



ISCHEMIA AND AGING ALTER SPREADING DEPOLARIZATION-RELATED TISSUE ACIDOSIS IN THE RAT CEREBRAL CORTEX

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INTRODUCTION

Cerebral ischemia and tissue pH: Metabolic acidosis causes cellular dysfunction and neuronal death due to the formation of lactic acid and the damage of oxidative phosphorylation. Local accumulation of lactate to cytotoxic levels may play a causal role in the generation and maturation of brain infarcts.

Spreading depolarization (SD): Spreading depolarizations may exacerbate ischemic injury via related atypical hemodynamic responses but their consequences on tissue pH changes are not yet understood.

Aging and SD: Aging predicts worse outcome from stroke and SD might play a potential role in the age related worsening of cerebral infarcts.

MATERIALS AND METHODS

- Animals: Young (8-10 weeks old) and Old (1.5 years old), male Sprague-Dawley rats (n=17)
- Anesthesia: isoflurane (1.5-2.2% in N₂O-O₂/2-1)
- Monitoring mean arterial pressure and arterial blood gases (left femoral artery catheter)
- Transient global forebrain ischemia induction: bilateral occlusion of the common carotid arteries ("two-vessel occlusion", ZVO)
- SD elicitation: topical 1M KCl
- Small, open craniotomy

Local field potential monitoring (DC-ECOG)
Laser-Doppler flowmetry (LDF)
pH-sensitive microelectrode

FIGURE 1. Experimental design

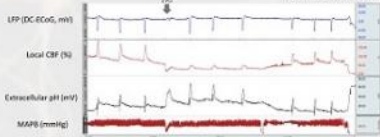


FIGURE 2. Simultaneously recorded parameters



FIGURE 3. Experimental protocol

ACKNOWLEDGEMENTS

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RESULTS

EVOKED SDs (1M KCl)

FIGURE 4. SD-associated pH changes



FIGURE 5. SD-coupled CBF changes

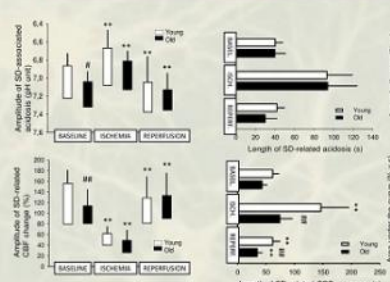


FIGURE 6. Representative figure of spontaneous SD occurrence

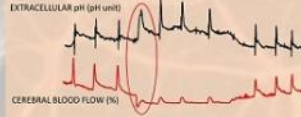
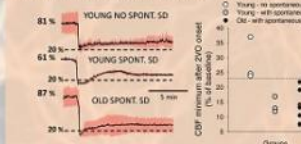


FIGURE 7. Characterization of CBF drop after ZVO onset



SPONTANEOUSLY OCCURRING SDs

FIGURE 8. Characterization of acidosis after ZVO onset

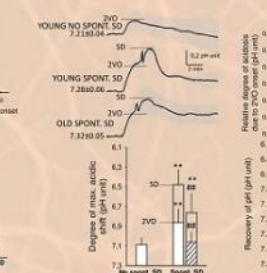


TABLE 1. Effects of aging on the SD-related acidosis

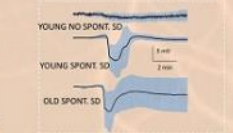
Phase	Amplitude of acidosis with SD (baseline SDs)	AUC of SD-related acidosis (ischemic SDs)
Baseline	~1.0	~1.0
Ischemia	~1.5	~1.5
Reperfusion	~1.0	~1.0

TABLE 2. Effects of aging on the SD-coupled CBF response

Phase	Amplitude of SD-coupled CBF response (baseline SDs)	AUC of SD-coupled CBF response (ischemic SDs)
Baseline	~1.0	~1.0
Ischemia	~1.5	~1.5
Reperfusion	~1.0	~1.0

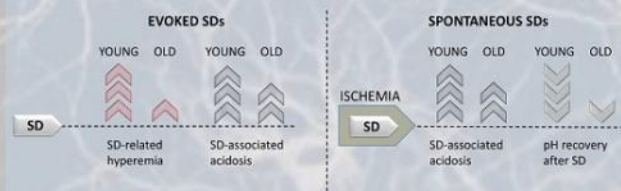
TABLE 3. Threshold of spontaneous SD occurrence

Spont. SD occurrence	CBF drop after ZVO onset (%)	Degree of acidosis after ZVO onset (pH units)	Spont. SD (Yes/No)
Young (n=5)	>20%	<0.2 pH units	NO
Young (n=5)	<20%	>0.2 pH units	YES
Old (n=4)	<20%	>0.2 pH units	YES



SUMMARY

- The magnitude of SD-related hyperemia is significantly smaller in the aged brain (evoked SDs).
- The SD-related acidosis is milder in the aged brain (evoked and especially spontaneous SDs).
- Tissue pH recovery after SD is hampered in the aged brain (spontaneous SDs).



CONCLUSION

- The density of the cerebral microvascular network decreases in the aged brain, the vascular wall becomes thickened and more rigid, vasoregulator signaling is less efficient, which could potentially diminish effective vasodilation.
- Glia/neuron ratio is increased in the aged brain, which may buffer tissue pH changes more effectively. Age related shrinkage of brain extracellular space may alter ionic diffusion and modulate the efficacy of proton pumps or acid transporters.
- Longer-lasting acidosis (even if it is mild) potentially contributes to lesion expansion.

SESSION TIME: 09:30 - 13:00
PRESENTATION TIME: 11:30 - 13:00

Poster Area

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POSTER CERTIFICATE

This is to certify that

Akos Menyhart

presented a poster entitled

Ischemia and aging alter spreading depolarization-related tissue acidosis in the rat cerebral cortex

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