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Short Communication

A mouse model of acute subdural hematoma under clinically realistic intensive care conditions: insights into effects on mitochondrial respiratory activity



Hannemann W[1], Sharon O[2], Kress Sa[1], Gröger M[1], Hoffmann A[1], Seifritz A[1], Kranz St[1], Calzia Enrico[1], Radermacher P[1], Kapapa T[2]

[1]Inst Anesthesiol Pathophysiol Process Eng, Ulm Univ, Germany; [2]Dept Neurosurg, Univ Hosp Ulm, Germany.

Corresponding author: enrico.calzia@uni-ulm.de

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Introduction

Acute subdural hematoma (ASDH) combines primary mass displacement with secondary injury [1], including blood-brain barrier breakdown and excitotoxicity [2] as well as mitochondrial dysfunction [3]. We characterised mitochondrial respiration after ASDH in a mouse model under intensive care monitoring.

Methods

ASDH was induced in adult mice (N = 10) by subdural injection of autologous blood (10 µL) using a dual burr-hole model. Intracranial pressure, brain tissue oxygen partial pressure, temperature and arterial pressure were monitored for up to 8 h. Untreated mice (N = 4) served as controls. Respiration of homogenised lesion-adjacent and lesion-distant tissue was measured by high-resolution respirometry using a substrate-uncoupler-inhibitor titration (SUIT) protocol [4]. Mass-specific oxygen flux, J_{O_2}, is given in pmol·s^{-1}·mg^{-1} as median [Q1; Q3]. Within-group comparisons were performed by the Wilcoxon signed-rank test ($p < 0.05$).

Results and discussion

Preliminary analyses showed markedly lower oxidative phosphorylation (OXPHOS) and electron transfer (ET) capacities, and higher LEAK-respiration in ASDH than in controls (Table 1). Within the ASDH group, respiration was lower in lesion-adjacent than in lesion-distant tissue ($p < 0.05$), whereas controls showed no such difference. The cytochrome *c* effect, defined as respiration before relative to after cytochrome *c* addition, was virtually absent in controls but marked in ASDH, particularly in lesion-adjacent tissue ($p < 0.05$). Thus, ASDH markedly impairs

mitochondrial respiration with a gradient between lesion-adjacent and lesion-distant tissue, and the cytochrome *c* response suggests alterations beyond reduced respiratory capacity. This reproducible model enables mechanistic investigations.

Table 1. Respiration of brain tissue homogenates. Median [Q1; Q3]. *$p < 0.05$, lesion-adjacent vs lesion-distant (Wilcoxon signed-rank test).

	ASDH lesion-adjacent	ASDH lesion-distant	Control adjacent region	Control distant region
OXPHOS capacity, J_{O_2} / [pmol·s^{-1}·mg^{-1}]	28.2 [19.9; 37.2]*	40.9 [39.9; 44.1]	85.7 [78.5; 91.0]	83.8 [76.9; 88.2]
electron transfer capacity, J_{O_2} / [pmol·s^{-1}·mg^{-1}]	32.9 [21.4; 48.7]*	76.3 [60.8; 85.6]	126.2 [120.3; 133.3]	135.3 [127.9; 141.2]
cytochrome *c* effect / [%]	53.1 [46.7; 61.1]*	78.0 [73.8; 84.0]	99.7 [99.0; 100.5]	95.3 [94.8; 96.7]
LEAK respiration [%]	0.58 [0.48; 0.69]*	0.47 [0.37; 0.53]	0.18 [0.17; 0.22]	0.19 [0.18; 0.20]

Conflicts of interest: The authors declare no conflict of interest.

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Author contributions: WH and OS contributed equally. WH and OS conducted the technical aspects of the experiment; WH performed and evaluated the respirometric measurements, and OS performed the neurosurgical procedures. SaK and MG conducted the non-neurosurgical procedures and were responsible for anaesthesiological and intensive care monitoring. AH was responsible for animal welfare and sample collection. AS and StK were responsible for sample processing and data management. EC contributed to experiment planning and supervised the respirometric analyses. PR and TK supervised the entire project as project leaders.

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