

GYRENCEPHALIC BRAINS TO MODEL STROKE IN THE HEART OF EU: WILL PIG OFFER NEW OPPORTUNITIES FOR AN OPTIMAL TRANSLATION?



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Linea 3: Cerebroprotección. 23 marzo 2023



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BACKGROUND

Animal models are required to study stroke and new treatments.

- The poor translationality of the preclinical research in stroke in rodents
- Get a “human-like” brain to model human stroke as free as possible of ethical corners

HHS Public Access
 Author manuscript
 Stroke. Author manuscript; available in PMC 2019 May 01.

Published in final edited form as:
 Stroke. 2018 May; 49(5): 1099–1106. doi:10.1161/STROKEAHA.117.018293.

The
 Miché
 Boltz

NEURAL REGE
 REVIEW

Large; human

Porcine **Primate** **Human**

- >60% white matter
- Permanent transcranial models
- Endovascular models
- T2W reveals swelling, MLS, and herniation
- FA decreases correlate with motor impairments

- >60% white matter
- Permanent/transient transcranial models
- Endovascular models
- Perfusion-diffusion mismatch
- FA decreases correlate with motor impairments

- >60% white matter
- Perfusion-diffusion mismatch
- Lesion volume, FA values, and MLS correlate with motor and neurological impairments

Erin E. Kaiser^{1,2}
 1 Regenerative Bi
 2 Neuroscience P
 3 Department of

Comp: Acute Use?

Aladdin Taha, Joaquim Bobi, Ruben Dammers, Rick M. Dijkhuizen, Antje Y. Dreyer, Adriaan C.G.M. van Es, Fabienne Ferrara, Matthew J. Gounis, Björn Nitzsche, Simon Platt, ... See all authors

Originally published 15 Feb 2022 | <https://doi.org/10.1161/STROKEAHA.121.036050>
 Stroke. 2022;53:1411–1422

International Journal of Molecular Sciences

MDPI

Review

Relevance of Porcine Stroke Models to Bridge the Gap from Pre-Clinical Findings to Clinical Implementation

Marc Melià-Sorolla¹, Carlos Castaño², Núria DeGregorio-Rocasolano¹, Luis Rodríguez-Fernández³, Antoni Dávalos³, Octavi Martí-Sistac^{1,4,5,6} and Teresa Casull^{1,5,6}

scientific reports

Check for updates

OPEN Endovascular model of ischemic stroke in swine guided by real-time MRI

D. Golubczyk¹, L. Kalkowski¹, J. Kwiatkowska¹, M. Zawadzki¹, P. Holak¹, J. Glodek¹, K. Milewska¹, A. Pomianowski¹, M. Janowski¹, Z. Adamiak¹, P. Walczak¹ & I. Malysz-Cymborska^{1,2}

Expertise

Germans Trias i Pujol Hospital
 Institut Català de la Salut



Dedicated facility



Abstract

Improving Large Animal Ischemic Stroke Models for Translational Studies in the Era of Recanalization

Shen Li and Marc Fisher

Originally published 12 Dec 2022 | <https://doi.org/10.1161/STROKEAHA.122.041354>
 Stroke. 2022;54:e16–e19

Abstract

Recanalization therapy with endovascular procedures has led to significant advances in the treatment of acute ischemic stroke.

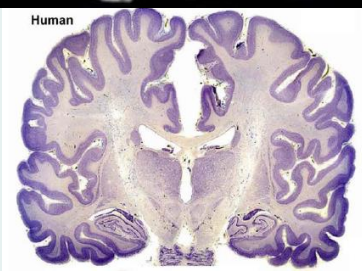
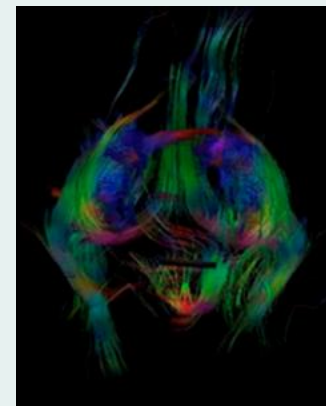
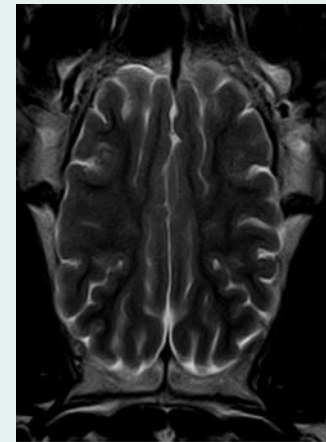
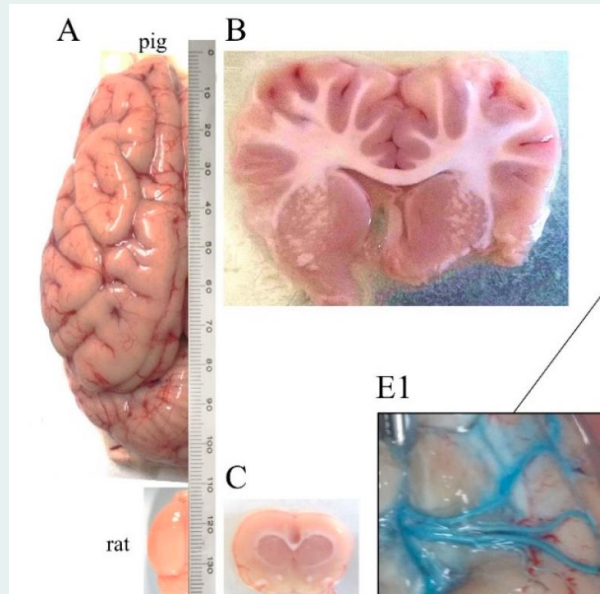
April 2022
 Vol 53, Issue 4

Stroke

January 2023
 Vol 54, Issue 1

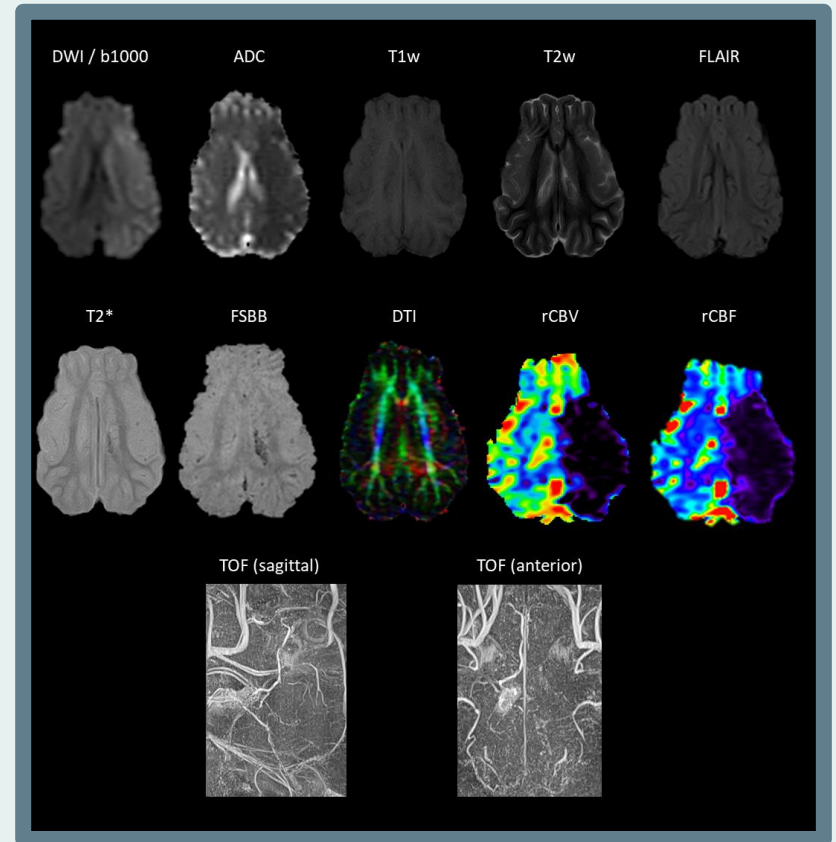
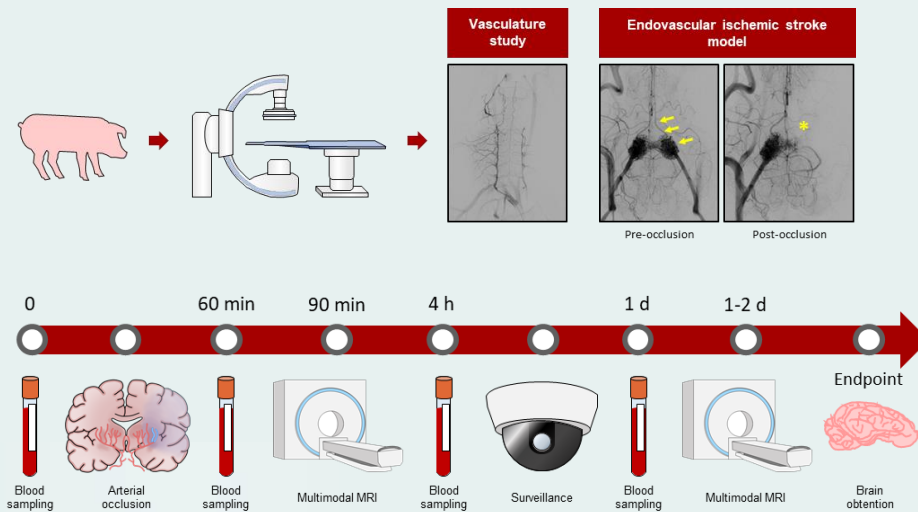
BIOFIDELIC TO HUMAN BRAINS

- Pigs vs rodents

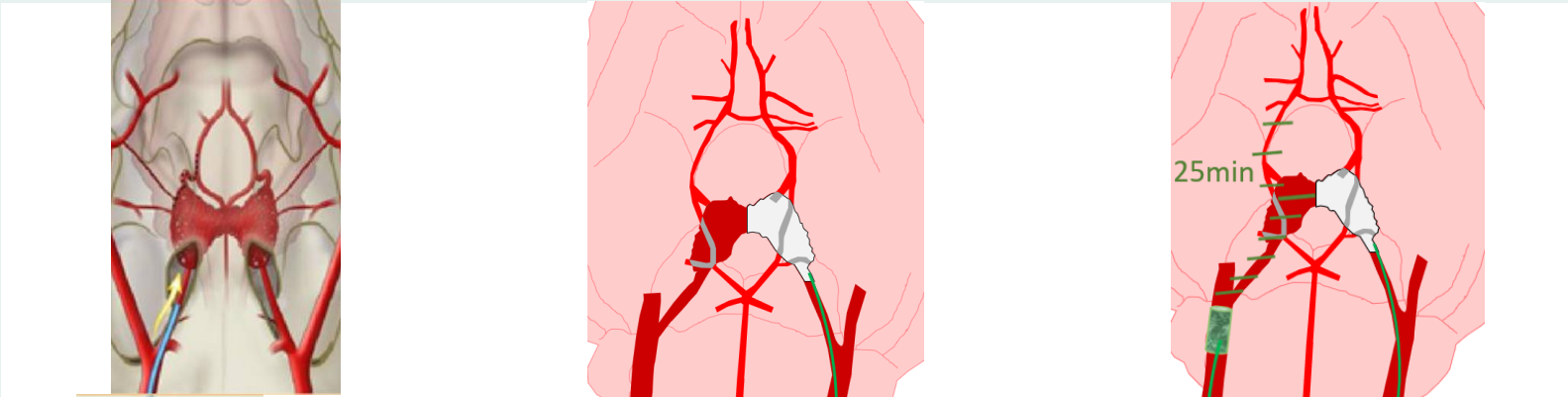


NEW ASSESSMENT OF MODELLING POSSIBILITIES & EXPERIMENTAL SET UP

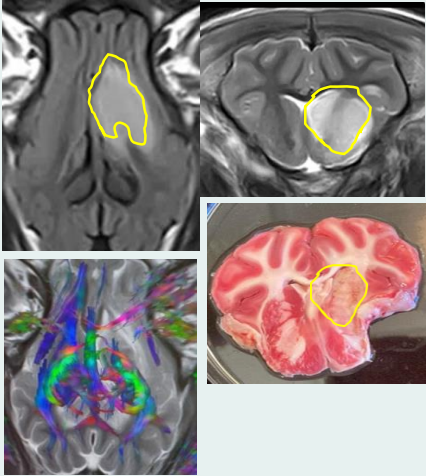
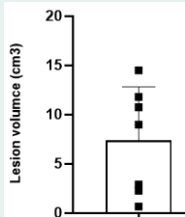
DUROC, LANDRACE, PIETRAIN,
MINIATURE PIG-SPECIPIG



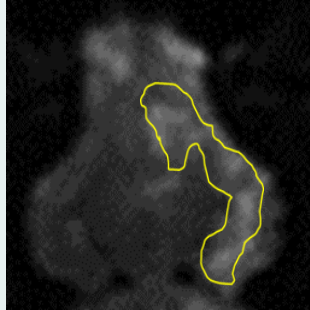
MODEL STROKE IN PIG IN A MINIMALLY INVASIVE WAY



Thrombin
 Thrombin+tPA
 Difficult to control the area and extent of the damage. Golubczyk et al, 2020



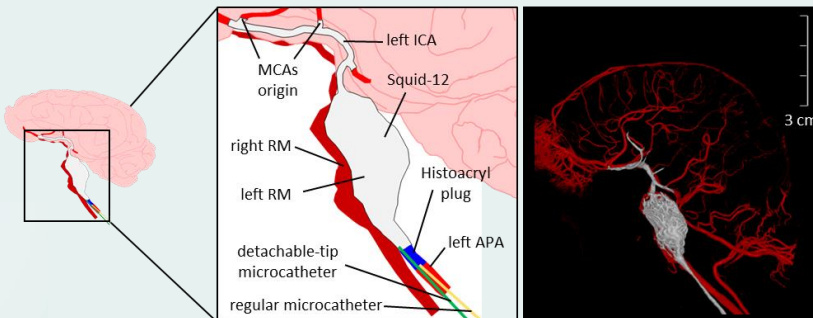
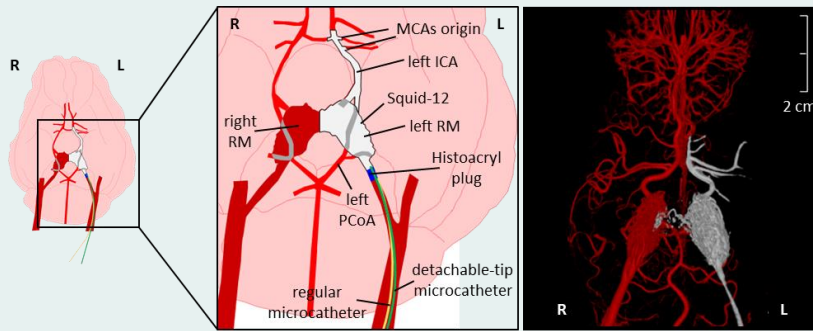
Permanent occlusion of one wing of the RM



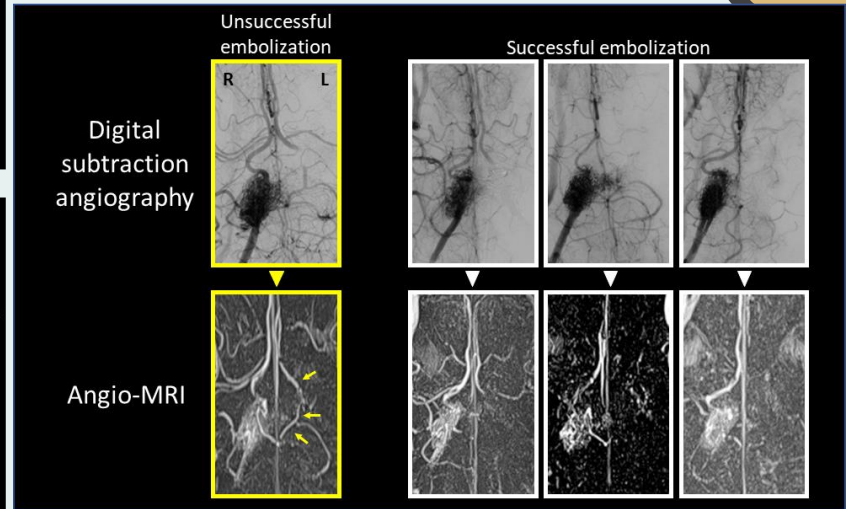
Transient occlusion affecting the left MCA area₅

SQUID-12+ THE PRESSURE COOKER TECHNIQUE

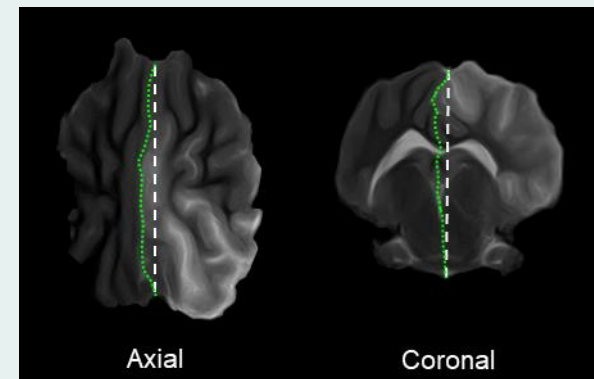
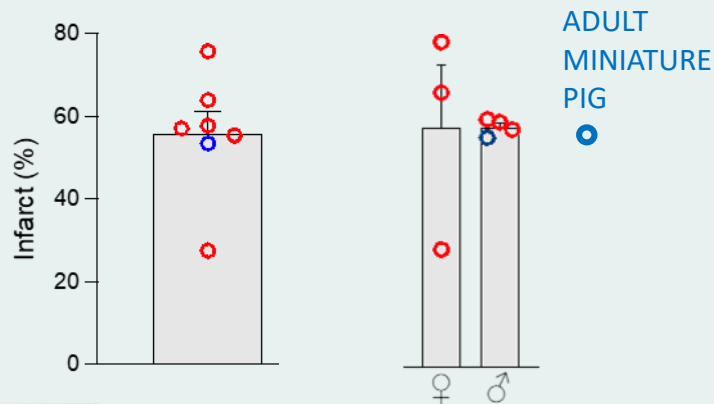
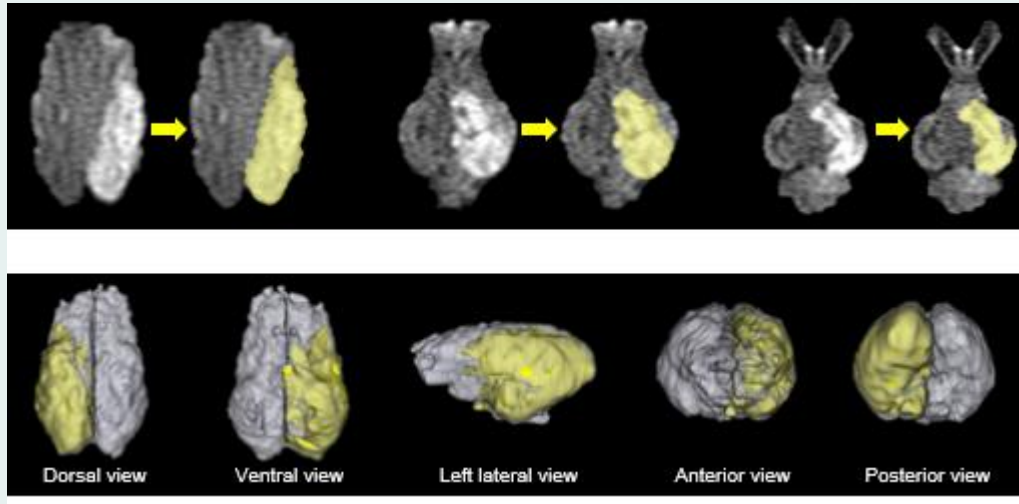
DUROC x LANDRACE BOTH SEXES



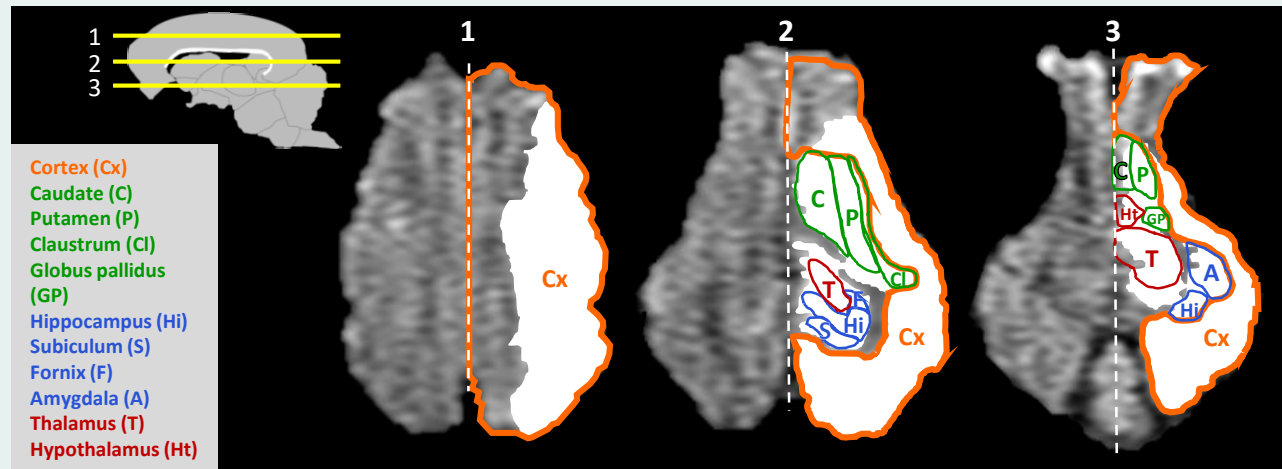
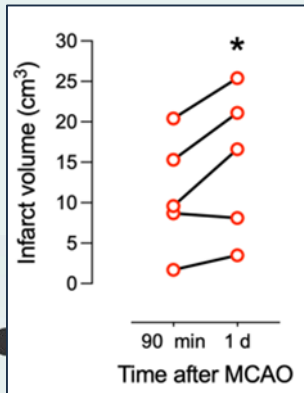
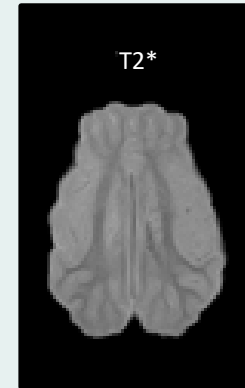
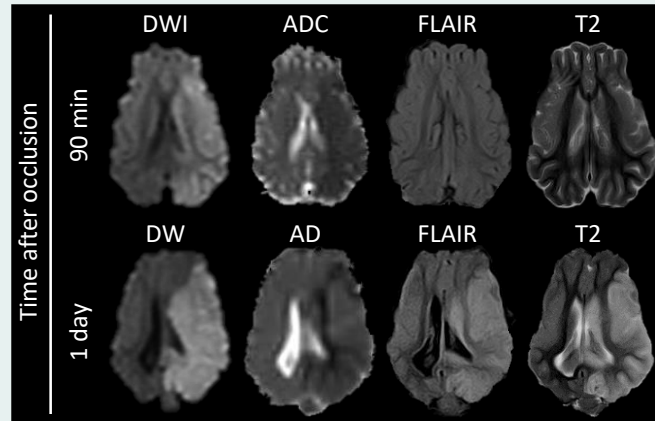
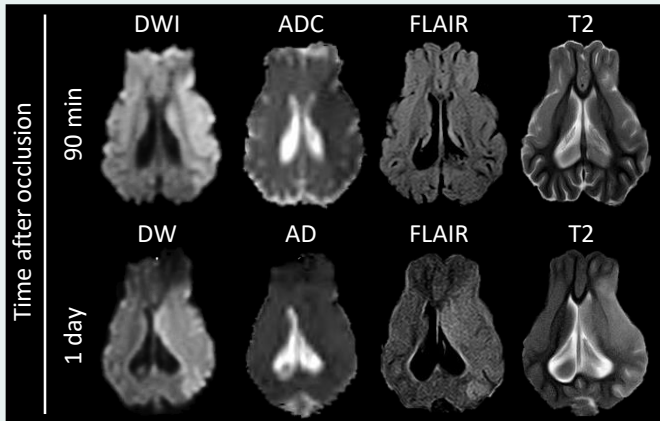
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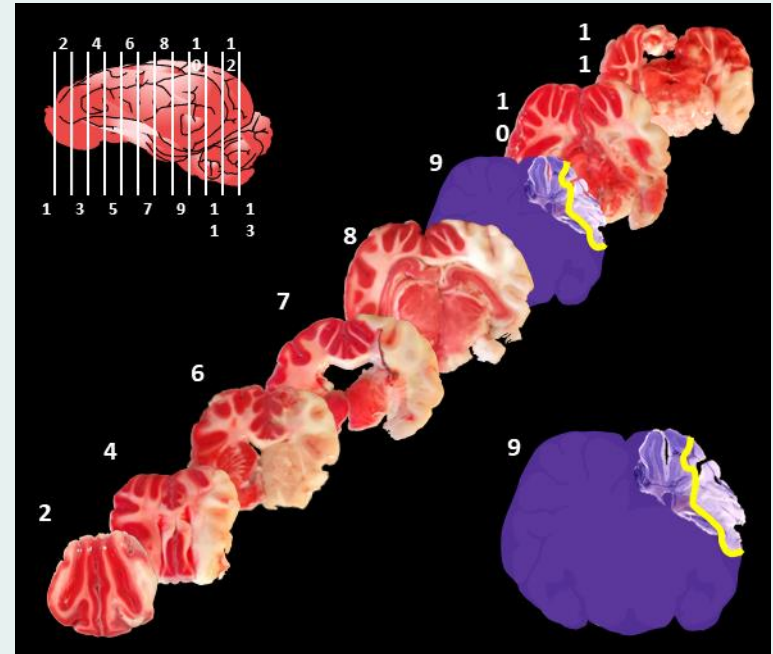
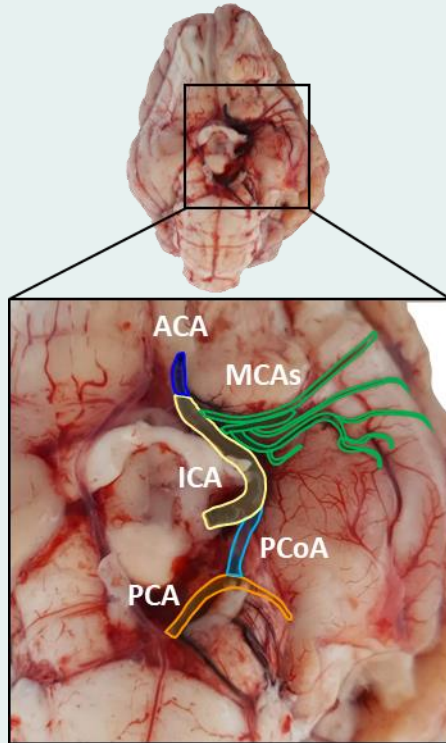
REPRODUCIBLE, MINIMALLY INVASIVE, ISCHEMIC STROKE MODEL



BRAIN AREAS AFFECTED



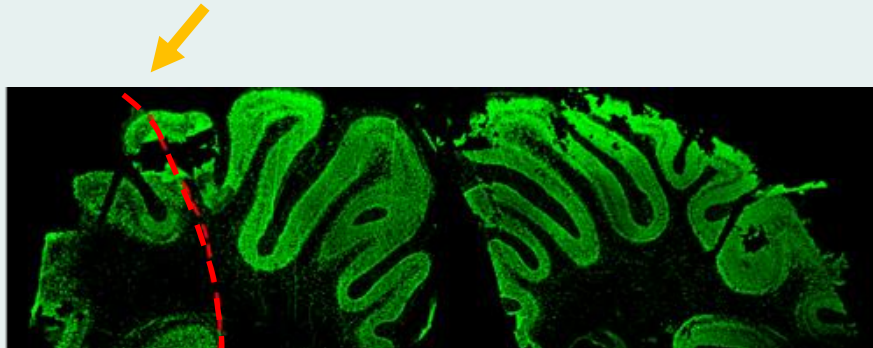
EX VIVO ASSESSMENTS



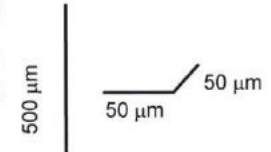
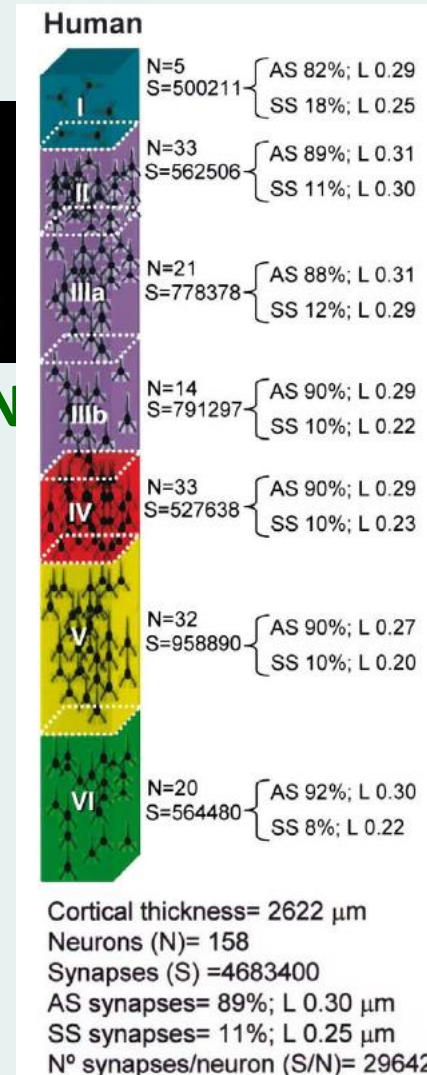
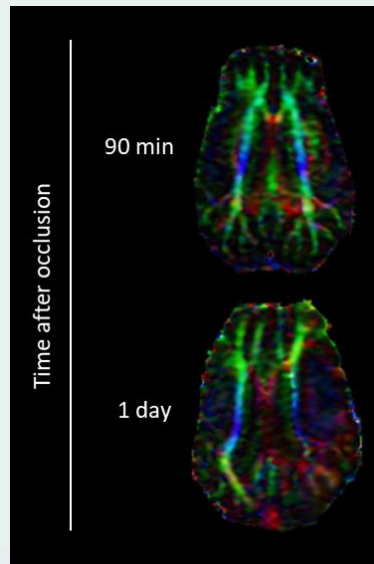
TTC stain

Nissl stain

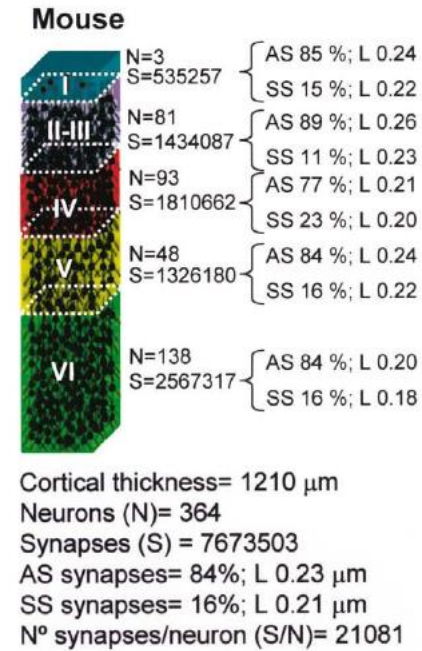
GREY AND WHITE MATTER DAMAGE



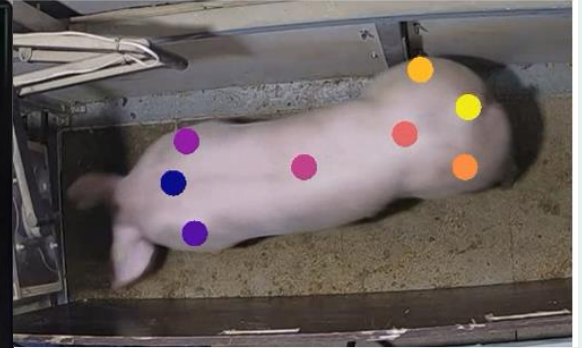
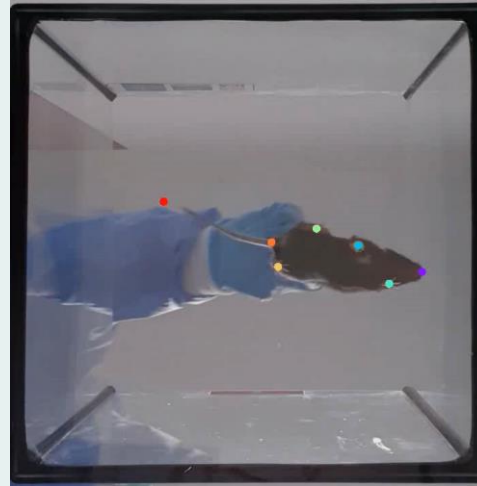
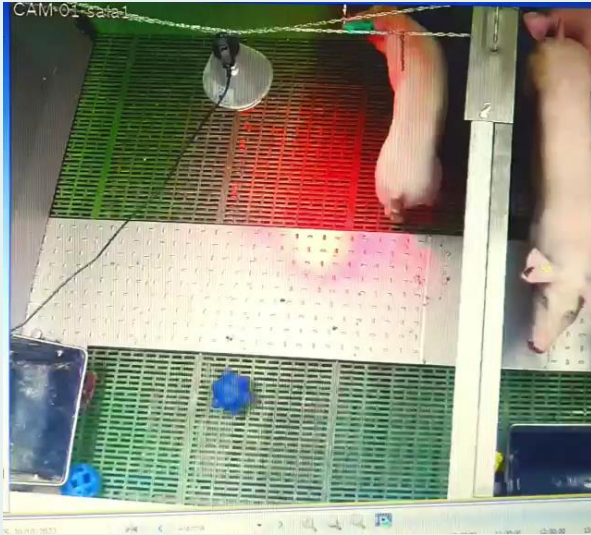
NeuN



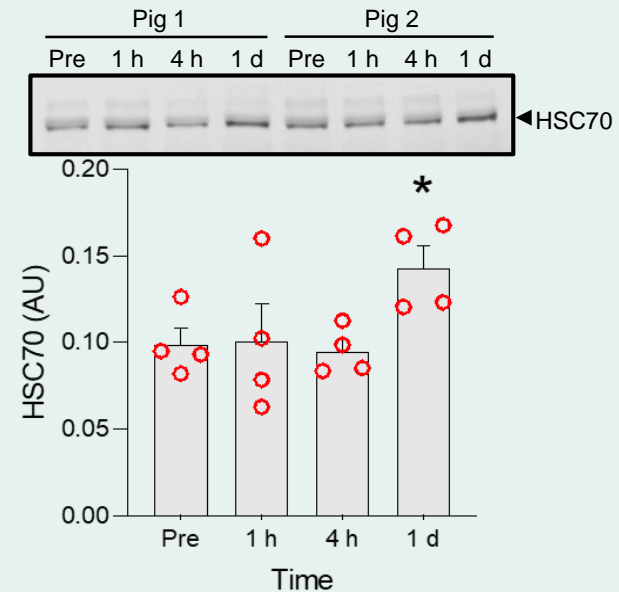
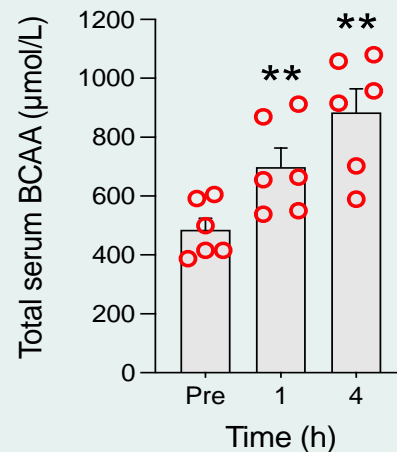
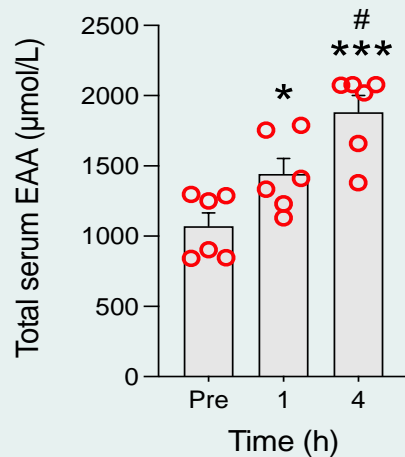
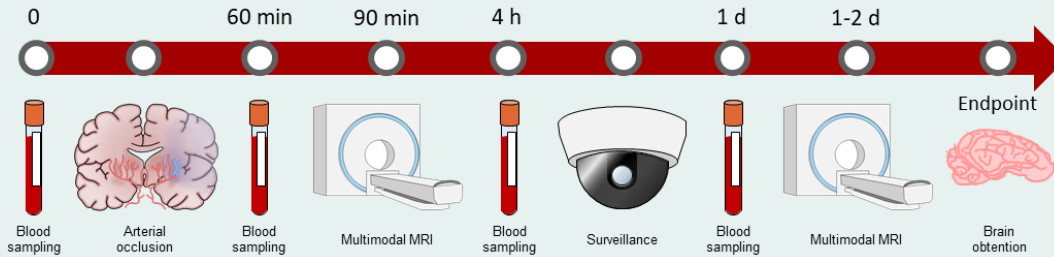
DeFelipe J. Rev. 2011



FUNCTIONAL IMPAIRMENT



BLOOD AA & PROTEIN STROKE BIOMARKERS

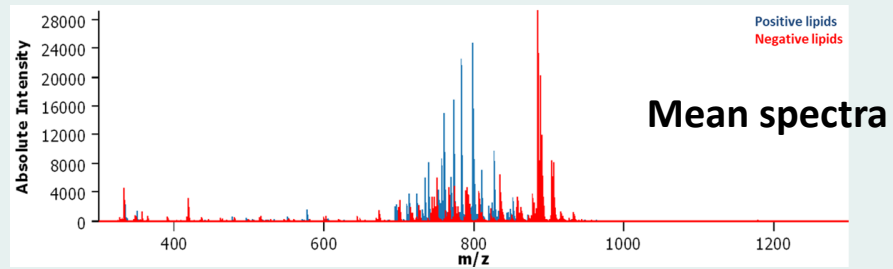


> JCI Insight. 2023 Feb 28;e163398. doi: 10.1172/jci.insight.163398. Online ahead of print.

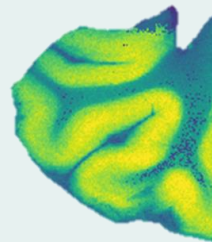
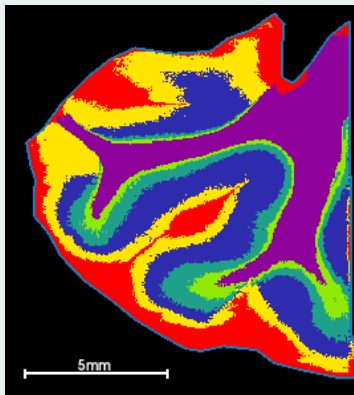
Establishment of a reproducible and minimally invasive ischemic stroke model in swine

Carlos Castaño¹, Marc Melià-Sorolla², Alexia García-Serran², Núria DeGregorio-Rocasolano², Maria Rosa García-Sort¹, María Hernandez-Pérez¹, Adrián Valls Carbó¹, Osvaldo A Pino³, Jordi Grifols⁴, Alba Iruela-Sánchez⁵, Alicia Palomar-García⁵, Josep Puig⁴, Octavi Martí-Sistac⁶, Antoni Davalos¹, Teresa Gasull²

BRAIN SPATIAL LIPIDOMIC STUDY

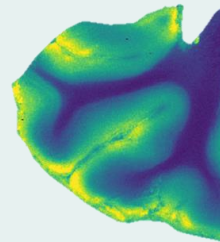


Positive lipids



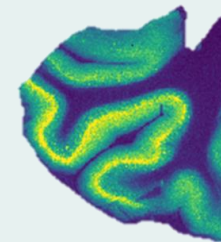
m/z= 801.540 [M+Na]⁺

phosphatidate



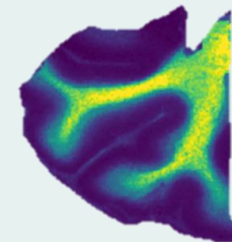
m/z= 697.464 [M+H]⁺

phosphatidylinositol



m/z= 872.541 [M+Na]⁺

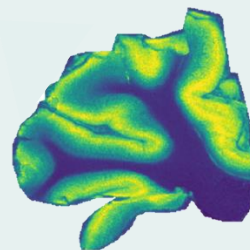
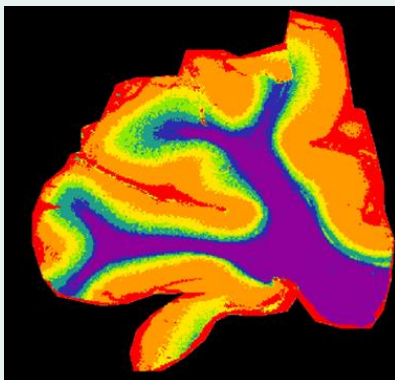
phosphatidylserine



m/z= 792.554 [M+H]⁺

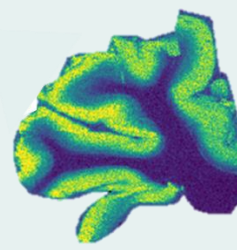
phosphatidylethanolamine

Negative lipids



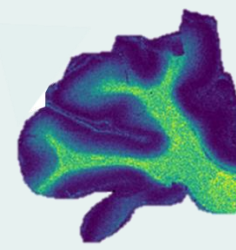
m/z= 885.551 [M-H]⁻

phosphatidylinositol



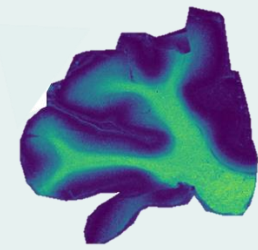
m/z= 792.554 [M-H]⁻

phosphatidylcholine



m/z= 862.610 [M-H]⁻

3-O-Sulfogalactosylceramide



m/z= 888.625 [M+Cl]⁻

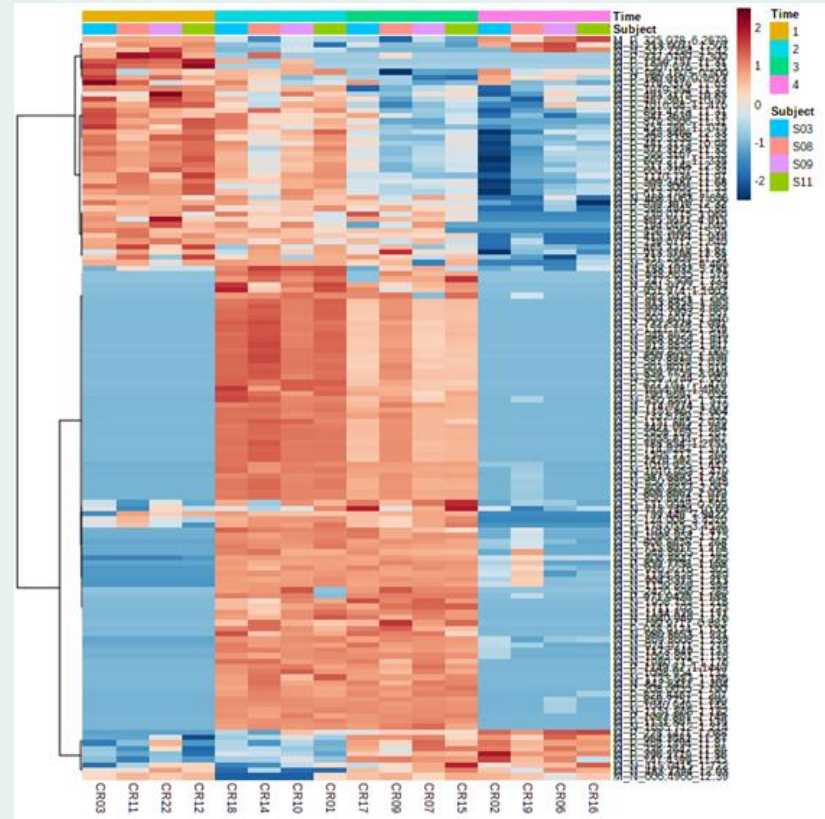
phosphatidylethanolamine

MIN  MAX

CURRENT COLLABORATIONS

RICORS

- Hospital Universitari Arnau de Vilanova/IRB Lleida/ Universitat de Lleida. **Metabolomics/Lipidomics in blood**
- We are currently collaborating with some international groups (**Tim Magnus/Eva Tolosa in Hamburg; Piotr Walczak Malysz-Cymborska in Poland/USA**) in inflammatory markers in blood.
- We have plenty of brain samples, fixed and cryopreserved and some freshly cryopreserved brain slices that could be used to study senescence-induced stroke or other interesting things.
- We have MRI-data





THANKS





THANKS