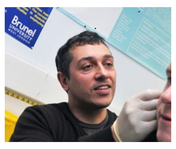

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The Existence of a 'Third Wind' Phenomenon in McArdle Disease.

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Introduction

In individuals with McArdle Disease exercise must begin at a very low relative intensity in recognition of muscle pain and the need to avoid muscle contracture and damage. This can result in the appearance of large molecular weight proteins in the general circulation posing a significant risk to renal function and, hence ultimately, to survival. Between 8-10 min of low intensity exercise 'second wind' is generally attained and is considered to be pathognomonic for McArdle disease[1] and marks a decrease in pain and heart rate. Some patients have however, reported that prolonged exercise of more than 2 hours results in another 'threshold' with further improvements in function and lessening of pathology-associated symptoms; a point that they themselves have coined 'Third Wind'. This has been the subject of much conjecture amongst members of our MDT as to whether it is an actual physical phenomenon or is psychological in nature.

Aims:

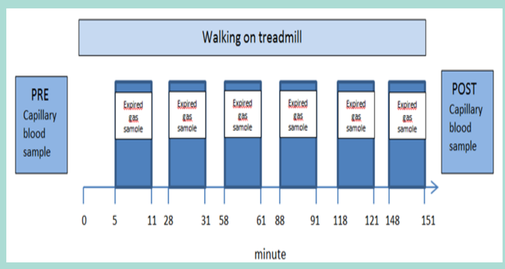
1: to establish whether or not 'Third Wind' is a physical phenomenon.

2: to attempt to run a 2.5h unbroken treadmill walk with a cohort of McArdle patients

3: to compare the McArdle group to a pathology-free control group.

Methods

Fourteen participants (6 McArdle and 8 control) walked at a self-selected pace on a motorised treadmill (Pulsar, HP Cosmos, Germany) for 151 min (2h 31min). An earlobe capillary blood sample was taken pre and post exercise to confirm absence of lactate. Expired gas was measured between min 5-11 of exercise to capture 'Second Wind' and each min by min assessment of the Rate of Perceived Pain (using the Borg CR10 Pain Scale)[2] and heart rate (Polar HR monitor, Polar Oy, Finland). Expired gas was then collected for 3 min and Rating of Perceived Exertion (RPE)[2] every 30 min during the walking protocol until min 151 when the exercise was terminated (i.e. at 2h 31 min of walking). Pre and post capillary blood samples were analysed for lactate concentration using an enzymatic-Amperometric analyser (Biosen C-line, EKF Diagnostics, Germany). The relative gram-use of fat and CHO was calculated from the expired gas[3], with16kJ per gram of CHO and 37kJ per g fat assumed.

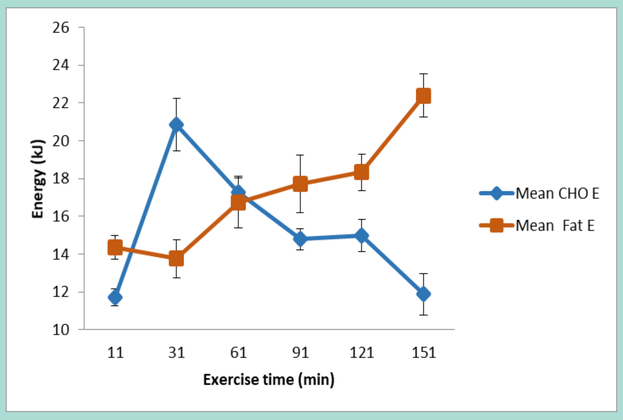


Participant	Age (yrs)	BMI ($kg \cdot m^{-2}$)	Highest $[La]_{blood}$ ($mmol \cdot L^{-1}$)	X Treadmill speed ($m \cdot s^{-1}$)	Distance in 2.5 hrs (km)	X HR (bpm)	RPE (min 11-151)
1	49	19	1.0	1.63	14.82	139	11,12,12,12,12
2	55	31	0.7	1.44	13.12	122	12,12,12,12,12
3	36	29	1.1	1.31	11.90	111	7,7,8,11,11
4	70	19	0.8	0.67	6.10	112	7,7,6,6,7
5	32	21	0.8	1.52	13.78	98	11,11,11,11,11
6	23	20	0.8	1.52	13.78	102	7,9,10,12,13

Experimental group: those with McArdle Disease

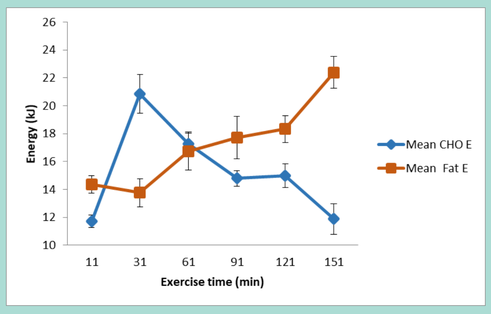
Results

The graph (right) shows the mean data for the 6 McArdle participants that completed the trial. A marked observable change can be seen at 121 min. There is a steeper rise in the slope of the fat curve indicating an increase in E from fat oxidn and a steeper decline in the CHO curve suggesting a reduction in the E derived from CHO.

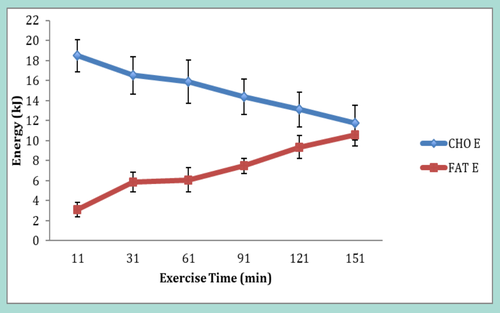


Results (cont)

When compared with the control group across the time period 11-151 min, there appears to be a sharp increase in CHO use in those with McArdle from minute 11-31 and then a steady increase in fat use with concomittent decrease in CHO use from min 31-151. In contrast for the control group there is an increase in fat use and concomittent decrease in fat use from the start.



McArdle Group



Control Group

Discussion

The main finding here is that of another apparent metabolic 'threshold', at 121 min, that can be objectively measured and which corresponds with the perception of those with McArdle Disease of a 'Third Wind'. Consistent with aim 1: 'Third Wind' can be confirmed as a physical phenomenon. Consistent with aim 2: all individuals with McArdle disease were unexpectedly able to complete 2.5h of exercise.

Aim 3 was also successfully achieved, but a difference is noted between those with McArdle disease and control participants. In the control group for min 11 there is a consistent rise in E derived from fat with a concomittent decrease in that derived from CHO. This is well-known response and one which is expected in those without pathology. In contrast, those with McArdle disease here had a sharp rise in the use of CHO from min 11-31. This is at odds with the 'norm' and reflects the increasing stabilisation following attainment of Second Wind and so, in the absence of muscle glycogen metabolism, this may be common in those with McArdle. The E deficit seen in the first 10 min is slowly rectified as increased blood flow ensures delivery of gluconeogenic substrate (glucose derived from liver glycogen and amino acids and glycerol from liver lipid catabolism) delivered via the general circulation, and from the slow to rise increase in local muscle fat oxidation.

Conclusion

Individuals with McArdle disease have a 'block' in normal CHO metabolism which restricts their exercise capacity and this is particularly pronounced at the start of any physical activity (PA). Beyond attainment of Second Wind the E demands of subsequent PA may be met by delivery of gluconeogenic substrate from the liver and local muscle fat oxidation. Question: are there other metabolic 'thresholds' either in McArdle Disease or, indeed, in other GSDs?

References

1. Vissing J: Haller RG. Ann Neurol. (2003); 54:539-542.

2. Borg GAV. *Borg's Perceived Exertion and Pain Scales*. Champaign Il. Human Kinetics, 1998.

3. Jeukendrup A; Gleeson M. *Sport Nutrition: an introduction to energy production*. Champaign Il. Human Kinetics, 2004.