population (Engel et al., 2003). Despite the best pharmacologic treatments available, 40% of patients remain refractory to therapy (Engel, 1998; Stephen et al., 2006). Epilepsy surgery is an alternative way to treat refractory patients and can achieve adequate results (Choi et al., 2008). However, it is highly invasive and technically difficult in deep areas of the brain (Wyllie et al., 1993). New and less invasive experimental techniques have been developed to achieve access to critical areas of the cerebral cortex for epilepsy treatment using the venous system (Henz et al., 2008; Bower et al., 2013). The aim of this study was to assess the feasibility and efficacy of minimally invasive transvenous mapping and ablation for the treatment of epilepsy using novel catheters in animal models.

Methods

Animal preparation

Eleven baboons (25—30 kg) and three canines (beagles) were studied under general anesthesia using isoflurane (1—3%). Intravenous heparin was given with a target ACT of 250 s. The studies were performed with the approval of the Mayo Clinic Institutional Animal Care and Use Committee.

Retrograde cerebral venous access and arterial access was obtained via the internal jugular vein, femoral vein, internal carotid artery, and femoral artery for angiography and mapping. A 4-Fr multipurpose catheter was inserted near the ostium of the jugular vein for venous angiography and in the internal carotid artery for arterial phase angiography. Both vessels were used for subsequent placement of mapping and ablation catheters in both the venous and arterial systems. Following transvenous mapping and ablation, craniotomy was performed with exposure of the parietal cortex. Induction, mapping, and ablation of the presumed seizure focus were then repeated under direct visualization through the craniotomy.

Electrical mapping and ablation

Transvenous mapping and ablation

Transvenous mapping of cortical electrograms from the occipital, temporal, and parietal lobes was performed through the cortical veins using the following experimental catheters: (1) over-the-wire 4.5-Fr mapping and temperature controlled irrigated ablation catheter (Fig. 1A) to negotiate the tortuous cortical veins and (2) a 4.5-Fr open-irrigation, balloon-virtual electrode venous ablation catheter (Fig. 1B) for larger lesion creation in the high impedance cerebral cortex environment. Mapping was also performed using commercially available catheters, a 2.7-Fr octapolar microelectrode catheter (Revelation Cardima$^{\text{TM}}$, Fremont CA) and a 6-Fr 4-mm tip, deflectable catheter (Blazer Boston Scientific$^{\text{TM}}$, Natick, MA). Electrograms were recorded using a multichannel recording system (Prucka$^{\text{TM}}$, General Electric, Milwaukee, USA) with filter settings of 0.5—500 Hz.

Seizures were induced by one of two techniques: pacing maneuvers (10 baboons) or cortical penicillin injection (4 baboons and 1 dog). The mapping catheter was navigated to cortical veins at different locations and pacing was performed at high (200 Hz) and low (50—200 Hz) frequencies. We obtained stimulation threshold values by varying energy from 2 to 20 mA at a pulse width of 2 ms and assessing for lowest value required for cerebral tissue activity. Pacing was then used to induce seizures. Alternatively, 2500 U of crystalline penicillin was injected over a skull aperture, in pre-determined areas located close to the site of catheter ablation. Penicillin injections induced large amplitude periodic epileptiform spikes. These injections were made to produce partial seizure activity in order to capture from the venous system brain signals close to ablation sites.

The induced seizure was mapped using the transvenously introduced catheter. Radiofrequency energy was delivered at pre-specified cortical locations using 500 kHz output of a generator grounded to two 100-cm^2 patches. Ablation settings were different for each catheter evaluated (Table 1). The operator specified the cortical location where RF energy was delivered, and the lesions were verified at necropsy. The local electrograms before and after ablation were recorded from the four electrodes at the ablation catheter tip in the venous system producing two bipolar signals.

Transcranial mapping and ablation

Following transvenous mapping and ablation, the penicillin-induced seizure was mapped on the cortical surface through a craniotomy. An experimental 'glove' catheter was then used to deploy larger lesions from the subdural space (Fig. 1C).

Magnetically-guided navigation

The NIOBE II system (Stereotaxis, Saint-Louis, MO, USA) utilizes a magnetic field to remotely navigate a micro-catheter (1.1 Fr) with magnetic steel in the tip. This system provides