



ACCLIMATION ALTERS STRESS GENE AND CYTOKINE EXPRESSION IN RAT LUNG

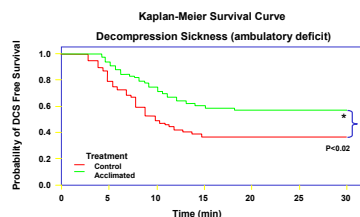
Ye Chen, Christine Schlaerth, Richard M. McCarron

Undersea Medicine Department, Combat Casualty Care Directorate, Naval Medical Research Center, Silver Spring, MD 20910



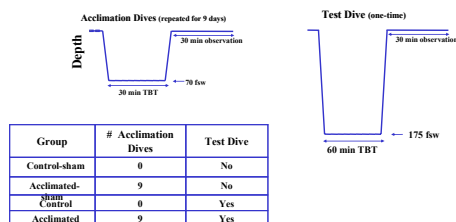
INTRODUCTION

Acclimation is the phenomenon by which an organism develops functional compensation over a period of time in response to a specific environmental factor. Our previous studies showed that animals acclimated to rapid decompression after repeated exposure to hyperbaric/decompressive stress. The goal of this study was to characterize the changes in inflammatory and stress related gene expression associated with acclimation to rapid decompression.

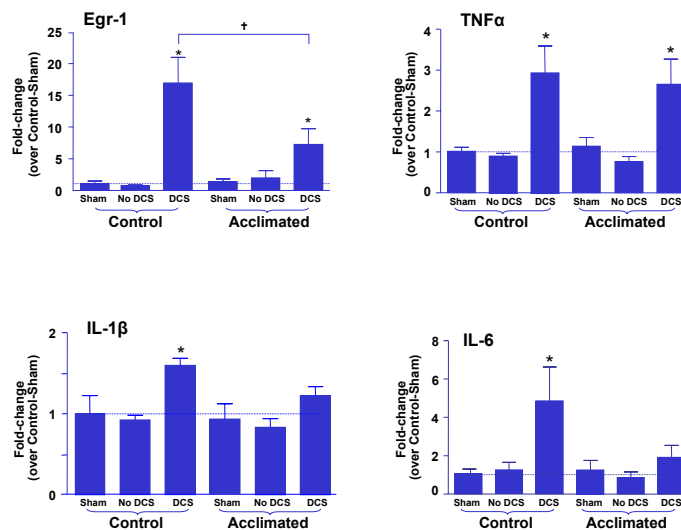


MATERIALS & METHODS

Rats were divided into 4 groups: (1) Control-sham: naïve rats; (2) Acclimation-sham: received 9 acclimation dives (70 fsw 30 min); (3) Control: received a test dive (175 fsw 60 min); and (4) Acclimation: received 9 acclimation dives and a test dive. After the test dive, rats were decompressed rapidly and observed for DCS (ambulatory deficit) by walking 30 min on a rotating cage. Total RNA was isolated from lung tissue and 13 genes were examined by real-time PCR.

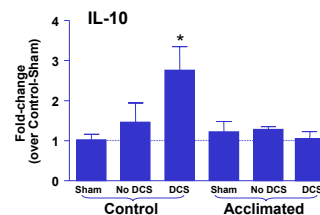


RESULTS



Gene List

- CD14 antigen (CD14)
- monocyte-chemoattractant-protein-1 (MCP-1)
- macrophage inflammatory protein-1b (MIP-1b)
- early growth response-1 (Egr-1)
- interferon gamma (IFNγ)
- interleukin 1 beta (IL-1b)
- interleukin 6 (IL-6)
- interleukin 10 (IL-10)
- selectin, endothelial cell (E-Selectin)
- transforming growth factor alpha (TGFα)
- tumor necrosis factor (TNFα)
- tumor necrosis factor receptor (TNFRI)
- vascular endothelial growth factor (VEGF)



RESULTS

The expression of immediate early gene/transcription factor Egr-1 was observed in both control and acclimated animals that had DCS, but not in non-DCS animals. The increase of Egr-1 in control-DCS was significantly greater than the acclimated-DCS animals. Both TNFα and IL-1β were significantly elevated in control-DCS animals. TNFα increased, while IL-1β decreased, in acclimated-DCS animals compared to control-DCS animals. Another cytokine, IL-6, also significantly increased in control-DCS but not in acclimated-DCS animals. Anti-inflammatory cytokine IL-10 significantly increased in control-DCS but not acclimated-DCS animals.

CONCLUSIONS

This study demonstrates that decompressive stress significantly increases expression of immediate early stress and cytokine genes in animals with DCS. Acclimated animals with DCS had decreased levels of immediate stress and cytokines gene expression. Our findings suggest a relationship among the significantly regulated factors. Decompression stress rapidly increased the transcription of Egr-1. Egr-1 protein binds to the TNFα promoter to increase transcription and release a cytokine cascade including IL-1β and TNFα initially, subsequently leading to the production of IL-6, as well as IL-10. This may produce a negative feedback on the cascade.



Acknowledgement: This study is supported by ONR grant work unit 600226N-0022-1-0000-0001 conducted according to the principles set forth in the "Guide for the Care and Use of Laboratory Animals" (NRC 1996) and was approved by the WRAIR/MRC IACUC. The opinions expressed here are those of the authors and do not reflect the official policy of the Department of the Navy, Department of Defense or the U.S. Government.