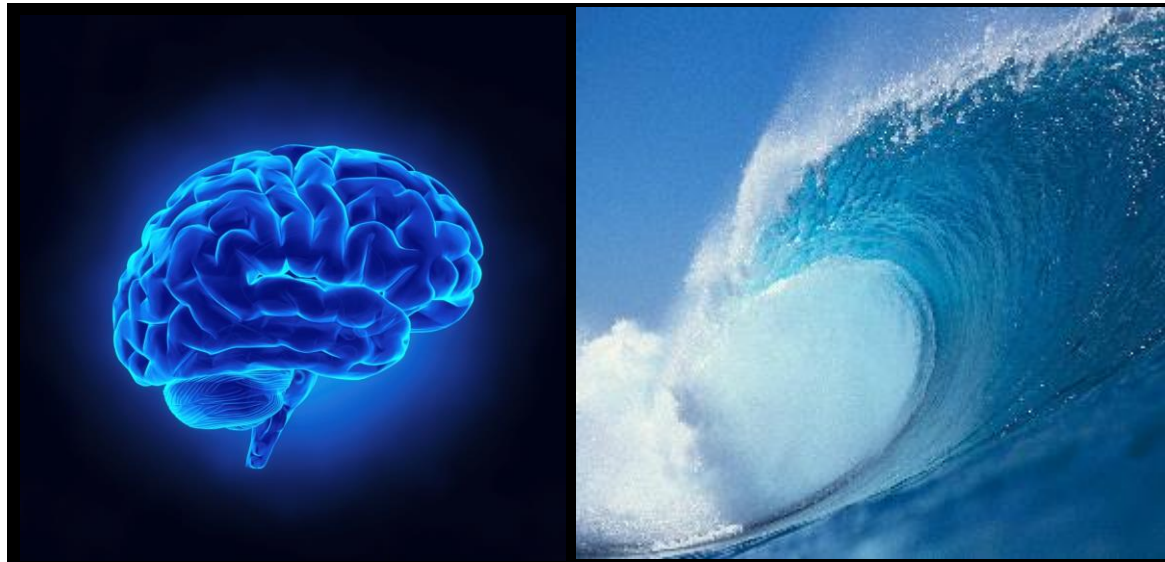


Tsunamis in the Brain

Discovery and potential significance of spreading depolarization



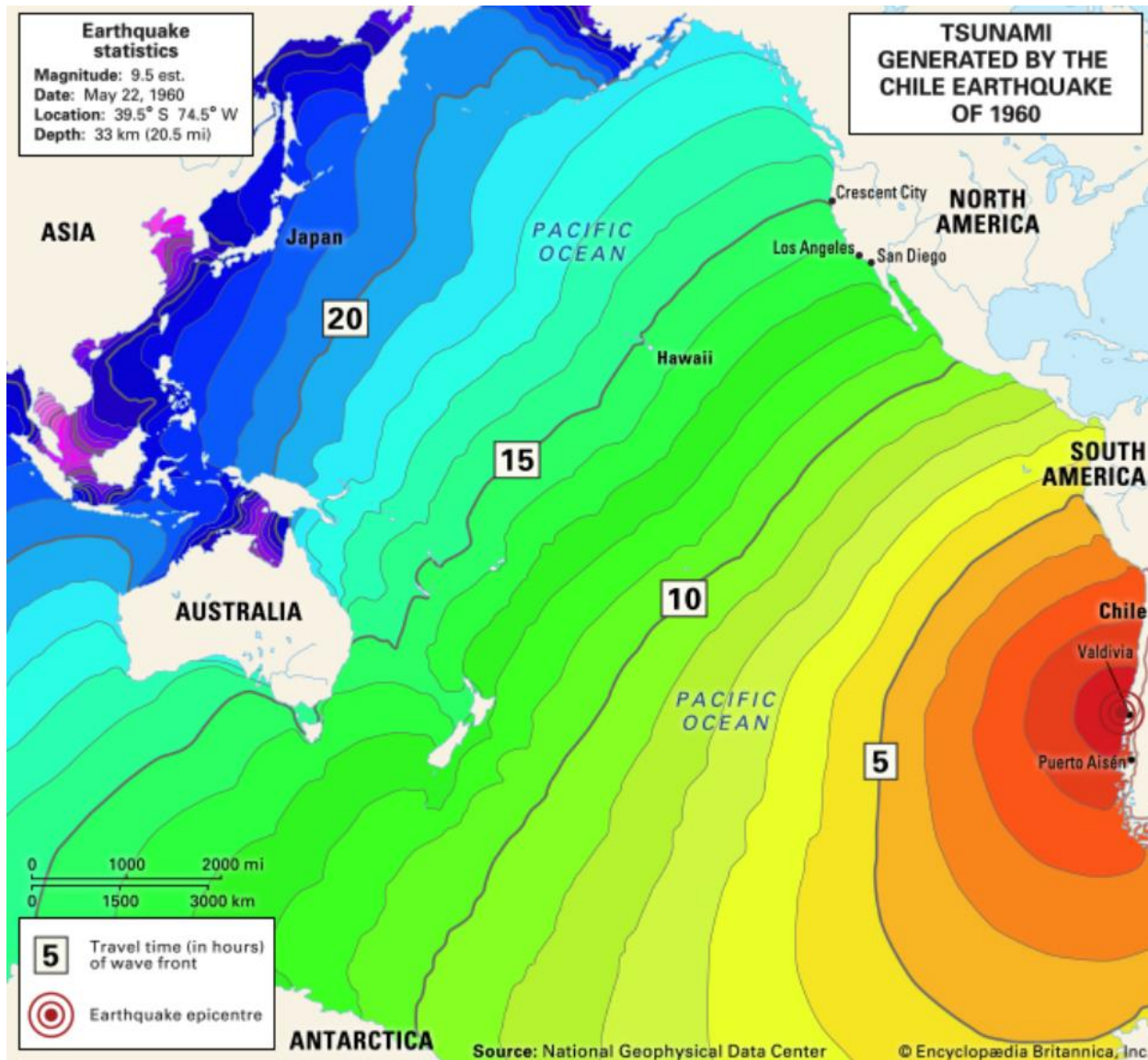
Bill Shuttleworth, PhD

Regents' Distinguished Professor & Dept. Chair
Dept Neurosciences, UNM HSC



SCHOOL OF
MEDICINE
DEPARTMENT OF
NEUROSCIENCES

IEEE SPMB
Saturday 7th December 2024



OUTLINE

▶ Introduction

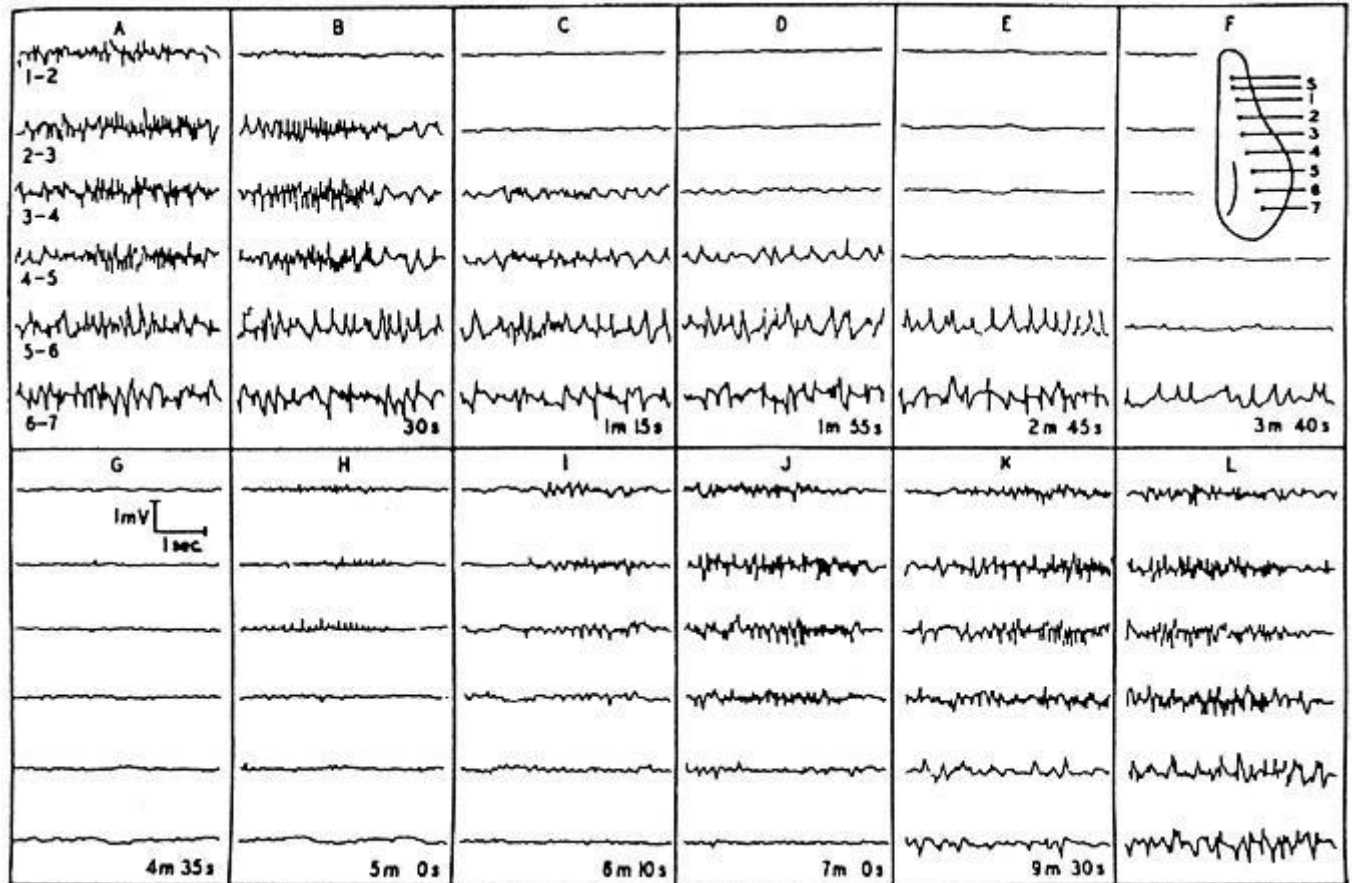
- Spreading Depolarizations (*“Brain Tsunamis”*)
- Migraine, Brain Injury

▶ Mechanisms & Translation to Practice

- Synaptic Depression
- Neuronal Injury
- Preventing SD Initiation

▶ Summary and Perspectives

SPREADING DEPRESSION



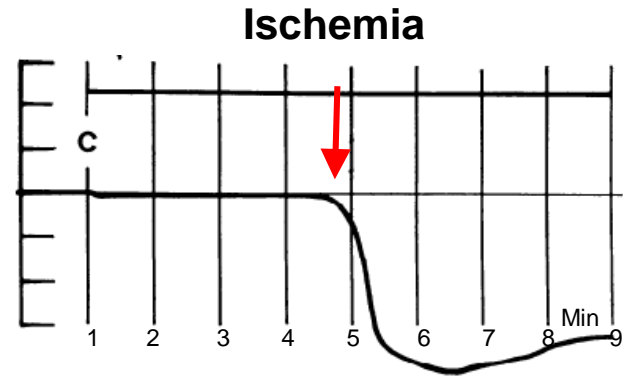
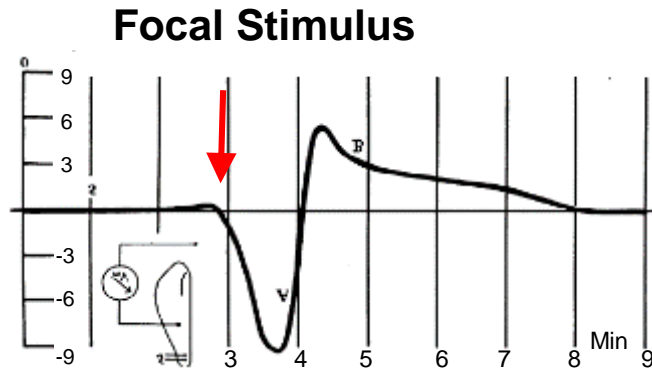
SPREADING DEPRESSION OF ACTIVITY IN THE CEREBRAL CORTEX*

ARISTIDES A. P. LEÃO
 Department of Physiology, Harvard Medical School,
 Boston, Massachusetts

(Received for publication August 14, 1944)

SPREADING DEPOLARIZATION

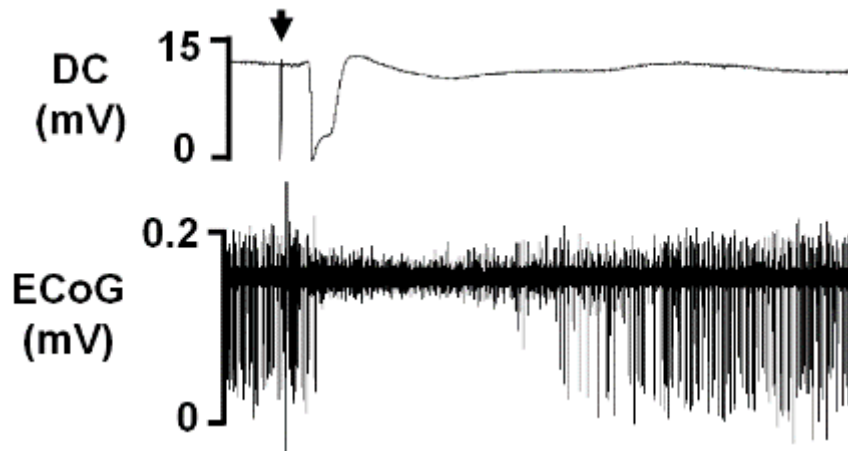
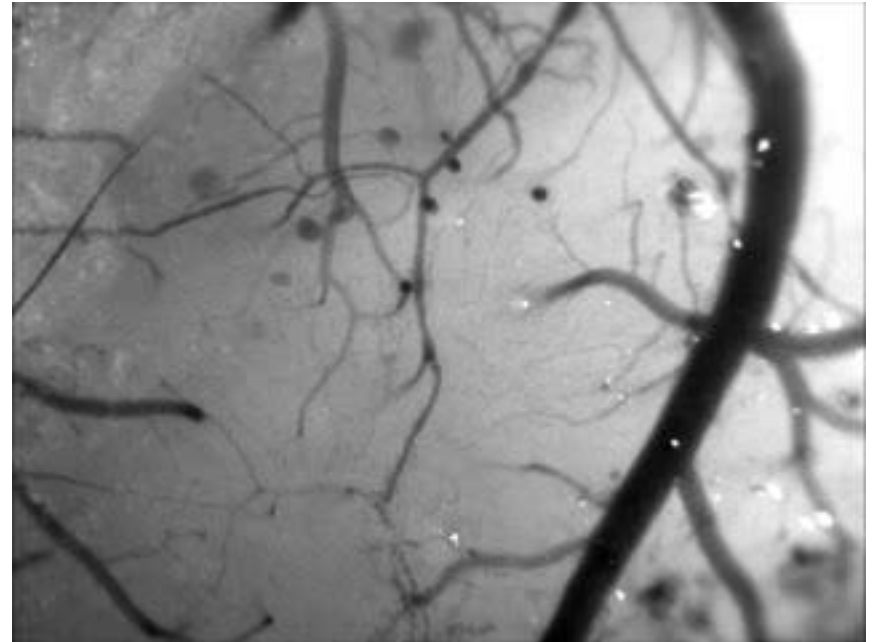
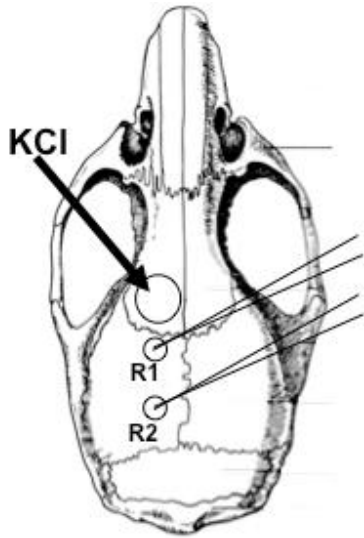
(Underlies Spreading Depression)



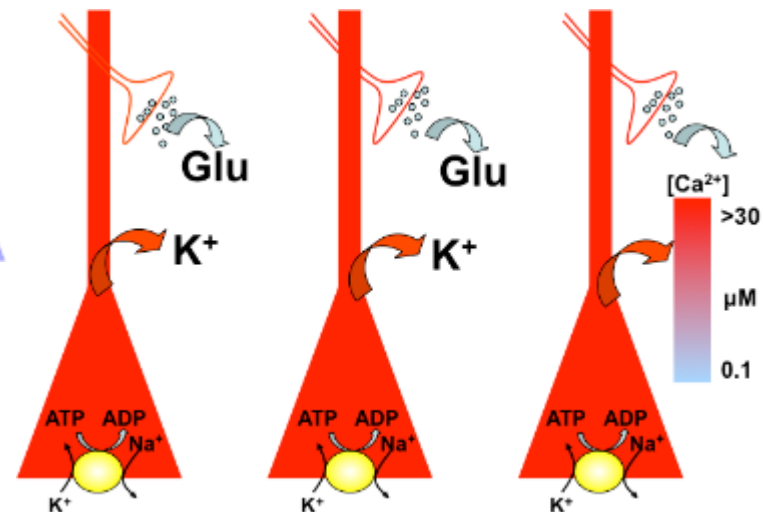
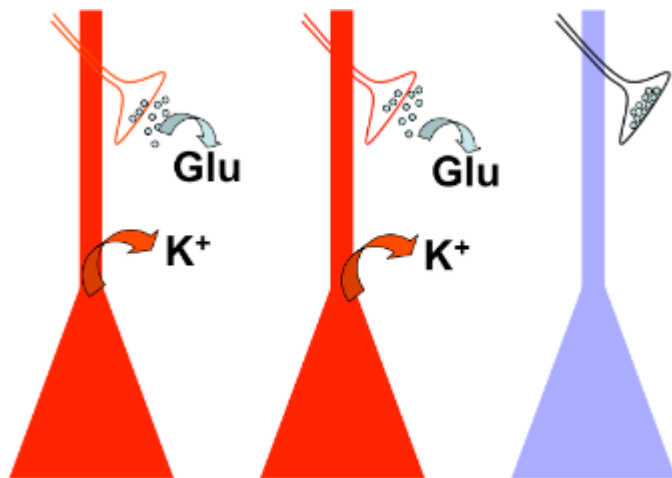
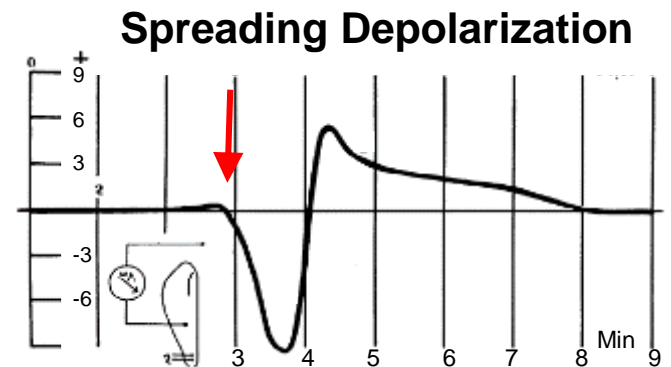
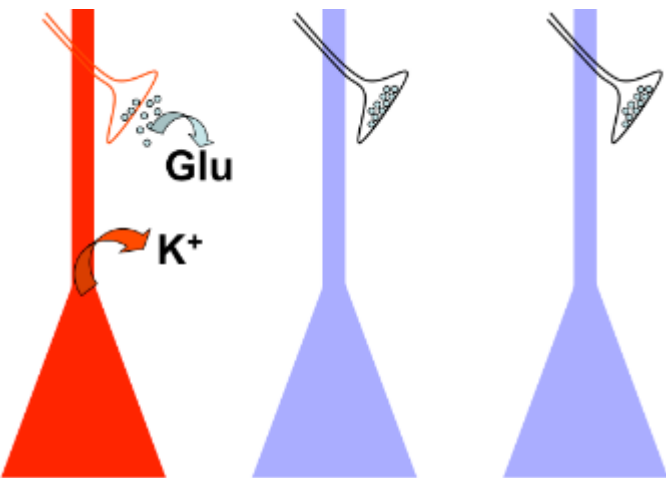
A, Leao, *Further observations on the spreading depression of activity in the cerebral cortex.*
J. Neurophysiol. 10 (1947) 409-414

Neurovascular Coupling

(anesthetized mice)



SPREADING DEPOLARIZATION



Spreading Depolarization (SD) is a Fundamental Brain Mechanism

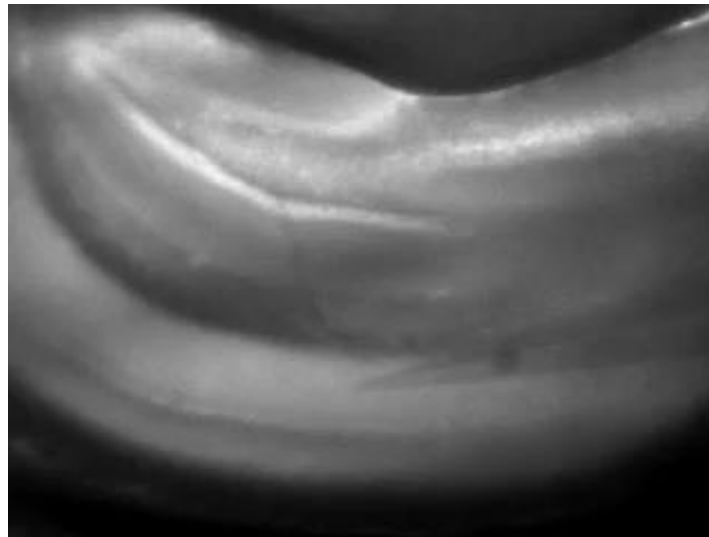
Across Species and Preparations

Isolated Retina from Chicken



Yu et al., PNAS 109 (2012) 2585-2589

Hippocampal Slice from Mouse



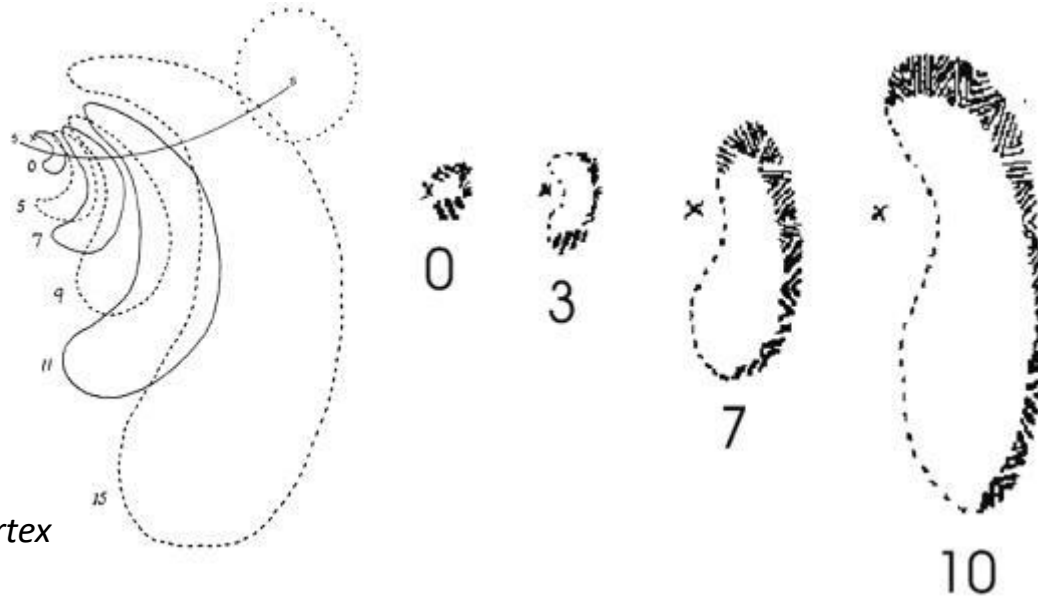
Shuttleworth Lab

Spreading Depolarization Underlies Migraine Aura?

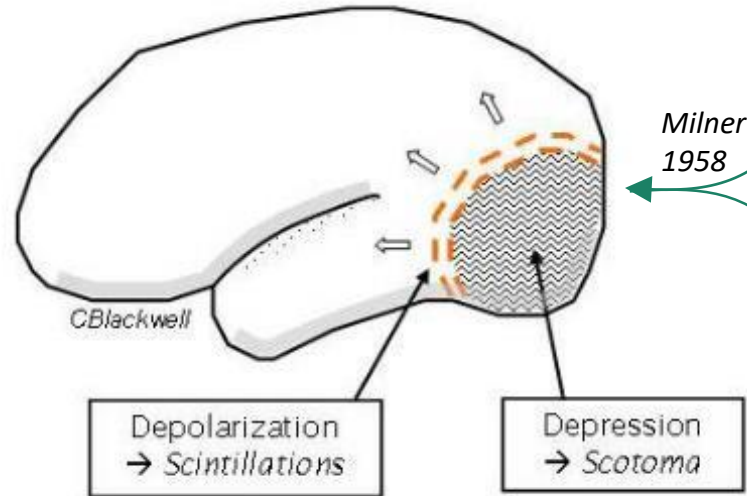
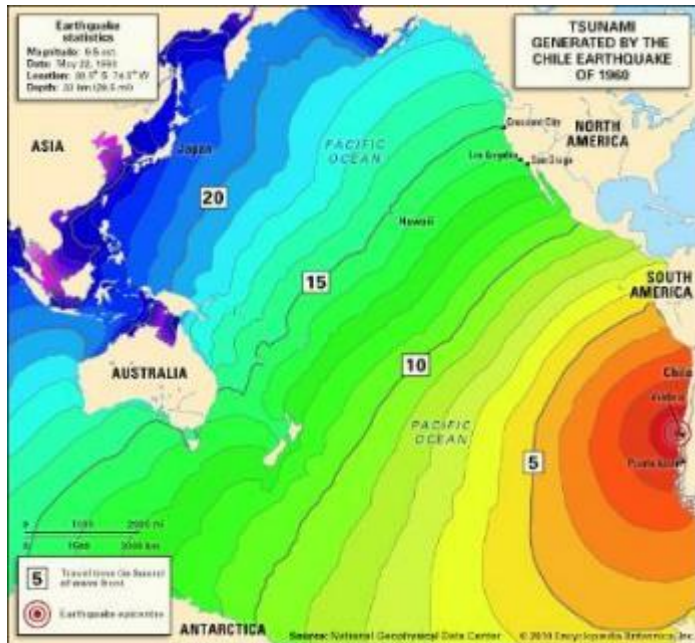


Lashley 1941

~3mm/min across visual cortex



Spreading Depolarization Underlies Migraine Aura?



Karl Lashley
1890-1958



Aristides León
1914-1993

Do Spreading Depolarizations Occur in Humans?

Many decades of evidence from animal studies suggested that these events likely contribute to human conditions – migraine, progression of stroke, TBI injury.

Do Spreading Depolarizations Occur in Humans?

Many decades of evidence from animal studies suggested that these events likely contribute to human conditions – migraine, progression of stroke, TBI injury.

BUT....

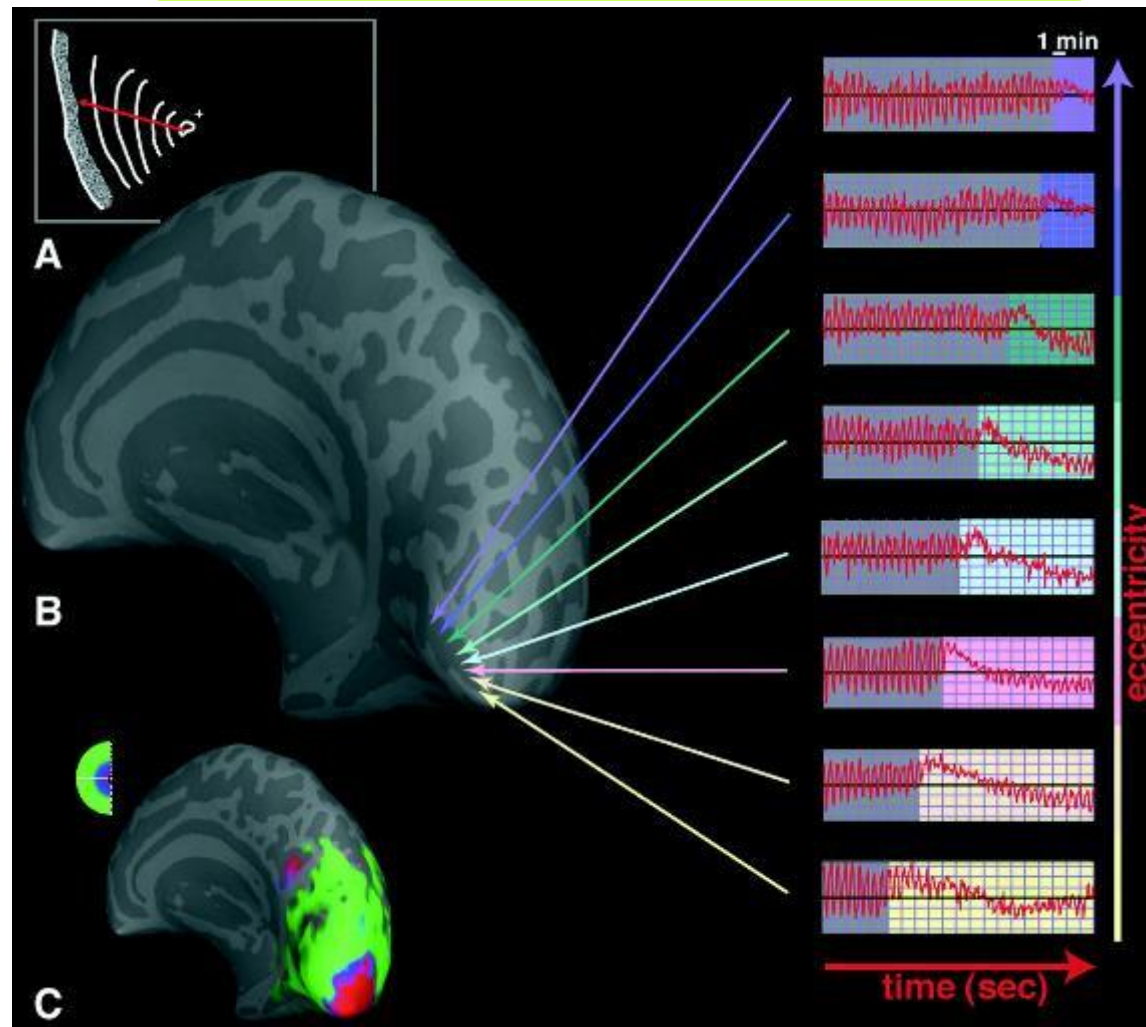
Almost universal rejection of idea that this was relevant for human patients (1947 to ~early 2000s)

- Not reported from EEG recordings
- Structure of human brain may not be suitable
- Neuron / glia ratio different
- Other mechanisms were considered more likely

Spreading Depolarizations Occur in Humans



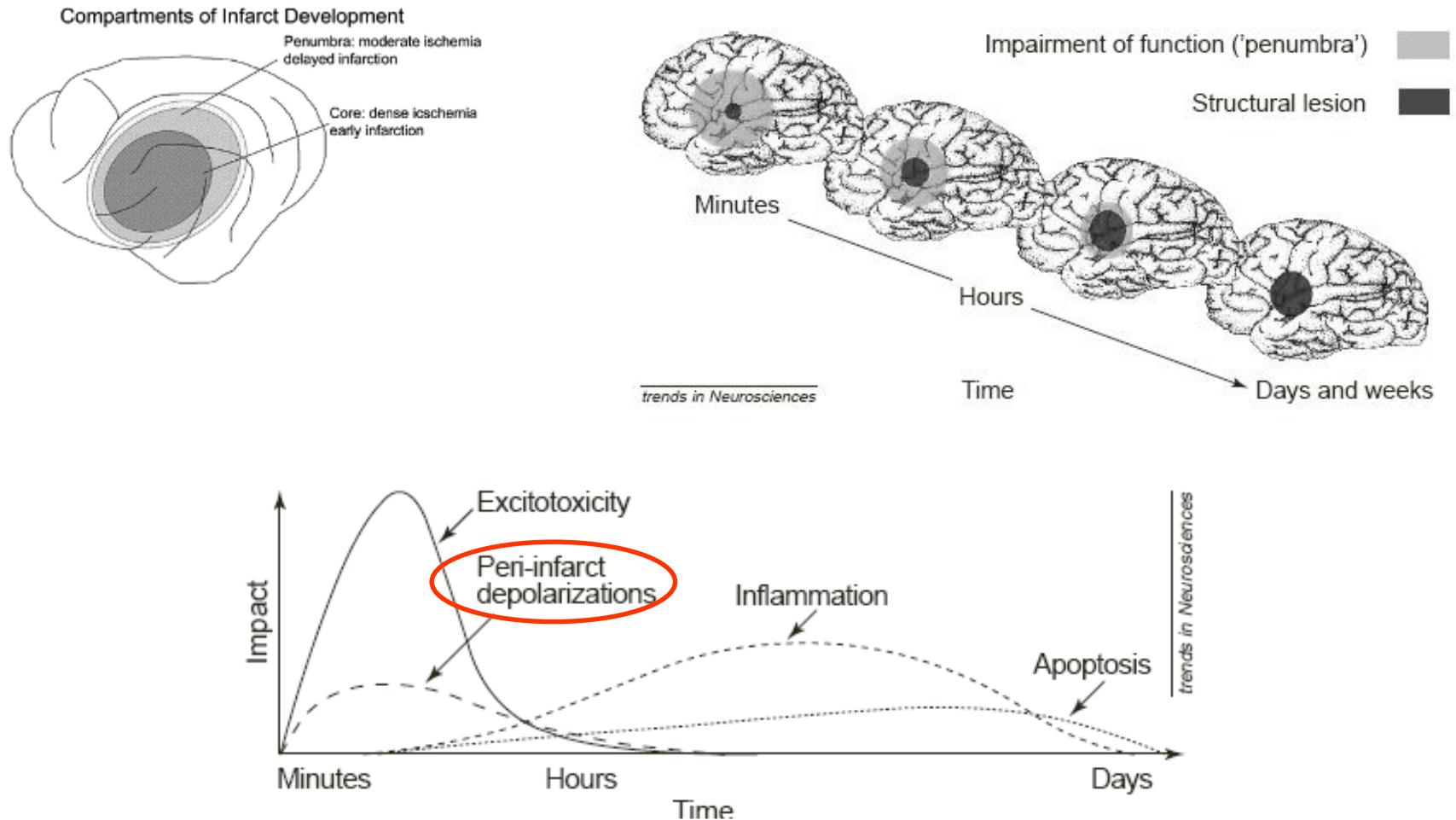
Spreading Depolarizations Occur in Humans



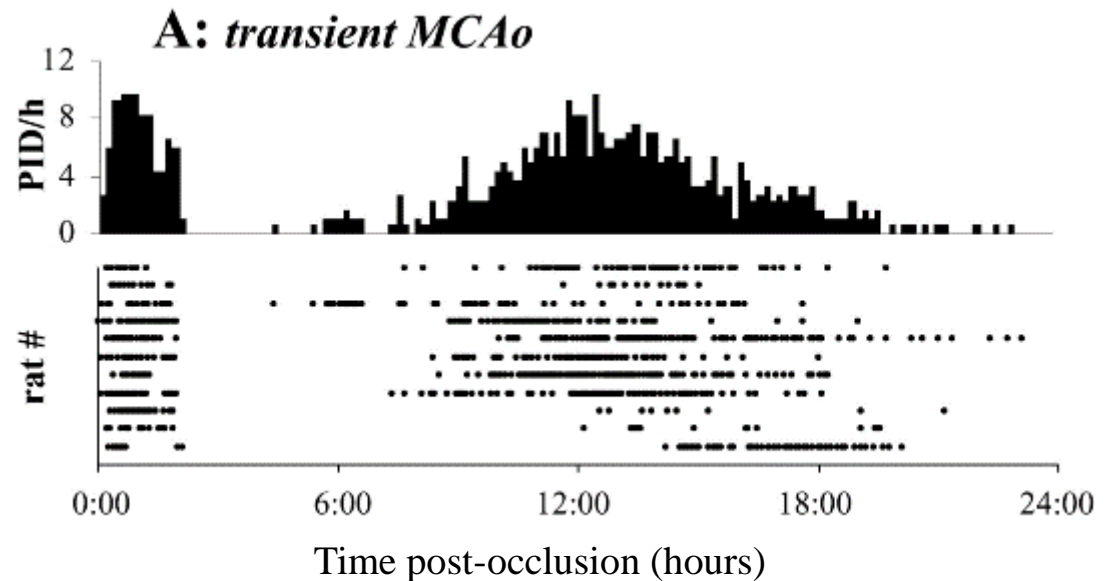
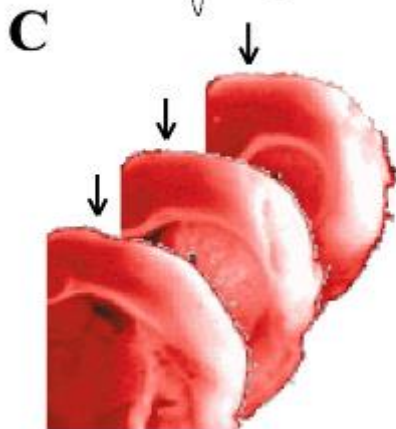
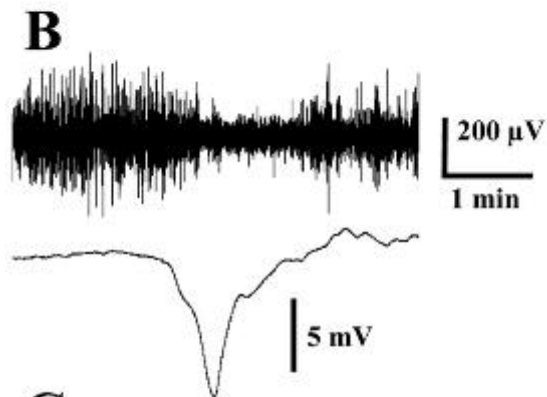
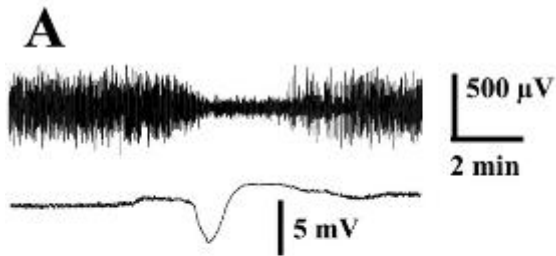
Mechanisms of migraine aura revealed by functional MRI in human visual cortex

Nouhine Hadjikhani^{*†}, Margarita Sanchez del Rio^{†‡}, Ona Wu^{*}, Denis Schwartz^{*}, Dick Bakker^{*}, Bruce Fischl^{*}, Kenneth K. Kwong^{*}, F. Michael Cutrer[§], Bruce R. Rosen^{*}, Roger B. H. Tootell^{*}, A. Gregory Sorensen^{*}, and Michael A. Moskowitz[§]

Progression of Brain Injury



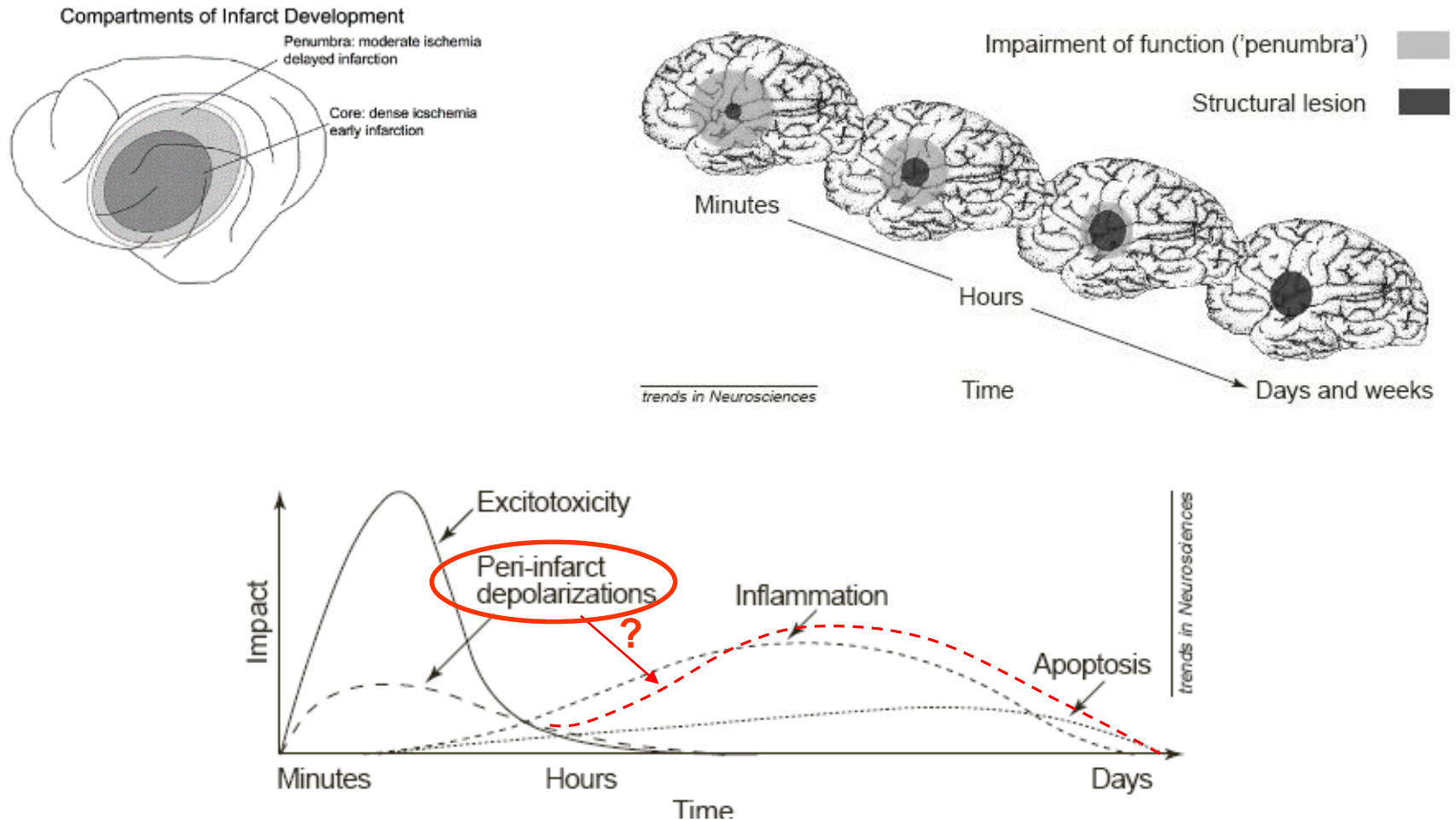
Spreading Depolarizations Occur Long after Initial Injury



“Delayed secondary phase of peri-infarct depolarizations after focal cerebral ischemia: relation to infarct growth and neuroprotection.”

JA Hartings et al., J Neurosci. 23 (2003) 11602-10.

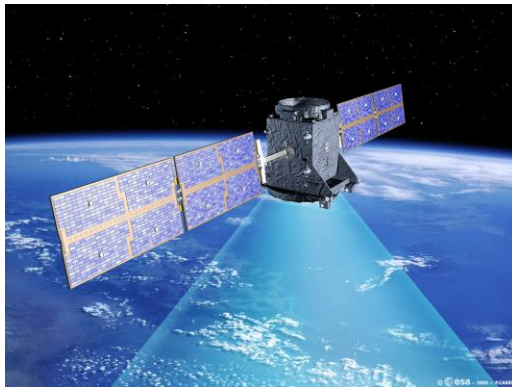
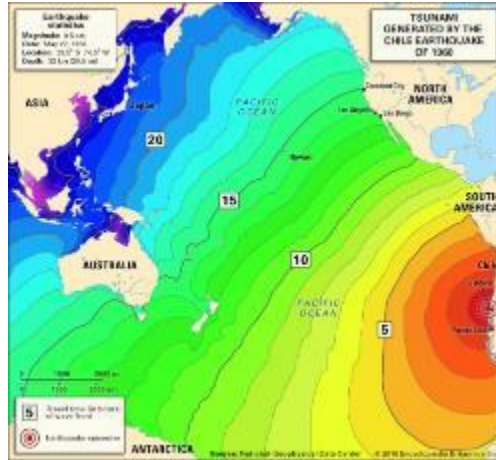
Progression of Brain Injury



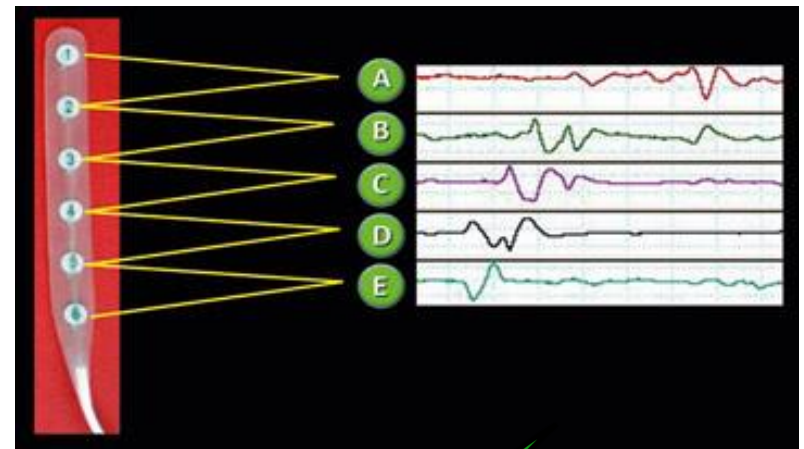
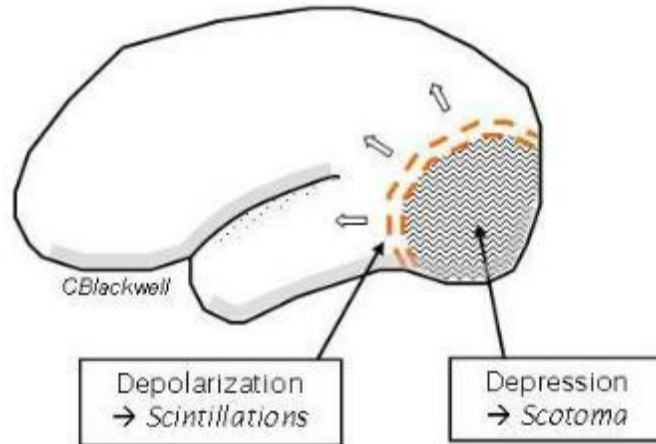
Modified from:

Dirnagl, U., Iadecola, C. & Moskowitz, M.A. *Trends in Neurosciences*. 22 (1999) 391-397.

Spreading Depolarizations are Difficult to Detect in Humans



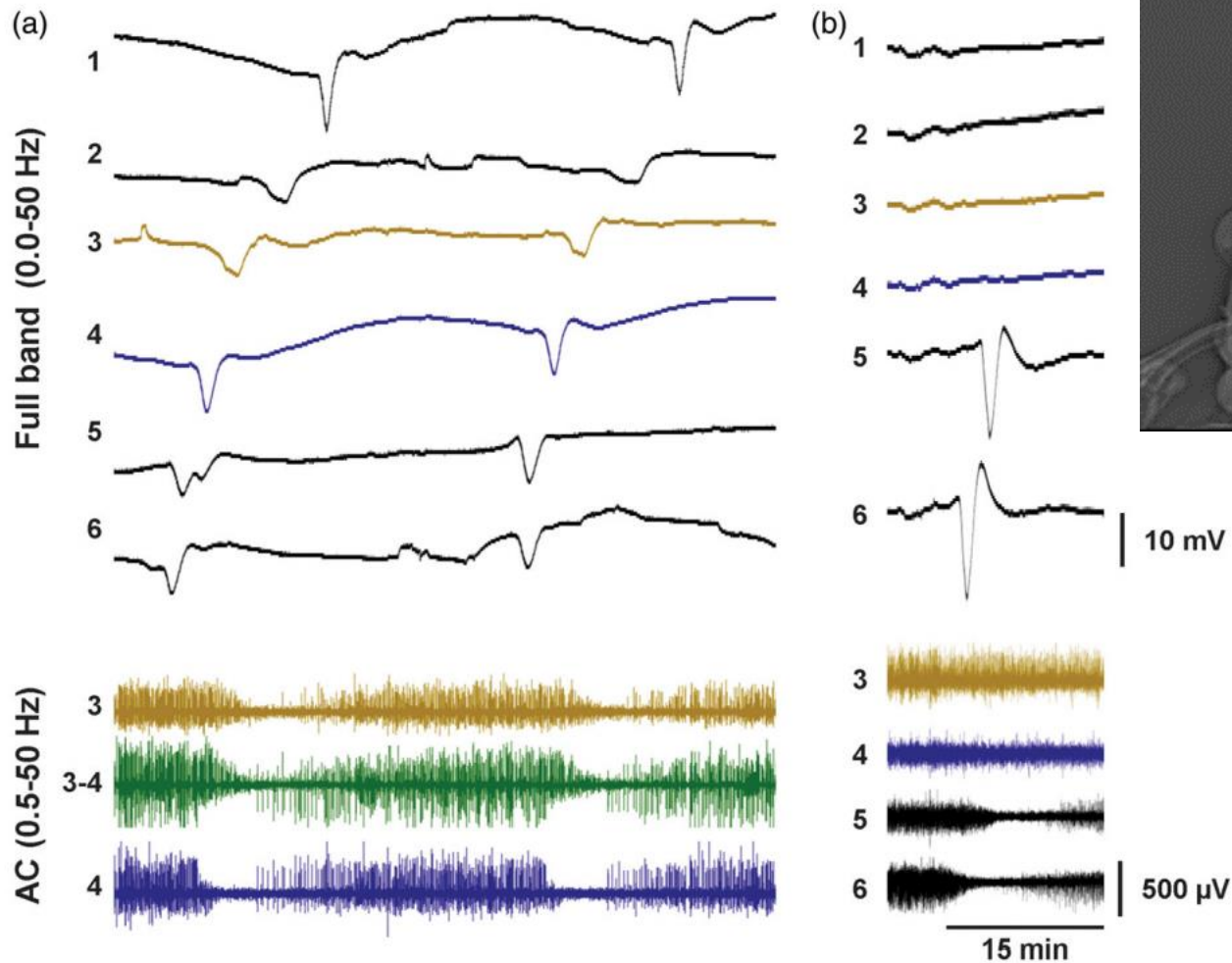
Spreading Depolarizations are Difficult to Detect in Humans



✗ (?)



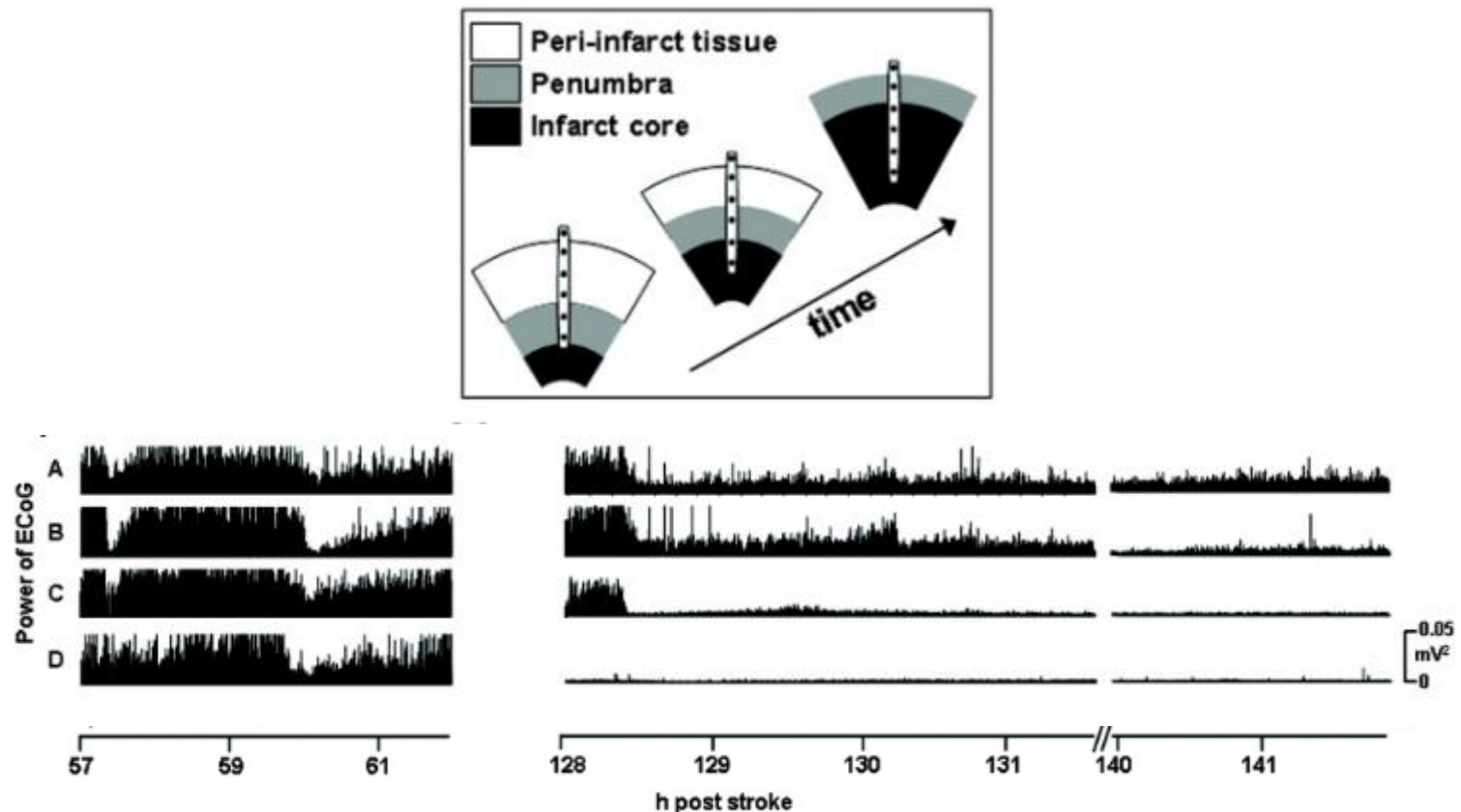
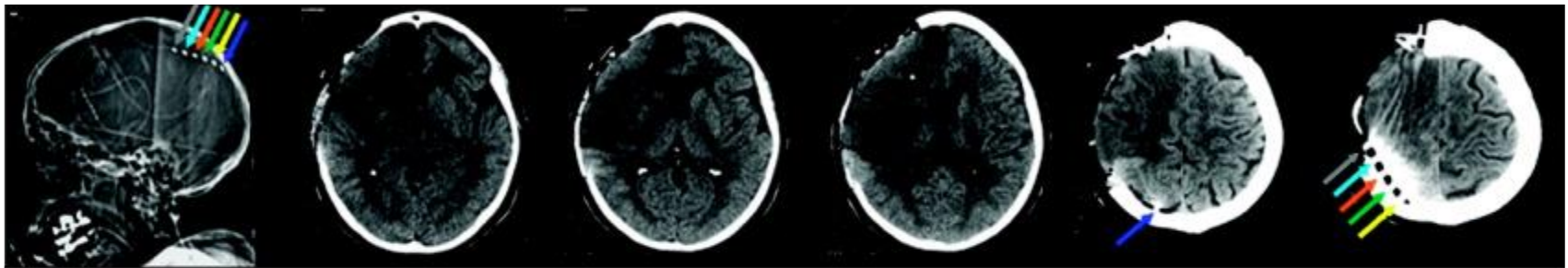
Subdural strip electrodes required for SD monitoring in ICU



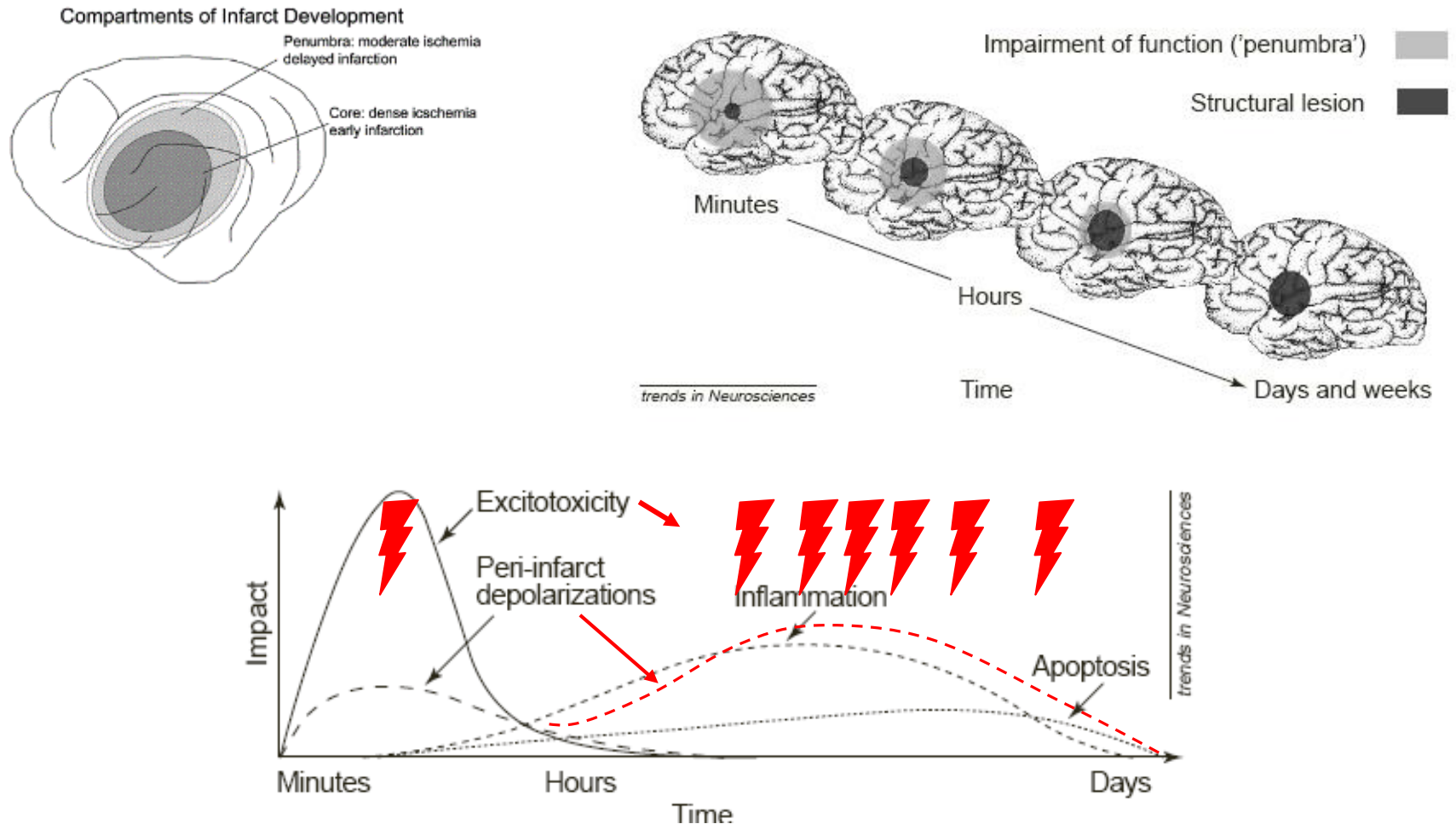
*Andrew Carlson, M.D.
Dept. Neurosurgery, UVA*

Hartings, Li, Hinzman, Shuttleworth, Ernst, Dreier, Wilson, Andaluz, Foreman & Carlson.
Direct current electrocorticography for clinical neuromonitoring of spreading depolarization.
J Cereb Blood Flow Metab. 37 (2017) 1857-1870.

Spreading Depolarizations contribute to injury at surprisingly late time points



A second update to traditional model of stroke progression

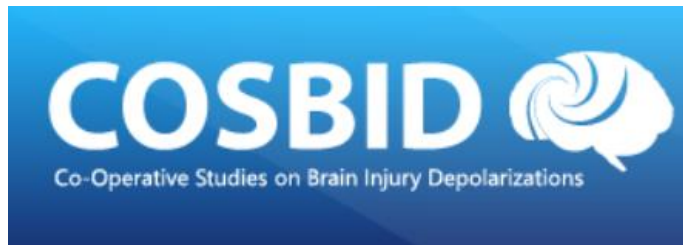


Modified from:

Dirnagl, U., Iadecola, C. & Moskowitz, M.A. *Trends in Neurosciences*. 22 (1999) 391-397.

International Consortium

(Basic Scientists and Clinical Investigators)



2009

www.cosbid.org

International Consortium

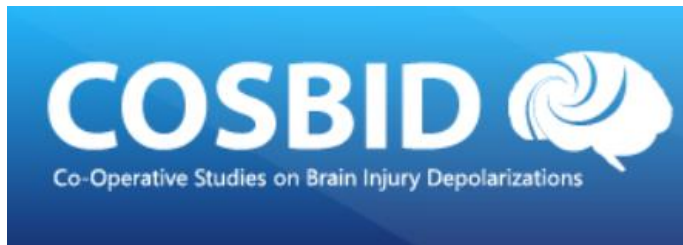
(Basic Scientists and Clinical Investigators)



2016



2024



www.cosbid.org

*Coming up:
Windsor, UK; December 2025*

Spreading Depolarization (SD) is a Fundamental Brain Mechanism

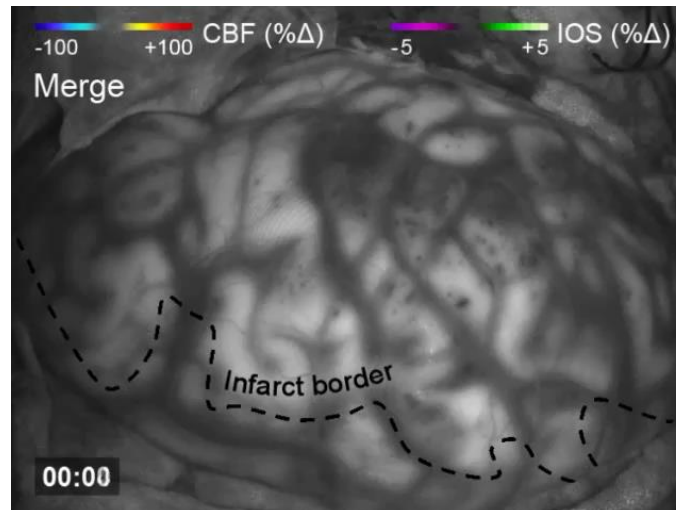
Across Species and Preparations

Anesthetized Pig



Santos et al., Neuroimage. 99 (2014) 244-55

Human, intraoperative recording



Woitzilk et al., Neurology 80 (2013) 244-55



Review Article

Clinical relevance of cortical spreading depression in neurological disorders: migraine, malignant stroke, subarachnoid and intracranial hemorrhage, and traumatic brain injury

Martin Lauritzen^{1,2}, Jens Peter Dreier^{3,4,5}, Martin Fabricius¹, Jed A Hartings⁶, Rudolf Graf⁷ and Anthony John Strong⁸

The continuum of spreading depolarizations in acute cortical lesion development: Examining Leão's legacy

Jed A Hartings^{1,2}, C William Shuttleworth³, Sergei A Kirov⁴, Cenk Ayata⁵, Jason M Hinzman¹, Brandon Foreman⁶, R David Andrew⁷, Martyn G Boutelle⁸, KC Brennan^{9,10}, Andrew P Carlson¹¹, Markus A Dahlem¹², Christoph Drenckhahn¹³, Christian Dohmen¹⁴, Martin Fabricius¹⁵, Eszter Farkas¹⁶, Delphine Feuerstein¹⁷, Rudolf Graf¹⁷, Raimund Helbok¹⁸, Martin Lauritzen^{15,19}, Sebastian Major^{13,20,21}, Ana I Oliveira-Ferreira^{20,21}, Frank Richter²², Eric S Rosenthal⁵, Oliver W Sakowitz^{23,24}, Renán Sánchez-Porrás²⁴, Edgar Santos²⁴, Michael Schöll²⁴, Anthony J Strong²⁵, Anja Urbach²⁶, M Brandon Westover⁵, Maren KL Winkler²⁰, Otto W Witte^{26,27}, Johannes Woitzik^{20,28} and Jens P Dreier^{13,20,21}

Recording, analysis, and interpretation of spreading depolarizations in neurointensive care: Review and recommendations of the COSBID research group

Jens P Dreier^{1,2,3}, Martin Fabricius⁴, Cenk Ayata^{5,6}, Oliver W Sakowitz^{7,8}, C William Shuttleworth⁹, Christian Dohmen^{10,11}, Rudolf Graf¹¹, Peter Vajkoczy^{1,12}, Raimund Helbok¹³, Michiyasu Suzuki¹⁴, Alois J Schiefecker¹⁵, Sebastian Major^{16,17}, Maren KL Winkler¹⁸, Eun-Jeung Kang¹⁹, Denny Milakara¹, Ana I Oliveira-Ferreira^{1,20}, Clemens Reiffurth^{1,3}, Gajanan S Revankar¹, Kazutaka Sugimoto¹⁴, Nora F Dengler^{1,12}, Nils Hechel^{1,13}, Brandon Foreman¹, Bart Feyen¹⁸, Daniel Kondziella¹⁷, Christian K Friberg², Henning Piligaard⁴, Eric S Rosenthal⁴, M Brandon Westover⁴, Anna Maslarova¹⁸, Edgar Santos⁴, Daniel Hertle⁴, Renán Sánchez-Porrás⁴, Sharon L Jewell¹⁹, Baptiste Balança^{20,21}, Johannes Platz²², Jason M Hinzman²³, Janos Lückl¹, Karl Scholnecht^{1,3,24}, Michael Schöll^{25,26}, Christoph Drenckhahn^{1,26}, Delphine Feuerstein¹, Nina Eriksen^{27,28}, Viktor Horsch²⁹, Julia S Bretz^{2,29}, Paul Jahnske²⁹, Michael Scheel²⁹, Georg Bohner²⁹, Egill Rostrop²⁷, Bente Pakkenberg^{28,30}, Uwe Heinemann^{1,31}, Jan Claassen¹, Andrew P Carlson³¹, Christina M Kowoll^{18,32}, Svetlana Lublinskaya^{33,34}, Yoash Chavdim^{33,34}, Ian Shalev³⁴, Alon Friedman^{33,35}, Gerrit Brinker³⁴, Michael Reiner³⁶, Sergei A Kirov³⁷, R David Andrew³⁸, Eszter Farkas³⁹, Erdem Güresir⁴⁰, Hartmut Vatter⁴¹, Lee S Chung⁴², KC Brennan⁴³, Thomas Lieutaud^{40,41}, Stephane Marinnesco^{40,41}, Andrew IR Maas⁴⁴, Juan Sahuquillo⁴², Markus A Dahlem⁴³, Frank Richter⁴⁴, Oscar Herreras⁴⁵, Martyn G Boutelle⁴⁶, David O Okonkwo⁴⁷, M Ross Bullock⁴⁸, Otto W Witte⁴⁹, Peter Martus⁵⁰, Arn MJM van den Maagdenberg^{51,52}, Michel D Ferrari⁵³, Rick M Dijkhuizen⁵³, Lori A Shutter^{47,54}, Norberto Andaluz⁵⁵, André P Schultze⁵⁶, Brian MacVicar⁵⁷, Tomas Watanabe⁵⁸, Johannes Woitzik⁵⁹, Martin Lauritzen⁵⁹, Anthony J Strong¹⁹ and Jed A Hartings^{23,54}

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DOI: 10.1177/0271678X16654496
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REVIEW

nature
medicine

The role of spreading depression, spreading depolarization and spreading ischemia in neurological disease

Jens P Dreier

NATURE MEDICINE VOLUME 17 | NUMBER 4 | APRIL 2011

Neuron

Volume 86, Issue 4, 20 May 2015, Pages 902–922

The Stroke-Migraine Depolarization Continuum

Jens P. Dreier^{1,2,3,*} and Clemens Reiffurth^{2,3}



Which Spreading Depolarizations Are Deleterious To Brain Tissue?

C. William Shuttleworth^{1,32*}, R. David Andrew², Yama Akbari³, Cenk Ayata⁴, Ramani Balu⁵, K. C. Brennan⁶, Martyn Boutelle⁷, Andrew P. Carlson⁸, Jens P. Dreier^{9,10,11,12,13}, Martin Fabricius¹⁴, Eszter Farkas¹⁵, Brandon Foreman^{16,27,29,30}, Raimund Helbok¹⁷, Nils Henninger¹⁸, Sharon L. Jewell¹⁹, Stephen C. Jones²⁰, Sergei A. Kirov^{21,22}, Britta E. Lindquist²³, Carolina B. Maciel²⁴, David Okonkwo³¹, Katelyn M. Reinhart¹, R. Meldrum Robertson²⁵, Eric S. Rosenthal²⁶, Tomas Watanabe²⁸ and Jed A. Hartings^{16,29,30}

Neurocrit Care (2020) 32:317–322

<https://doi.org/10.1007/s12028-019-00776-7>

What Should a Clinician Do When Spreading Depolarizations are Observed in a Patient?

Raimund Helbok^{1*}, Jed A. Hartings^{2,3,4}, Alois Schiefecker¹, Baptiste Balança^{5,6,7,8}, Sharon Jewell^{9,15}, Brandon Foreman^{2,3,4,10}, Ari Ercole¹¹, Ramani Balu¹², Cenk Ayata¹³, Laura Ngwenya^{2,3,4,10}, Eric Rosenthal¹⁴, Martyn G. Boutelle¹⁵, Eszter Farkas¹⁶, Jens P. Dreier^{5,17,18,19,20}, Martin Fabricius²¹, C. William Shuttleworth²² and Andrew Carlson²³

Neurocrit Care (2020) 32:306–310

<https://doi.org/10.1007/s12028-019-00777-6>

OUTLINE

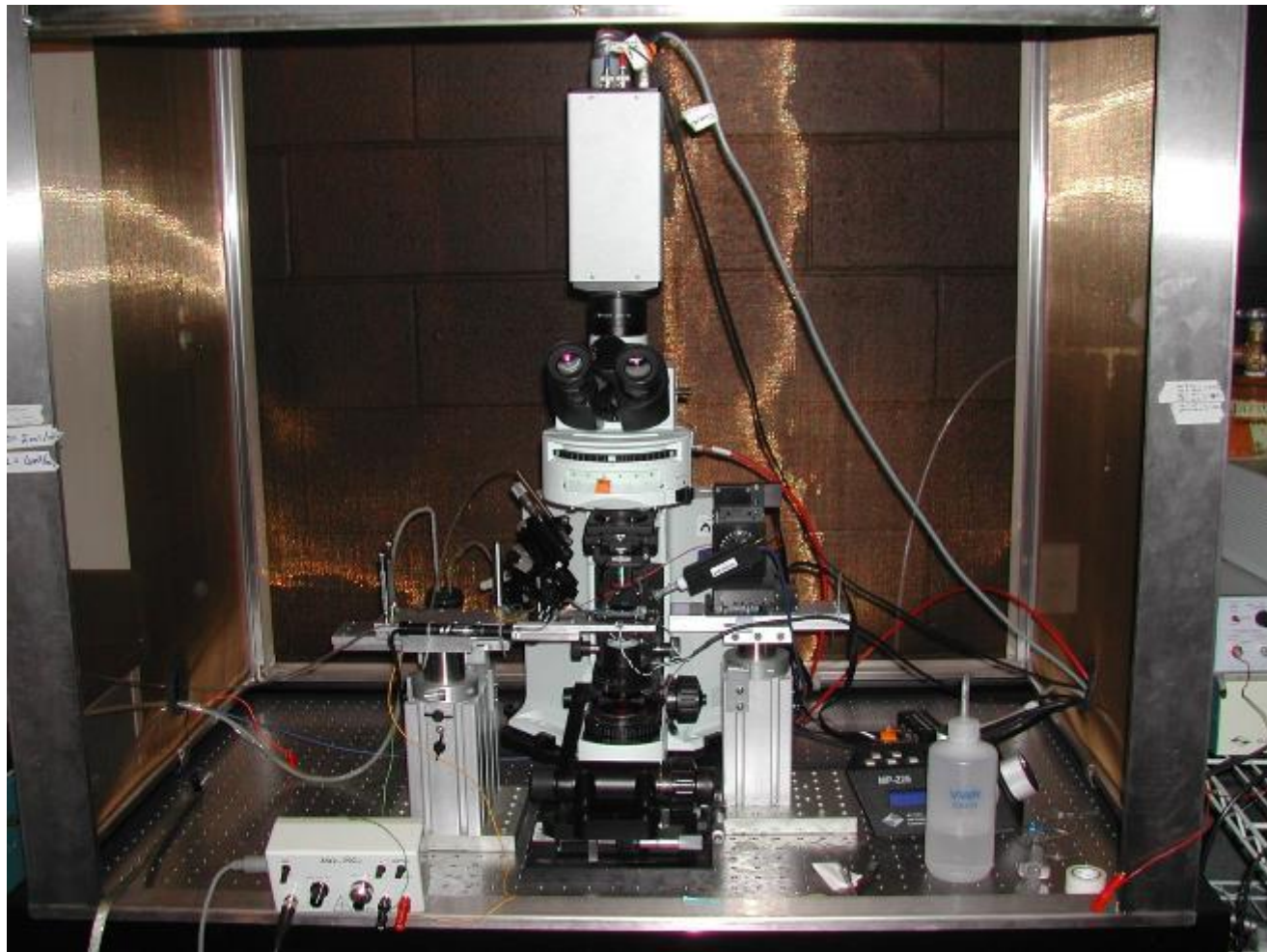
► Introduction

- Spreading Depolarizations (*“Brain Tsunamis”*)
- Migraine, Brain Injury

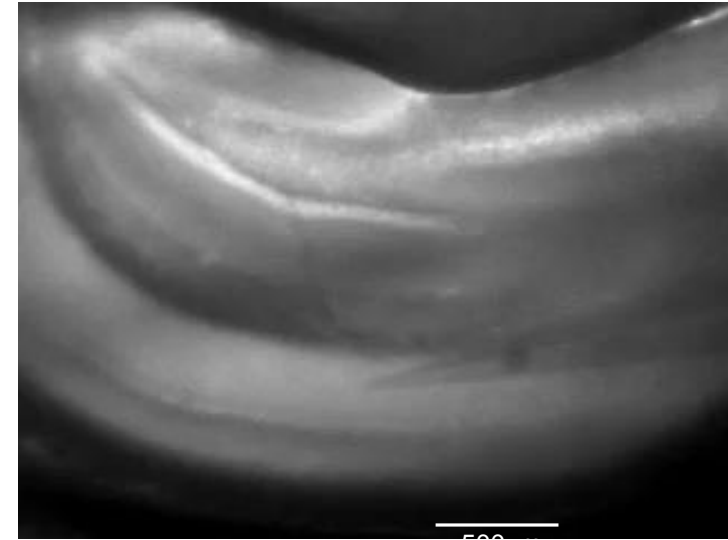
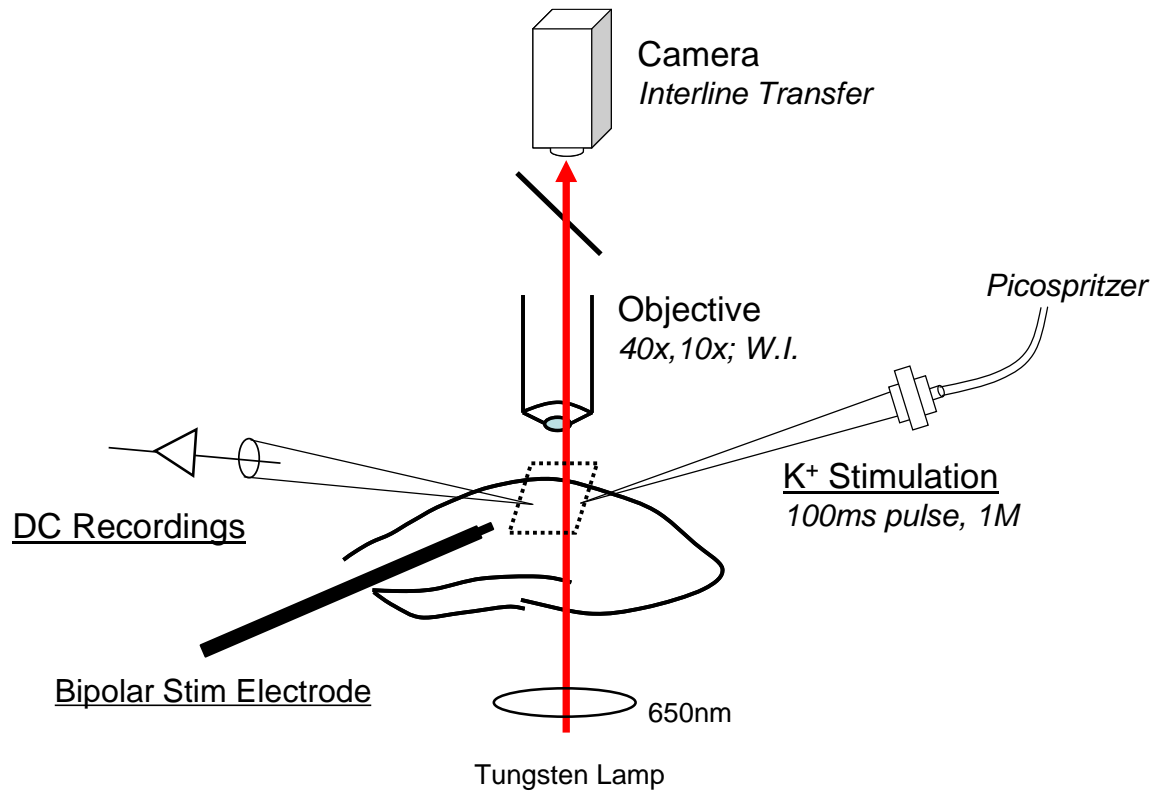
► **Mechanisms & Translation to Practice**

- Synaptic Depression
- Neuronal Injury
- Preventing Initiation

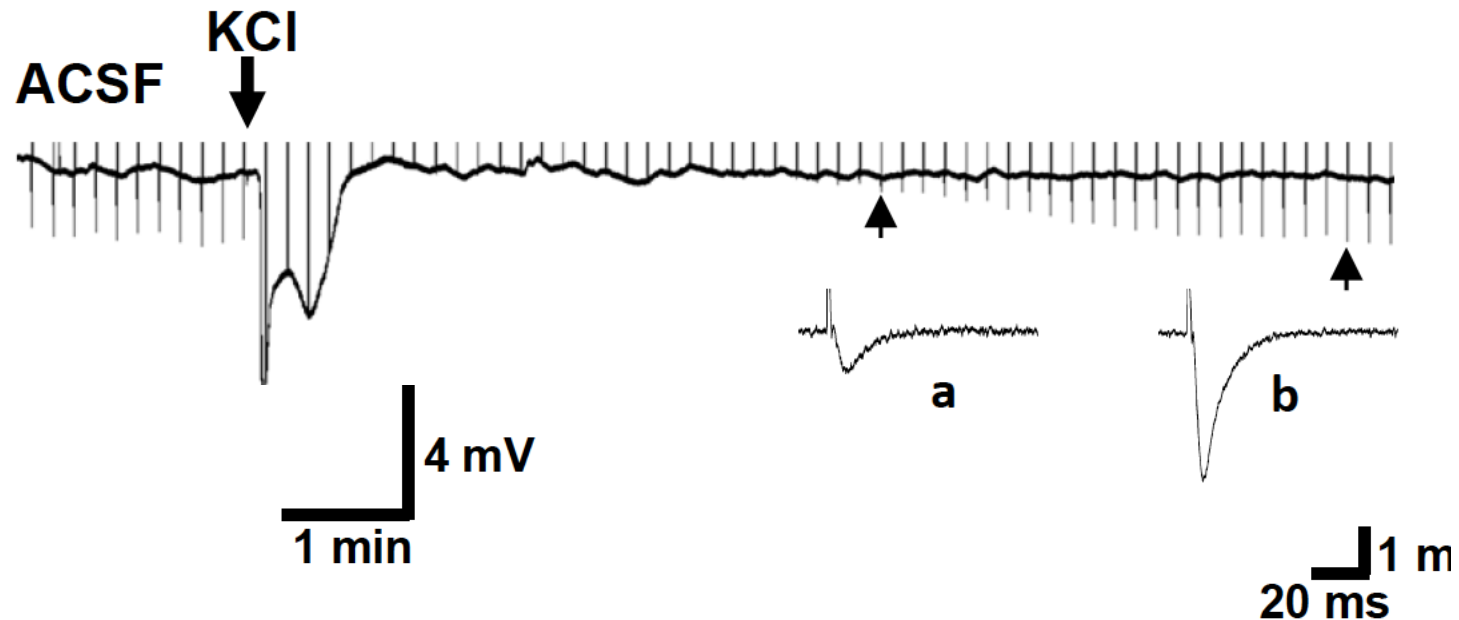
► Summary and Perspectives



Spreading Depolarization in a Brain Slice



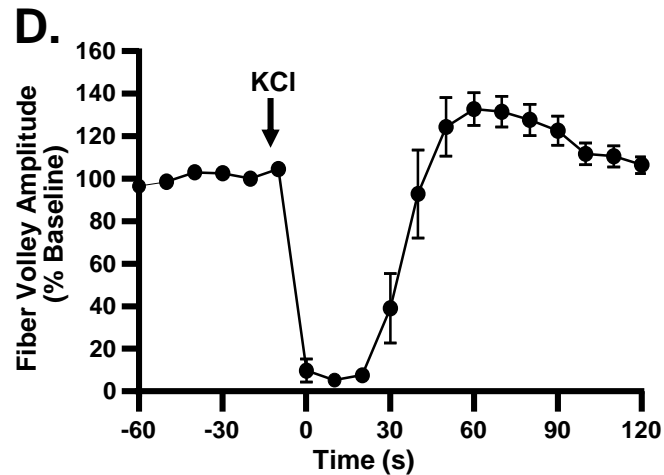
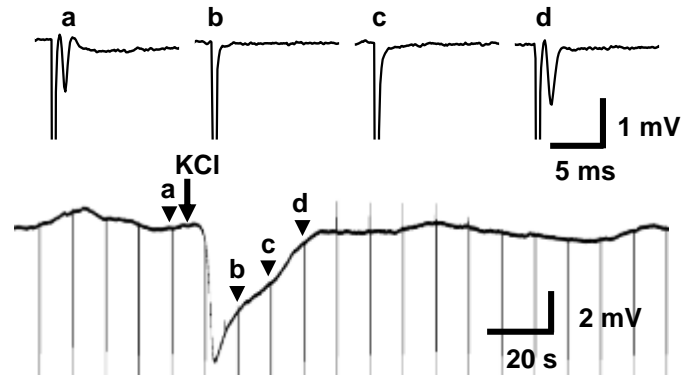
Long Suppression of Evoked Synaptic Potentials after SD



Potential Mechanisms for Prolonged Suppression of Synaptic Activity :

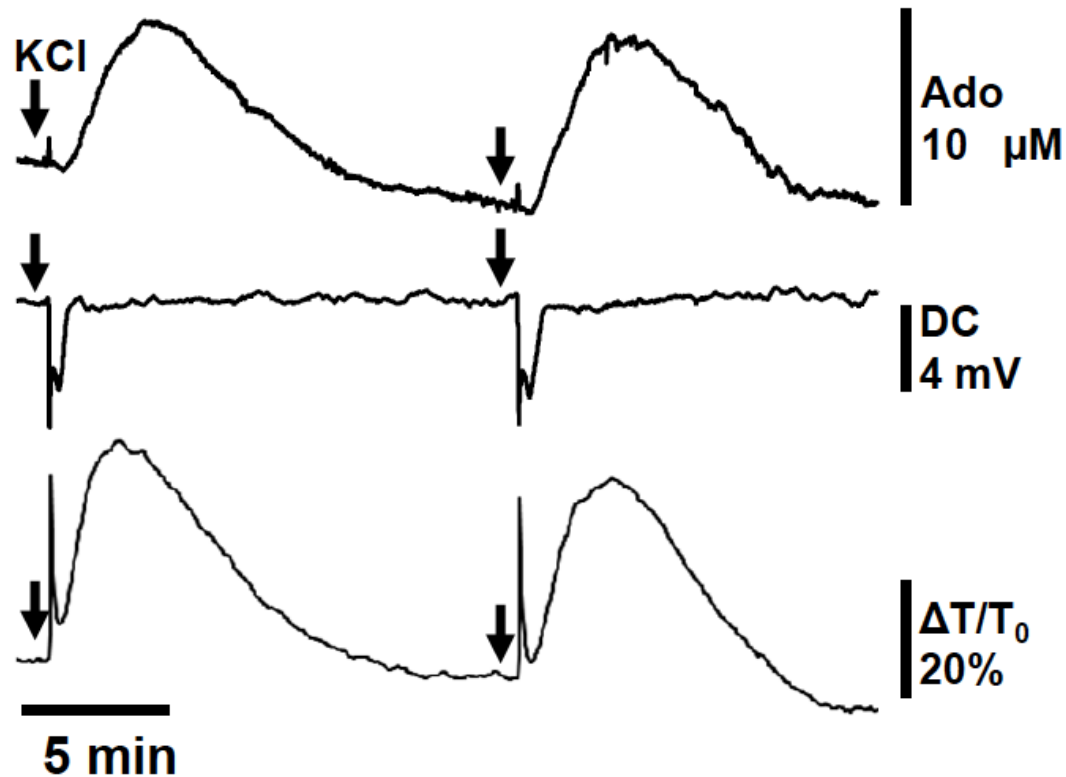
- ▶ *Depolarization Block?*
- ▶ *Dendritic Spine Retraction?*
- ▶ *Adenosine Accumulation?*

Brief Period of Action Potential Failure

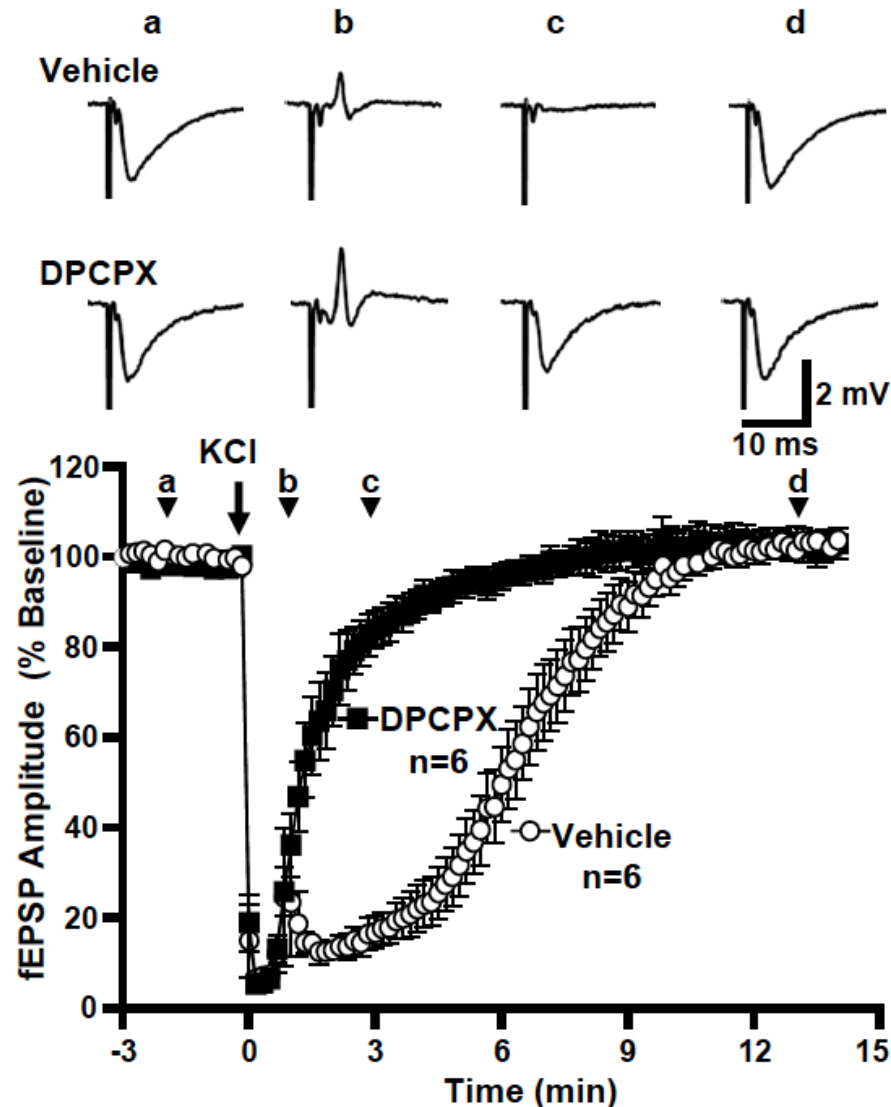


Extracellular Adenosine Accumulation

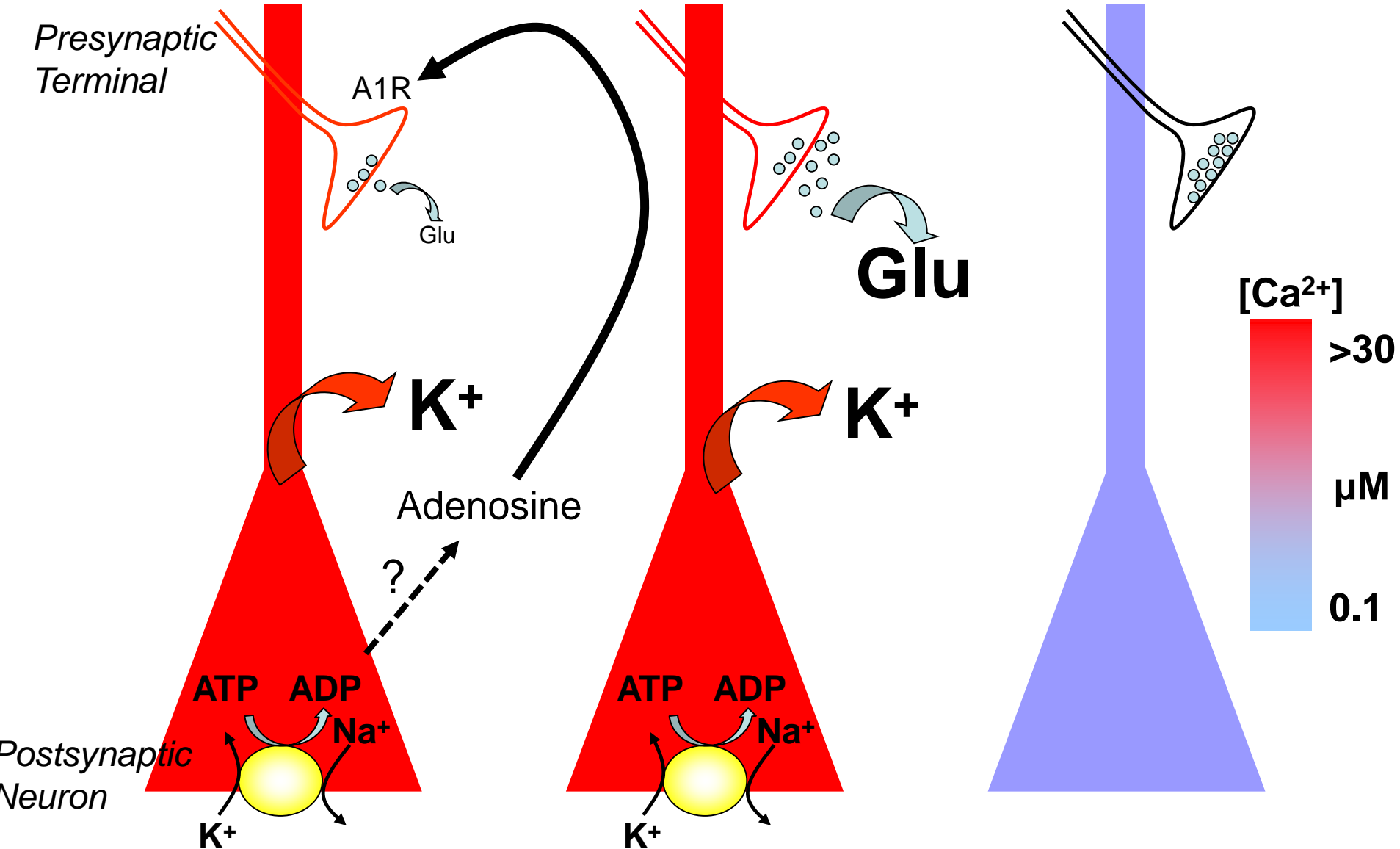
(Electrochemical detection – Sarissa probes)



A1 receptor activation mediates prolonged secondary suppression of epsps



SD PROPAGATION



ADENOSINE RECEPTOR ACTIVATION IS RESPONSIBLE FOR PROLONGED DEPRESSION OF SYNAPTIC TRANSMISSION AFTER SPREADING DEPOLARIZATION IN BRAIN SLICES

B. E. LINDQUIST AND C. W. SHUTTLEWORTH*

Department of Neurosciences, University of New Mexico School of Medicine, 1 University of New Mexico, Albuquerque, NM 87131, USA

Journal of Cerebral Blood Flow & Metabolism
Volume 34, Issue 11, November 2014, Pages 1779–1790
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<https://doi.org/10.1038/jcbfm.2014.146>



Original Article

Spreading Depolarization-Induced Adenosine Accumulation Reflects Metabolic Status *In Vitro* and *In Vivo*

Britta E Lindquist and C William Shuttleworth



Original Article

Evidence that adenosine contributes to Leao's spreading depression in vivo

Britta E Lindquist and C William Shuttleworth

JCBFM

Journal of Cerebral Blood Flow & Metabolism
2017, Vol. 37(5) 1656–1669
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► Introduction

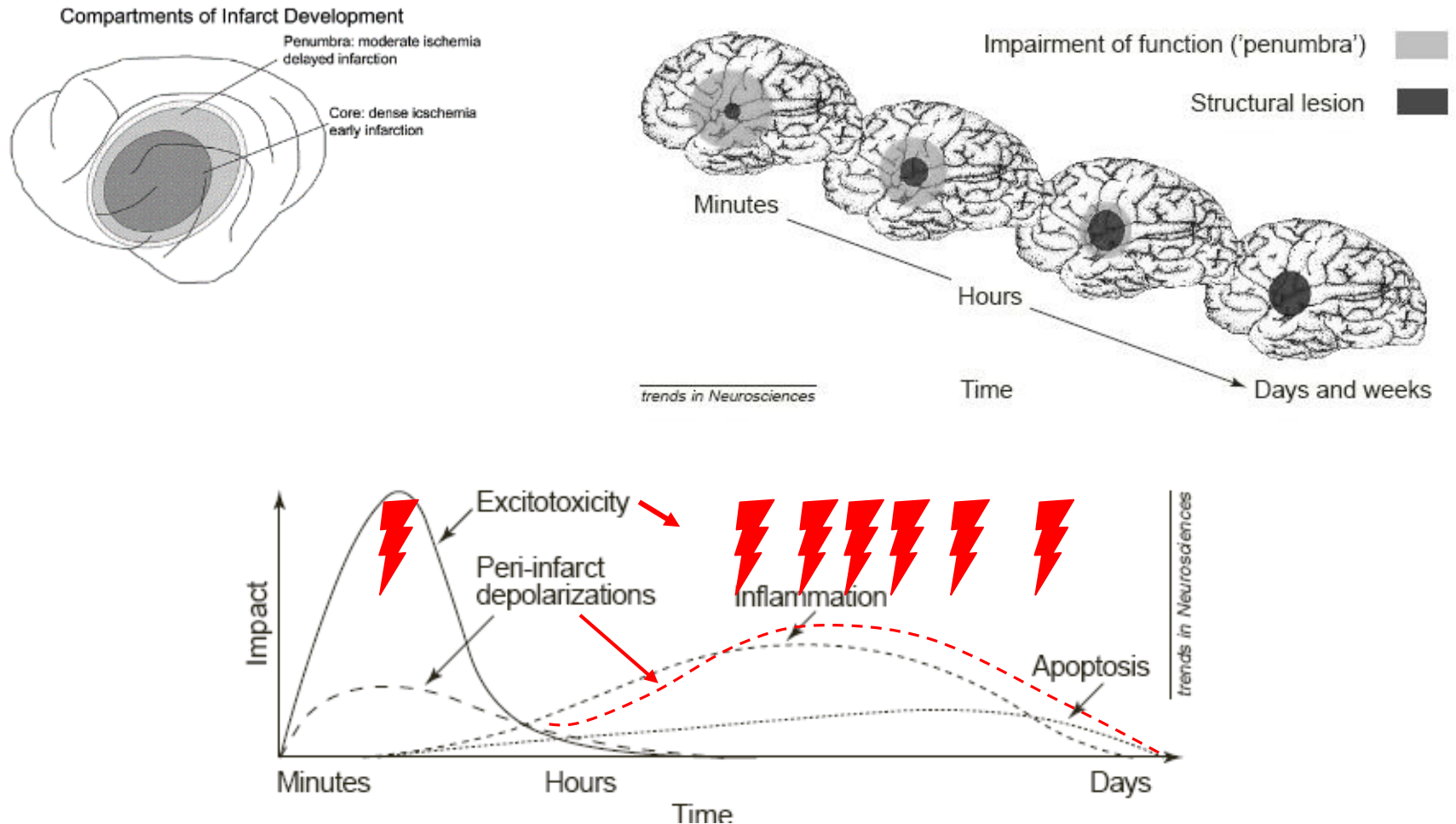
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- Neuronal Injury
- Preventing Initiation

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A second update to traditional model of stroke progression



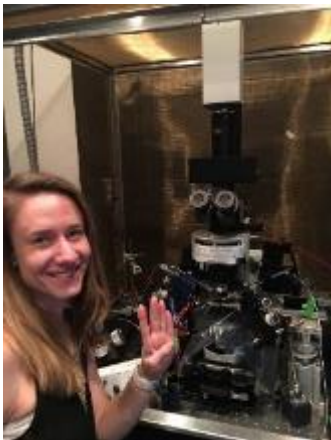
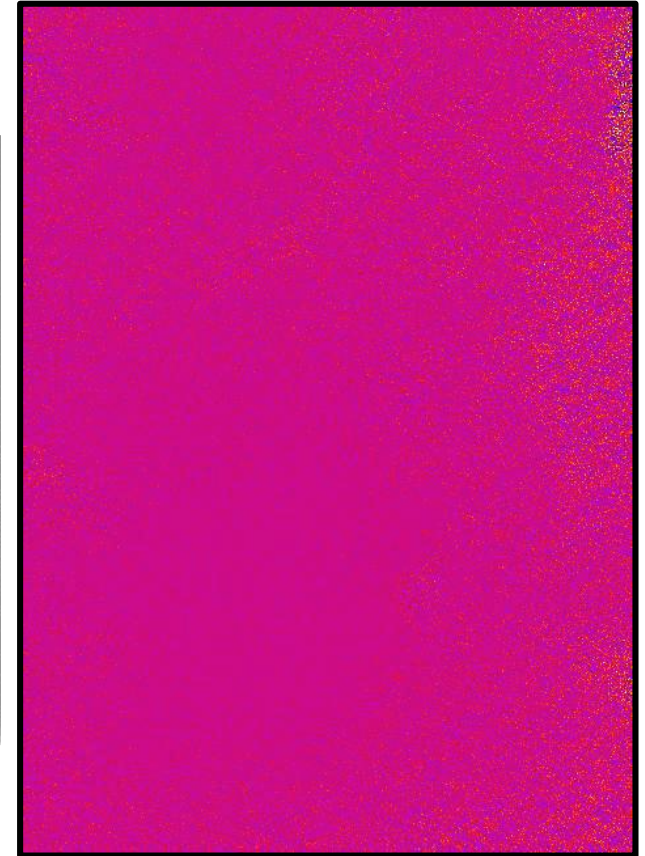
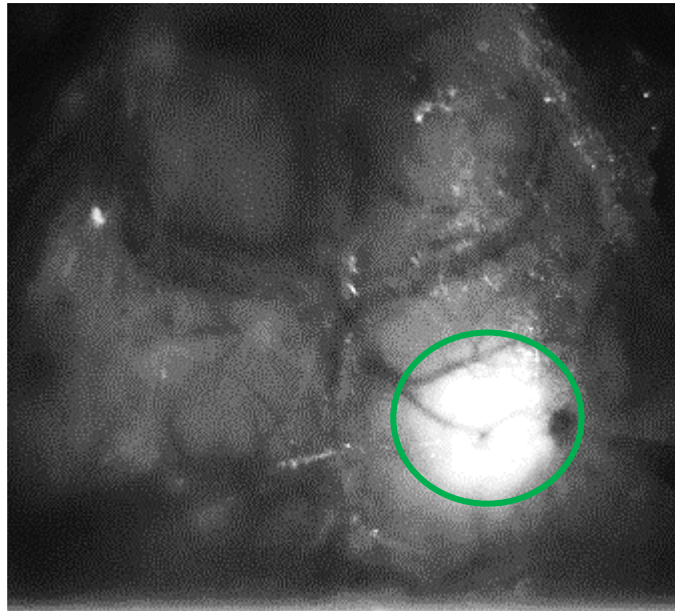
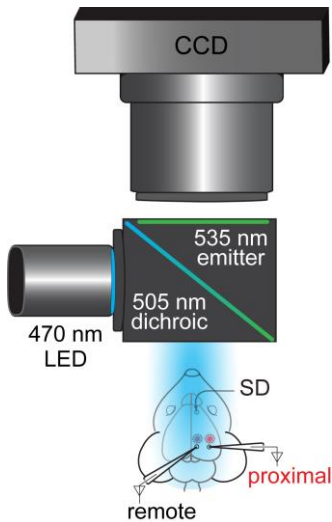
Modified from:

Dirnagl, U., Iadecola, C. & Moskowitz, M.A. *Trends in Neurosciences*. 22 (1999) 391-397.

A burst of excitotoxicity, time locked to SD

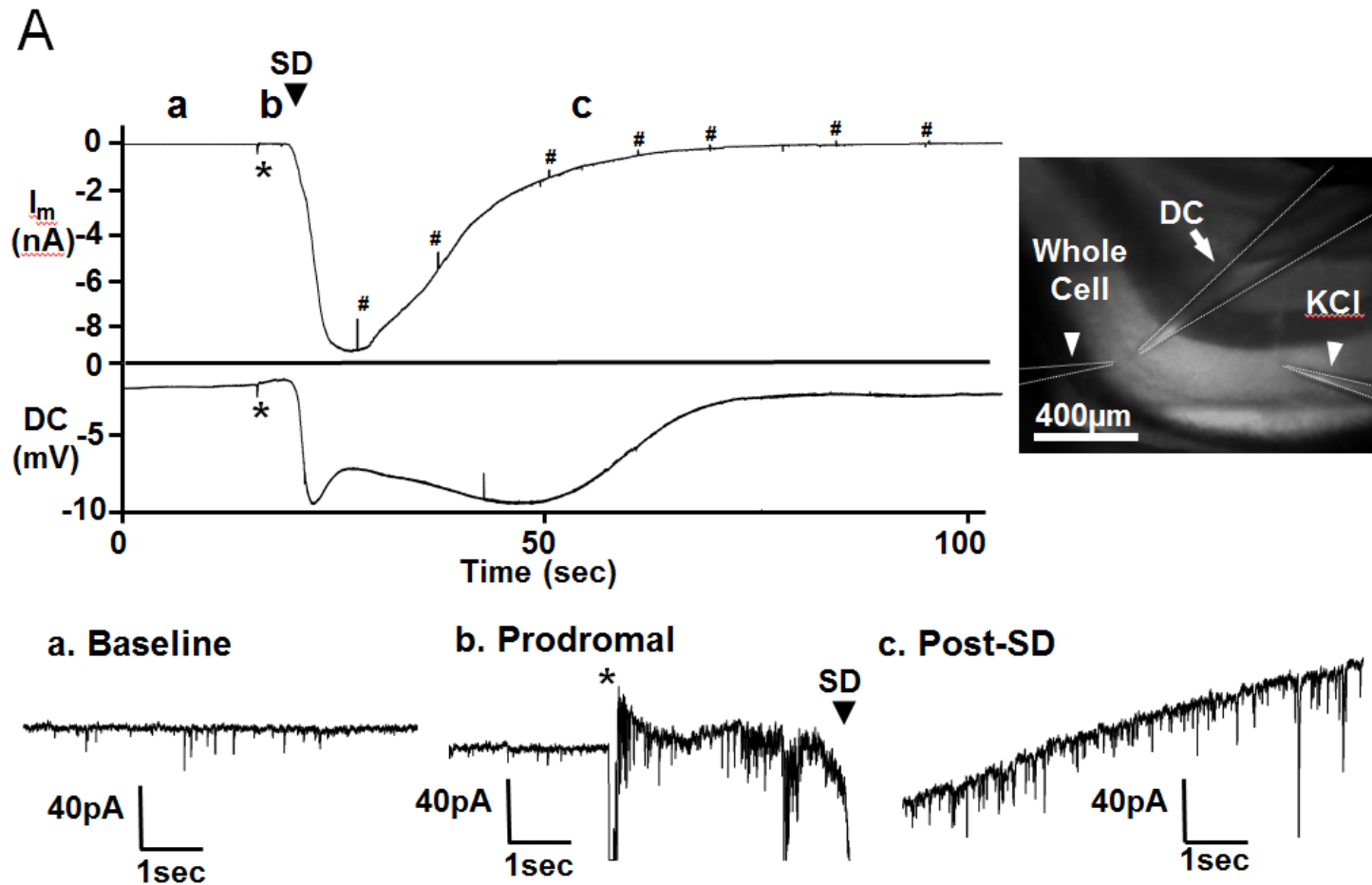
(basal glutamate low around stroke, until SD hits)

iGluSnFR cortical injection

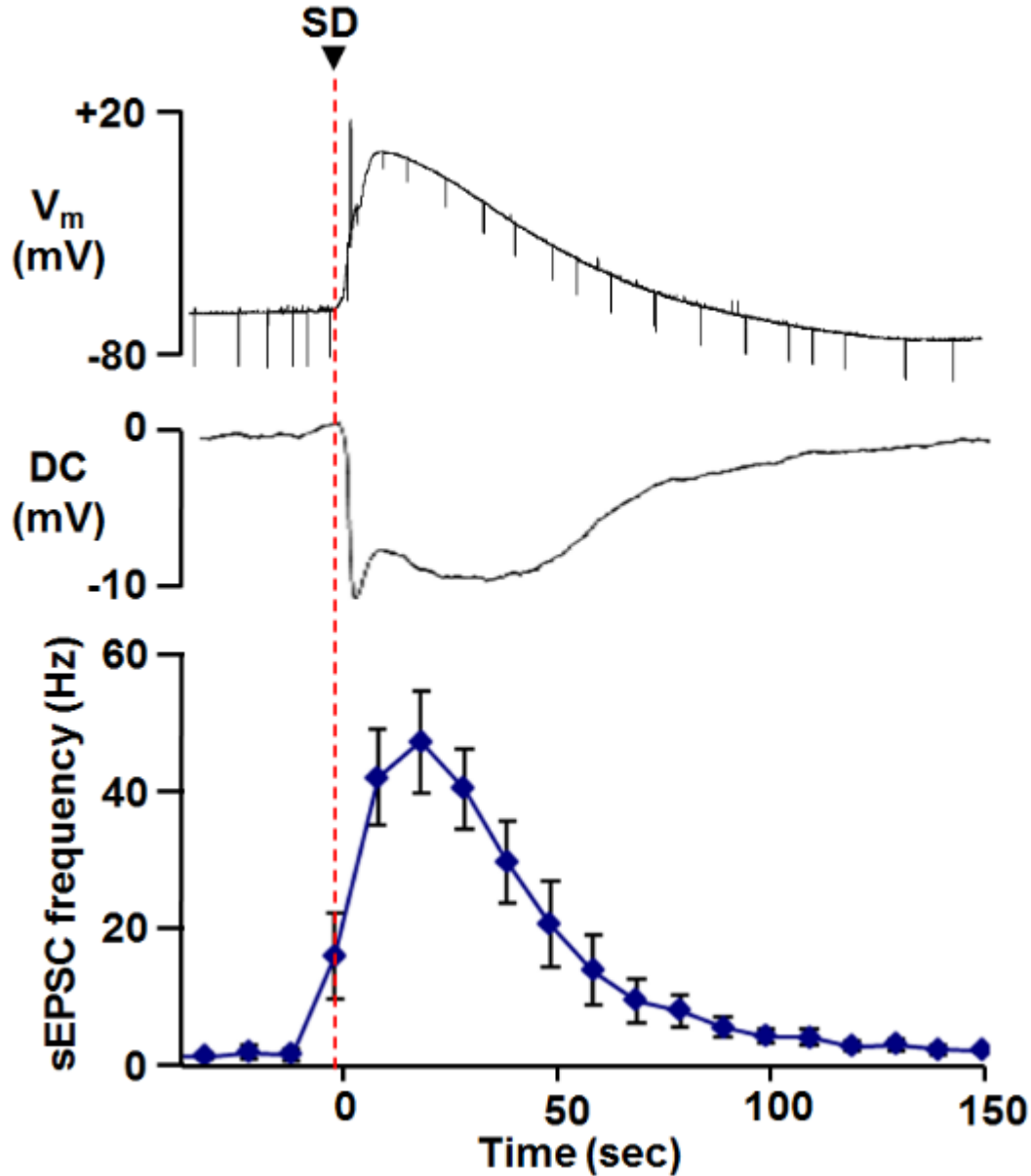


Kate Reinhart

Excitation in the late phase of SD (1)

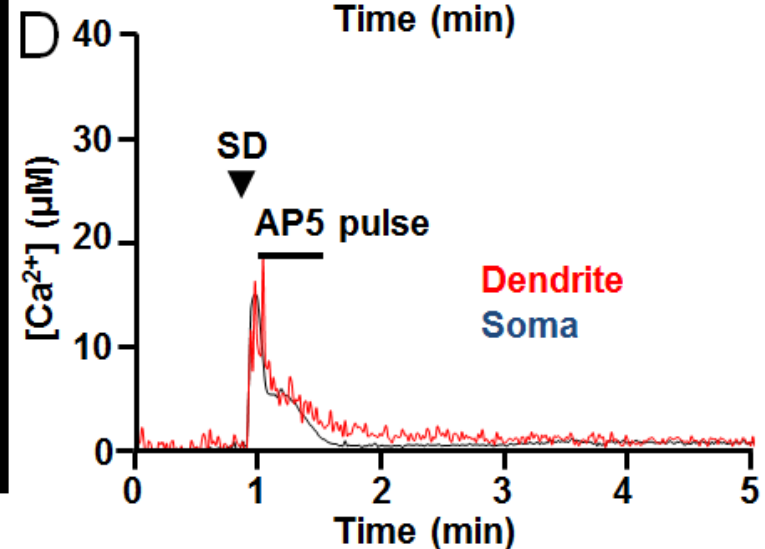
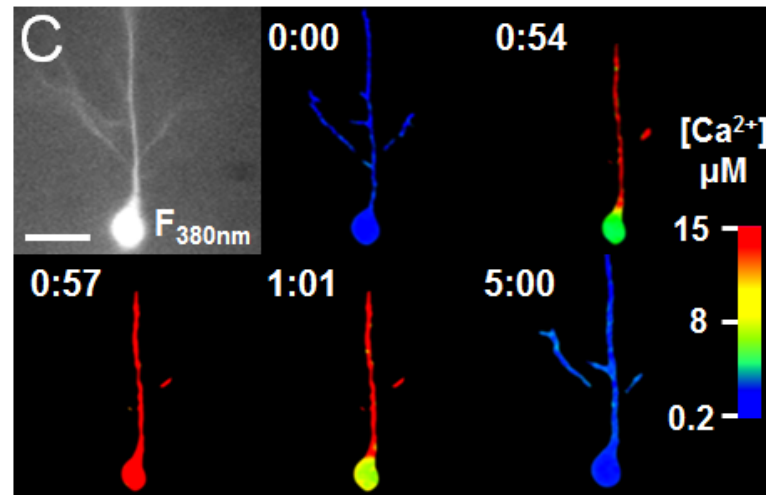
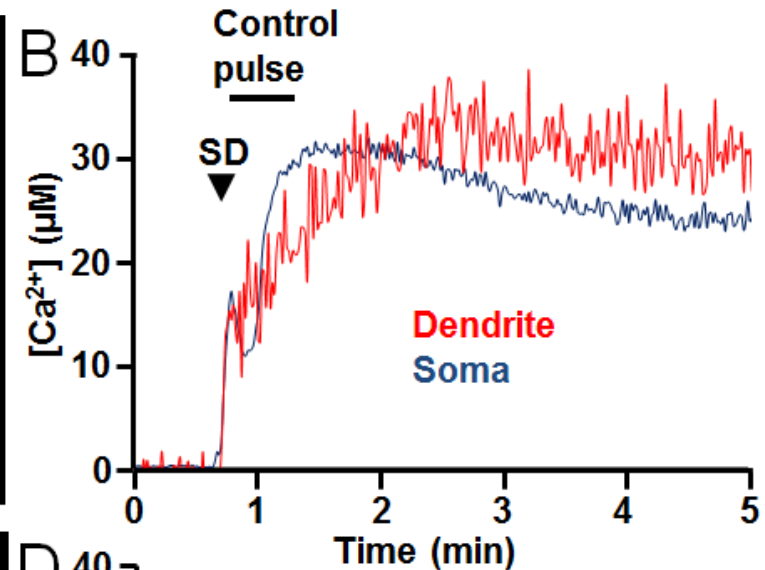
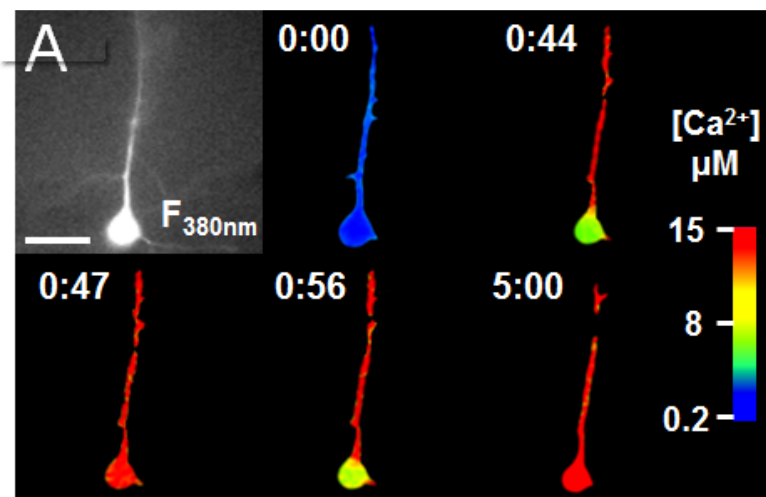


Excitation in the late phase of SD (2)

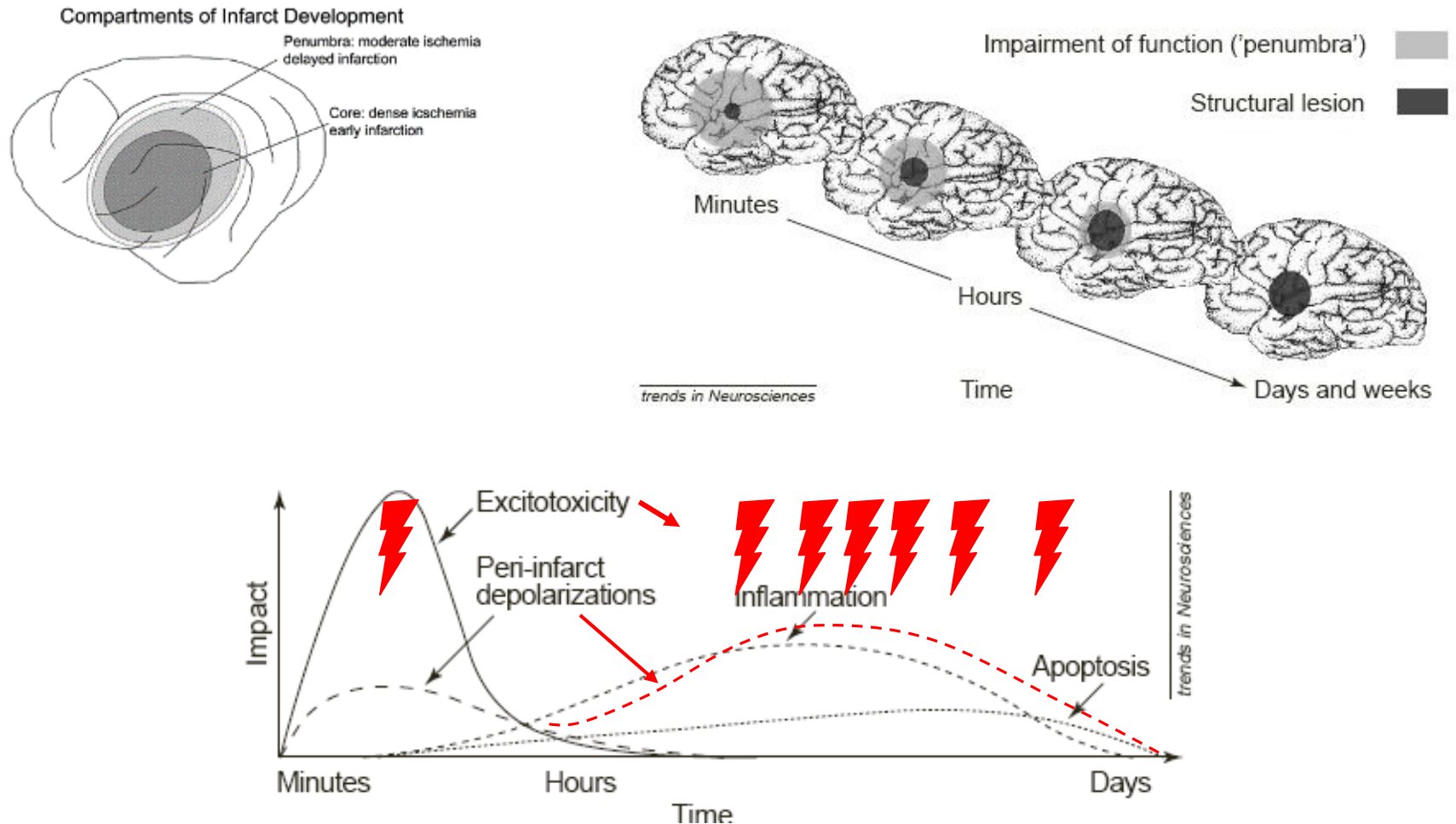


Isamu
Aiba

Sustained Dendritic Ca^{2+} Elevations in the late SD phase (Metabolically-compromised neurons)



A second update to traditional model of stroke progression



Modified from:

Dirnagl, U., Iadecola, C. & Moskowitz, M.A. *Trends in Neurosciences*. 22 (1999) 391-397.

Targeting Glutamate Overload with Ketamine

Case Report

Preliminary Evidence That Ketamine Inhibits Spreading Depolarizations in Acute Human Brain Injury

Oliver W. Sakowitz, MD; Karl L. Kiening, MD; Kara L. Krajewski, BA; Asita S. Sarrafzadeh, MD; Martin Fabricius, MD; Anthony J. Strong, MD; Andreas W. Unterberg, MD; Jens P. Dreier, MD
(*Stroke*. 2009;40:e519-e522.)

doi:10.1093/brain/aws152

Brain 2012; 135; 2390–2398 | 2390

BRAIN
A JOURNAL OF NEUROLOGY

Effect of analgesics and sedatives on the occurrence of spreading depolarizations accompanying acute brain injury

Daniel N. Hertle,¹ Jens P. Dreier,² Johannes Woitzik,³ Jed A. Hartings,⁴ Ross Bullock,⁵ David O. Okonkwo,⁶ Lori A. Shutter,⁴ Steven Vidgeon,⁷ Anthony J. Strong,⁷ Christina Kowoll,⁸ Christian Dohmen,⁸ Jennifer Diedler,⁹ Roland Veltkamp,⁹ Thomas Bruckner,¹⁰ Andreas W. Unterberg,¹ Oliver W. Sakowitz¹ and for the Cooperative Study of Brain Injury Depolarizations (COSBID)

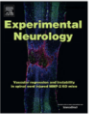
Experimental Neurology 305 (2018) 121–128



Contents lists available at ScienceDirect

Experimental Neurology

journal homepage: www.elsevier.com/locate/yexnr



Research paper

Ketamine reduces deleterious consequences of spreading depolarizations

Katelyn M. Reinhart, C. William Shuttleworth*

Department of Neurosciences, University of New Mexico School of Medicine, United States



Received: 15 March 2023 | Revised: 10 June 2023 | Accepted: 6 July 2023

DOI: 10.1111/jnc.15923

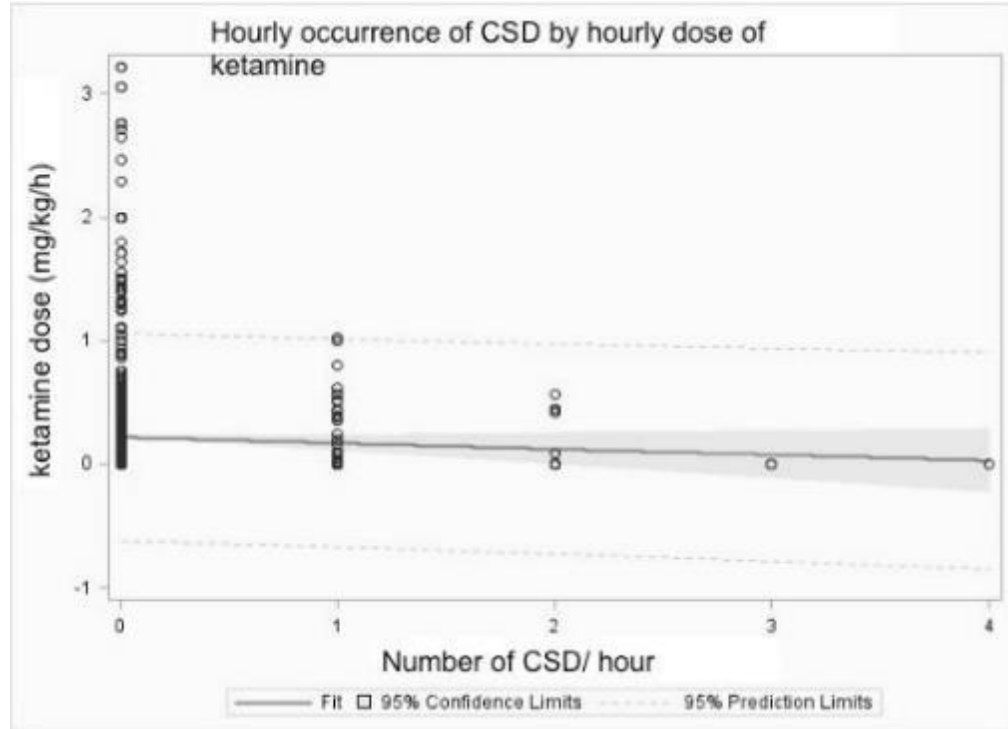
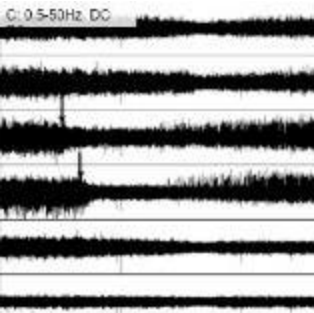
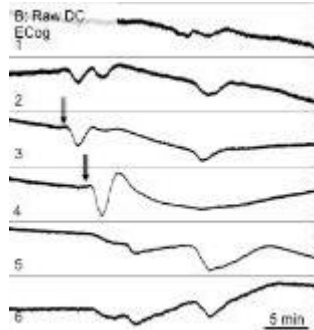
ORIGINAL ARTICLE

Journal of Neurochemistry **JNC** WILEY

Ketamine improves neuronal recovery following spreading depolarization in peri-infarct tissues

Katelyn M. Reinhart^{1,2} | Russell A. Morton¹ | K. C. Brennan² | Andrew P. Carlson³ | C. William Shuttleworth¹

Targeting Glutamate Overload with Ketamine



10 subjects, 1642 hours of Ecog.
Strong dose dependent effect
observed at doses >1.15mg/kg/h.
OR=13.838, 95% CI= 1.99-1000

JNS

CLINICAL ARTICLE

J Neurosurg 130:1513–1519, 2019

Spreading depolarization in acute brain injury inhibited by ketamine: a prospective, randomized, multiple crossover trial

Andrew P. Carlson, MD, MS-CR,¹ Mohammad Abbas, MD,¹ Robert L. Alunday, MD,¹
Fares Qeadan, PhD,² and C. William Shuttleworth, PhD³

Departments of ¹Neurosurgery, ²Internal Medicine, and ³Neurosciences, University of New Mexico School of Medicine, Albuquerque, New Mexico

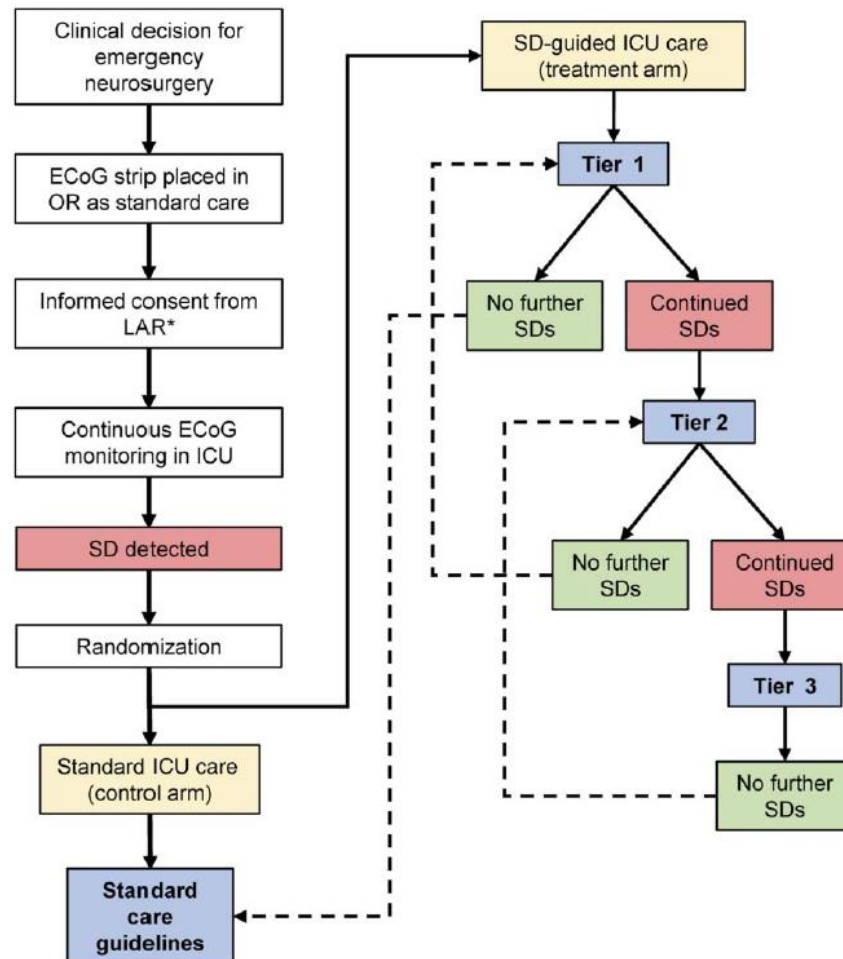
Targeting Glutamate Overload with Ketamine

CLINICAL PROTOCOLS

Improving Neurotrauma by Depolarization Inhibition With Combination Therapy: A Phase 2 Randomized Feasibility Trial

Jed A. Hartings, PhD*, Jens P. Dreier, MD*^{§||¶#}, Laura B. Ngwenya, MD, PhD*, Ramani Balu, MD, PhD**^{††}, Andrew P. Carlson, MD^{‡‡},
Brandon Foreman, MD*^{§§}

Neurosurgery 93:924–931, 2023



OUTLINE

► Introduction

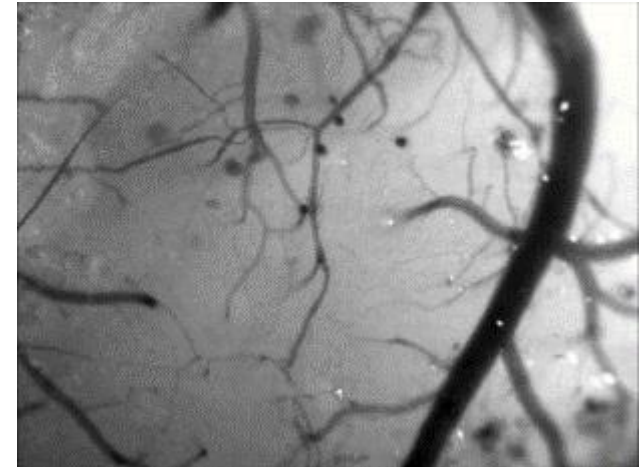
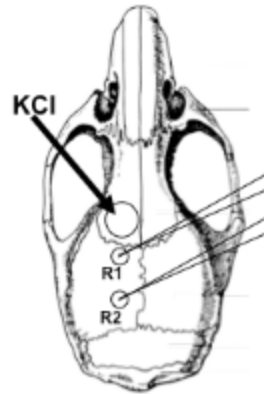
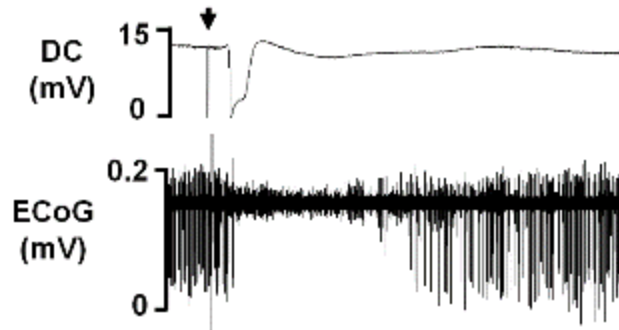
- Spreading Depolarizations (“*Brain Tsunamis*”)
- Migraine, Brain Injury

► Mechanisms and Translation to Practice

- Synaptic Depression
- Neuronal Injury
- Preventing Initiation

► Summary and Perspectives

Generation of SD by neurosurgical procedures (anesthetized mice)



Neurological Research

A Journal of Progress in Neurosurgery, Neurology and Neuro Sciences

ISSN: 0161-6412 (Print) 1743-1328 (Online) Journal homepage: <http://www.tandfonline.com/loi/ynr20>



Taylor & Francis
Taylor & Francis Group

Vascular, electrophysiological, and metabolic consequences of cortical spreading depression in a mouse model of simulated neurosurgical conditions

Andrew P Carlson, Russell E Carter & C William Shuttleworth



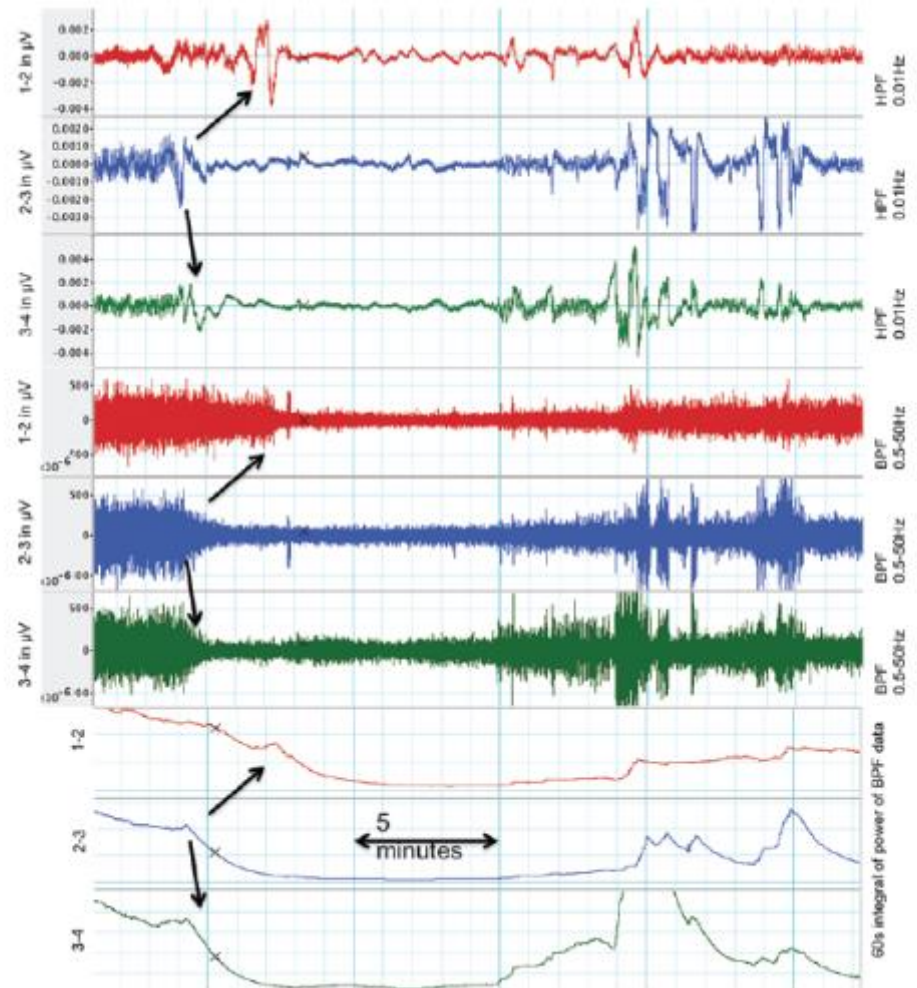
Andrew Carlson
Dept Neurosurgery

Operating Room Recordings

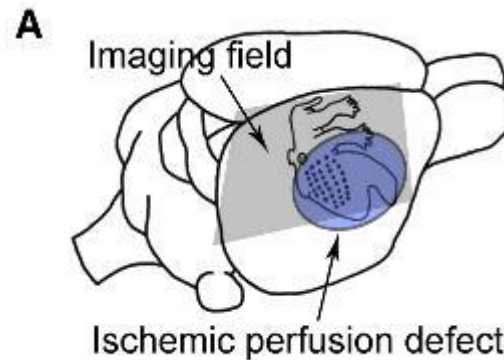


Cortical spreading depression occurs during elective neurosurgical procedures

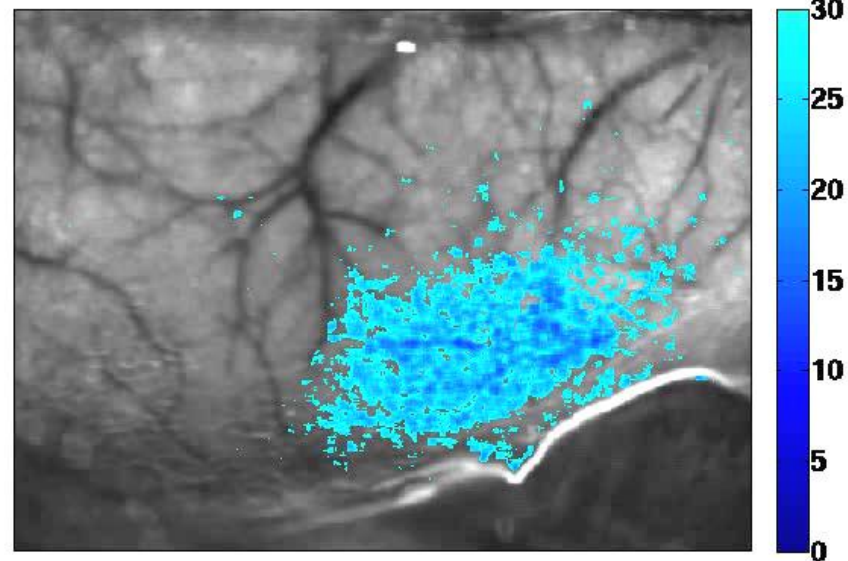
Andrew P. Carlson, MD, MSCR,¹ C. William Shuttleworth, PhD,² Brittany Mead, BS,¹ Brittany Burlaw, BS,¹ Mark Krasberg, PhD,¹ and Howard Yonas, MD¹



Generation of SD in focal stroke (anesthetized mice)

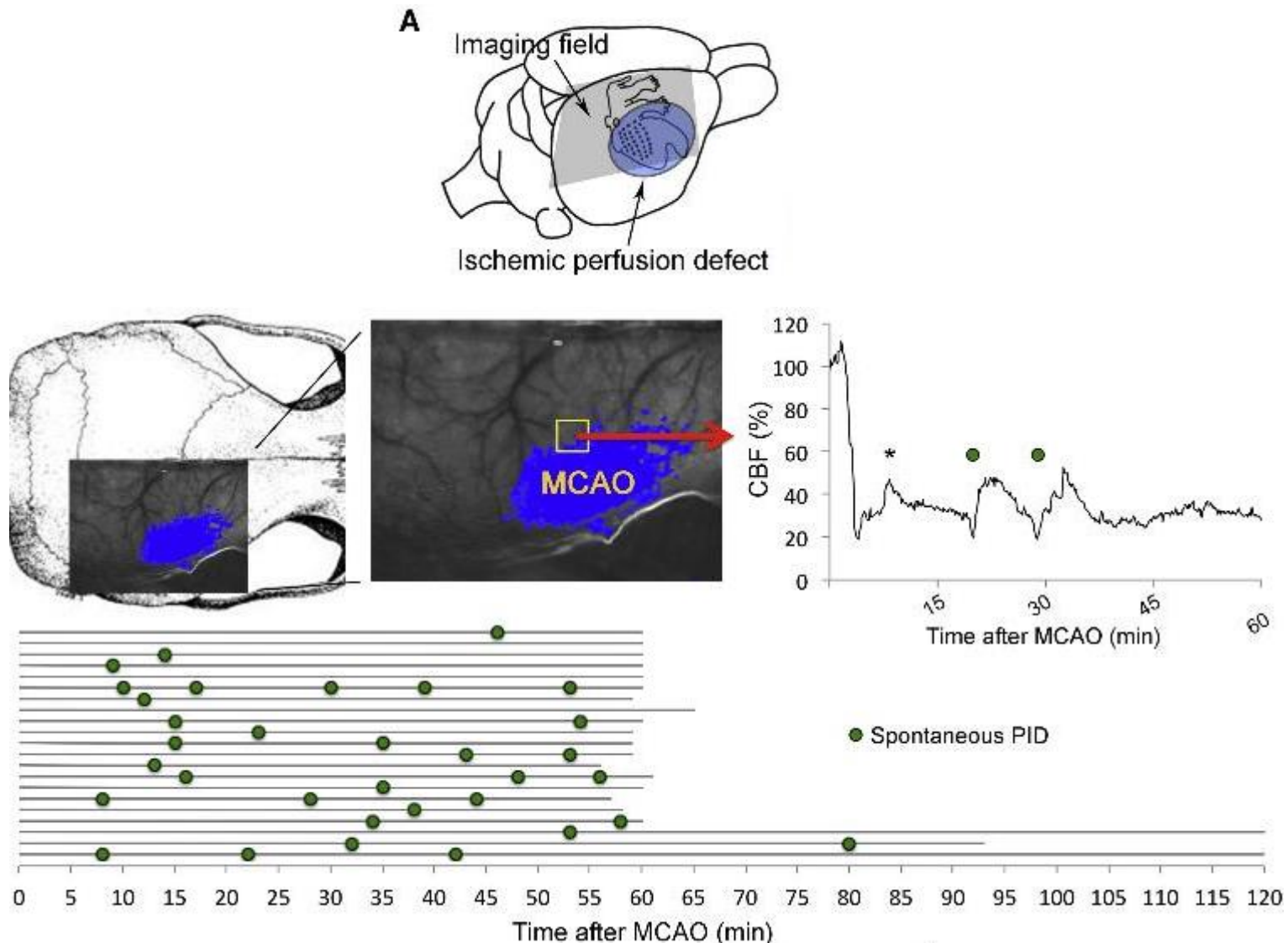


Time: 15.5 min

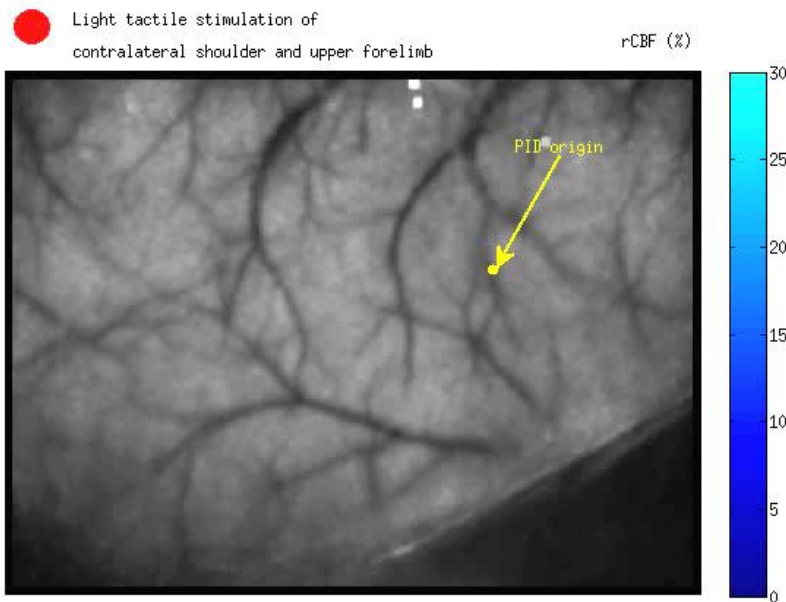
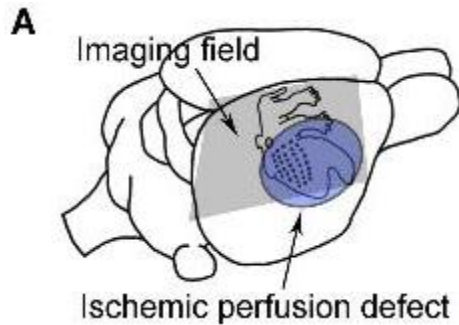


Cenk Ayata
Dept Neurology
Harvard, MGH

“Spontaneous” generation of SD in focal stroke (anesthetized mice)



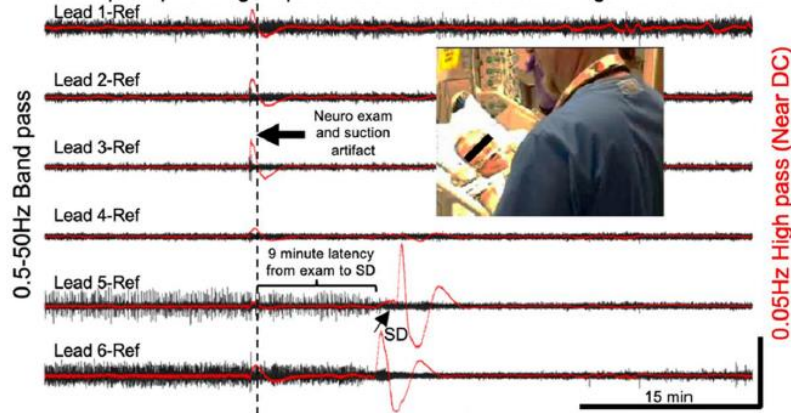
Sensory stimulation and generation of SD in focal stroke (anesthetized mice)



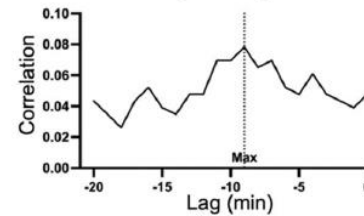
Cenk Ayata
Dept Neurology
Harvard, MGH

Potential Interventions

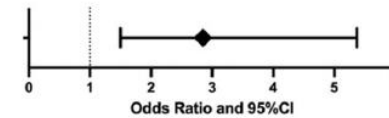
A: Example Spreading Depolarization on ECoG occurring after stimulation



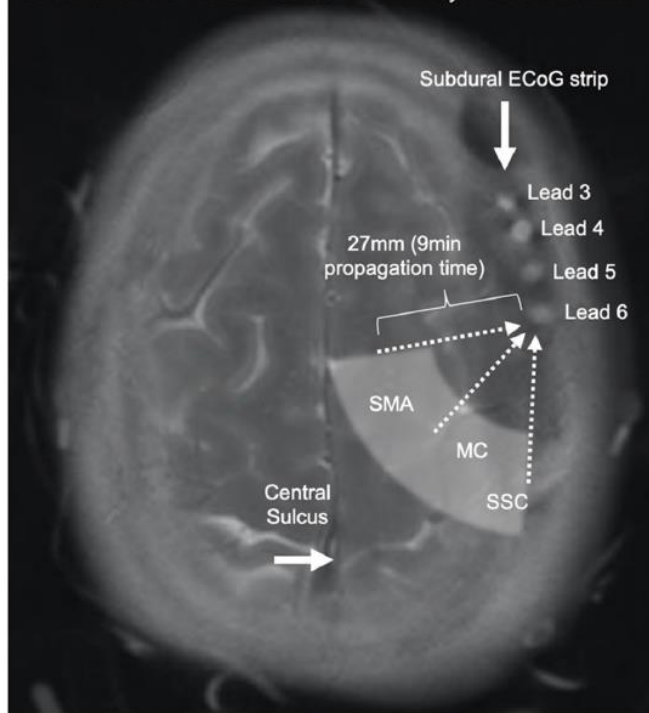
B: Highest correlation of stimulation and SD occurs at 9 min negative lag



C: Odds of SD 9 min after stimulation



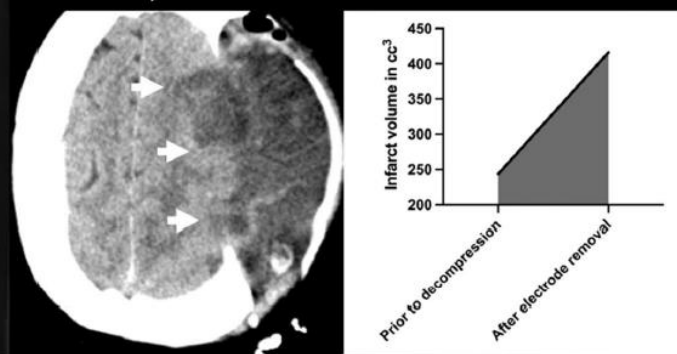
D: Plausible SD initiation zone: left sensory/motor/SMA cortex



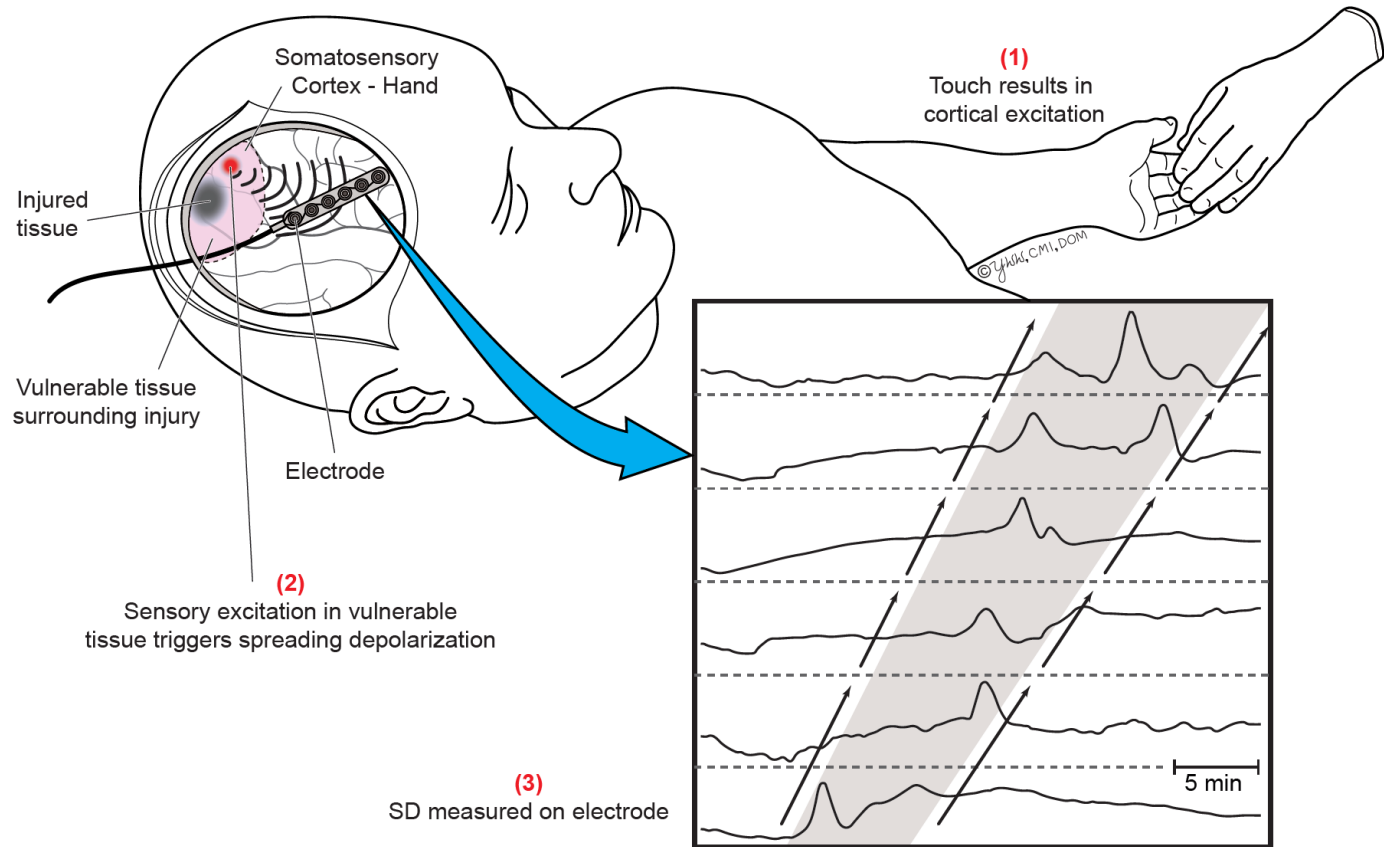
E: SD initiation zone at infarct border in infarct penumbra



F: Infarct expansion and edema at 1 week



Potential Interventions



Translational Stroke Research
<https://doi.org/10.1007/s12975-022-01014-7>

ORIGINAL ARTICLE



Is the Human Touch Always Therapeutic? Patient Stimulation and Spreading Depolarization after Acute Neurological Injuries

Andrew P. Carlson¹ · Herbert T. Davis² · Thomas Jones³ · K. C. Brennan⁴ · Michel Torbey⁵ · Rosstin Ahmadian⁶ · Fares Qeadan⁷ · C. William Shuttleworth⁸

Received: 18 January 2022 / Revised: 21 February 2022 / Accepted: 23 March 2022

OUTLINE

► Introduction

- Spreading Depolarizations (*“Brain Tsunamis”*)
- Migraine, Brain Injury

► Mechanisms & Translation to Practice

- Synaptic Depression
- Neuronal Injury
- Preventing Initiation

► Perspectives & Conclusions

Perspectives (1)

- SD field is likely to grow rapidly

Non-invasive detection in patients will increase numbers being examined in an expanded number of disorders

- Translational potential appears high

As a fundamental brain mechanism, features are very well conserved across broad range of species

Targeting SD as an “upstream” has a number of advantages over targeting subsequent intracellular signaling cascades

SD studies underway in diverse clinical conditions

Migraine

Ischemic Stroke

Trauma

Subarachnoid Hemorrhage

Brain Death

Seizures

Sudden Unexpected Death in Epilepsy

Subdural Hematoma

Concussion

Electroconvulsive Therapy

Glioblastoma

** Ongoing UNM & UVA studies*

Perspectives (2)

Non-invasive detection methods may include:

- Scalp EEG
- Functional Near Infrared Spectroscopy (fNIRS)
- Functional Ultrasound (fUS)
- *Others?*



Correlates of spreading depolarization in human scalp electroencephalography

Christoph Drenckhahn,^{1,2} Maren K. L. Winkler,¹ Sebastian Major,^{1,2,3} Michael Scheel,⁴ Eun-Jeung Kang,^{1,3} Alexandra Pinczolits,^{1,5} Cristian Grozea,⁶ Jed A. Hartings,⁷ Johannes Woitzik,^{1,5} and Jens P. Dreier^{1,2,3} for the COSBID study group

5780

IEEE JOURNAL OF BIOMEDICAL AND HEALTH INFORMATICS, VOL. 28, NO. 10, OCTOBER 2024



Real-Time Non-Invasive Imaging and Detection of Spreading Depolarizations through EEG: An Ultra-Light Explainable Deep Learning Approach

Yinzhe Wu[✉], Student Member, IEEE, Sharon Jewell, Xiaodan Xing[✉], Yang Nan[✉], Anthony J. Strong[✉], Guang Yang[✉], Senior Member, IEEE, and Martyn G. Boutelle[✉]

communications medicine

ARTICLE

<https://doi.org/10.1038/s43856-023-00344-3>

OPEN

Check for updates

Noninvasive and reliable automated detection of spreading depolarization in severe traumatic brain injury using scalp EEG

Alireza Chamanzar^{✉ 1,2}, Jonathan Elmer³, Lori Shutter^{✉ 4}, Jed Hartings⁵ & Pulkit Grover^{✉ 1,2}

COMMUNICATIONS MEDICINE | (2023)3:113 | <https://doi.org/10.1038/s43856-023-00344-3> | www.nature.com/commsmed

Perspectives (3)

- Development of automated detection will be important for SD-targeted therapies in the ICU
- Novel bioassays could also be helpful for bedside monitoring

Review Article

Recording, analysis, and interpretation of spreading depolarizations in neurointensive care: Review and recommendations of the COSBID research group

Neurocrit Care (2017) 35:5160–5175
<https://doi.org/10.1007/s12028-021-01228-x>


JCBFM

Journal of Cerebral Blood Flow & Metabolism
2017, Vol. 37(5) 1595–1625
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DOI: 10.1177/0271678X16654496
journals.sagepub.com/home/jcbfm
SAGE

**NEUROCRITICAL
CARE SOCIETY**

ORIGINAL WORK

Development and Evaluation of a Method for Automated Detection of Spreading Depolarizations in the Injured Human Brain

Sharon Jewell^{1,2}, Stephen Hobson³, Grant Brewer³, Michelle Rogers¹, Jed A. Hartings⁴, Brandon Foreman⁵, José-Pedro Lavrador⁶, Michael Sole³, Clemens Pahi⁷, Martyn G. Boutelle¹ and Anthony J. Strong^{2*} 



Research article

Received: 10 December 2013, Revised: 16 December 2014, Accepted: 23 February 2015, Published online in Wiley Online Library: 27 March 2015

(wileyonlinelibrary.com) DOI: 10.1002/nbm.3288

**NMR
IN BIOMEDICINE**

Measurement of distinctive features of cortical spreading depolarizations with different MRI contrasts

S. Umesh Rudrapatna^{a*}, Arend M. Hamming^{a,b}, Marieke J. H. Wermer^b, Annette van der Toorn^a and Rick M. Dijkhuizen^a

Conclusions

- SDs are real in humans
 - Contribute to migraine, acute brain injury*
 - Likely a range of other disorders*
- SD causes secondary injury progression and there is a large window of opportunity to target SD in the neuroICU
 - First trials underway targeting SDs with ketamine*
- There are multiple strategies that could mitigate injury caused by SD
 - Pharmacologic, physiological interventions, minimal stimulation, metabolic supplementation, astrocyte activation*
- The role for SDs in other neurological/psychiatric conditions is an area of emerging interest
 - Will benefit greatly from improved non-invasive detection*

Acknowledgements



Shuttleworth Lab:

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Jordan Weisend
Michael Bennett
Alissa Cabada-Gomez

Past Lab Members:

Kate Reinhart, Ph.D.
Britta Lindquist, MD, Ph.D.
Isamu Aiba, Ph.D.
Russell Carter, Ph.D.
Jessica Seidel, Ph.D.
Rob Dietz MD, Ph.D.
Thom VanderJagt, Ph.D.
Zuzana Sumbalova Ph.D.
Kevin Rowland, Ph.D.
Meg Hoskison, Ph.D.
Angela Brennan, Ph.D.



New Mexico Spreading
Depolarization Consortium

SD colleagues:

Andrew Carlson, M.D.

UNM Neurosurgery; now UVA

Russell Morton, Ph.D.

UNM Neurosciences

Chris Abbott, M.D.,

Davin Quinn, M.D.

UNM Psychiatry

Michel Torbey, M.D.

UNM Neurology

KC Brennan, M.D.

University of Utah

Jed Hartings, Ph.D.

University of Cincinnati

COSBID consortium

Support:

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NIGMS: P20 GM109089

NCATS: UL1TR000041

