

Severe Obstructive Sleep Apnea Disrupts Vigilance-State-Dependent Metabolism

Felix Schmidt ^{1,2}, Nora Nowak ³, Patrick Baumgartner ^{1,2}, Thomas Gaisl ^{1,2}, Stefan Malesevic ^{1,2}, Bettina Streckenbach ³, Noriane A. Sievi ², Esther I. Schwarz ^{1,2}, Renato Zenobi ³, Steven A. Brown ^{4†}, Malcolm Kohler ^{1,2,5*,†}

Online Data Supplement

This supplementary information contains:

Methods

Supplementary Table S1

Results

Supplementary Table S2

Supplementary Figure S1

METHODS

Table S1: Stratification of 149 suspected OSA patients out of cross-sectional nested case-control study by Nowak et al. 2021. This secondary analysis focus on stratification 2.

		OSA			Control		
	All participants	stratification 1 ODI>30 or (ODI>10 & ESS>10)	stratification 2 ODI>30 & ESS>10	stratification 3 ODI>30	stratification 1 ODI<5 or (ODI<10 & ESS<11)	stratification 2 ODI<10 & ESS<11	stratification 3 ODI<10
Number of subjects (N)	149	51	18	36	33	26	47
Age, mean (SD), years	53.3 (13.7)	55 (13.4)	51.6 (10.2)	53.6 (13)	48.5 (14.6)	49.7 (14.3)	49.3 (14.6)
male sex, n (%)	108 (72.5%)	35 (68.6%)	13 (72.2%)	26 (72.2%)	20 (60.6%)	17 (65.4%)	30 (63.8%)
BMI, mean (SD), kg/m2	30.1 (6.6)	33 (6.5)	33.1 (6.7)	34 (6.5)	27.2 (6.1)	28 (6.4)	27.1 (5.5)
active smoker, n (%)	31 (20.8%)	17 (33.3%)	7 (38.9%)	14 (38.9%)	6 (18.2%)	5 (19.2%)	10 (21.3%)
former smoker, n (%)	53 (35.6%)	16 (31.4%)	4 (22.2%)	9 (25%)	11 (33.3%)	10 (38.5%)	16 (34%)
AHI at diagnosis, mean (SD), events per hour	19.6 (17)	34.8 (18)	42.9 (15)	42.7 (15)	5.9 (5)	5.3 (3)	6.4 (5)

ODI₄% at diagnosis, mean (SD), events per hour	20.8 (17.5)	38.3 (17.5)	46.5 (14.7)	46.8 (13.2)	4.4 (2.7)	5 (2.6)	5.2 (2.6)
ESS at diagnosis, mean (SD), points	8.9 (4.5)	11 (4.8)	14.2 (2.8)	10 (5.2)	7.4 (3.4)	6 (2.4)	9.4 (4.5)

Definition of abbreviations: AHI: apnea-hypopnea-index; BMI: body mass index; ESS: Epworth Sleepiness Scale; ODI: oxygen desaturation index.

RESULTS

Table S2: 18 identified compounds showed weak to strong evidence for a difference in breath profiles of symptomatic OSA patients compared to controls.

Metabolite	Key biochemical metabolism ¹	Selected other linking pathways ^{1,2}	Evidence level
Deoxyribose	Energy metabolism	Glucuronate interconversions/ Pentose phosphate pathway; Purines & Pyrimidine	$p \leq 0.05$
Glycerate	Carbohydrate metabolism	Glucuronate interconversions/ Pentose phosphate pathway; Glycolysis; Gluconeogenesis; Glyoxylate cycle; ...	$p \leq 0.1$
Pyruvate	Carbohydrate metabolism	Glycolysis & Gluconeogenesis; TCA cycle; Pentose phosphate pathway; Amino acids pathways; Pyruvate turnover; ...	$p \leq 0.005$
Lactate	Carbohydrate metabolism	Glycolysis & Gluconeogenesis; Propanoate metabolism; Pyruvate turnover; ...	$p \leq 0.05$
Malate	Carbohydrate metabolism	TCA cycle; Glyoxylate metabolism; Pyruvate metabolism; ...	$p \leq 0.05$
Succinate	Carbohydrate metabolism	TCA cycle; Amino acids pathways, Pyruvate metabolism, Propanoate & Butanoate metabolism	$p \leq 0.1$
Glyoxylate	Carbohydrate metabolism	Glyoxylate metabolism; Purine metabolism; Amino acids pathways; ...	$p \leq 0.05$

Hydroxypyruvate	Carbohydrate metabolism	Glyoxylate metabolism; Glycine, serine and threonine metabolism	$p \leq 0.1$
Succinate semialdehyde	Carbohydrate metabolism	Butanoate metabolism; Glutamate decarboxylation pathway	$p \leq 0.005$
Hydroxybutanoate	Carbohydrate metabolism	Butanoate metabolism; Ketone body pathway; ...	$p \leq 0.05$
Hydroxypropanoate	Nucleotide metabolism	Propanoate metabolism; Pyrimidine metabolism; ...	$p \leq 0.05$
Aminobutanoate	Amino acid metabolism	Butanoate metabolism; Glutamate decarboxylation pathway; Alanine, aspartate and glutamate metabolism; Arginine and proline metabolism; ...	$p \leq 0.005$
Malonate semialdehyde	Amino acid metabolism	Propanoate metabolism; Various amino acid pathways; Pyrimidine metabolism	$p \leq 0.005$
Acetoacetate	Amino acid metabolism	Butanoate metabolism; Various amino acid pathways; Ketone body pathway	$p \leq 0.005$
Carnitine	Lipid metabolism	Fatty acid metabolism; transport	$p \leq 0.005$
Dehydrocarnitine	Lipid metabolism	Fatty acid metabolism; transport	$p \leq 0.005$
Acetylcarnitine	Lipid metabolism	Fatty acid metabolism; transport	$p \leq 0.05$
Acrylcarnitine	Lipid metabolism	Fatty acid metabolism; transport	$p \leq 0.05$

¹ Key pathways according KEGG release 102.0; ² Identified pathways by MetaboAnalyst 5.0; TCA - tricarboxylic acid cycle; ... - indicates many more linking pathways exists.

SUPPLEMENT FIGURE

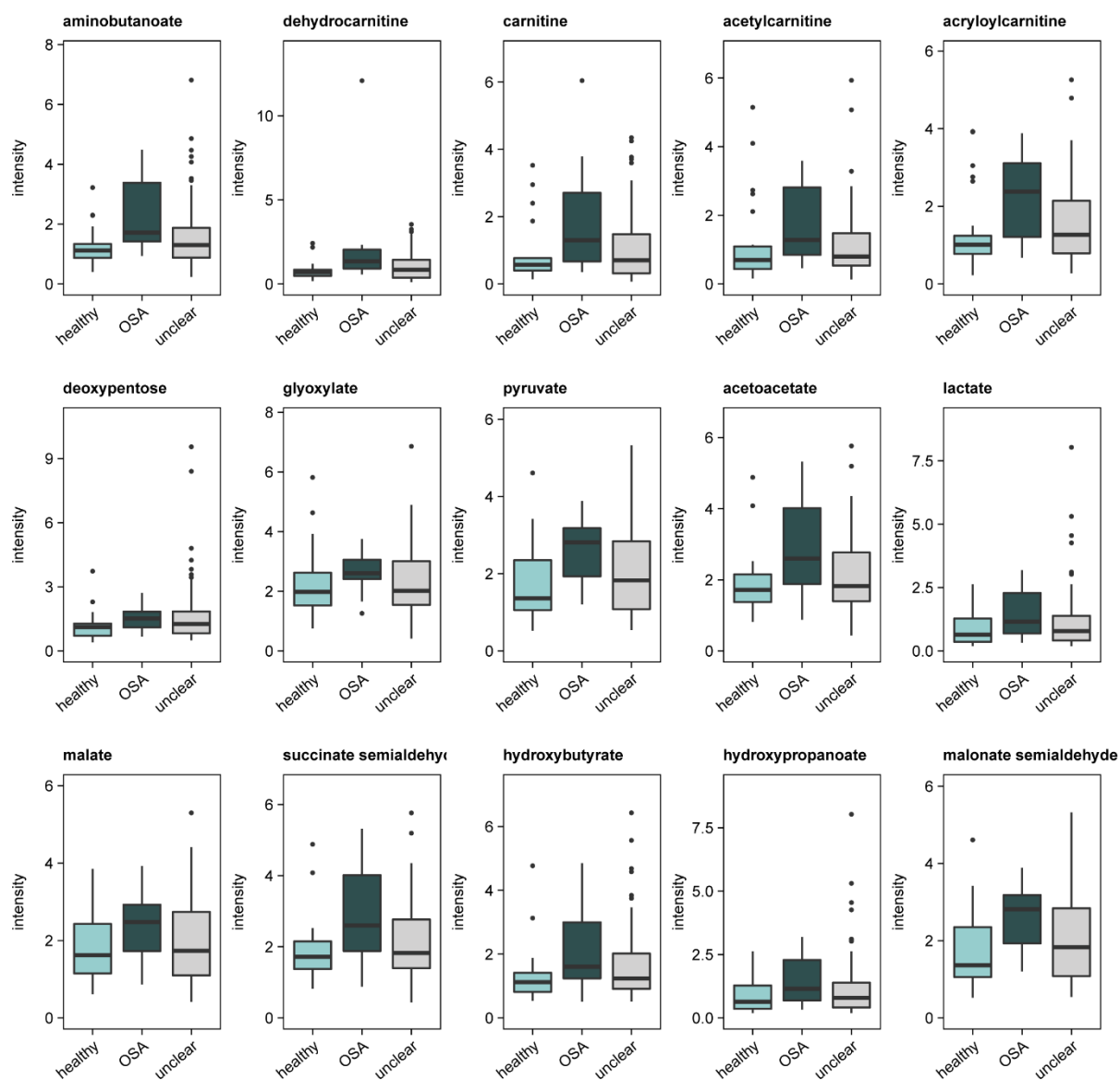


Figure S1: 15 compounds with moderate or strong evidence for a difference are shown in boxplots. Boxplots (center line: median, box limits: 25th and 75th percent quantile, whisker length: 1.5 interquartile range). OSA - symptomatic OSA (symptomatic OSA was defined as ODI > 30 events/h and an ESS > 10 points); Healthy - controls (selected according to an ODI < 10/h and an ESS < 11 points); Unclear – other subjects (not stratified in OSA or Control group; see Table E1)