

5th Congress of the European Academy of Neurology

Oslo, Norway, June 29 - July 2, 2019

Teaching Course 16

**Traumatic Brain Injury, stroke and subarachnoid
haemorrhage - How to Make an Impact in neurocritical care
management and research (Level 2)**

**Spreading depolarizations and spreading ischemia
in TBI, stroke and SAH**

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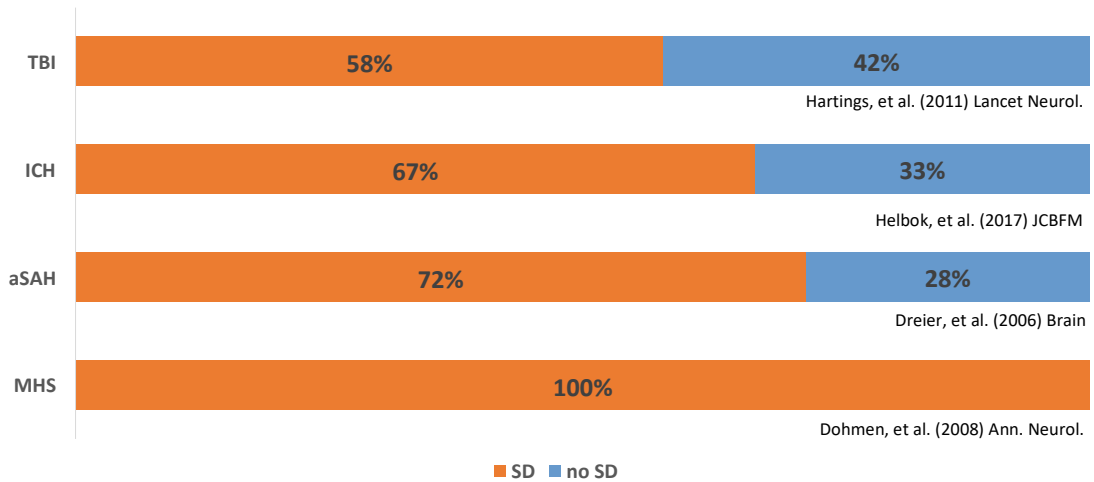
Spreading depolarizations and spreading ischemia in TBI, stroke and SAH

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Center for Stroke Research Berlin
Charité, Berlin

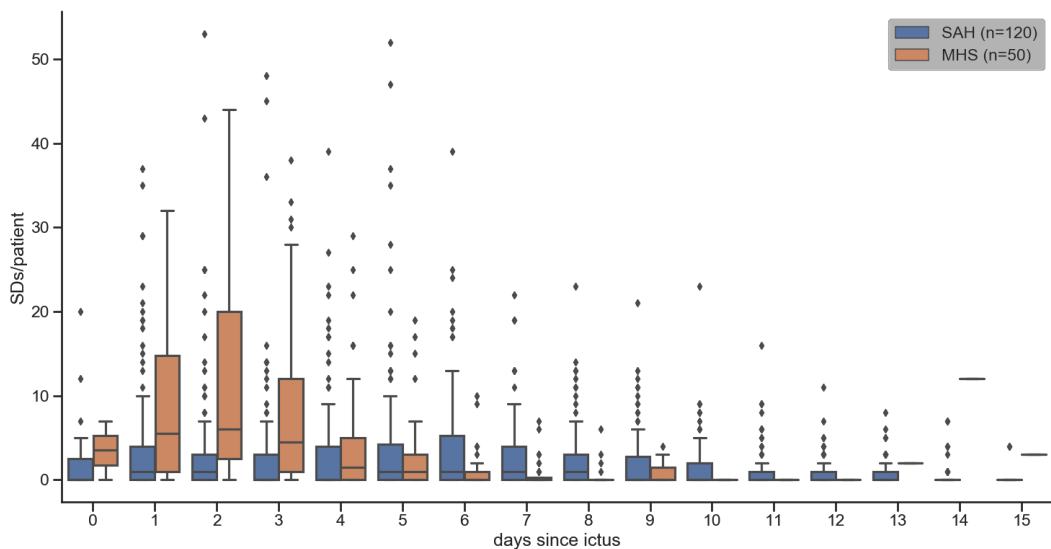
Conflict of interest

- No disclosures

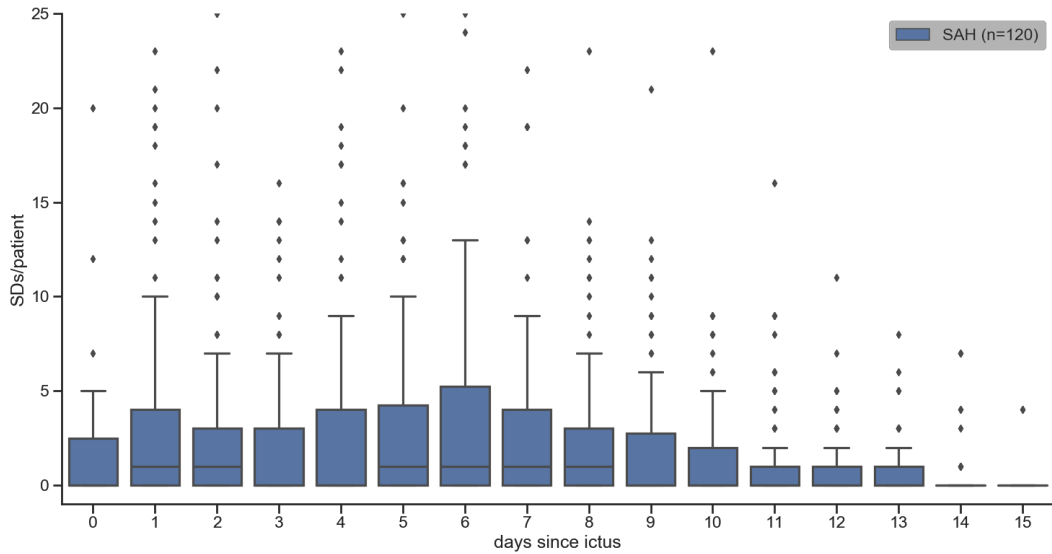
Spreading depolarizations in human diseases



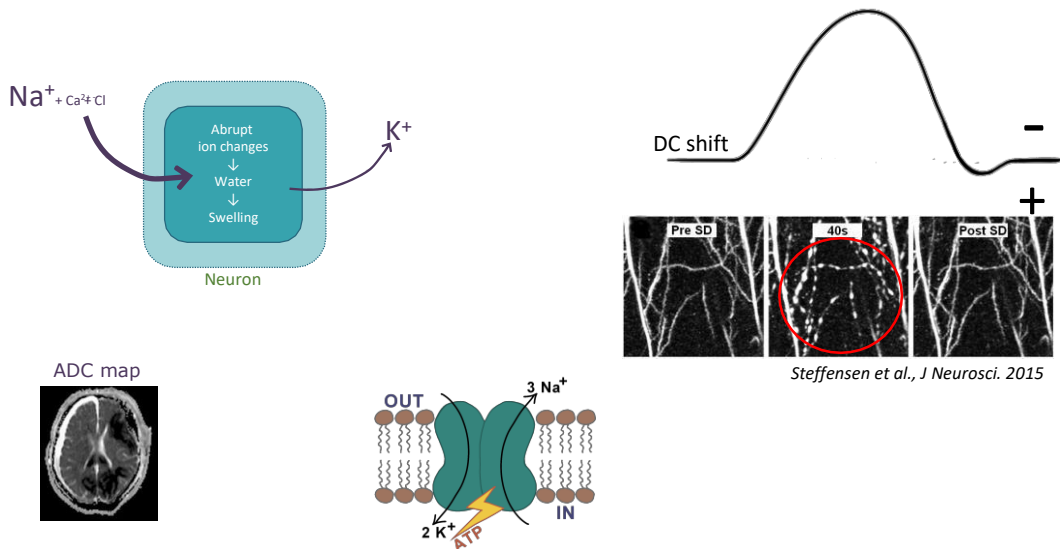
Spreading depolarizations in human diseases



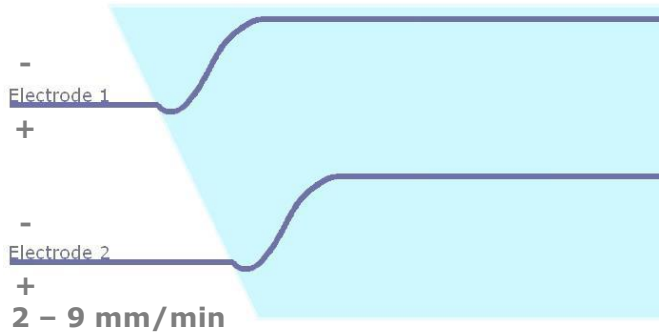
Spreading depolarizations in human diseases



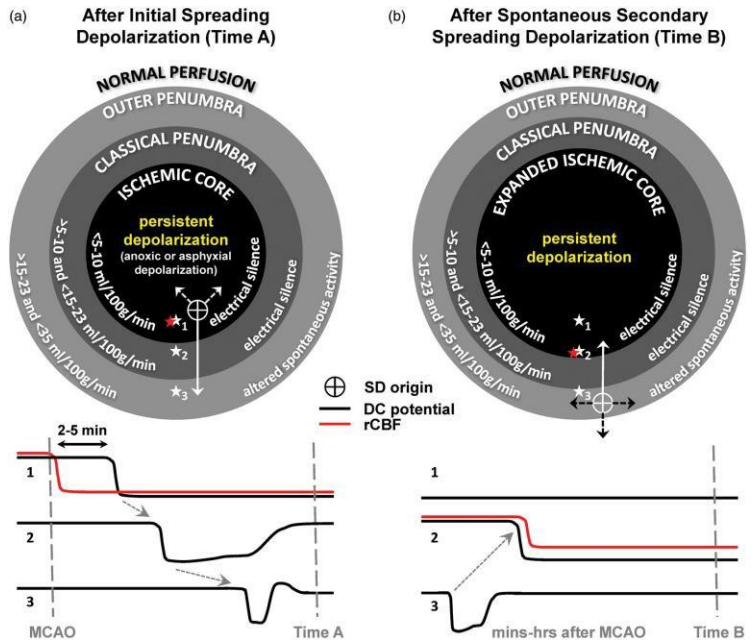
SD is electrophysiological correlate of cytotoxic edema



The spreading depolarization continuum



The spreading depolarization continuum



Hartings, et al. (2017) JCBFM

Ion concentrations during SD

	Physiological	Spreading Depolarization
[K ⁺] _i (mM)	134	106
[K ⁺] _o (mM)	2.3–3.1	35–60
[Na ⁺] _i (mM)	10	35
[Na ⁺] _o (mM)	146–154	57–59
[Ca ²⁺] _i (mM)	0.06 * 10 ⁻³	25 * 10 ⁻³
[Ca ²⁺] _o (mM)	1.2–1.3	0.08
[Cl ⁻] _o (mM)	145–148	95
Extracellular space (%)	18–22	5–9
Membrane potential (mV)	-70	-10

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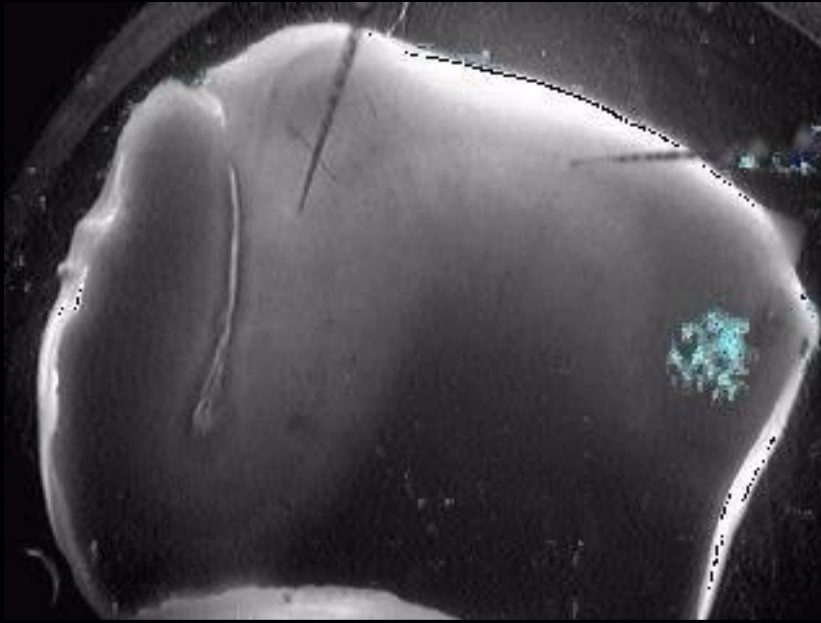
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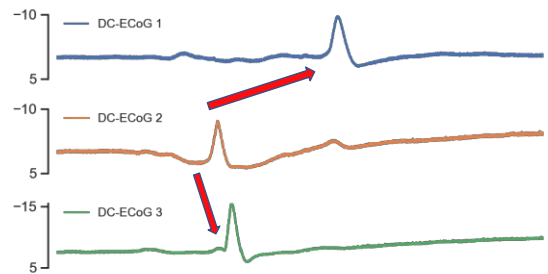
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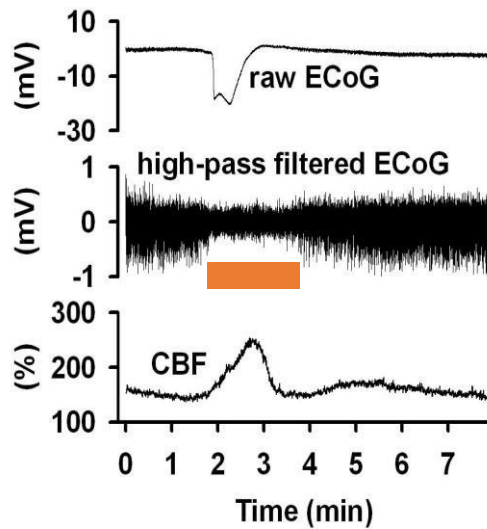
Spreading depolarization in human brain tissue



Spreading depolarization and spreading depression



Spreading depolarization and spreading hyperemia in rat cortex

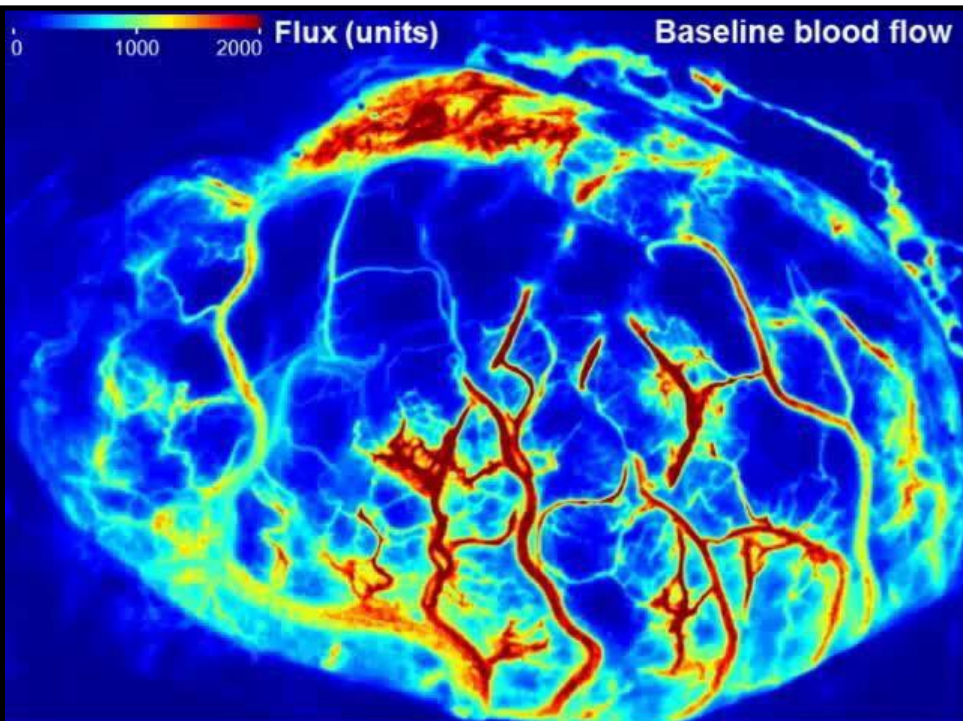


CHARITÉ

CSB

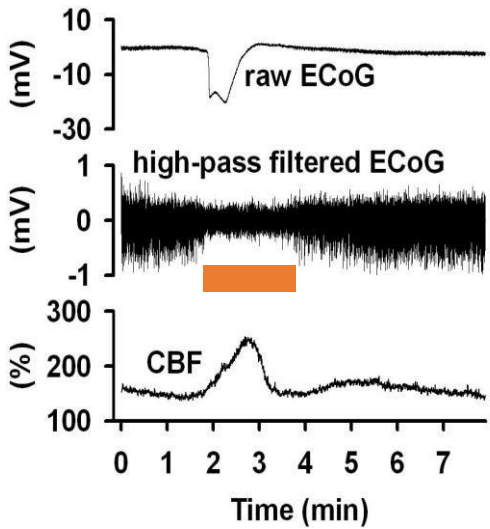
COSBID
Co-Operative Studies on Brain Injury Consequences

Protect Brain – Prevent Complications – Restore Function

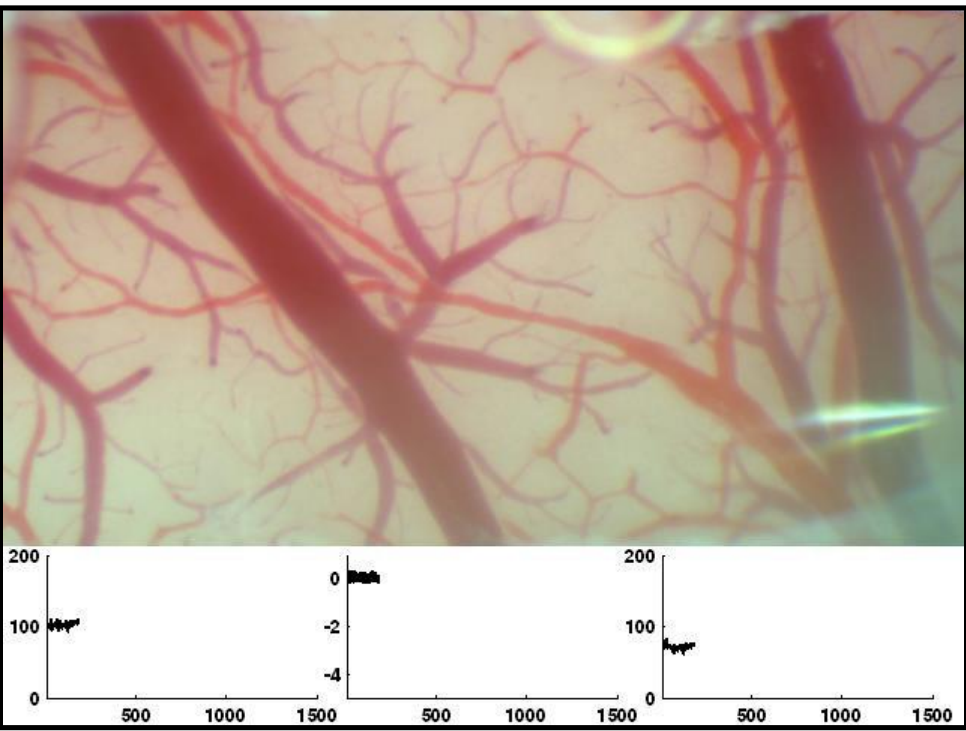


Woitzik, et al.
(2013) Neurology

Blood flow responses to spreading depolarization



Protect Brain – Prevent Complications – Restore Function



Cortical spreading ischaemia is a novel process involved in ischaemic damage in patients with aneurysmal subarachnoid haemorrhage

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The term cortical spreading depolarization (CSD) describes a wave of mass neuronal deactivations and water. Clusters of prolonged CSDs were measured time-locked to progressive CSD-induced tone alterations in resistance vessels, causing either transient hyperperfusion (in healthy tissue) or hypoperfusion (inverse haemodynamic response = cost at risk for progressive damage, which has so far only been shown experimentally). Here, study in 19 patients with aneurysmal subarachnoid haemorrhage, using novel subdural neous laser-Doppler flowmetry (LDF) and direct current-electrocorticography, combined pressure of oxygen (pO₂). Regional cerebral blood flow and electrocorticography were isolated CSDs occurred in 12 patients and were associated with either physiological, although the physiological haemodynamic response caused tissue hyperemia, the inverse of prolonged CSDs were measured in five patients in close proximity to structural brain clusters were associated with CSD-induced spreading hypoperfusions, which were significantly longer in duration (up to 144 min) than those of isolated CSDs. Thus, oxygen depletion caused by the inverse haemodynamic response may contribute to the establishment of clusters of prolonged CSDs and lesion progression. Combined electrocorticography and perfusion monitoring also revealed a characteristic vascular signature that might be used for non-invasive detection of CSD. Low-frequency vascular fluctuations (LF-VF) (f < 0.1 Hz), detectable by functional imaging methods, are determined by the brain's

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Propagation of cortical spreading depolarization in the human cortex after malignant stroke

ABSTRACT

Objective: To investigate electrodynamic response to cortical spreading depolarization in the peri-infarct region. **Methods:** In this prospective observational case study, we used a novel technology to measure cerebral blood flow in patients with postoperative occurrence of cortical spreading depolarization during recording strip for electrocorticography and infarct

Results: In 7 of 20 patients, 1.9 blood flow changes occurred during a 20-minute period. Thirteen events: response, and 4 by decrease of blood flow. Propagation and propagation area from 0.1 to 4.8 cm². Intrinsic frequency vascular fluctuations were suppressed (number of 56 ± 82 cortical spreading depolarization progression of 30 ± 13 cm² was detected in 5 of 7 patients). **Conclusions:** We visualize the spatiotemporal propagation of cortical spreading depolarization in the human cerebral cortex intraoperatively. In patients with depolarizations with either hyperemic or hypoxic that, in patients with focal ischemia, cortical spreading depolarization causes a breakdown of electrochemical gradients following acute brain injury, and also elicits dynamic changes in regional cerebral blood flow that range from physiological neurovascular coupling (hyperemia) to pathological inverse coupling (hypoperfusion). In this study, we determined whether pathological inverse neurovascular coupling occurred as a mechanism of secondary brain injury in 24 patients who underwent craniotomy for severe traumatic brain injury.

Inverse neurovascular coupling to cortical spreading depolarizations in severe brain trauma

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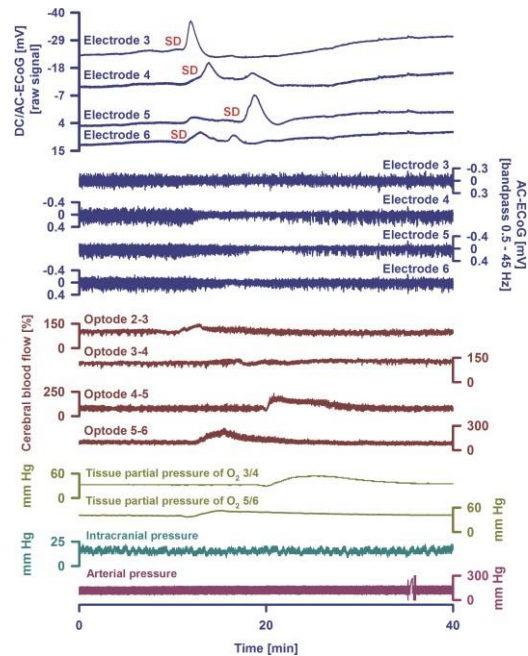
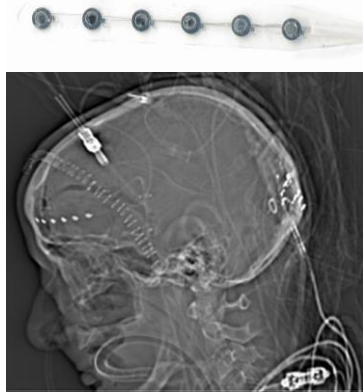
See <https://doi.org/10.1093/brain/awz241> for a scientific commentary on this article.

Cortical spreading depolarization causes a breakdown of electrochemical gradients following acute brain injury, and also elicits dynamic changes in regional cerebral blood flow that range from physiological neurovascular coupling (hyperemia) to pathological inverse coupling (hypoperfusion). In this study, we determined whether pathological inverse neurovascular coupling occurred as a mechanism of secondary brain injury in 24 patients who underwent craniotomy for severe traumatic brain injury.



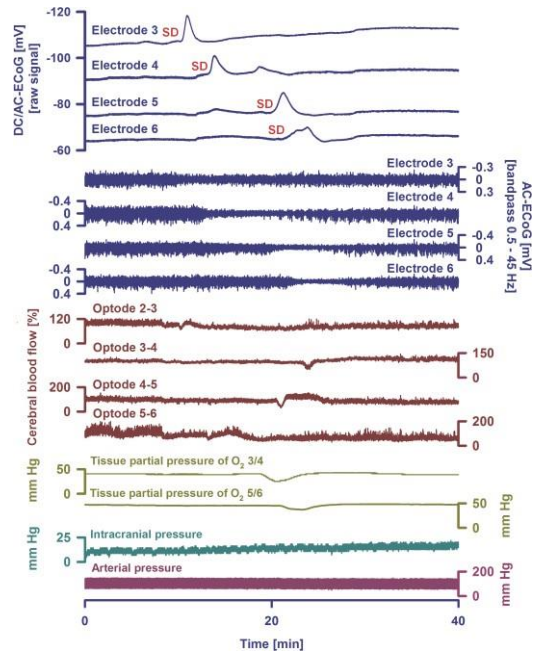
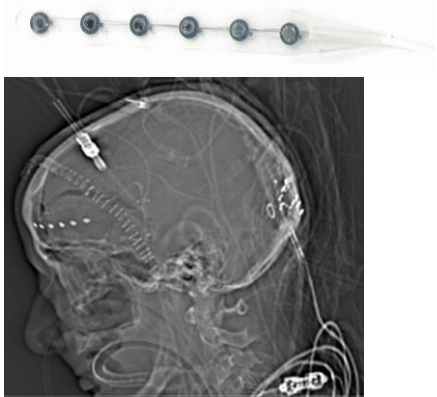
Protect Brain – Prevent Complications – Restore Function

Spreading hyperemia and spreading hyperoxia in response to spreading depolarization

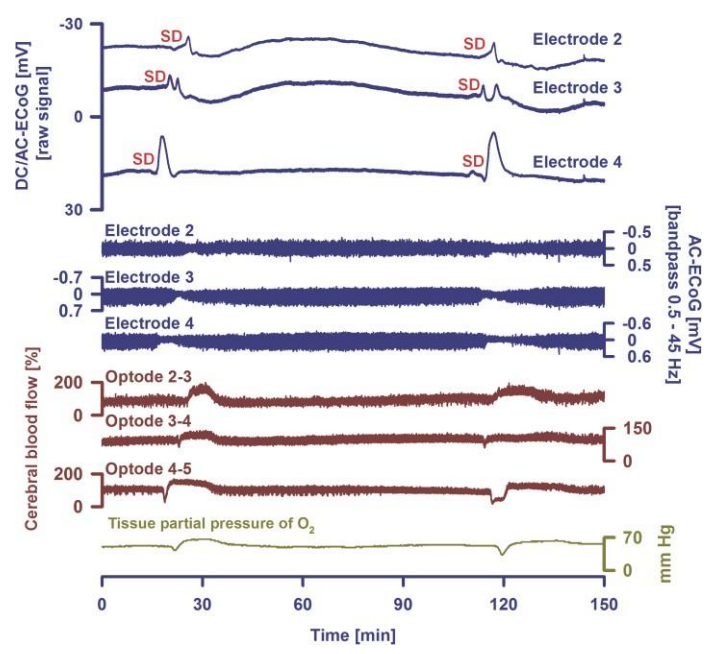
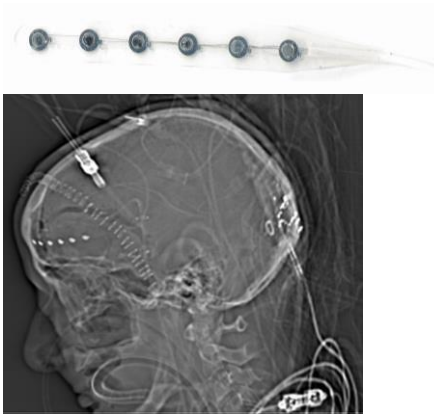


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Spreading ischemia and spreading hypoxia in response to spreading depolarization



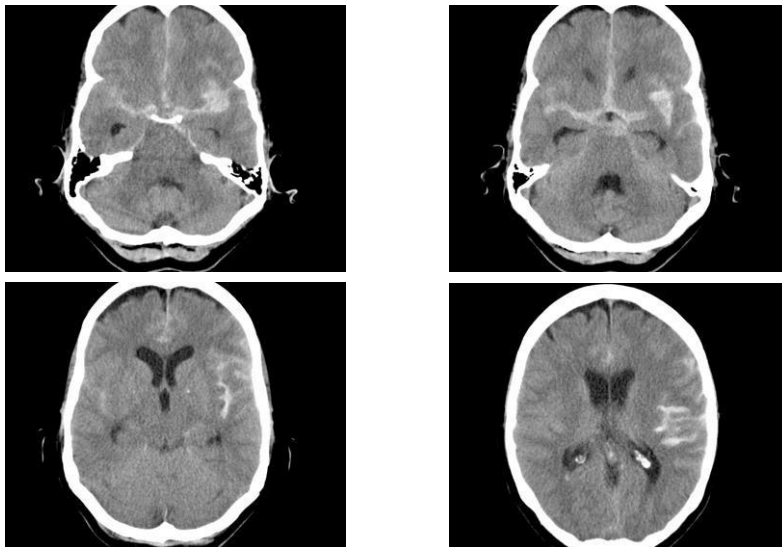
Transition from spreading hyperemia/hyperoxia to spreading ischemia/hypoxia



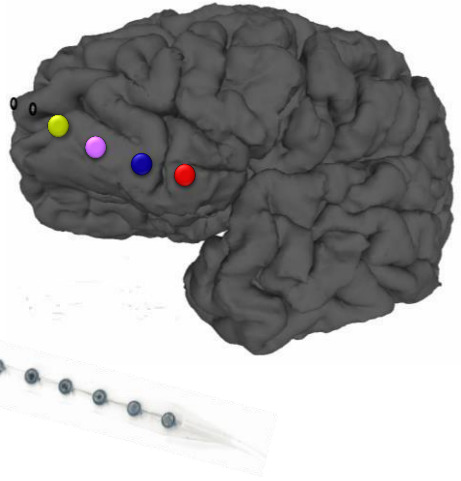
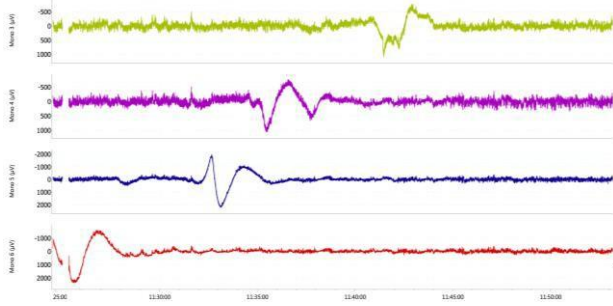
SDs associated with transient neurological deficit

- 56 years old female patient
- Initial symptoms:
 - Bilateral headache
 - decreased consciousness (GCS 11)
 - aphasia.
- aSAH from aneurysm of the left MCA (6 mm), H&H ° 3, WFNS ° 4
- No headache history, no isolated migraine aura

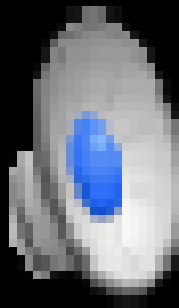
Initial CT scan



SD patterns



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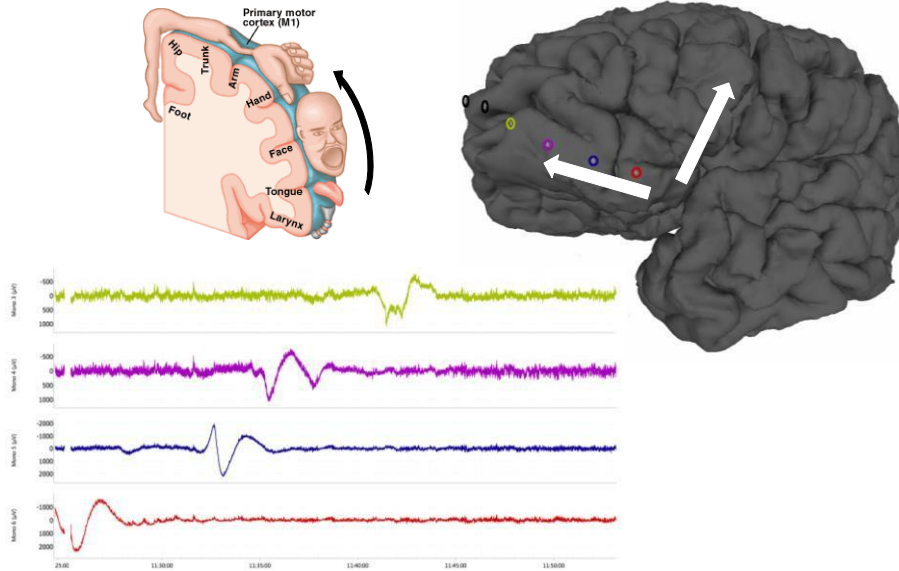


Milakara, et al.
(2017) Neuroimage Clin.

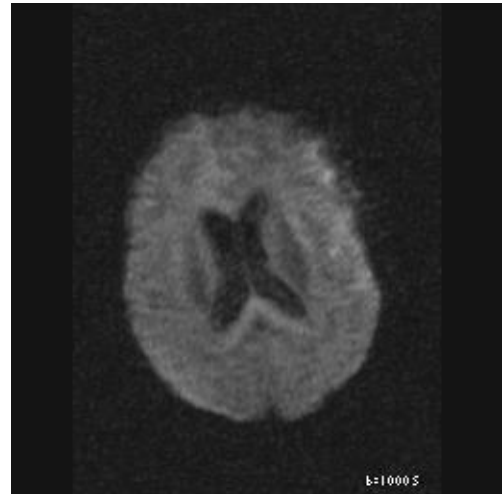
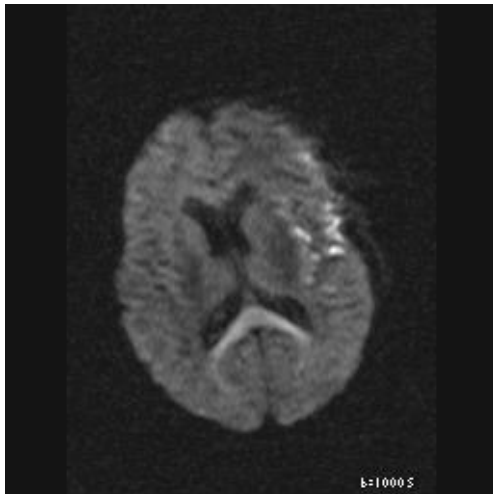


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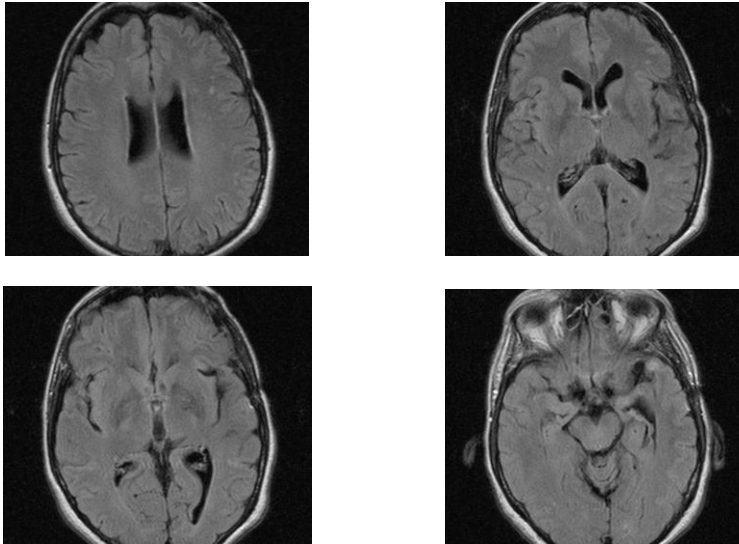
SD patterns



Early MRI



Follow up MRI



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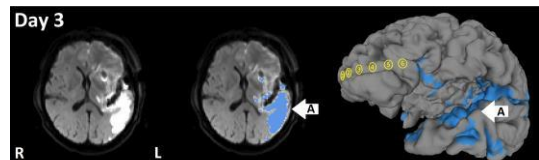
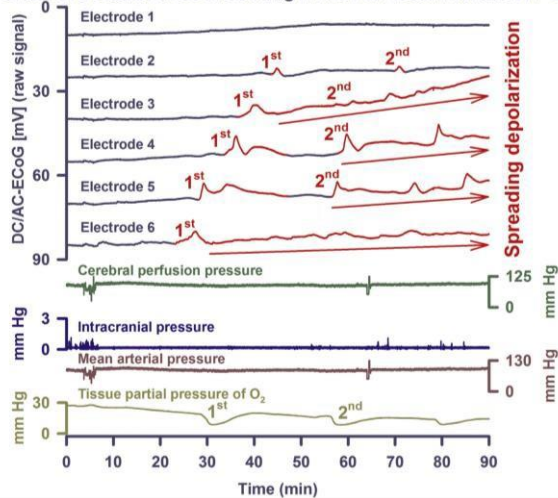
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Protect Brain – Prevent Complications – Restore Function

Spreading Depolarization and lesion progression

Onset of a cluster of SDs resulting in the new local infarction in 'B'



Milakara, et al. (2017)
Neuroimage Clin.

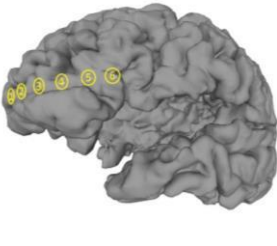
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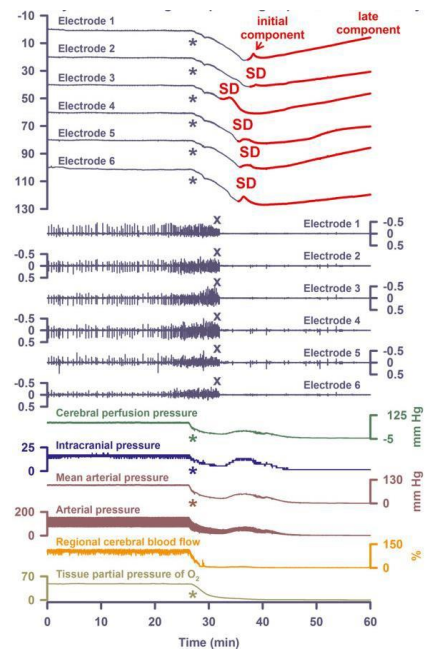
COSBID
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Protect Brain – Prevent Complications – Restore Function

Terminal spreading depolarization and nonspreading depression after cardiac arrest



Dreier, Major, et al. (2018) Annals of Neurology



Summary

- SDs occur frequently in TBI, ICH, SAH and MHS patients
- Spreading ischemia occurs in TBI, SAH and MHS and leads to prolonged depolarizations and additional tissue hypoxia
- Clustered SDs are associated with unfavorable outcome
- SDs occur in the early phase of development of new lesions
- SD monitoring may help to predict new lesions/infarcts and identify patients requiring additional or intensified therapy.

Acknowledgment

Charité, Berlin

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Jens Dreier
Coline Lemale
Clemens Reiffurth
Viktor Horst
Vasilis Kola
Karl Schoknecht

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Martin Lauritzen, Copenhagen
Raimund Helbok, Innsbruck
Anthony Strong, London
...



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Further information

- www.cosbid.org
- braintsunamis.org

The screenshot shows a web browser window with the URL icsid2020.univ-lyon1.fr/en/pages/icsid-2020-organizing-committee. The page features a large graphic with the text "ICSID 2020 International Conference on Spreading Depolarizations" and "LYON, FRANCE 18-20 APRIL". Below the graphic, there is a navigation menu with "Home", "Organizing committee", "Lyon", and "Contact". The "Organizing committee" section lists the "Conference chair" as Baptiste Balanca, MD PhD, and the "Co-Chair" as Stéphane Marinesco, PhD and Moncef Berhouma, MD.



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