Heritability of the mammalian dive response

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Introduction

The heart and brain are organs that are vitally dependent upon a continuous supply of oxygen. Interruption of oxygen supply for only a short time, as occurs during sleep apnea, stroke or heart disease, can cause permanent damage or death. The mammalian dive response is a conserved physiological trait that arises from natural selection, reflecting genotypic adaptations to prolonged apnea or asphyxia. The response is observed in both aquatic (Butler and Jones 1997), and semi-aquatic (rat and musk rat, Drummond and Jones 1979; McCulloch, Ollenberger et al. 1997) mammals, preventing permanent damage of heart and brain during prolonged apnea. A similar, although less prominent, type of response also occurs in man (Lindholm, Sundblad et al. 1999), making studies on appropriate animal models particularly relevant to humans.

Previous studies have shown a great variability in the human dive response and individual factors such as age and diving experience have been suggested to modify the bradycardia (Manley 1990; Lin and Hong 1996). It is known that that several factors induce or modify these cardiovascular responses, such as arterial hypoxia and hypercapnia, cessation of respiratory movements, and face immersion (Butler and Jones 1997; Lindholm, Sundblad et al. 1999). Even though the physiological mechanism of this response has been thoroughly investigated (Butler and Jones 1997; Lundgren and Miller 1999), no study has investigated the genetic basis of this physiological trait. However, recent research have shown that the response is repeatable within the same subject over years [Peter Lindholm, Pers. Comm.] suggesting that the trait is heritable (Terblanche, Fahlman et al. 2004).

Simple genetic traits represent only a small portion of the total genetic contribution to human health problems. Most traits with great impact on human health are complex, involving many genes that can interact with one another and with environmental factors, making the prediction of disease state for a given genotype a difficult task. For this reason, we used crosses between inbred strains of rats as a model system to study the complex genetics underlying the highly conserved mammalian dive response. The reduced intra-strain variability enabled us to maximize inter-strain variability, thus isolating strains with an outstanding dive response and those with little or no response. We therefore compared the dive response in strains of inbred and outbred rats. Rats are an excellent animal model as inbred strains are readily available, they are semi-aquatic animals that are easily trained (Galef 1980; Ollenberger, Matte et al. 1998) and possess a strong dive response during forced as well as voluntary dives (McCulloch, Ollenberger et al. 1997).

Acknowledgement: Research support came from a NSERC Discovery grant to DRJ. The experiments reported herein were approved by the UBC Animal Care Committee. We would like to thank Diana Temple for editorial help and Liz Montcalm-Smith for helping us print this poster. We also thank Shawn Soutierre for helpful comments on the experimental design for this project.

Objective

1. **Determine if the mammalian dive response is heritable.**
2. **Determine if this trait is dominant and controlled by a single gene.**

Methods

Animals: **18 male animals were used. 12 animals from two inbred strains (S1 and S2) and 6 animals from an outbred strain (S3).**

Training: **Newly weaned animals (~100 g) were trained to dive twice daily. Dive durations were increased based on the comfort of the animal until a maximum of 40 sec.**

Surgery: **At a body mass of ~150 g, ECG electrodes were implanted subcutaneously under gas anaesthesia. Electrodes exited in the neck and were anchored to the underlying tissue.**

Experiments: **After 4 days of recovery, animals were dived once for 40 sec for 3 days.**

Results

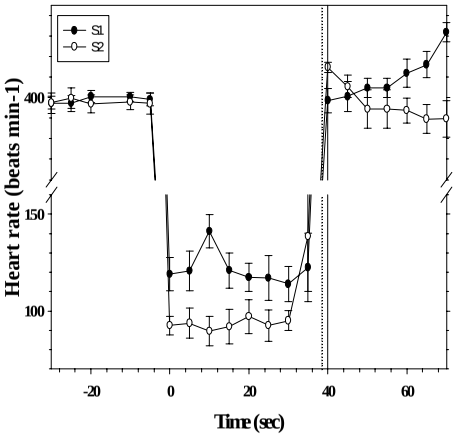
-Body mass ranged from 169.2 to 206.9 g during experimental dives and there were no differences between strains.

-Pre-dive resting heart rate variability was > 80% higher in the outbred strains as compared with the inbred strains.

-Heart rate variability during diving was > 19% higher in the outbred strain as compared with the inbred strains.

-Resting *f*H before diving was not different between inbred strains (S1: 400.0 ± 18.6 beats min^{-1} vs. S2: 395.0 ± 18.1beats • min^{-1}) but there was a significant difference in the diving bradycardia (S1: 120.9 ± 24.5 beats • min^{-1} vs. S2: 92.8 ± 21.2 beats • min^{-1}).

-There were no differences in post-dive *f*H between inbred strains (S1: 410.0 ± 30.8 beats • min^{-1} vs. S2: 400.9 ± 31.5 beats • min^{-1}).



Summary

-Reduced genetic variability of the inbred strains as comapred with the outbred strain reduced biological variability in heart rates. These data show that a significant portion of heart rate control is genetic.

-There was a significant difference in the dive response between inbred strains which shows that a portion of the mammalian dive response is heritable.

Point of contact

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