How do we explain exercise intolerance in CFS/ME?

CFS/ME MC Amsterdam

- Why do we do it: concept
- How do we do it
- A few results

CFS/ME

Chronic activity of immune system

- Chronic infection
- Auto-immune
- Allergy

Sickness response:

- Motivational state:

- stay in your hole (at home)
  ("fatigue")

- Reduction of energy loss
- Safer Lion neighbour

Sickness response:

Energy

- Reduce perfusion of skin, brain,
- muscles etc

- Reduce carbohydrate metabolism
- of muscles

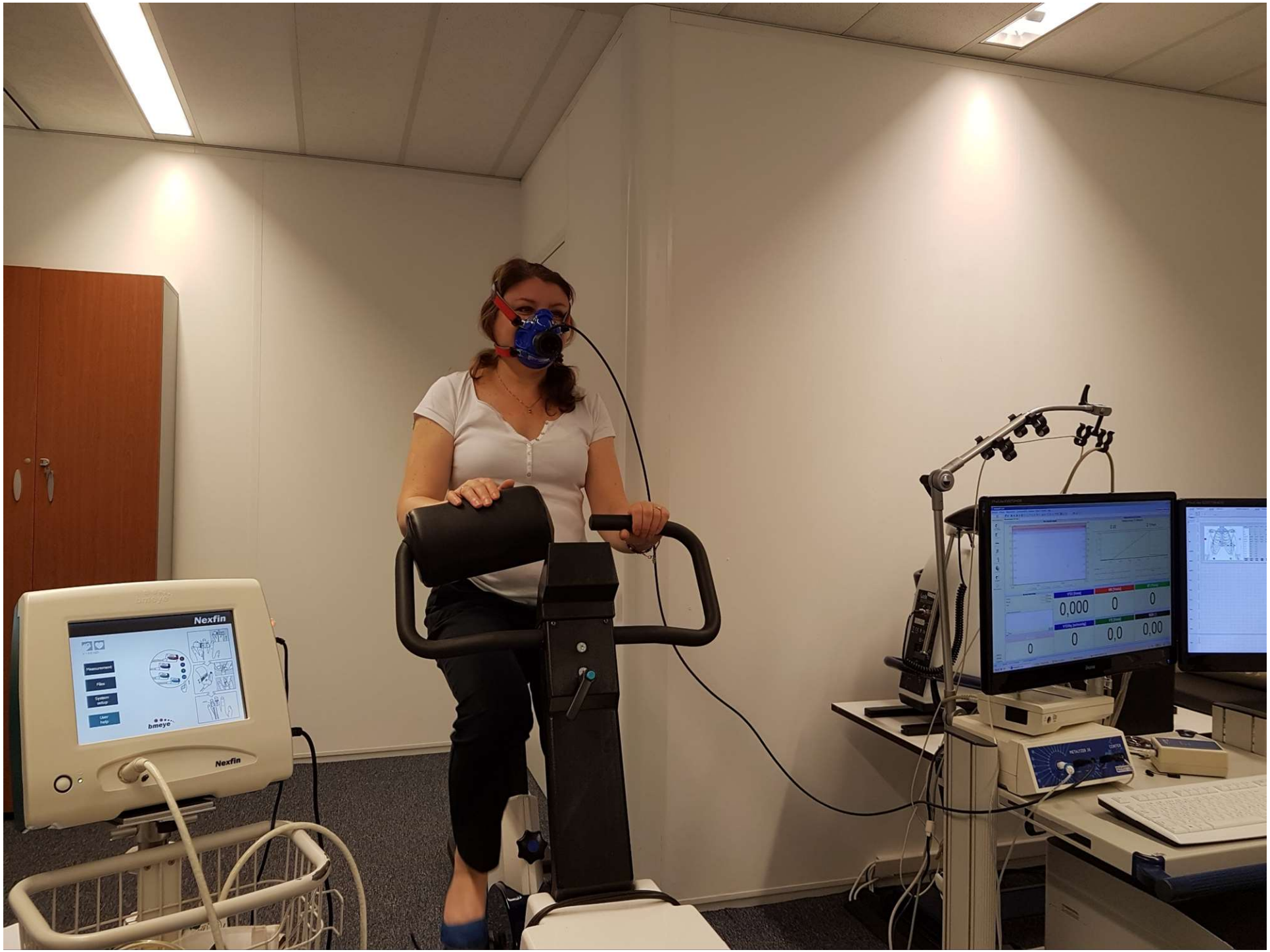
We decided to study the energy production of the muscles during stress and the adaptation of the body to increasing physical load

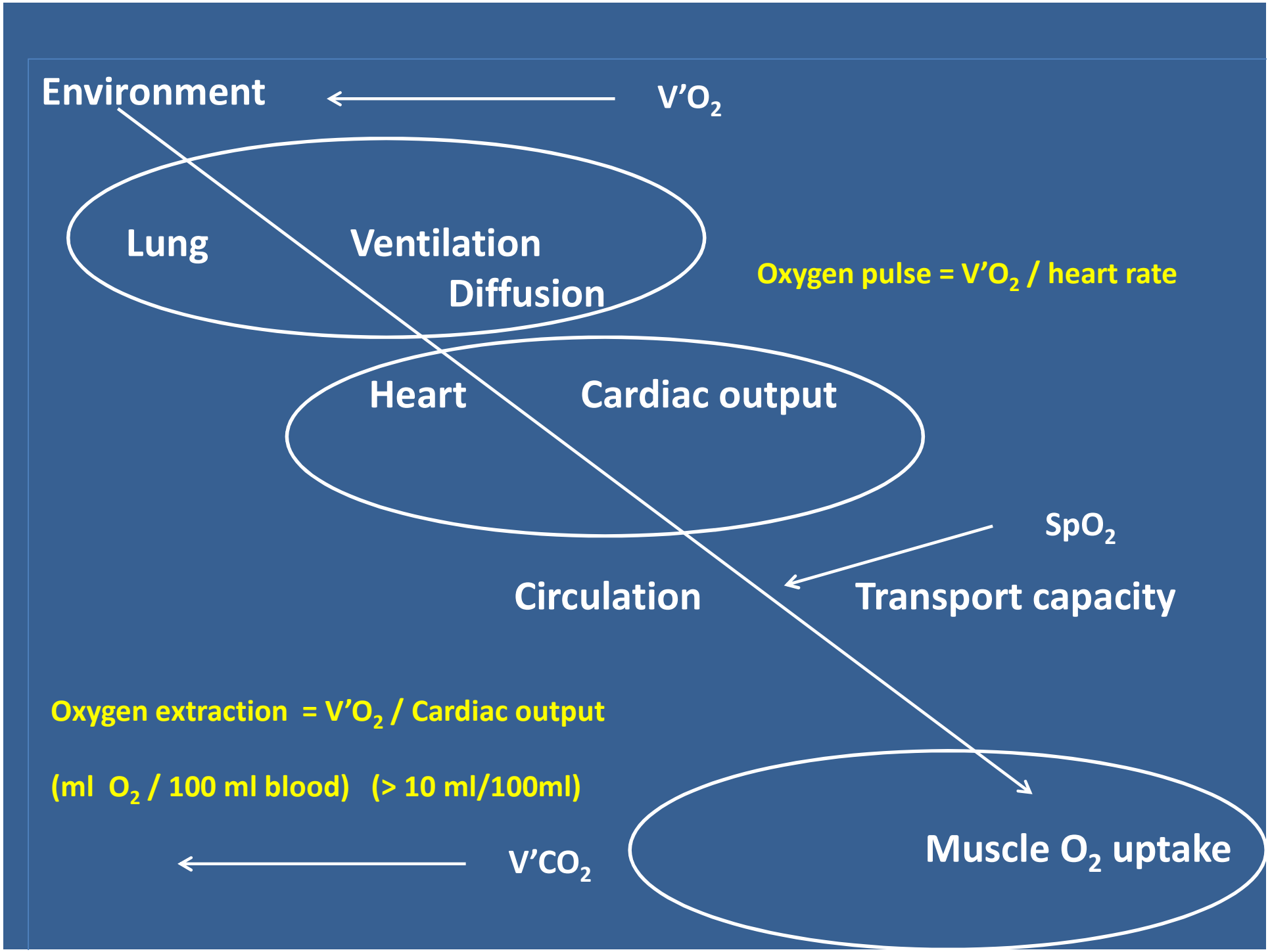
Cardiopulmonary exercise test

Diagnostic:

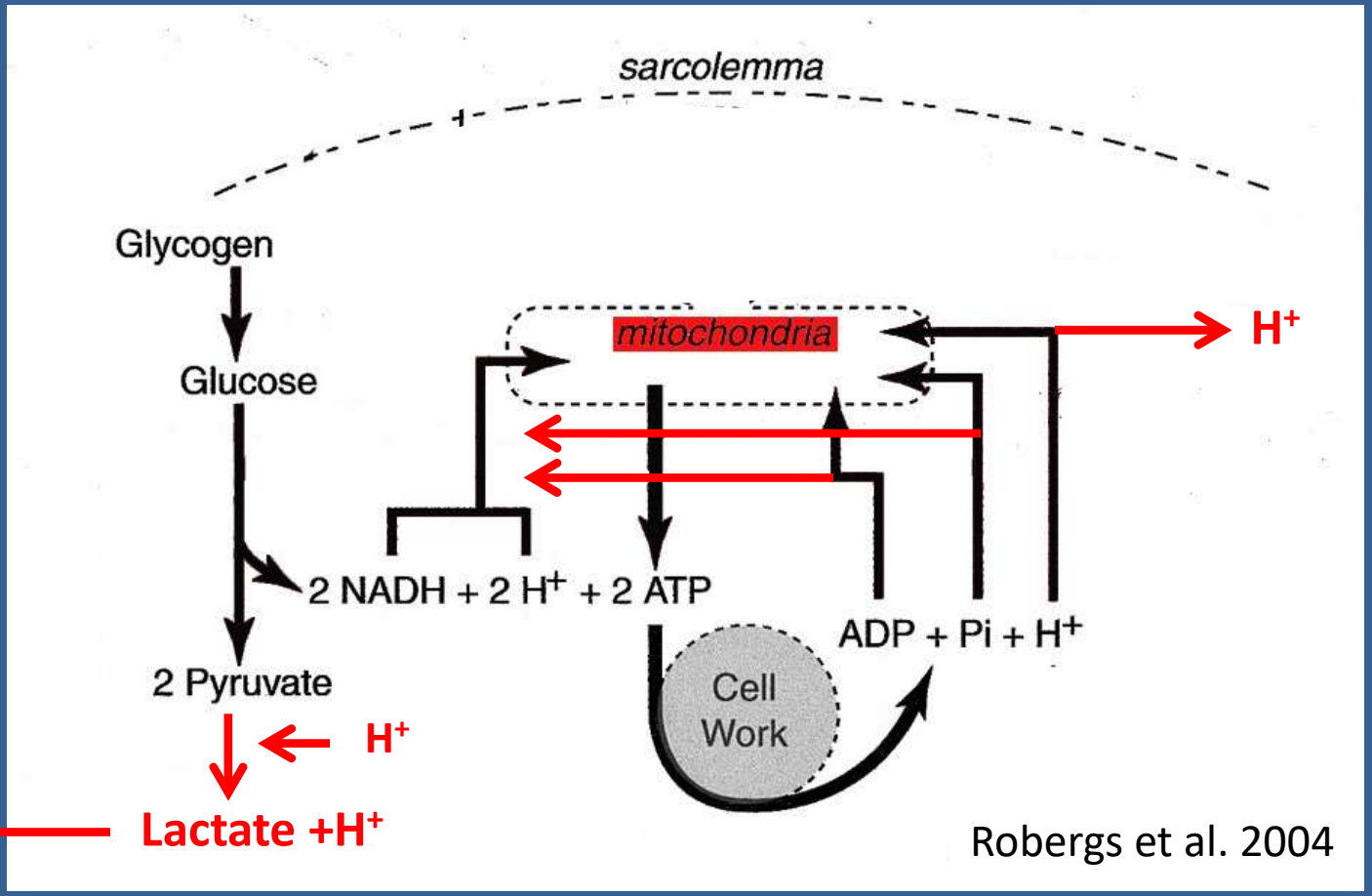
limiting factor: lungs, heart, circulation, blood, muscles

Severity of impairment


Nexfin
Measurement
Files
System setup
User help
bmeye
Nexfin


Environment
V'O2
Lung
Ventilation
Diffusion
Oxygen pulse = V'O2 / heart rate
Heart
Cardiac output
SpO2
Circulation
Transport capacity
Oxygen extraction = V'O2 / Cardiac output
(ml O2 / 100 ml blood) (> 10 ml/100ml)
V'CO2
Muscle O2 uptake

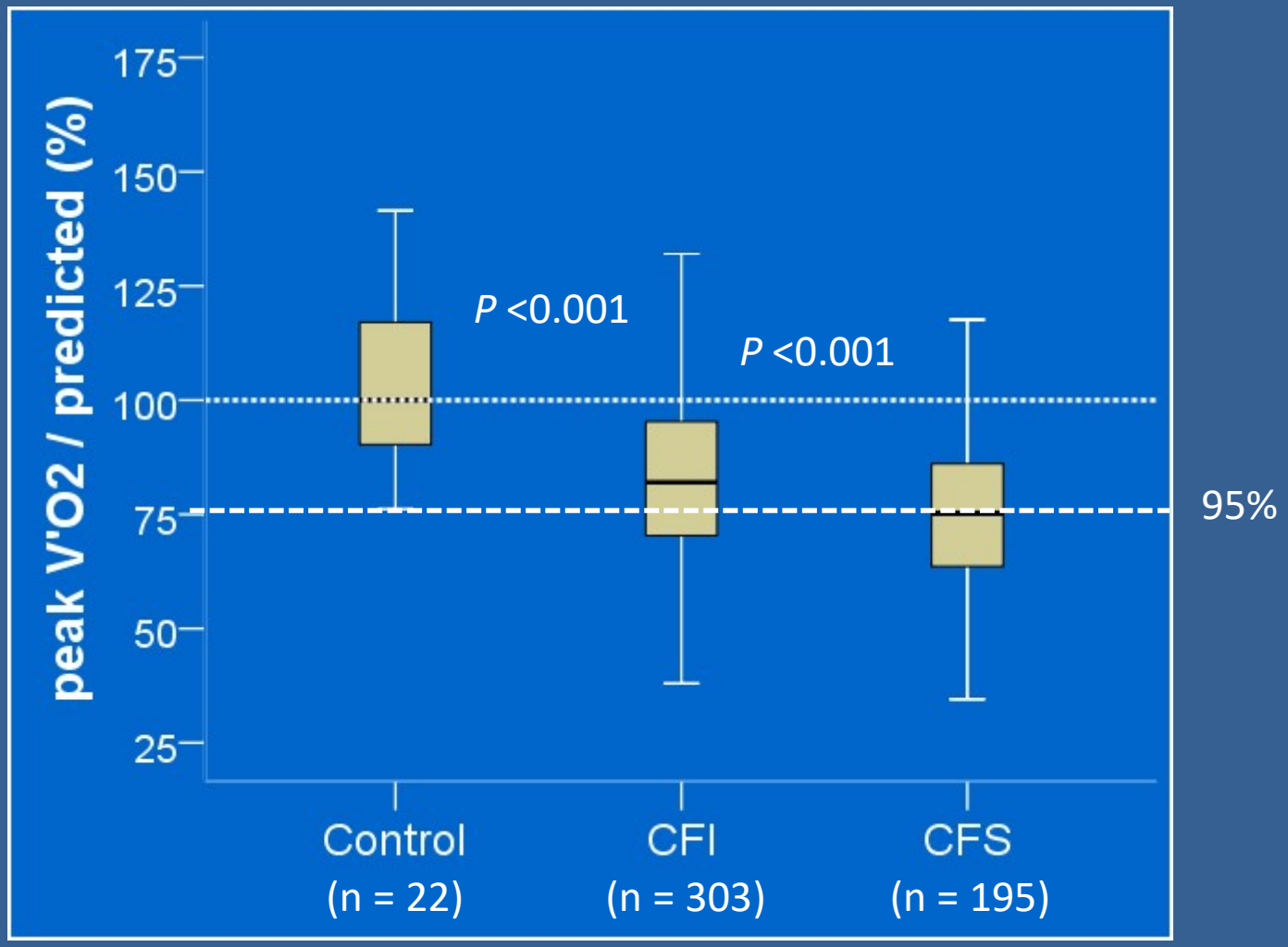
ADP, Pi and H^+ are recycled in mitochondria



Robergs et al. 2004

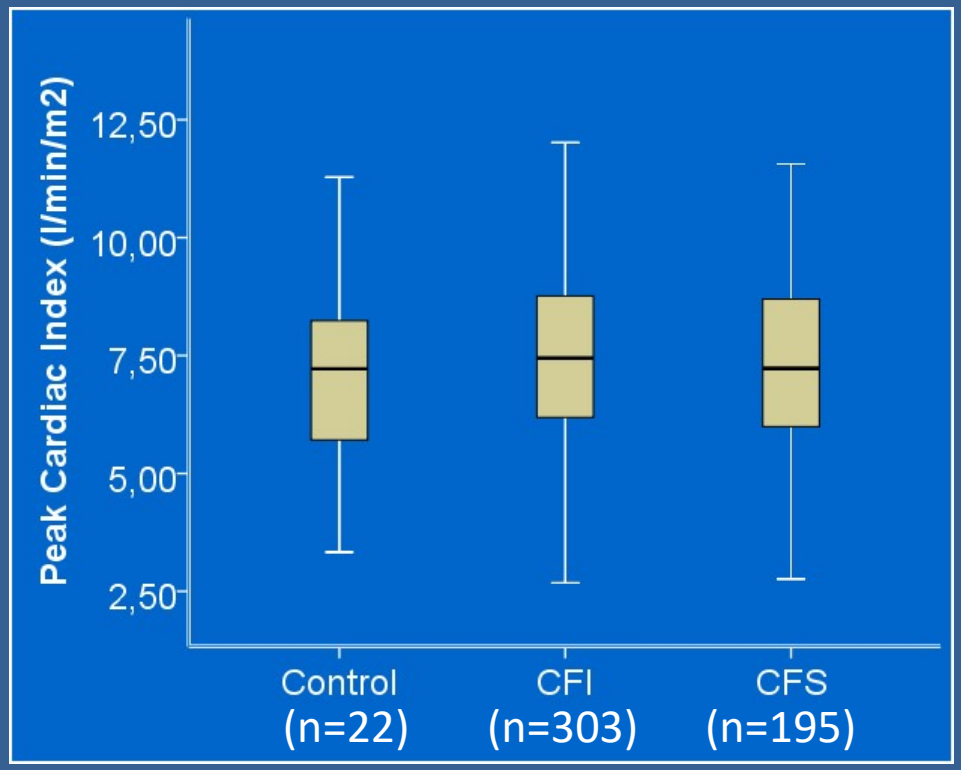
Peak V'O2 is lower in CFI and CFS patients expressed as percentage of sedentary reference (Gläser 2009 SHIP study)

(Tukey post hoc)



Cardiac Index was not different

(ANOVA)



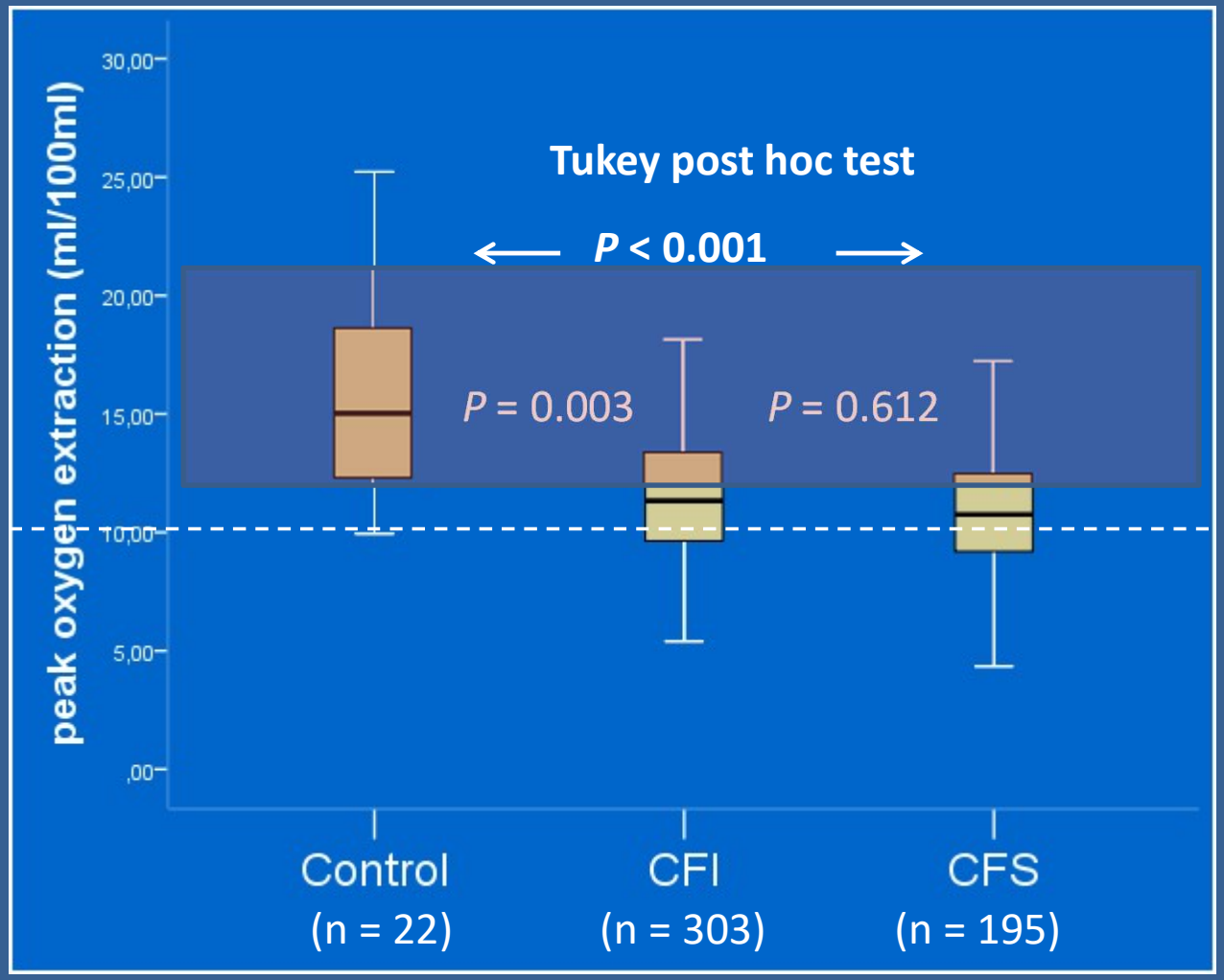
Continuous pulse contour analysis

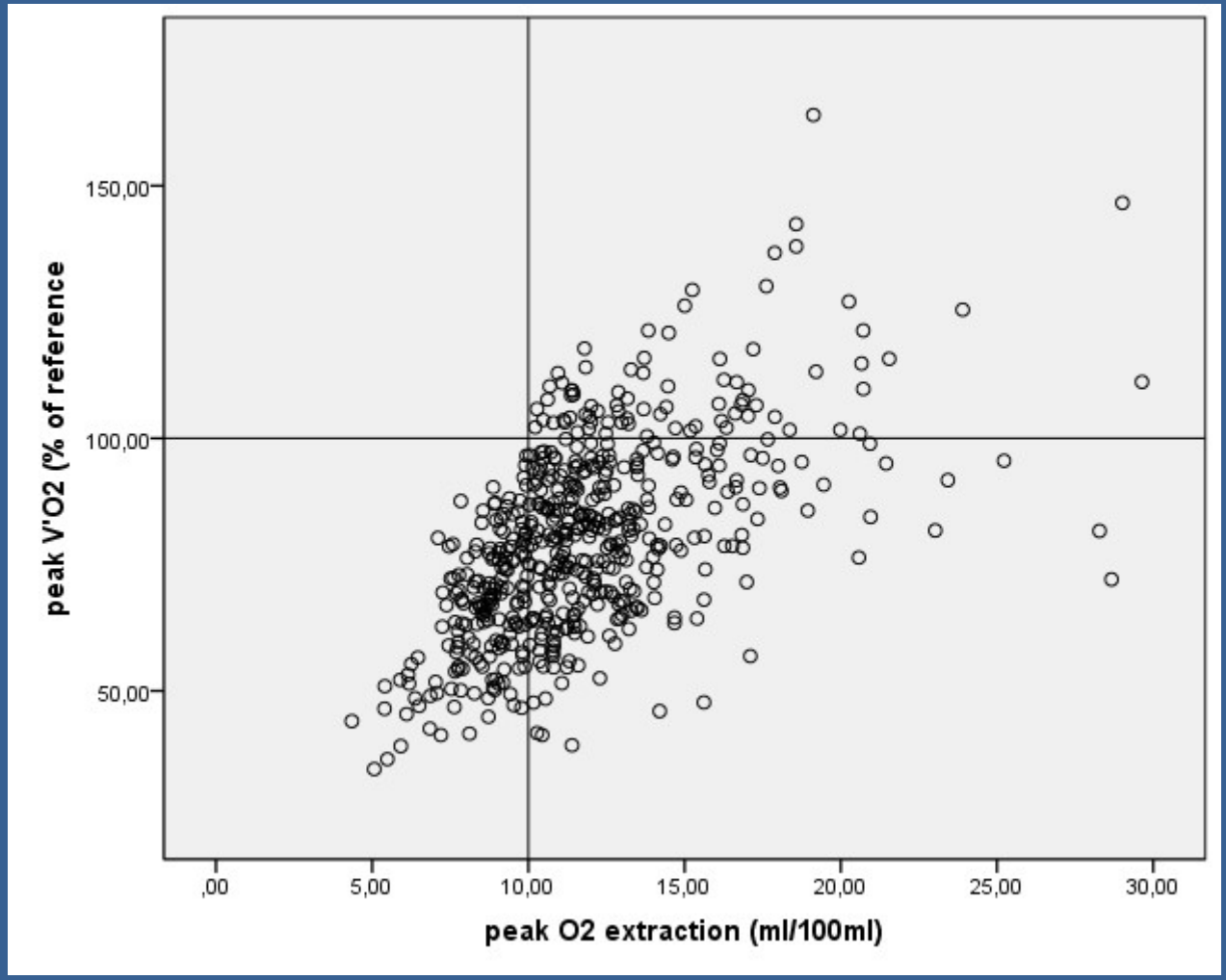
Environment

Lung	Ventilation Diffusion
Heart	**Cardiac output**
Circulation	Flow
	Transport capacity
Muscle	

Peak oxygen extraction by muscle cells was lower in CFI and CFS patients

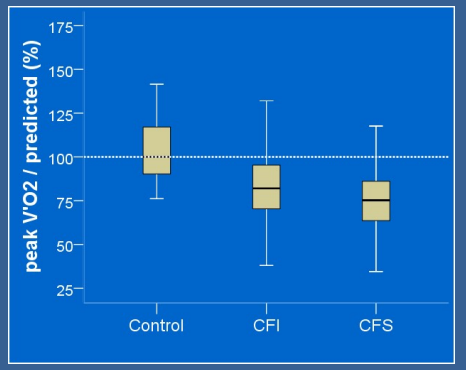
(O_2 extraction = $V'O_2$ / Cardiac output)



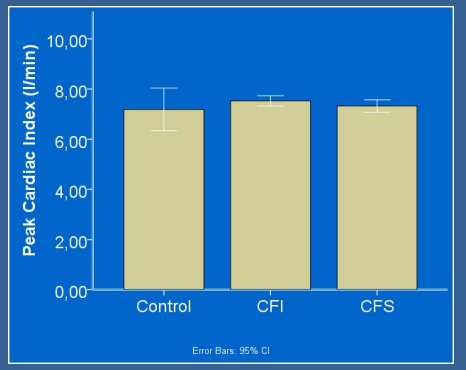

peak V'O2 (% of reference
150,00
100,00
50,00
,00
5,00
10,00
15,00
20,00
25,00
30,00
peak O2 extraction (ml/100ml)

This retrospective study indicates I:

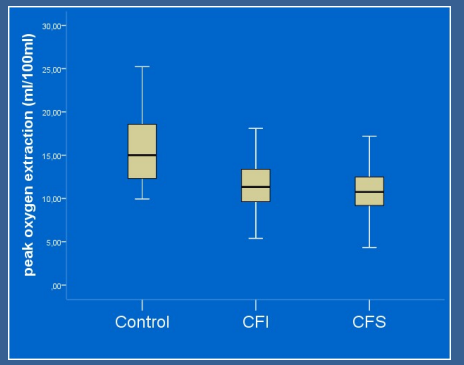
Peak O_2 uptake is low in CFS patients



Circulation is not different



Peak oxygen extraction is low in CFS patients



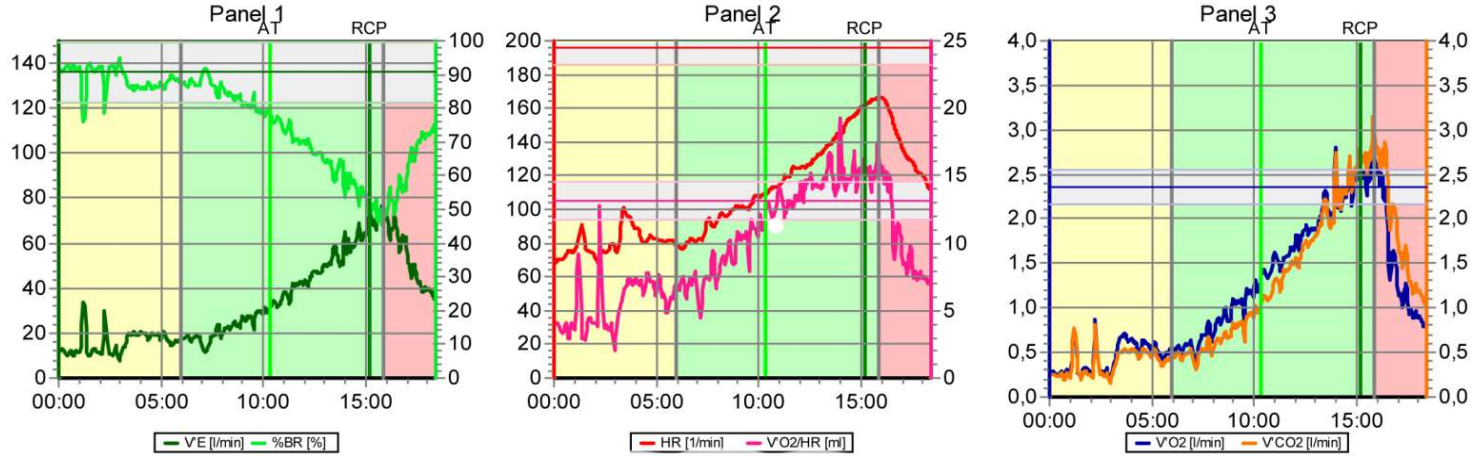
CVS Centrum Amsterdam

Harbor-UCLA 9-Panel Plot

Name:					
ID:	**A11**	Weight:	74 kg	Lean Body Weight:	-
Age:	22 years	Height:	176 cm	BSA:	1,91 m^2
Sex:	female	Physician:		BMI:	24 kg/m^2

Date:	2-5-2013, 10:56	Workload Protocol:	Ramp protocol 25 Watt/min
Duration of Test:	0:18:24		
Operator:	1. Dr R.C.W. Vermeulen		

CPX-Testing Device: MetaLyzer 3B - R2	Ambient Conditions
Exercise Device: Lode Excalibur Sport (911900)	Temperature: 24,3 °C
ECG12-Testing Device: CardioCollect	Pressure: 1019 mbar

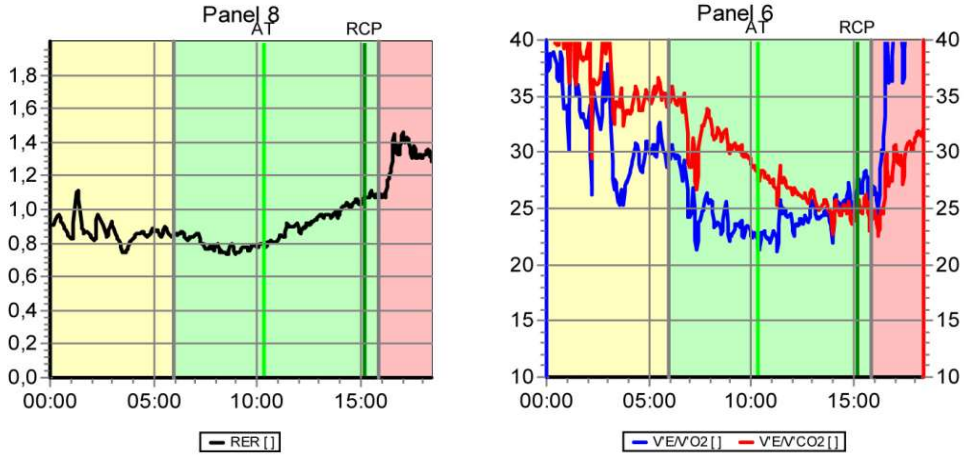


O_2 extraction: 13.84 ml/100ml

ΔQ'/ΔV'O2: 5.85

Lactate: 2' after 11.10 mmol/l

Lactate/V'O2: 5.31 mmol/l/l



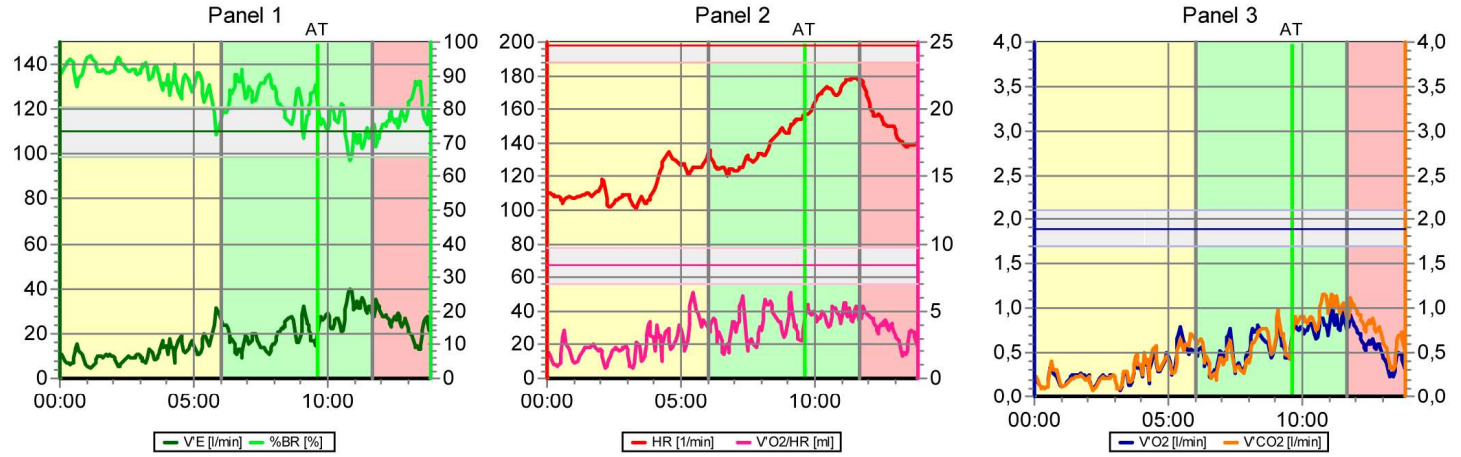
CVS Centrum Amsterdam

Harbor-UCLA 9-Panel Plot

Name:					
ID:	**V2626**	Weight:	60 kg	Lean Body Weight:	-
Age:	19 years	Height:	159 cm	BSA:	1,65 m^2
Sex:	female	Physician:		BMI:	24 kg/m^2

Date:	24-7-2013, 10:20	Workload Protocol:	Ramp Protocol 15 Watt/min
Duration of Test:	0:13:52		
Operator:	1. Dr R.C.W. Vermeulen		

CPX-Testing Device: MetaLyzer 3B - R2	Ambient Conditions
Exercise Device: Lode Excalibur Sport (911900)	Temperature: 27,2 °C
ECG12-Testing Device: CardioCollect	Pressure: 1012 mbar

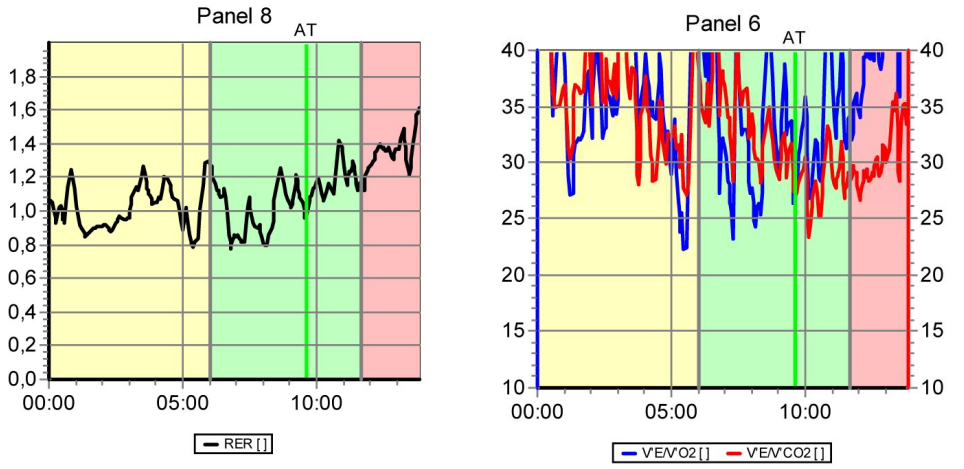


O_2 extraction: 5.40 ml/100ml

ΔQ'/ΔV'O2: 15.20

Lactate 2' post: 12.10 mmol/l

Lactate/V'O2: 21.12 mmol/l/l



CVS Centrum Amsterdam

Harbor-UCLA 9-Panel Plot

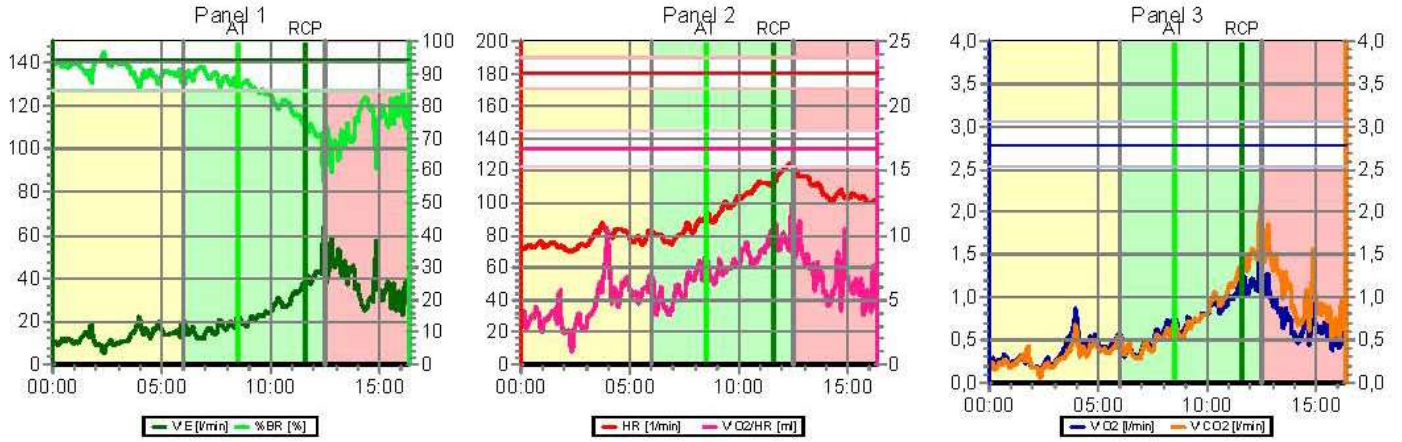
CORTEX

Name:					
ID:	**V2651**	Weight:	73 kg	Lean Body Weight:	-
Age:	45 years	Height:	177 cm	BSA:	1,90m^2
Sex:	male	Physician:		BMI:	23kg/m^2

Date:	17-10-2013, 11:34	Workload Protocol:	Ramp protocol 20 W/min
Duration of Test:	0:16:21		
Operator:	1. Dr R.C.W. Vermeulen		

CPX-Testing Device: MetaLyzer 3B - R2
Exercise Device: Lode Excalibur Sport (911900)
ECG12-Testing Device: CardioCollect

Ambient Conditions
Temperature: 24,4 °C
Pressure: 1003 mbar

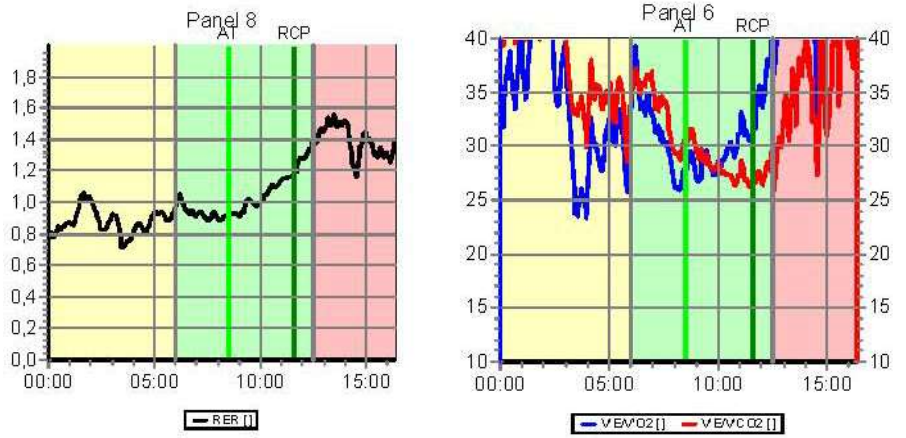


O_2 extraction: 9.54 ml/100ml

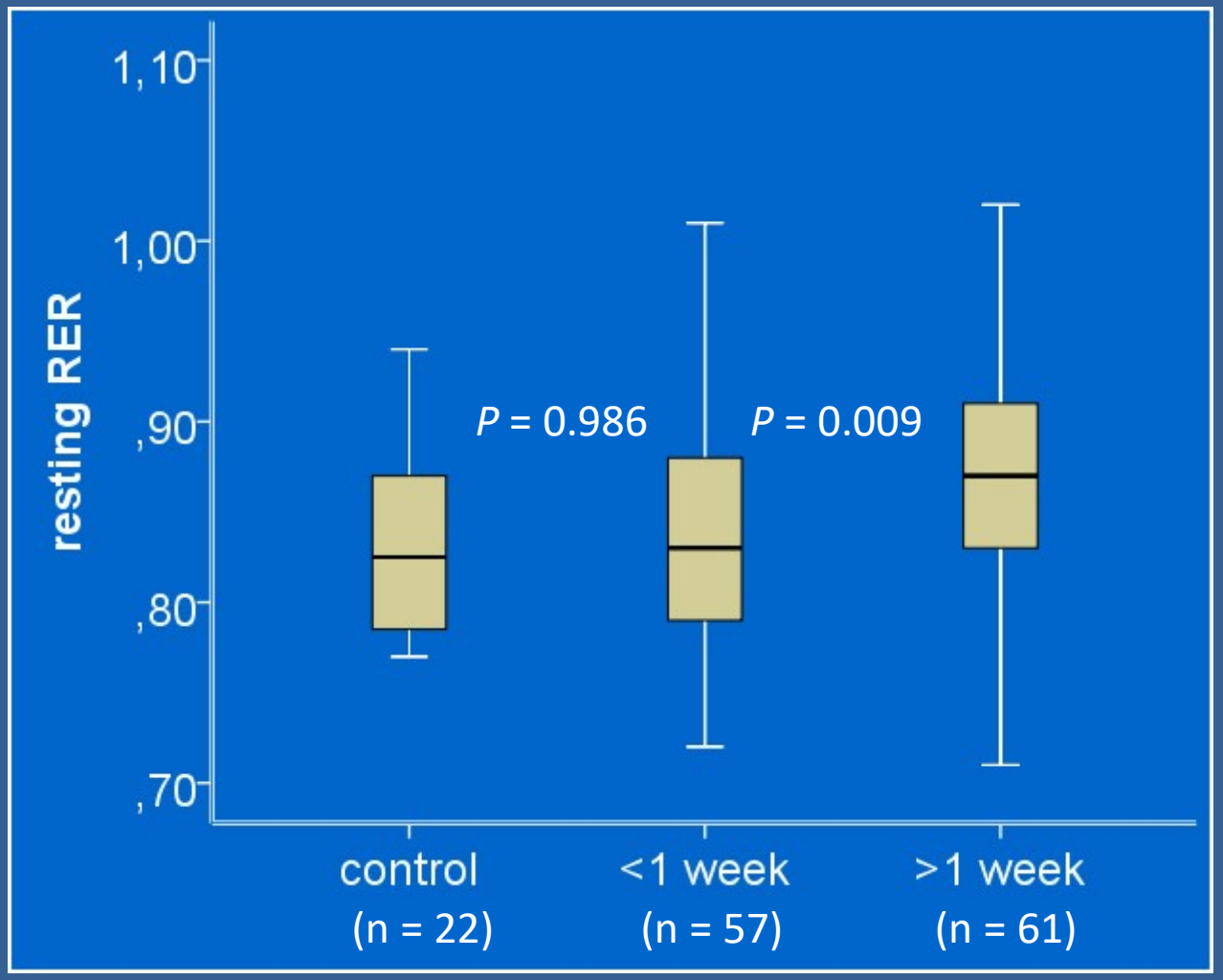
ΔQ'/ΔV'O2: 8.53

Lactate: 2' after 6.00 mmol/l

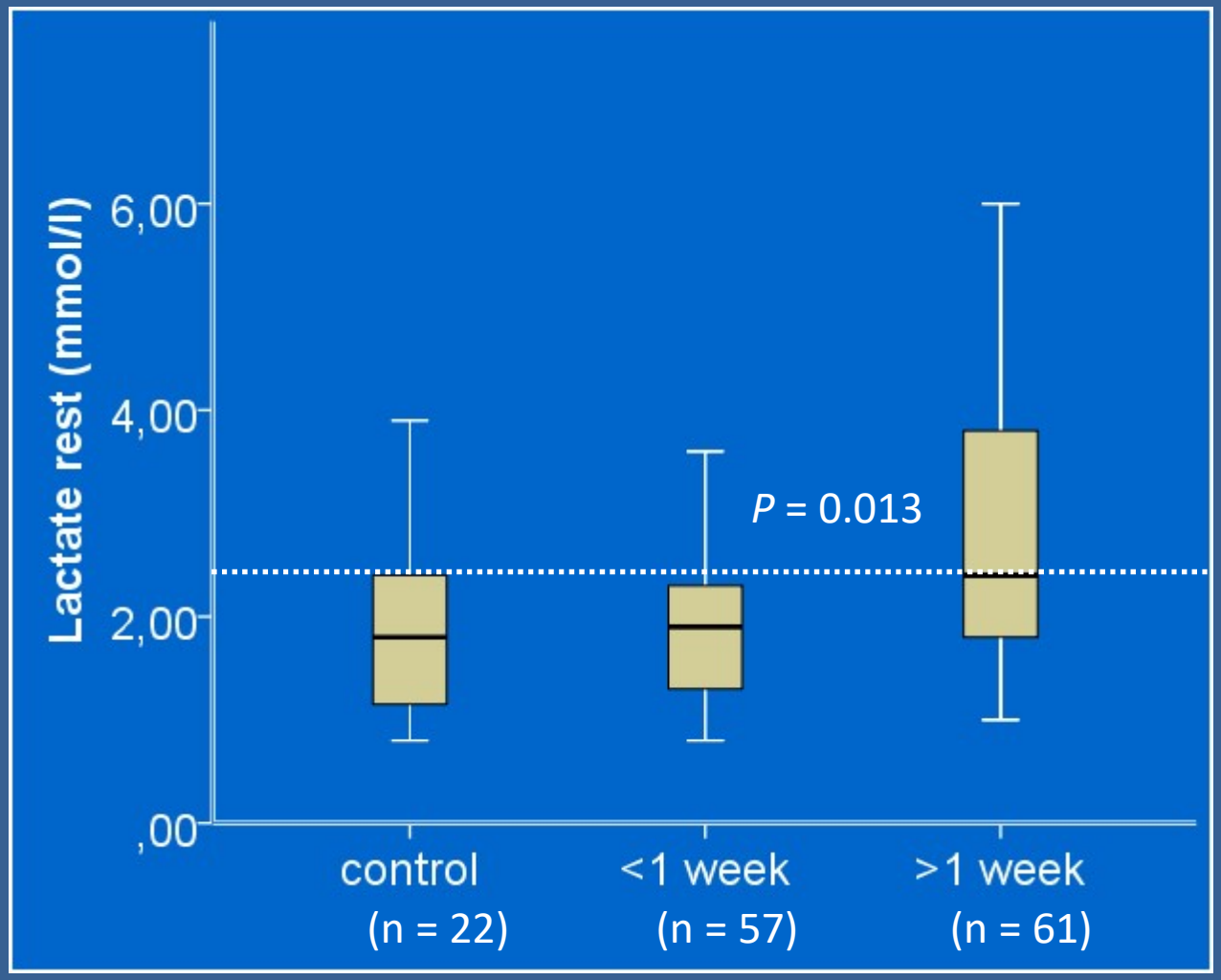
Lactate/V'O2: 7.09 mmol/l/l



Resting Respiratory Exchange Ratio is high in CFS patients with a start in > 1 week (Tukey post hoc)

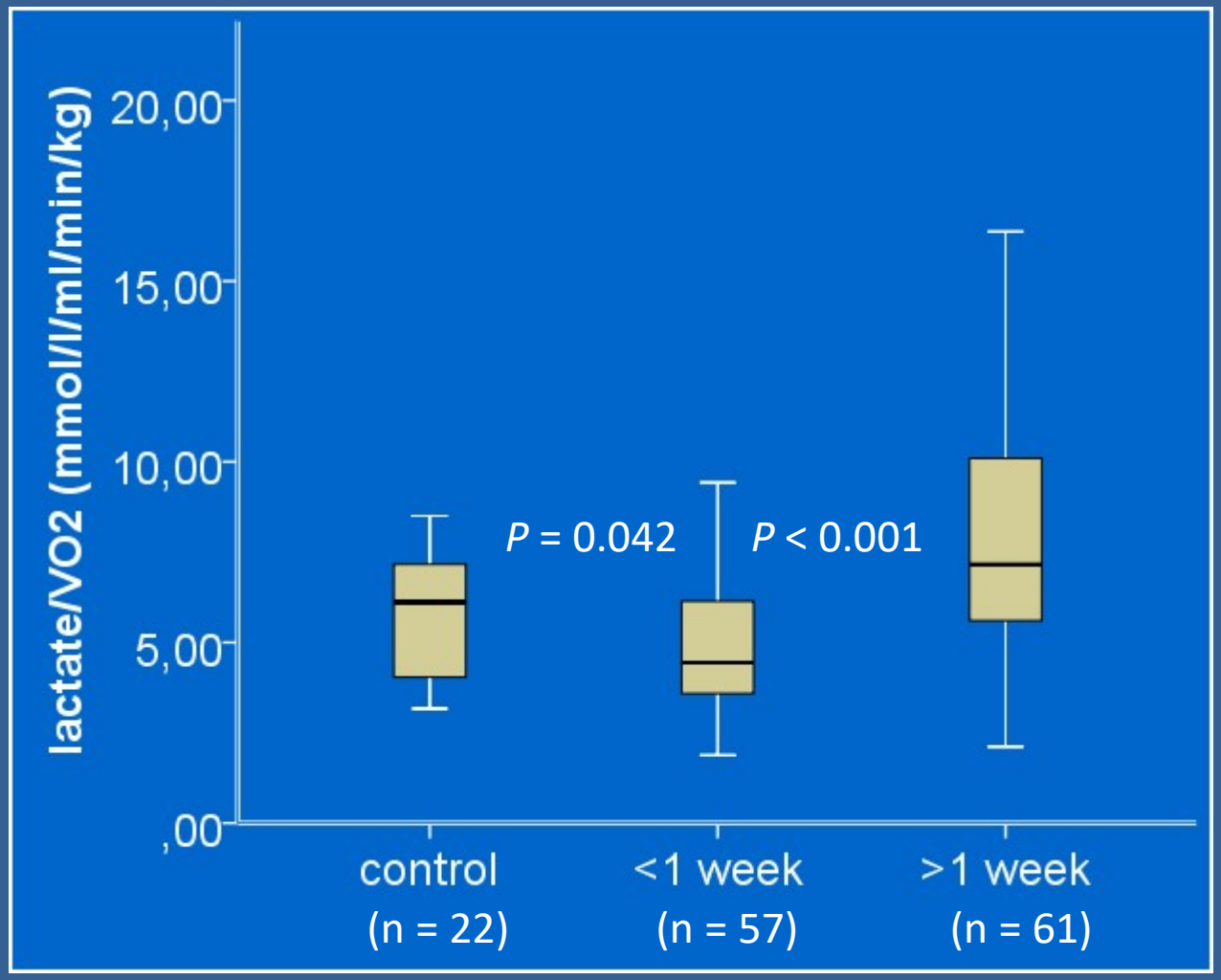


Resting lactate is high in CFS patients with a start in > 1 week (Tukey post hoc)



Lactate/oxygen uptake is low in CFS patients with a start in < 1 week and high in > 1 week

(Tukey post hoc)

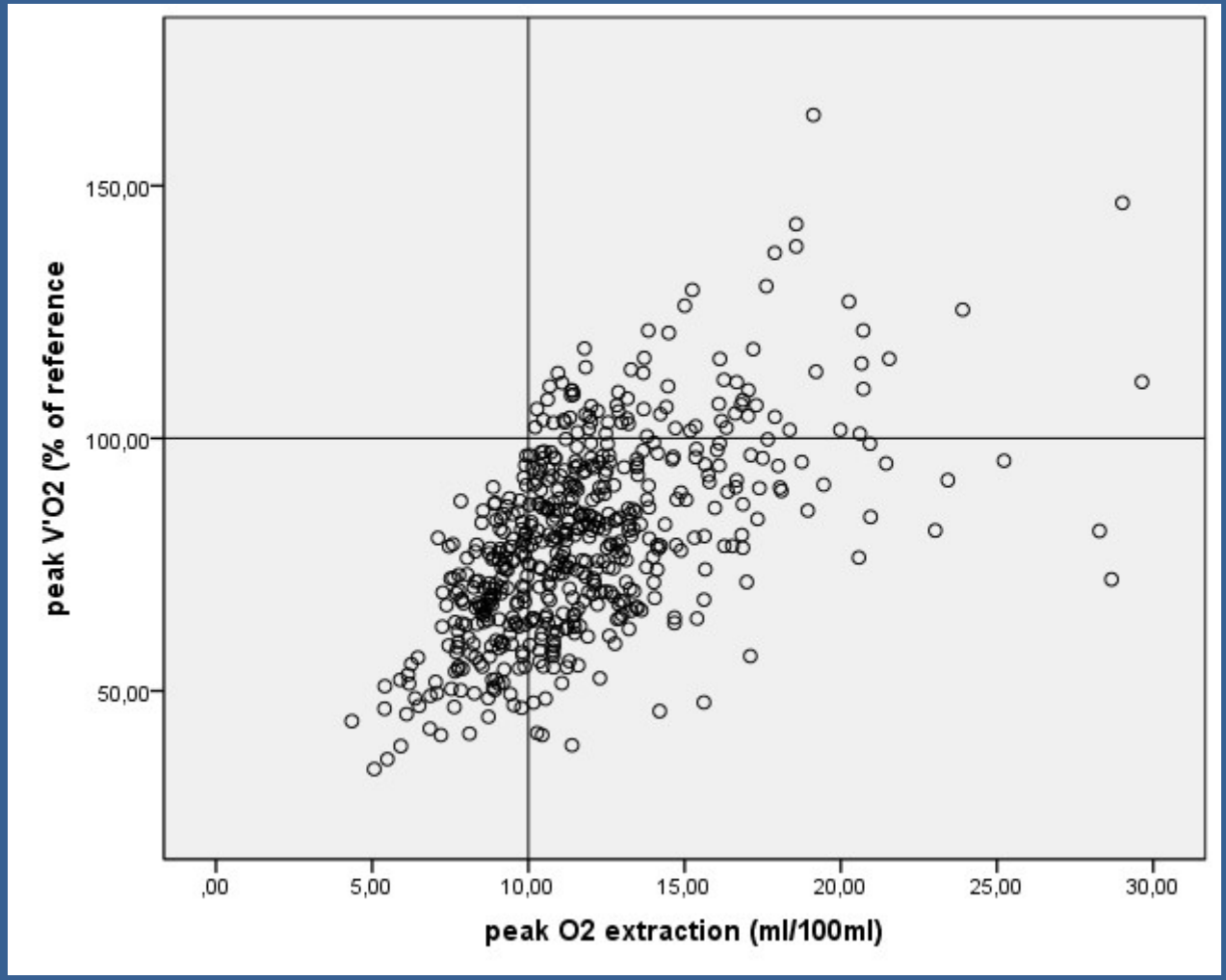


This retrospective study indicates that:

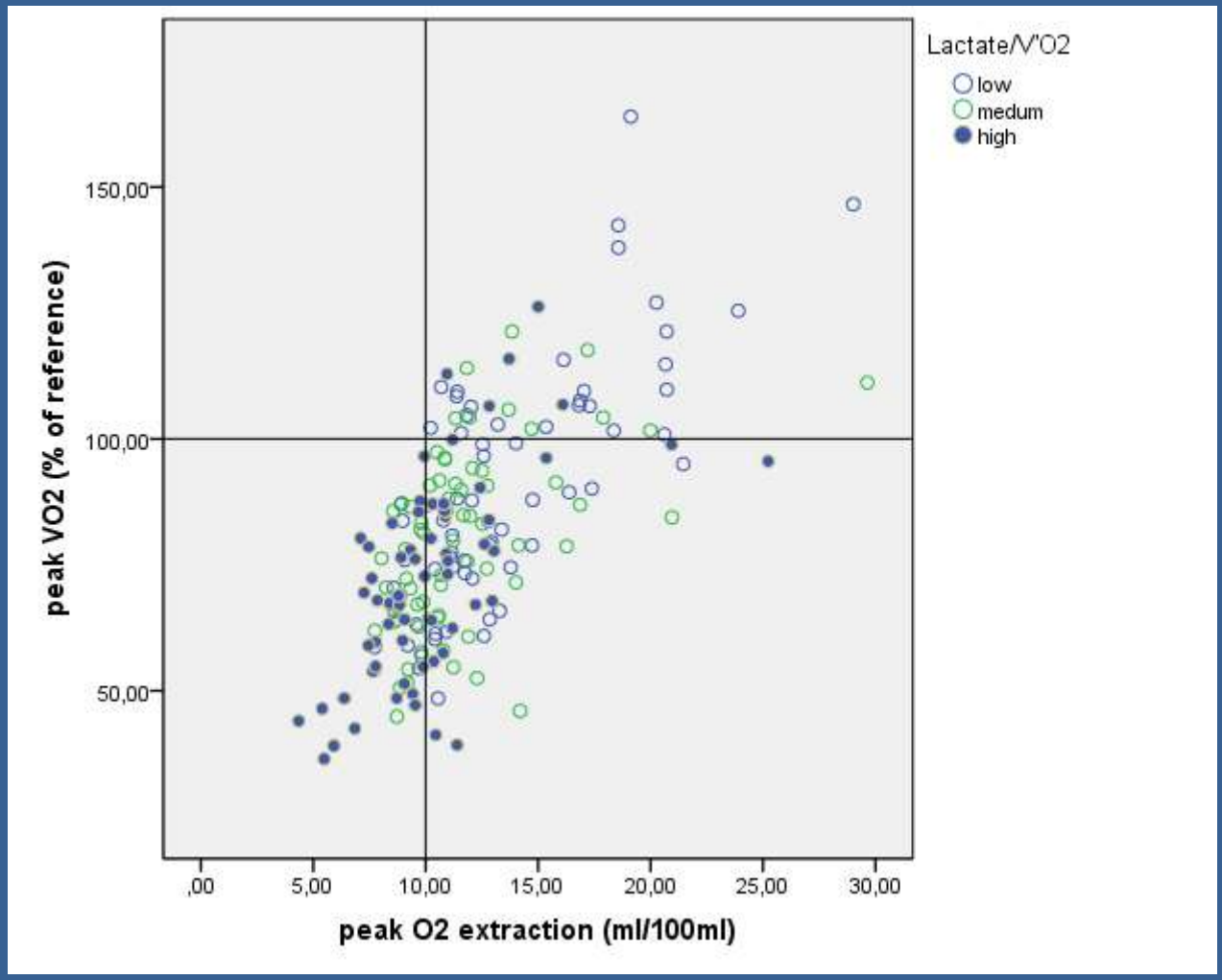
The low peak V'O2 in CFS is caused by
impaired production of ATP in muscle cells

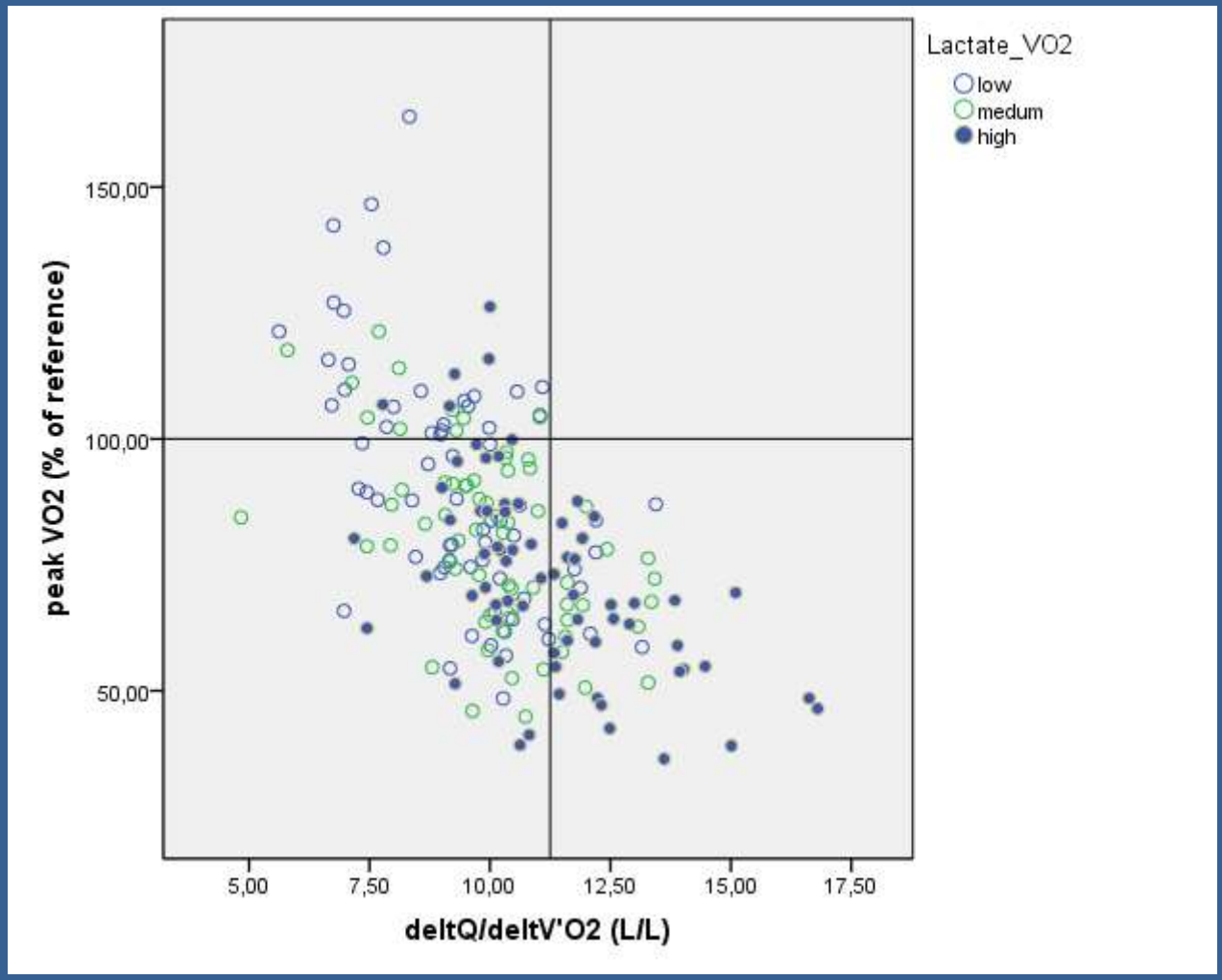
Sudden onset CFS: low lactate
Caused by downregulation?

Gradual onset CFS: high lactate
Caused by mitochondrial pathology?


peak V'O2 (% of reference
150,00
100,00
50,00
,00
5,00
10,00
15,00
20,00
25,00
30,00
peak O2 extraction (ml/100ml)

		N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Minimum	Maximum
						Lower Bound	Upper Bound		
lactate/ΔV'O2	0	39	8,9723	4,16743	,66732	7,6214	10,3232	3,45	21,12
	1	102	6,4171	2,55835	,25331	5,9146	6,9196	2,11	16,37
	2	61	5,3340	2,01965	,25859	4,8167	5,8512	1,88	12,08
	Total	202	6,5834	3,06349	,21555	6,1583	7,0084	1,88	21,12
Lactate/ΔV'CO2	0	39	5,2697	2,28297	,36557	4,5296	6,0097	2,35	11,87
	1	118	3,8814	1,43150	,13178	3,6204	4,1424	1,39	9,27
	2	62	3,5241	1,16532	,14800	3,2281	3,8200	1,49	7,17
	Total	219	4,0274	1,65769	,11202	3,8067	4,2482	1,39	11,87
Lactate/Watt	0	39	,06442	,030088	,004818	,05467	,07418	,025	,146
	1	117	,04889	,018360	,001697	,04553	,05226	,018	,101
	2	63	,04564	,016633	,002096	,04145	,04983	,018	,098
	Total	219	,05072	,021417	,001447	,04787	,05358	,018	,146


Lactate/V'O2
low
medum
high
150,00
100,00
50,00
peak VO2 (% of reference)
,00
5,00
10,00
15,00
20,00
25,00
30,00
peak O2 extraction (ml/100ml)


Lactate_VO2
low
medum
high
150,00
100,00
50,00
peak VO2 (% of reference)
5,00
7,50
10,00
12,50
15,00
17,50
deltQ/deltV'O2 (L/L)