

EFFECT OF GLUTATHIONE DEPLETION AND AGE ON SKELETAL MUSCLE PERFORMANCE DURING A CHRONIC STRETCH-SHORTENING CONTRACTION EXPOSURE

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INTRODUCTION

The age distribution of the workforce in the United States is predicted to shift to older workers (Bureau of Labor Statistics, 1999). We have recently shown in a rat model that aging has a profound effect on the ability of skeletal muscle to adapt to repetitive mechanical loads (Cutlip et al., 2006). Oxidative stress production following high-intensity mechanical loading has been suggested to lead to negative changes in force production (McArdle et al., 2001), especially with aged skeletal muscle. Modulating the oxidative stress profile and quantifying the resulting adaptive response would prove beneficial in broadening our understanding with respect to repetitive-loading induced adaptations.

Glutathione is a major antioxidant in the cell and serves various functions such as directly acting as a reducing agent and recycling radicals generated from other antioxidant molecules. Glutathione depletion can be accomplished using L-Buthionine Sulfoximine (BSO), which is an irreversible inhibitor of γ -glutamylcysteine synthase (GCS). BSO has been well-documented both physiologically and biochemically to chronically deplete levels of glutathione, and animals dosed with BSO would be expected to be more vulnerable to mechanical loading-induced oxidative stress and performance deficits.

The effect of age and glutathione depletion on the ability to adapt to a chronic exposure of stretch-shortening cycles (SSCs) has not

been studied. We hypothesized that age and glutathione depletion negatively affects the ability to adapt to repetitive exposures of SSCs.

METHODS

All testing was performed on male Fischer Brown Norway Hybrid rats (F344 x BN F1, N = 32) obtained from the National Institutes on Aging colony. Young adult (N=16, 330g \pm 28 g SD, 12 weeks of age) and old (N= 16, 588g \pm 32 g SD, 30 months) rats were housed in an AAALAC accredited animal quarters. Young adult (N=8) and old (N=8) animals were dosed with 10mM of BSO in drinking water. The response of the dorsiflexor muscles to isometric and stretch-shortening contractions (SSC) were quantified *in vivo*. Young and old rats underwent exposure to 8 sets of 10 SSCs, 3 times/week, for 4.5 weeks duration. Performance was assessed by isometric testing and dynamic muscle function testing via a single SSC (Table 1).

Table 1. Experimental Protocol

Step	Young BSO and Vehic(N=16)	Old BSO and Vehic (N=16)
1	Isometric Test (90 deg)	Isometric Test (90 deg)
2	1 Stretch-Shortening Contraction 70°-140°-70° ankle angle @ 500 deg/s	1 Stretch-Shortening Contraction 70°-140°-70° ankle angle @ 500 deg/s
3	8 sets of 10 intermittent Stretch-Shortening Contractions at 90°-140°-90° ankle angle @ 60 deg/s	8 sets of 10 intermittent Stretch-Shortening Contractions at 90°-140°-90° ankle angle @ 60 deg/s
4	Isometric Test (90 deg)	Isometric Test (90 deg)
5	1 Stretch-Shortening Contraction 70°-140°-70° ankle angle @ 500 deg/s	1 Stretch-Shortening Contraction 70°-140°-70° ankle angle @ 500 deg/s

The performance parameters used to evaluate the force changes were isometric force, F_{max} (i.e, the maximum force

achieved in the eccentric contraction), and negative work (eccentric work). These parameters were generated from the pre-test isometric (step 1) and the pre-test SSC (step 2).

RESULTS AND DISCUSSION

The isometric force of both the young BSO and vehicle group improved over the 4.5 week exposure while the old groups remained static (Fig 1). The peak eccentric force (F_{max}) and negative work both showed similar patterns as the isometric force (Figs 2 and 3).

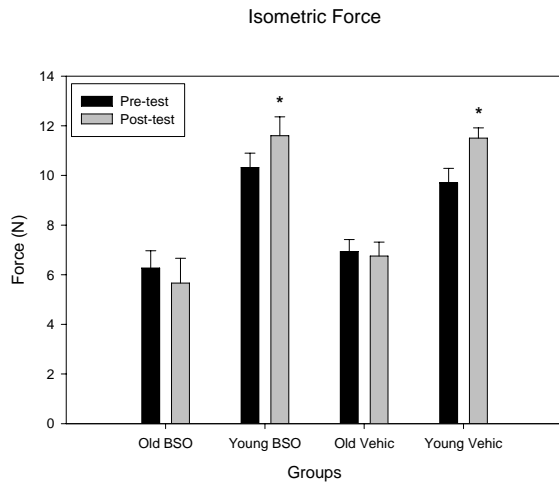


Figure 1: Isometric Force of the old and young BSO and vehicle treated groups.

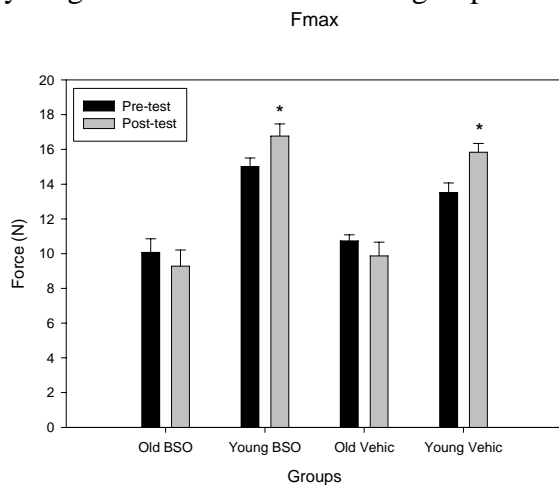


Figure 2: Peak eccentric force of the old and young BSO and vehicle treated groups.

SUMMARY

The young BSO and vehicle groups adapted positively to the chronic exposure while the old animals did not. Glutathione depletion did not have a negative effect on performance in either age group. These results suggest that compensatory mechanisms are age-dependent and allow for adaptation to repetitive mechanical loads even when the glutathione pathway is compromised.

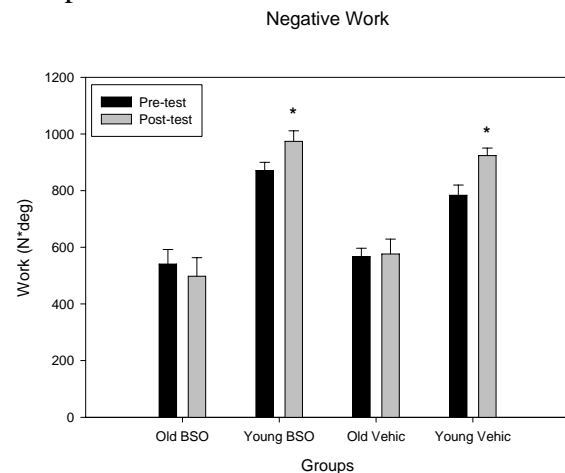


Figure 3: Negative Work of the old and young BSO and vehicle treated groups.

DISCLAIMER

The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the National Institute for Occupational Safety and Health.

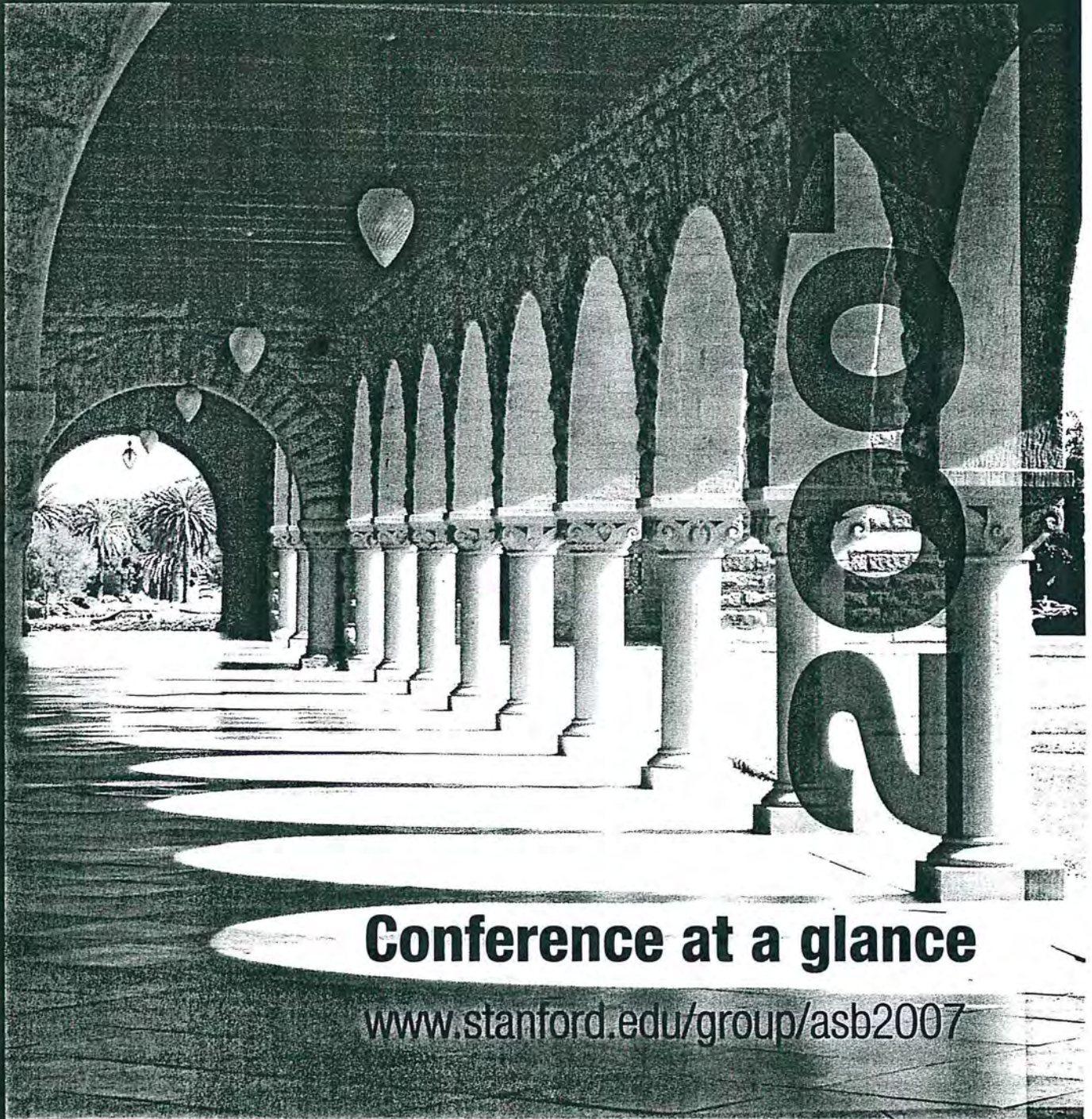
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