Structure and function of Cortical Dysplasias

In a BCNU model

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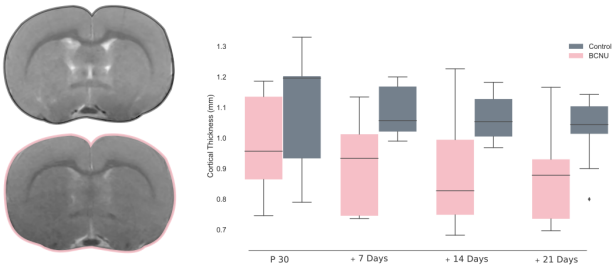

Figure 1. Cortical thickness comparision between control group and treatment (BCNU) along 7,14,21 after P30. Control in lightgray and BCNU in lightpink. p<0.05.

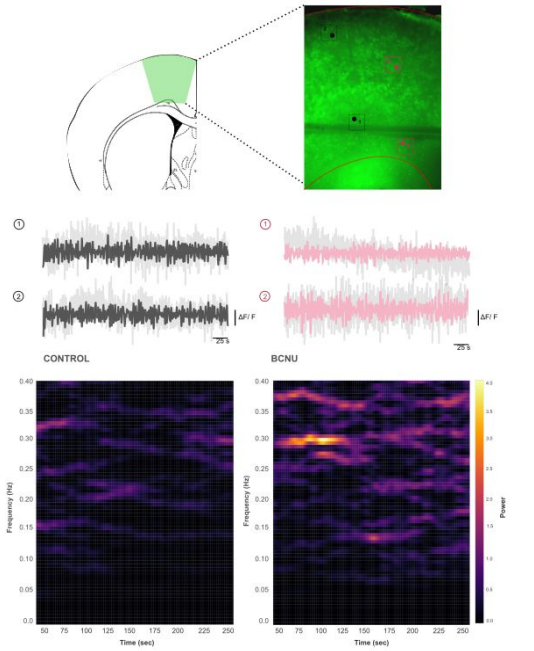

Figure 2. A qualitative results of the calcium activity FOV in green and of neurons responses in control cortex (lightgrey) and BCNU (lightpink). There are dubstancial difference between their power activities at basal treatment and posterior to pilocarpine(external stimulus) as well.

Introduction

Focal cortical dysplasias (FCD), are characterized by dyslaminated cortex, blurring of the gray/white matter interface and variable architectural abnormalities (Guerrini *et al.,* 2015). Their characterization and classification are limited, as they are often underdiagnosed, and may even go undetected for years. It is difficult to detect FCDs, as they are often subtle, variable in extension, cell morphology, and localization. Approximately 27% of those malformations generate chronic and medically refractory epilepsy (Rakhade & Jensen, 2009). And it is unknown how these subtle morphological abnormalities can lead to epilepsy.
In our work we use the BCNU model of cortical dysplasia in rodents, seeking the anatomical and functional differences between dysplasias and the healthy cortex, and their susceptibility to generate epileptic seizures in response to an exogenous stimulus.

Methods

BCNU treatment (n=4) *Treatment group*. In pregnant rats, we induce carmustine (BCNU) 20mg/Kg at 15 days of gestation. *Control group*. We injected a similar volume of BCNU doses. We selected (n=4) males at 25 postnatal days we took anatomical **MRI** T2 images (7T Pharmascan Bruker BioSpin GmbH, Ettlingen, Germany) (TR= 200 ms; TE=35ms; flip angle, 30°; slice thickness, 80 μm; FOV, 25.6x25.6; the number of averages, 6; matrix size, 384x384). **MRI sequence** We scanned each animal 7,14,21 days after P30 with the same T1 sequence. **Calcium imaging ex vivo** n= 6 brains of the *Treatment group* and n=6 of *Control group* were recorded with calcium imaging technique in a stereoscope fluorescence microscope (Leica M205 FCA) coupled with a CCD camera. Each brain slice (230 um) was permeabilized with Fluo-4AM for 1 hour at atmospheric conditions (CO2 5%, 32°C, O2 2%). We record each slice activity following the next sequence: Basal activity with ACSF perfusion (**3 min**), Pilocarpine stimulus (**13 min**: 10 seconds Basal-30 seconds Pilocarpine 300 uM, rest of ACSF perfusion), break of 15 min with ACSF solution, KCl stimulus (**13 min:** 10 seconds Basal-30 seconds KCl 140 mM, rest of ACSF perfusion).

Results

We found a cortical thickness difference between groups (Figure 1) and cell malformations and disarrangement as well in the motor cortex. Their physiology shows that the cortical dysplasias have a greater power activity (Figure 2) and more structured network when an external stimulus occurs. With this work, we found that anomalies in anatomy lead a plastic change in function.

Guerrini, R., Duchowny, M., Jayakar, P., Krsek, P., Kahane, P., Tassi, L., ... Blumcke, I. (2015). *Diagnostic methods and treatment 1options for focal cortical dysplasia. Epilepsia, 56(11), 1669–1686.*
Rakhade, S. N., & Jensen, F. E. (2009). Epileptogenesis in the immature brain: emerging mechanisms. *Nature Reviews Neurology*, *5*(7), 380.