



17th Annual COSBID Meeting –
Elsinore, Denmark September 10-11, 2015



THE IMPACT OF AGE ON THE EVOLUTION OF SPREADING DEPOLARIZATION TRIGGERED DURING GLOBAL FOREBRAIN ISCHEMIA IN THE RAT

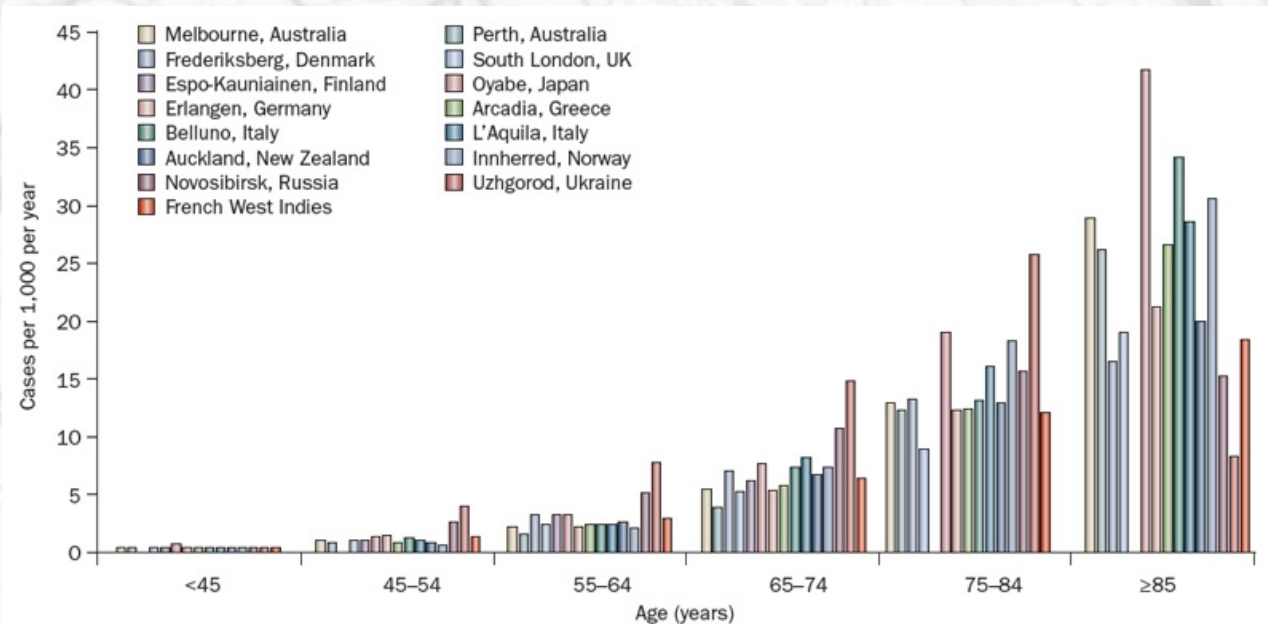
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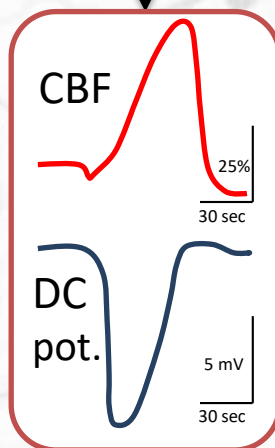
15 million people suffer stroke worldwide each year. (World Health Report – 2002)
 Stroke was the second most frequent cause of death worldwide in 2011, accounting for 6.2 million deaths (~11% of the total).
 Strokes can and do occur at ANY age (WHO, 2012).

The incidence of stroke increases with age!

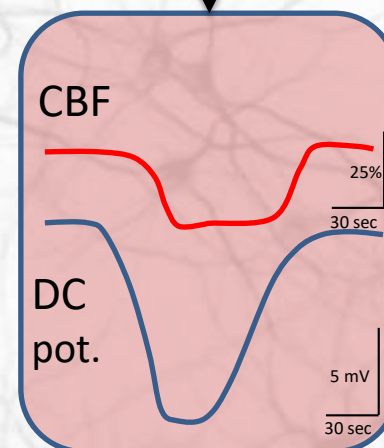


SD OCCURENCE

FACT: The incidence of ischemic stroke increases with age.
QUESTION: What is the impact of aging on SDs and related hemodynamic responses under physiological and ischemic conditions?

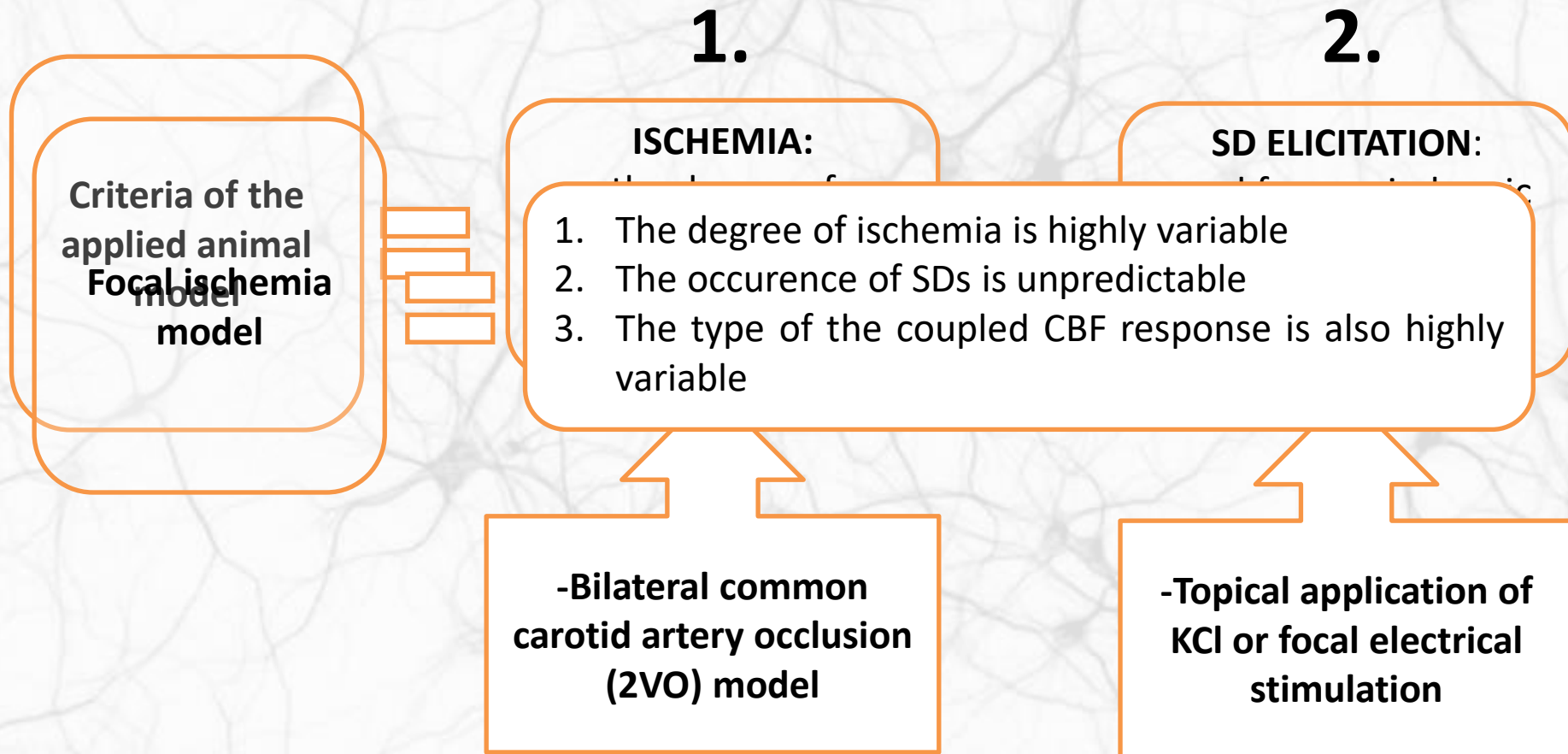


-transient hyperemia
 -short DC potential shift

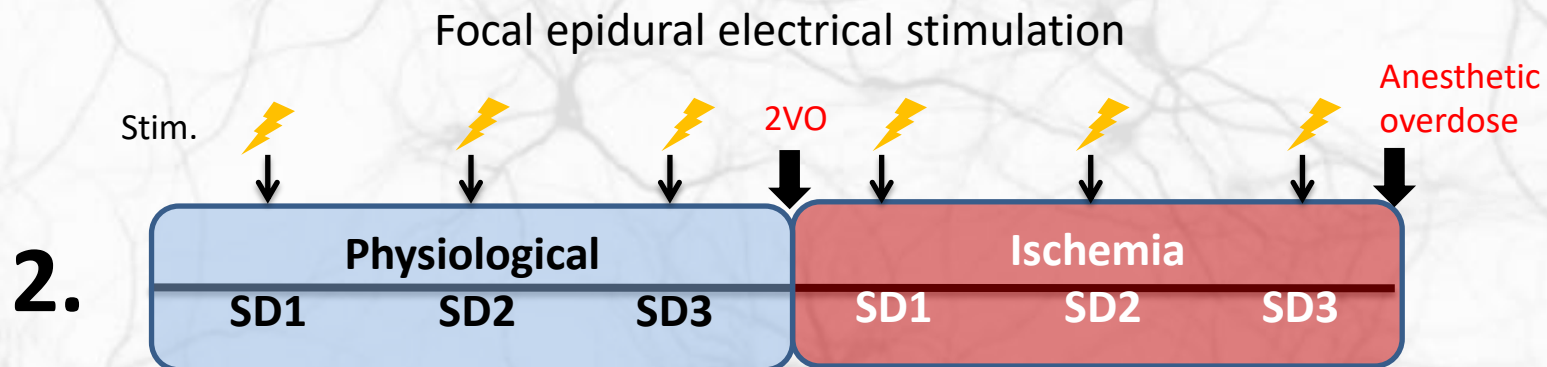
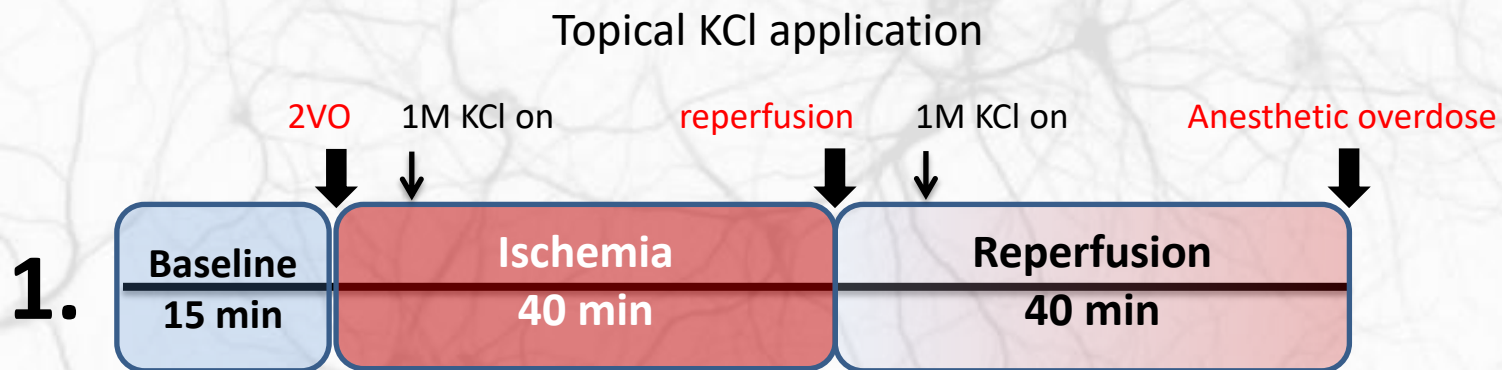


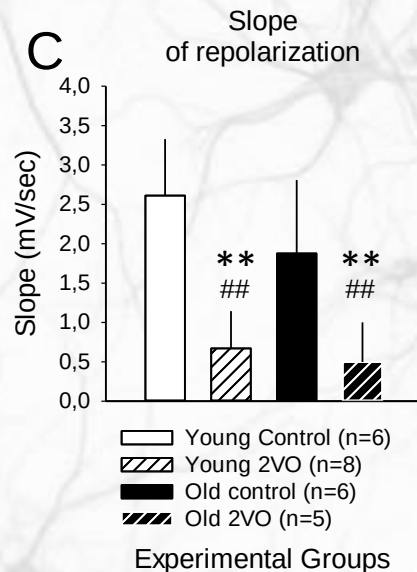
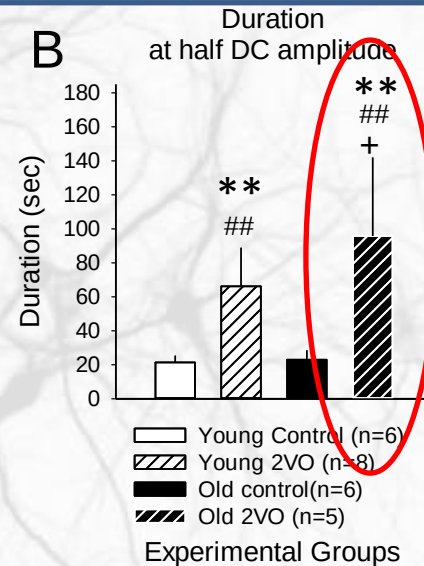
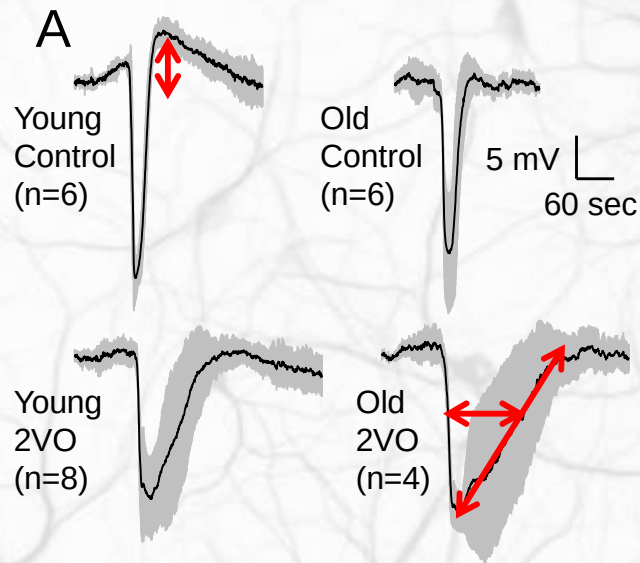
-spreading ischemia
 -long lasting DC potential shift

SD induction in a global ischemia model

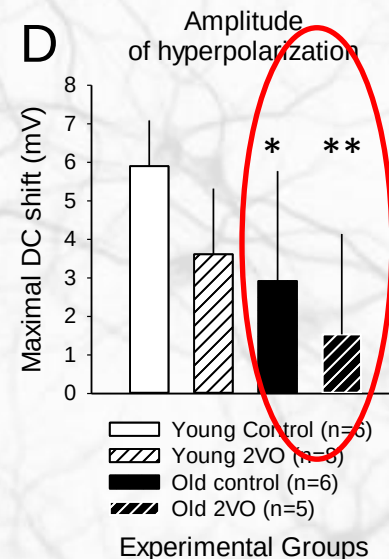


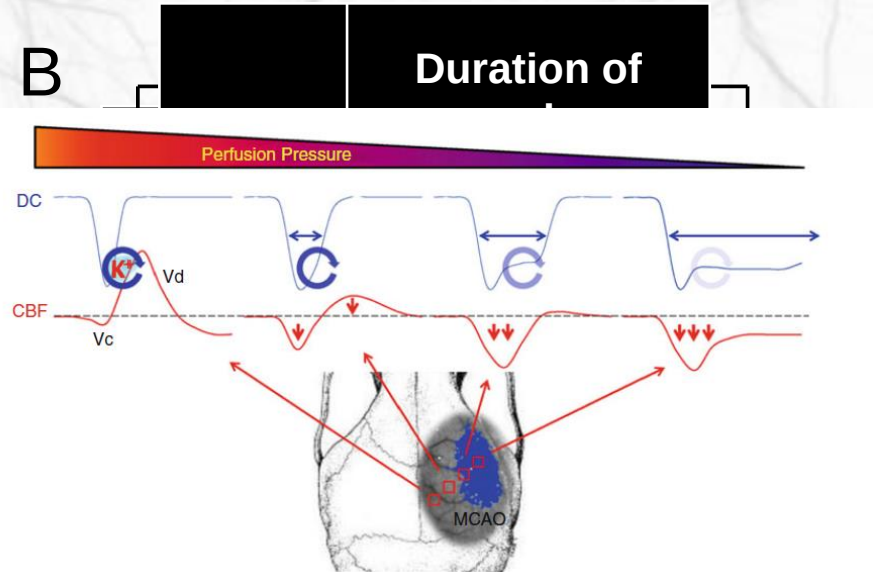
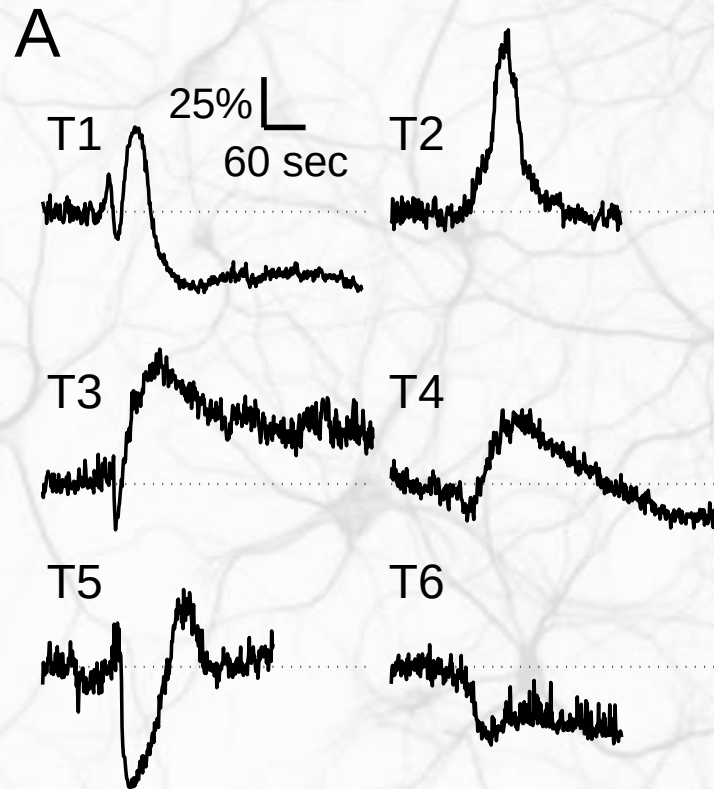
We used anesthetised rats
 Induction of global forebrain ischemia
 Electrophysiology
 Laser Doppler Flowmetry





Post hoc: LSD (Fisher):
 **: vs. Young Control
 ##: vs. Old control
 +: vs. Young 2VO
 $p^+ < 0.05$
 $p^{**}, p^{##} < 0.01$

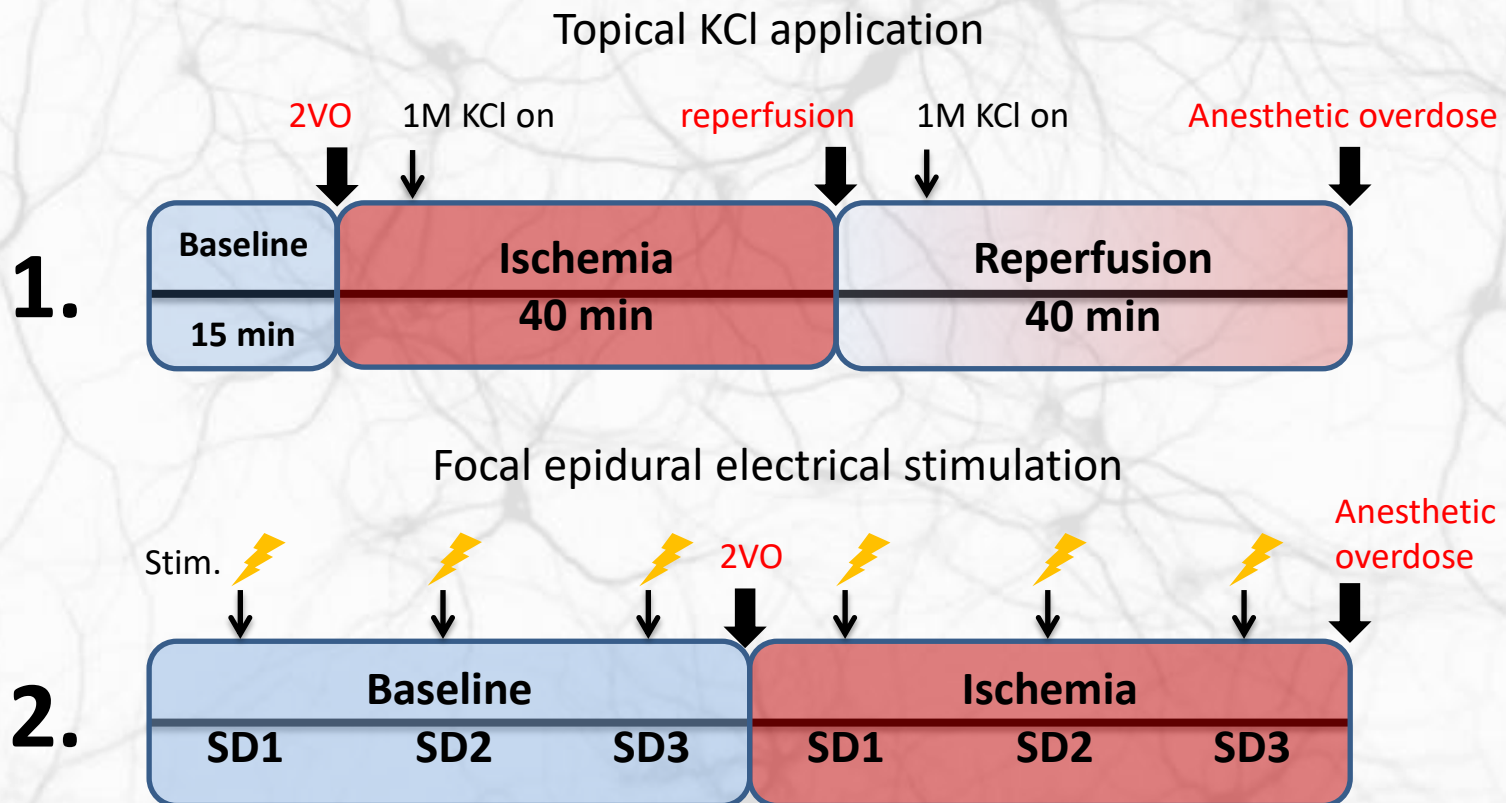




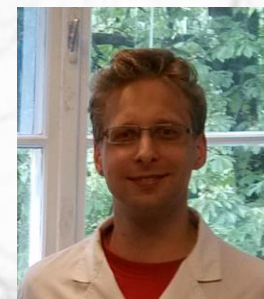
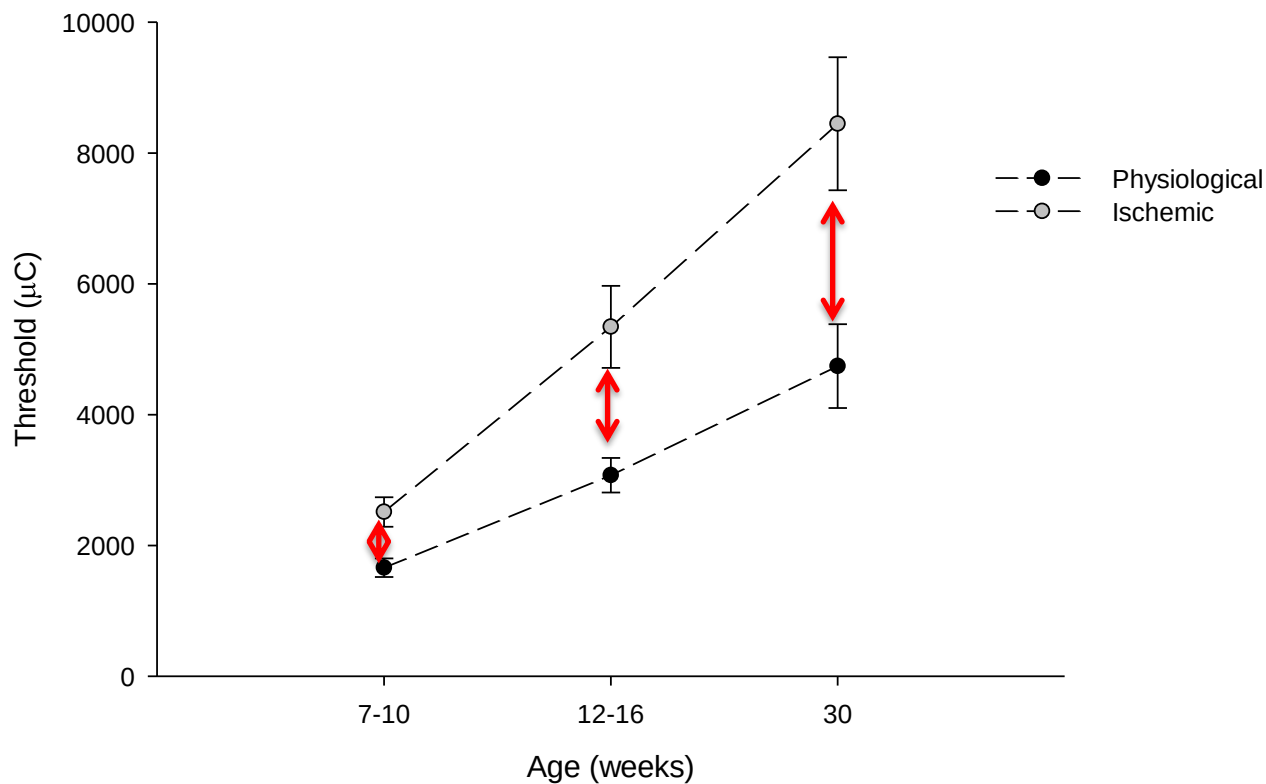
1	Old Control	Hoffmann and Ayata, 2013 4.6±5.2
On F=	Old 2VO	1344±1047**

Experimental groups
One-way ANOVA: $F=10.855^{**}$

We used anesthetised rats
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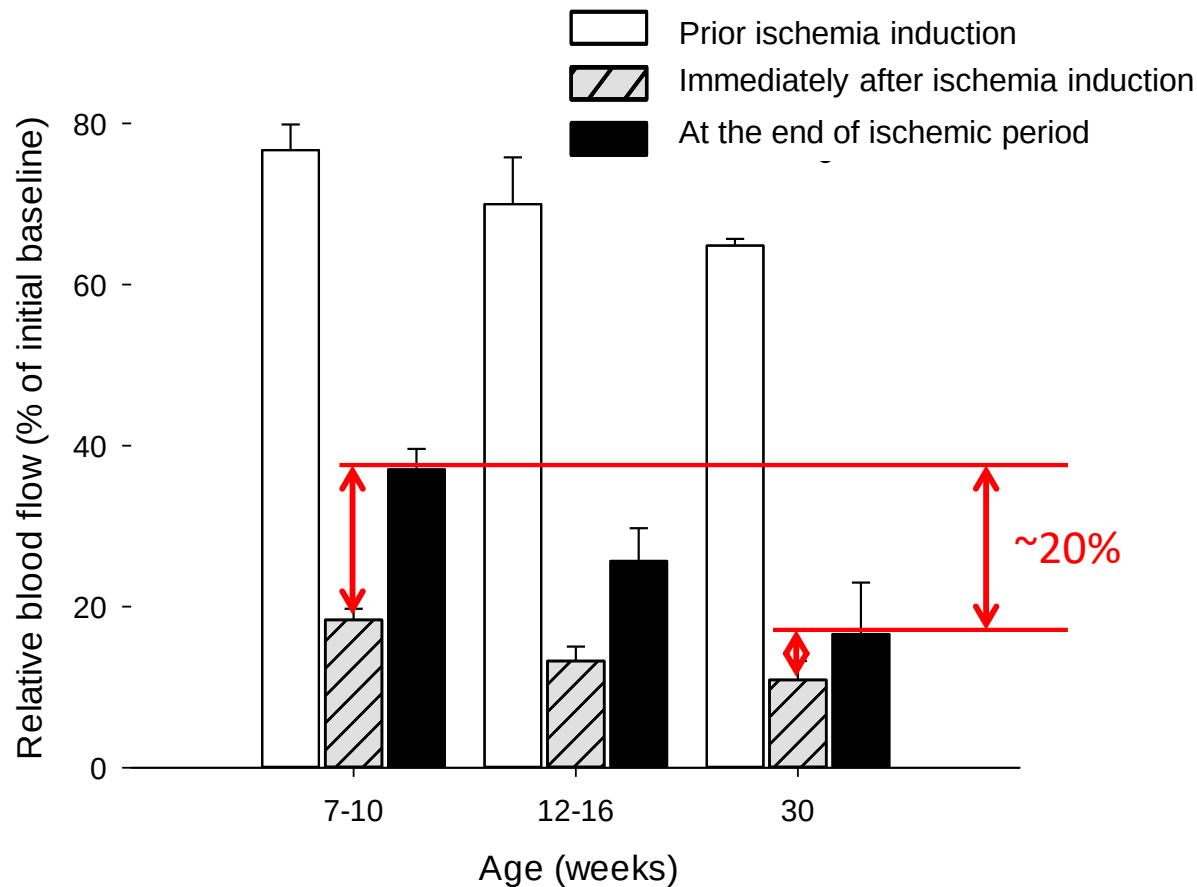


Spreading depolarization thresholds



Péter Hertelendy

Levels of local CBF taken at selected time points



Péter
Hertelendy

AGING

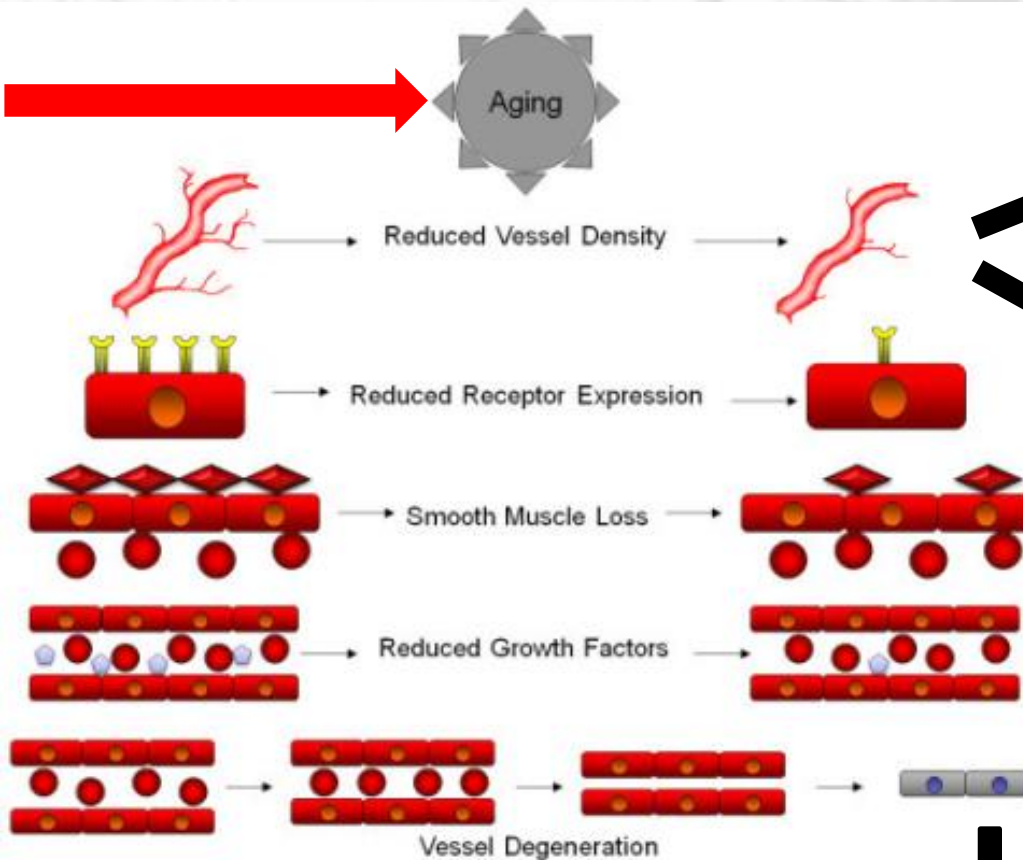
In the AGED BRAIN
SDs have a higher threshold of elicitation

ISCHEMIA

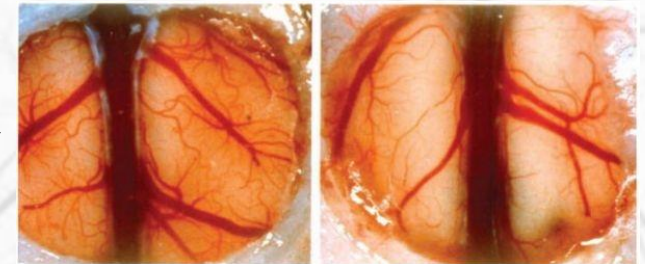
Once SD occurs during ISCHEMIA

- Aging, superimposed on ischemia impedes the recovery from spreading depolarization.
- Spreading ischemia occurs at increased frequency in the aged brain.
- Perfusion deficit deepens progressively in the aged but not in the young brain (possibly because spreading ischemia aggravates perfusion deficit in the aged ischemic brain).

⇒ Tissue damage is more probable.



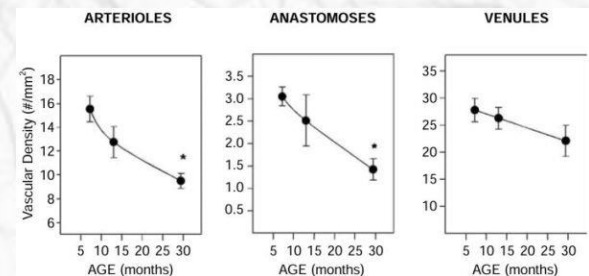
Petcu EB et al., 2010



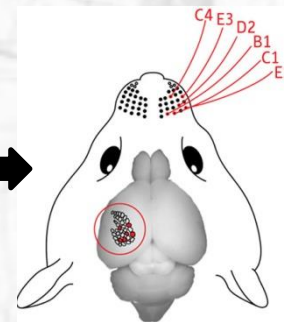
ADULT (13-months)

AGED (29-months)

Sonntag et al., 1997



Sonntag et al., 1997



Thank you for your attention!

Group of Experimental Neuroimaging



Ferenc Bari, Professor, Dean, research group leader, manager



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Undergraduate students:



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Borbála Szepes

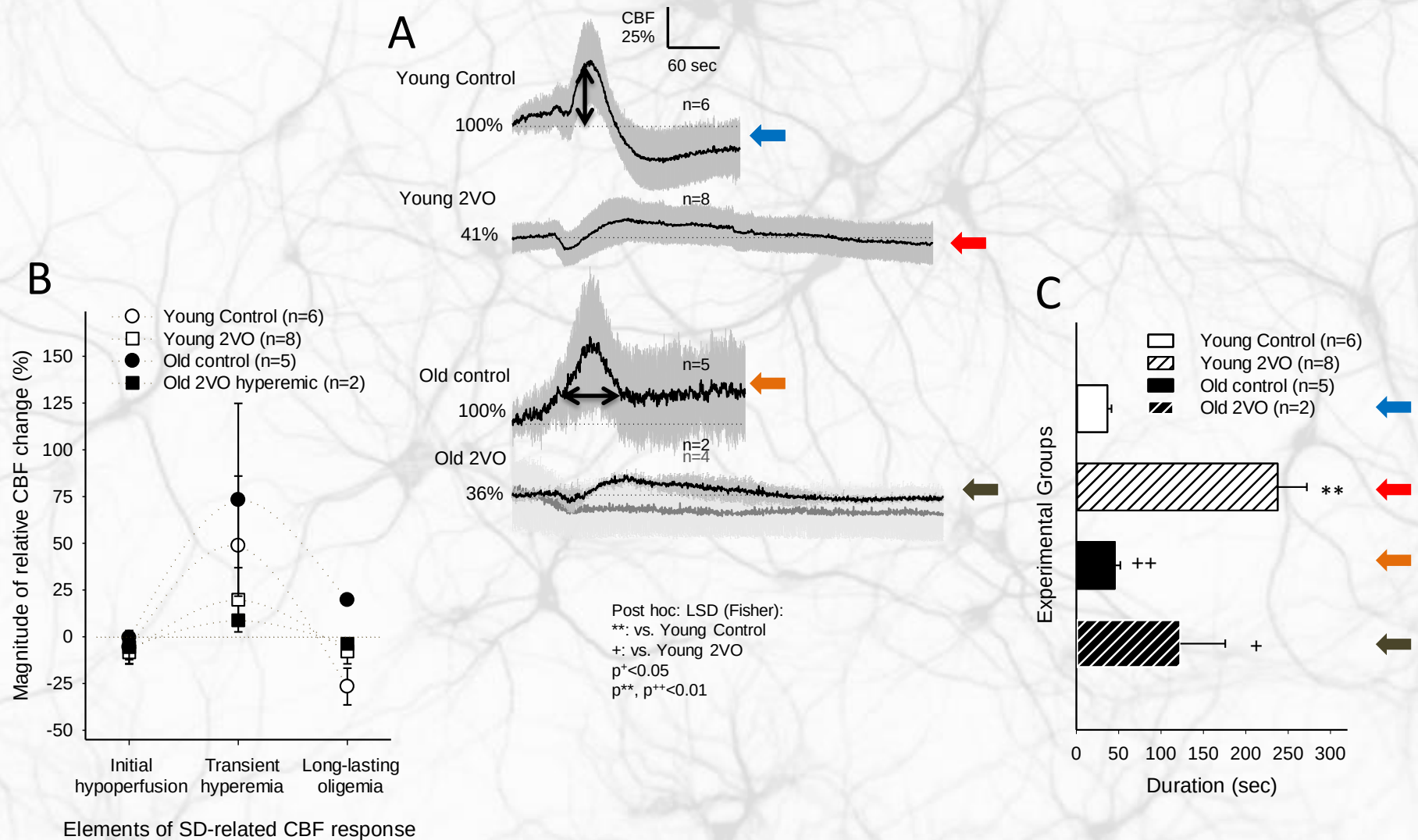


Réka Tóth



Tamás Kiss

Quantitative analysis of SD1-related CBF responses



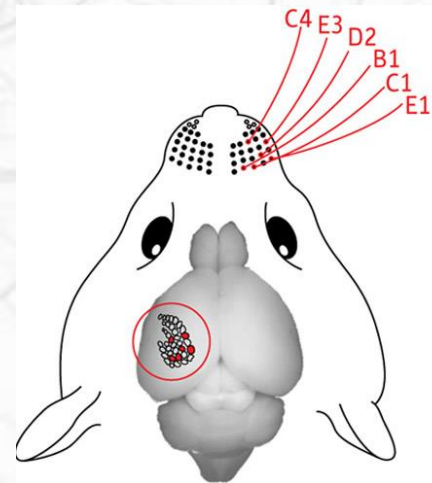


Aging impairs neurovascular coupling

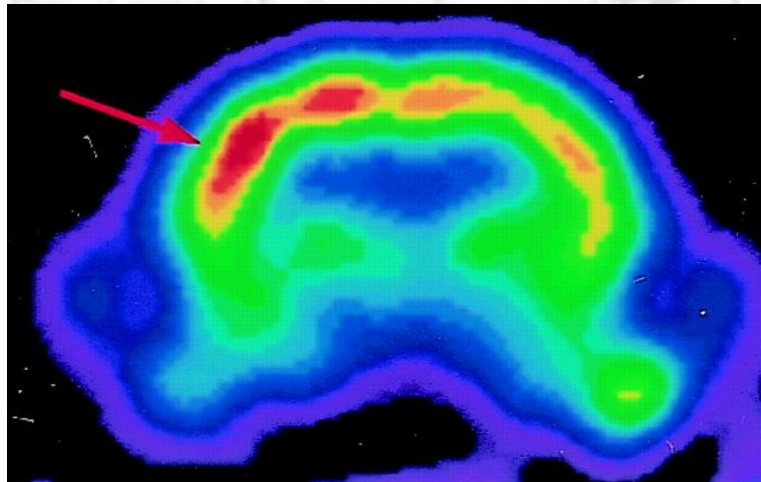
Whisker stimulation in mice

→ Electrical activity → Functional hyperemia

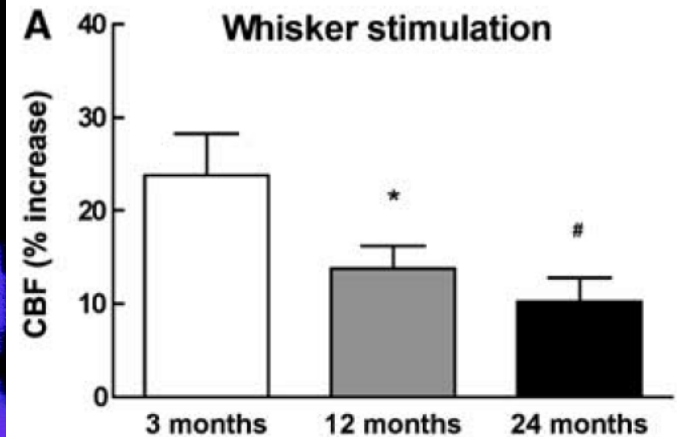
Age-dependent decrease
in the magnitude of
functional hyperemia



(Akemann et al., 2010)



(Phelps, PNAS, 2000)

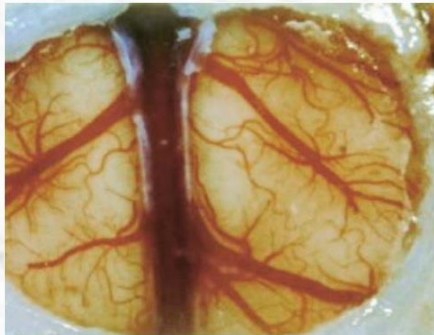


(Park et al., JCBFM, 2007)

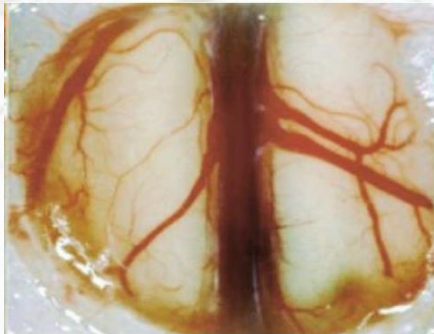


Cerebral microvascular rarefaction during aging

Cranial window in
Brown-Norway rat

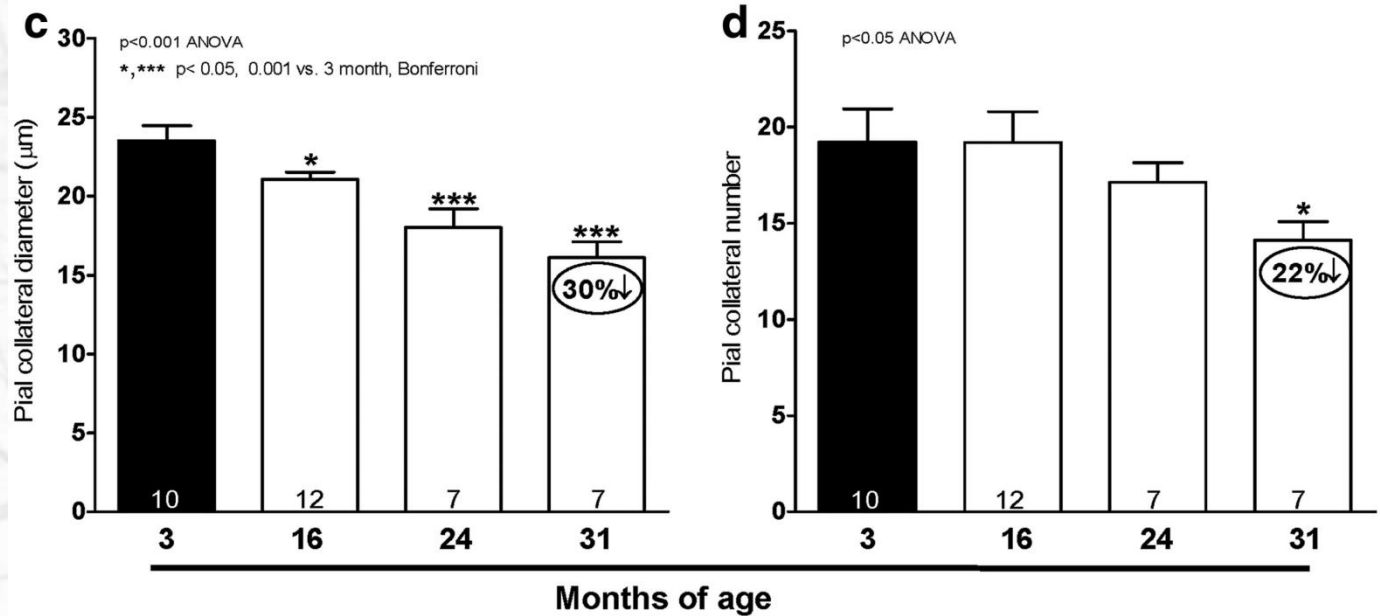


13 months old



26 months old

Quantitation of pial arteriolar rarefaction
in C57BL/6 mice

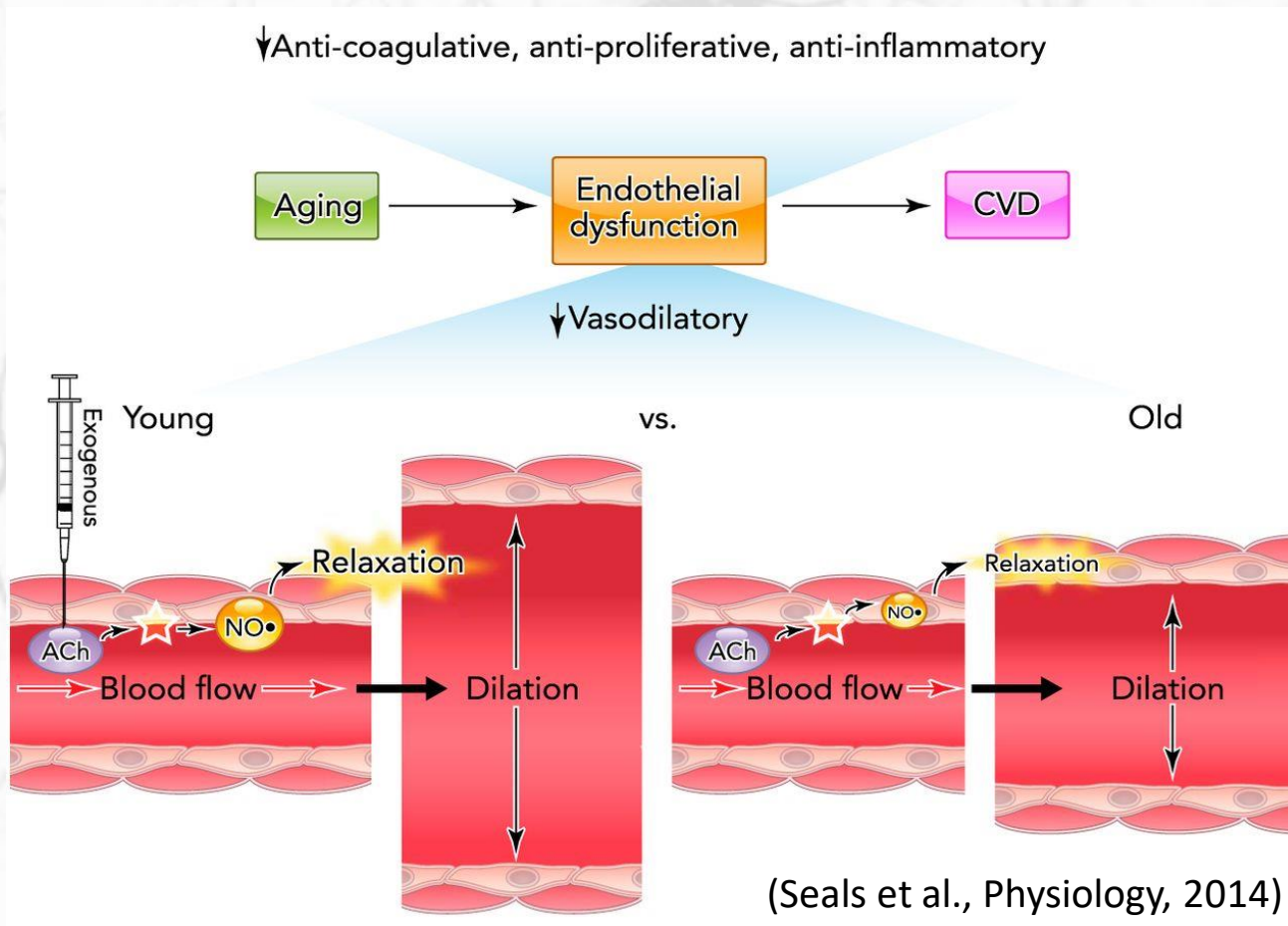


(Faber et al., Arterioscler Thromb Vasc Biol 2011)

(Middle et al.,
Ageing Res Rev 2003)



Age-related vascular endothelial dysfunction





Summary

In the aged brain
SDs occur less frequently and have a higher threshold of elicitation

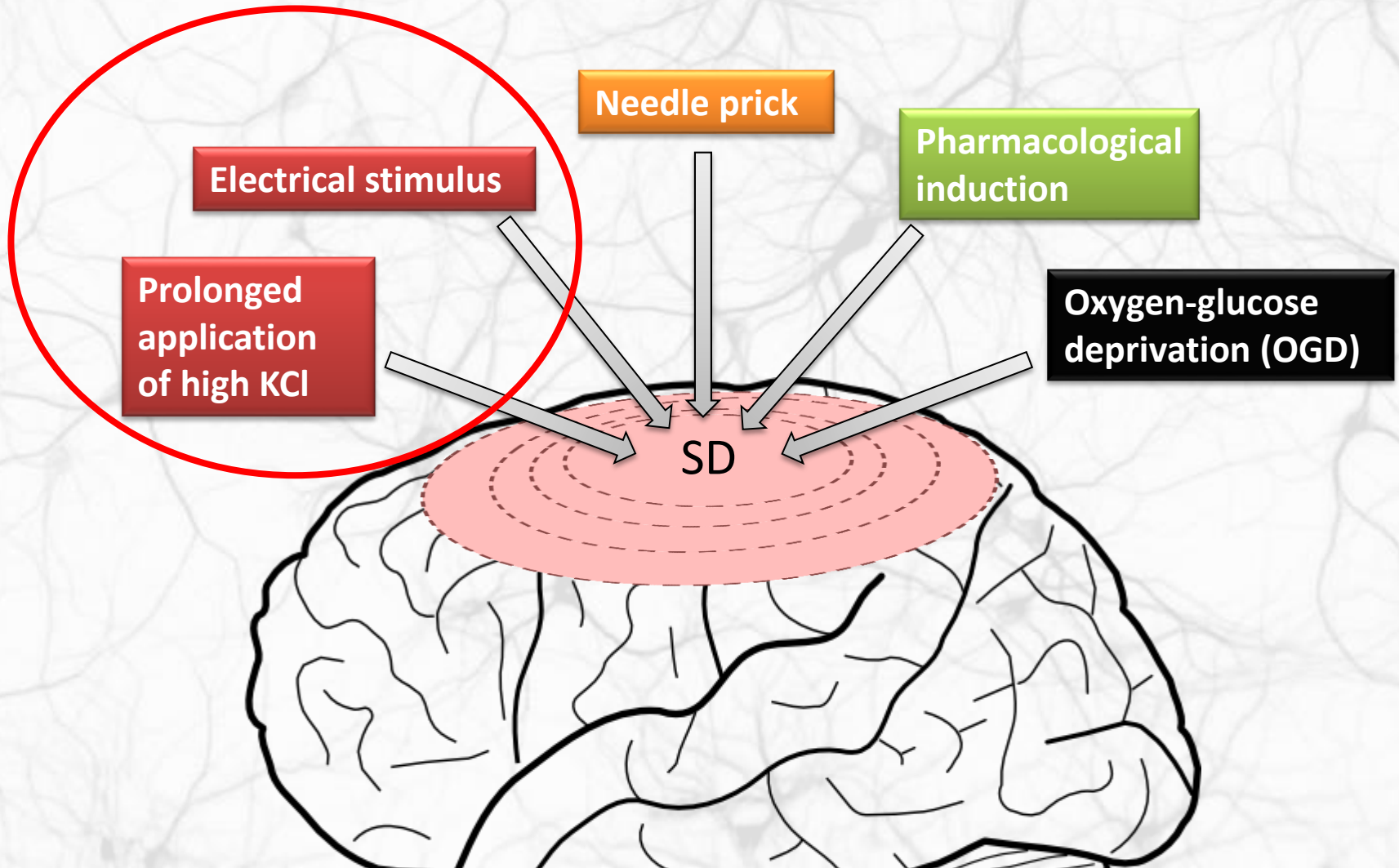
BUT

Once SD occurs during ischemia

- SD is likely coupled with adverse hemodynamic response
- SD duration is considerably longer
- Tissue damage is more probable



Experimental elicitation of SD



Methods

