Characterisation of Central Chemoreception and Cardioregulation in Sudden Unexpected Death in Epilepsy

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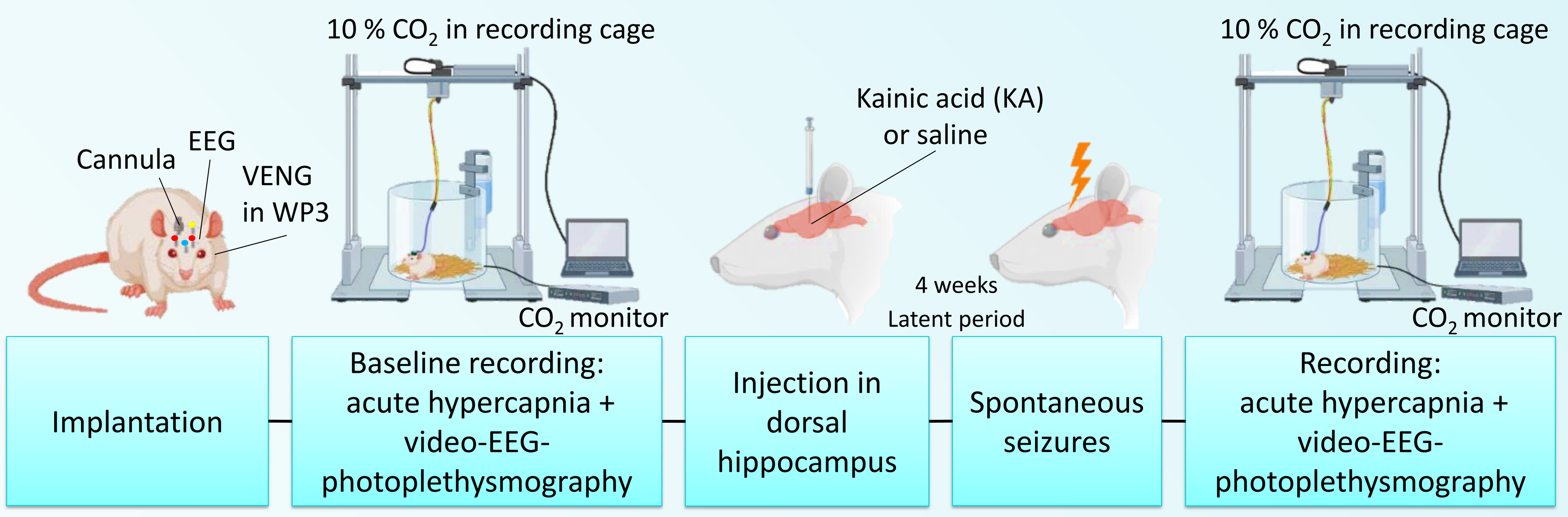
Abstract

This study investigates the role of dysregulated central ventilatory chemoreception (CVC) and cardiac abnormalities in Sudden Unexpected Death in Epilepsy (SUDEP) in the kainc acid rat model. Autonomic dysregulation prior to SUDEP has been recognized, especially respiratory arrest but also cardiac dysregulation[1]. The project aims to (1) analyze Central ventilatory chemoreception and heart rate progression in epileptic rats, induced by kainic acid, (2) to explore neuromodulator immunolabeling in relevant brainstem and cortical regions, and (3) compare vagus nerve signals in high CO2 conditions in epileptic and healthy animals.

Methodology

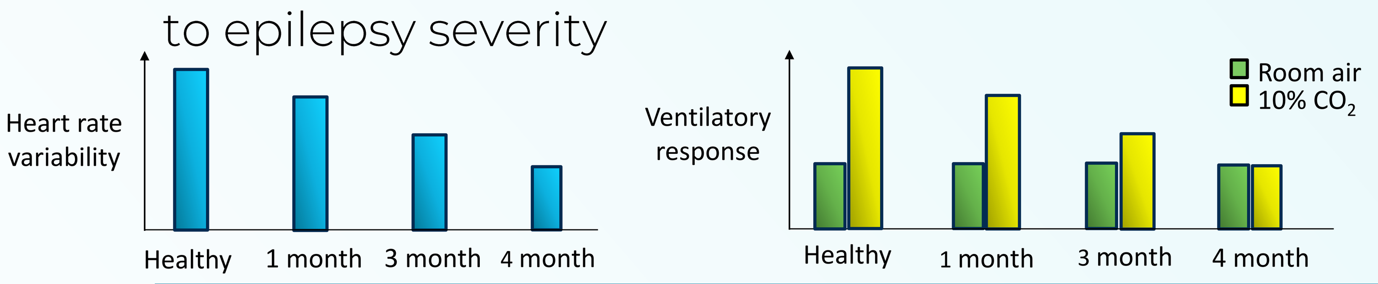


Introduction

Central apnea emerges to be the key contributor for Sudden unexpected death in epilepsy (SUDEP). Particularly dysregulation of central ventilatory chemoreception (CVC)[1], the system detecting changes in PCO2 levels, is postulated to play a role in SUDEP, accompanied by autonomic anomalies such as cardiac dysregulation. Currently, vagus nerve stimulation (VNS) is used as an adjunctive treatment for SUDEP and is also shown to activate chemosensitive and cardioregulatory pathways[2]. This research project aims to fill in the gaps in the molecular understanding of SUDEP pathophysiology, particularly focusing on central chemoreceptive and cardioregulatory centers.

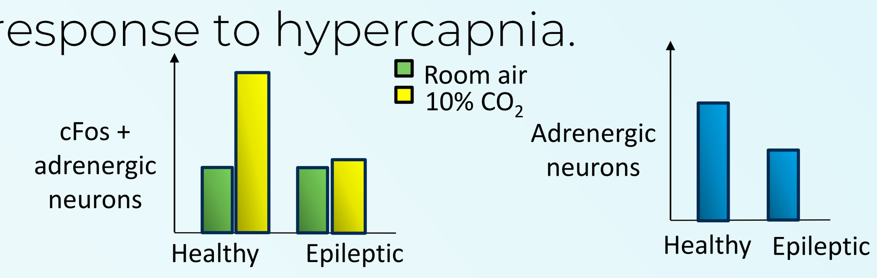
WP1

The cardiorespiratory response with severity of seizure in a model of refractory epilepsy. We expect that heart rate variability and ventilatory response will be attenuated parallel to epilepsy severity



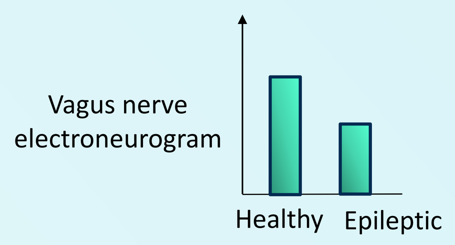
WP2

Central cardioregulatory changes after severe seizures. We expect that Severe epilepsy will alter the immunolabelling of cardio regulatory regions and their activation in response to hypercapnia.



WP3

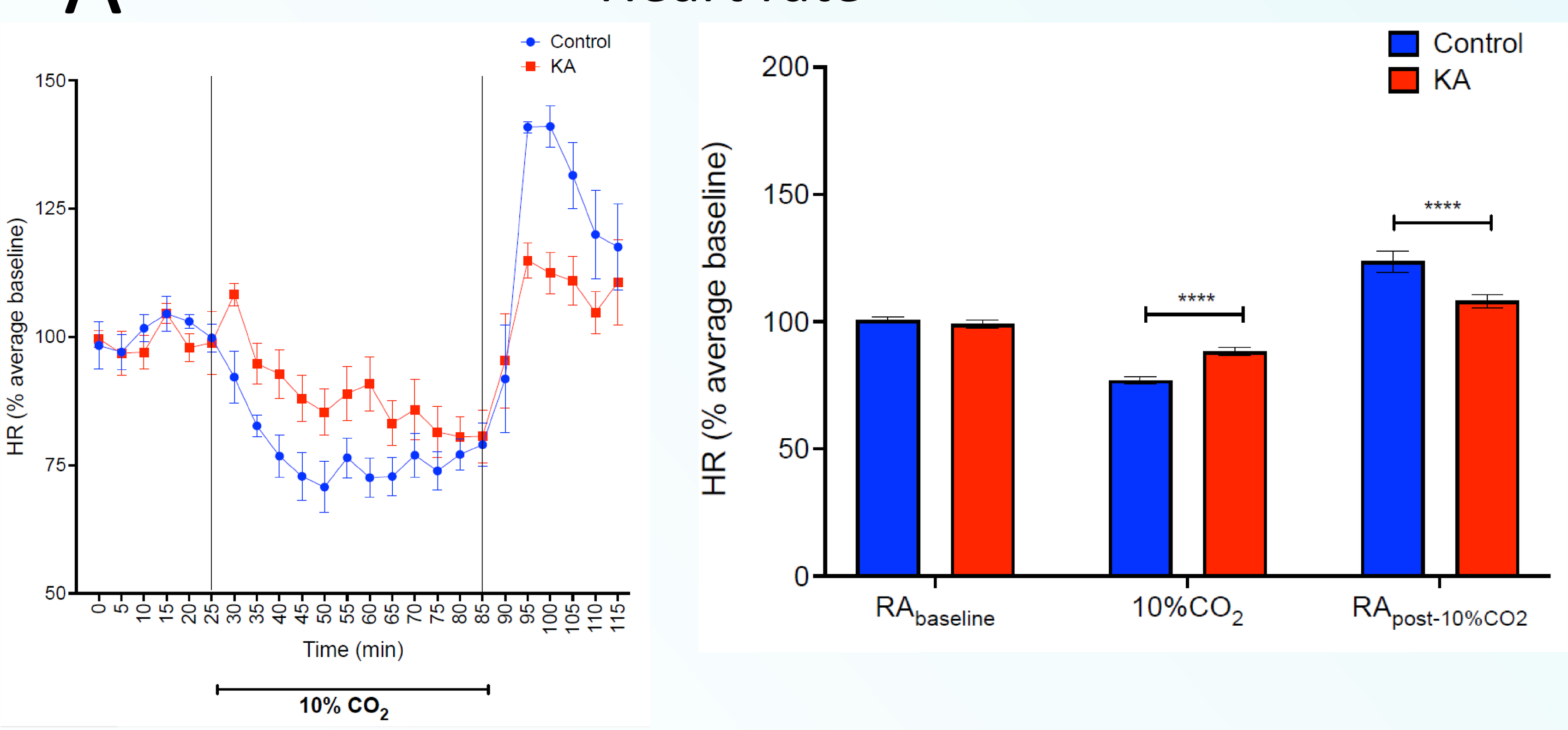
VENG recordings during hypercapnia challenge in epileptic and healthy animals. We anticipate that vagus nerve electroneurogram signal to CO2 in KA rats will be attenuated with increasing cardiac dysfunction in parallel to the severity of epilepsy.



Preliminary results

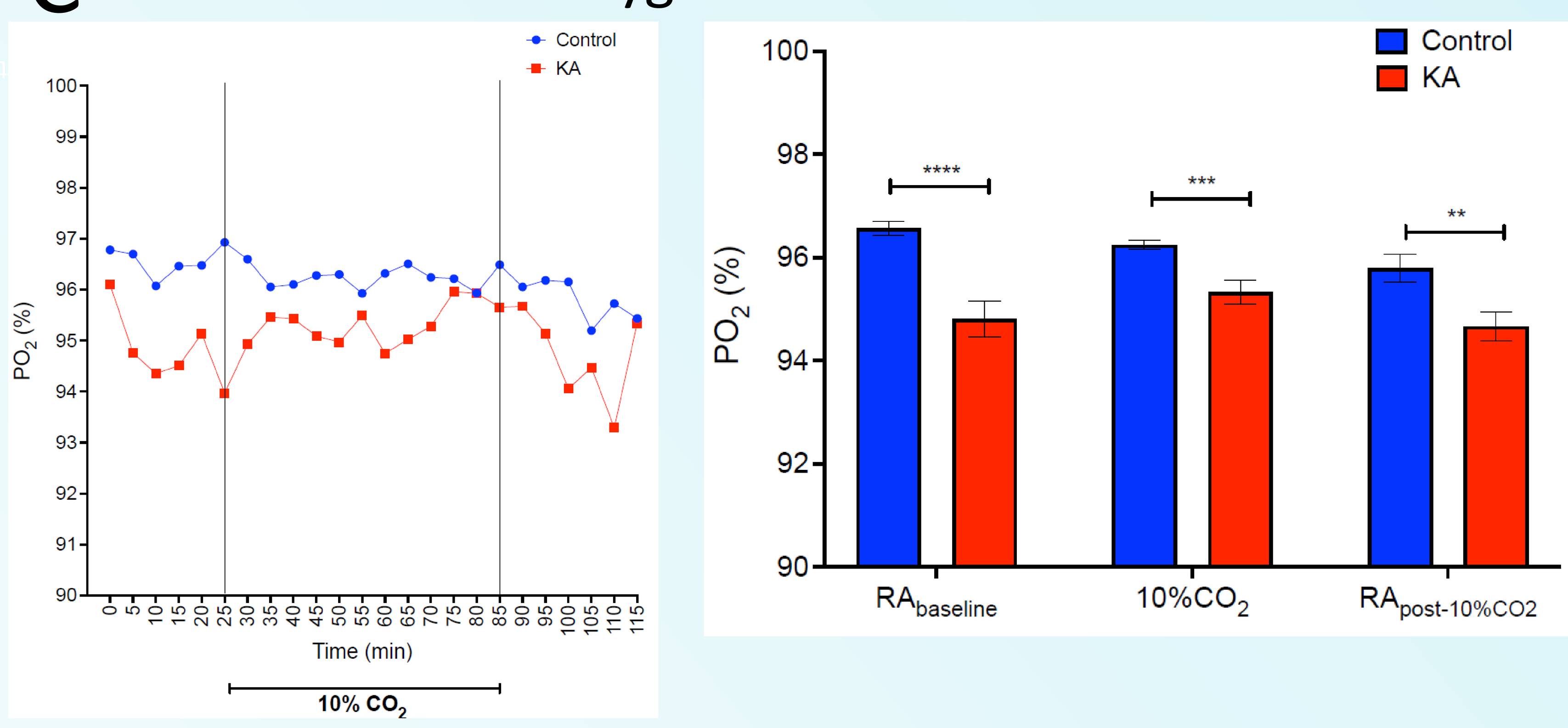
A

Heart rate



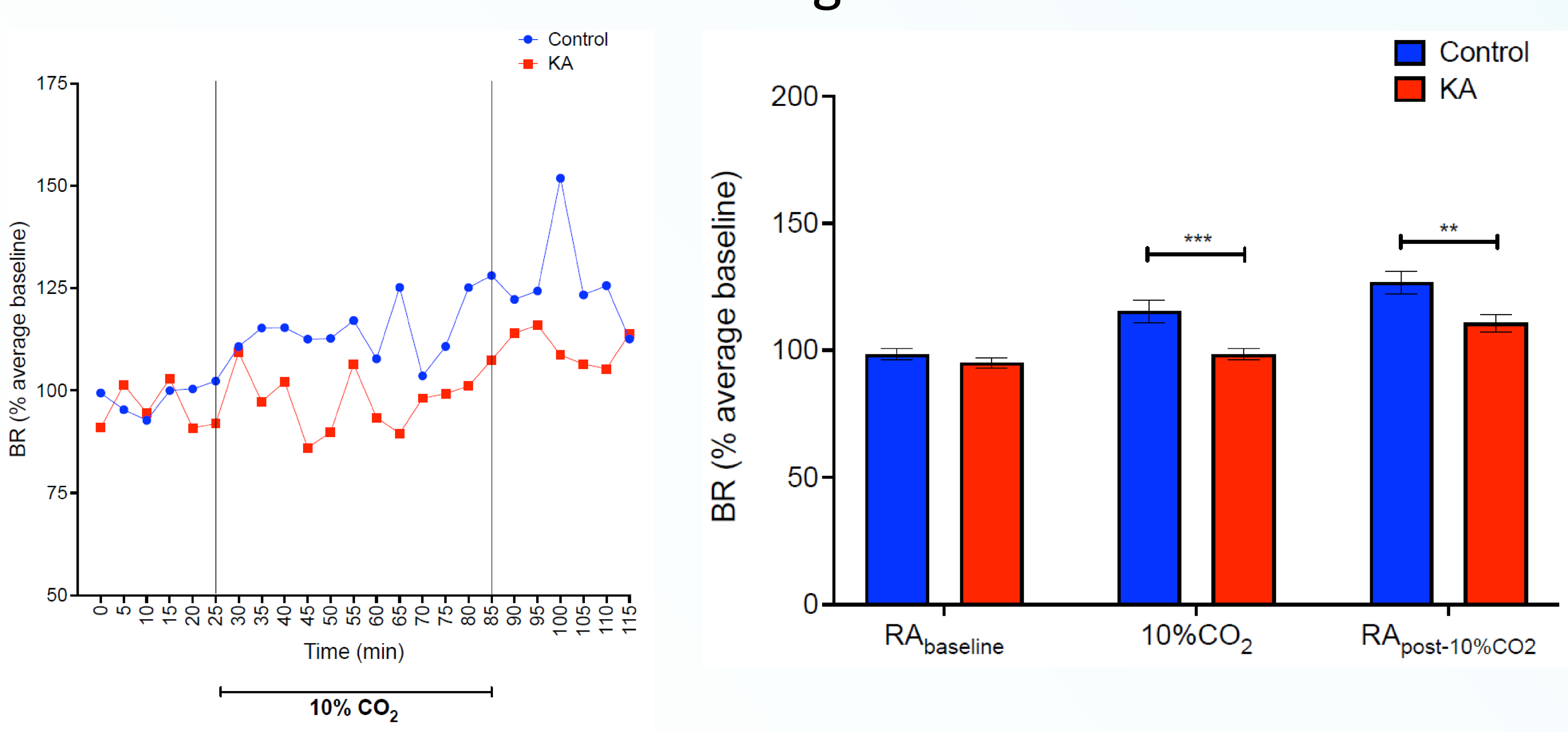
C

Oxygen saturation



B

Breathing rate



Photoplethysmography recording for heart rate (A), breathing rate (B) and oxygen saturation (C) before, during and after 1 hour of 10% CO_2 challenge.

A) There was no differences in the heart rate during baseline between the kainic acid rats and the healthy controls, but there was a significant attenuation during and after the challenge.

B) We observe the same tendency in the breathing rate with less increase in the kainic acid group.

C) Oxygen saturation in epileptic rats was inferior to healthy controls before, during and after the CO_2 challenge.

References

[1] Stewart, M. J Physiol Sci, 2018, [2] Guyenet, P.G. Compr Physiol, 2014

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