CHAPTER FIVE:

DISCUSSION

SUMMARY

The present study sought to determine whether the SR of skeletal muscle from aged animals is more susceptible to the deleterious effects of ROS. The study concluded that uptake and release rates are decreased in SR from aged animals. Also, HOCl affects Ca^{2+} uptake by similar extents in adult and aged animals. H_2O_2 evokes greater Ca^{2+} release is aged animals. This suggests that Ca^{2+} release channel of aged animals is more susceptible to ROS.

GENERAL DISCUSSION

Animal studies show that muscle mass and force decreases, but the extent of reduction varies from muscle to muscle (Klitgaard et al., 1989; Eddinger et al., 1995; Lynch et al., 1993; Brown and Hasser, 1996). Klitgaard and coworkers showed a 29% decrease in force production in the soleus (a slow muscle) between 9 and 24 months, with no further changes at 29 months. Larsson and Edström (1986) found no difference in force production between young (6 mo.) and old (20-24 mo.) in the soleus or tibialis anterior when the cross-sectional area (CSA) was asserted in the results. The force production of skinned fibers from the extensor digitorum longus (EDL) in rats aged 9 and 30 months showed no difference (Eddinger et al., 1985). But, they also found a increase in the force production of the soleus from old rats. Lynch et al.(1993), also found no significant differences in force in the EDL between adult and old rats using skinned fibers. The soleus force production of these rats was unchanged. In a study by Brown and Hasser (1996), they found a significant age-related decrease in muscle mass after 28 months in male Fischer 344/Brown Norway hybrids. The study showed a muscle mass reduction in the soleus (18%), extensor digitorum longus (EDL-16%), plantaris (37%), and gastrocnemius (38%).

In this present study, it was concluded that a reduction in the gastrocnemius was apparent in the aged (27mo) rats in comparison to the adult (12mo) rats. This held despite normalization in body mass. Rabon (unpublished data) showed no significant difference between 12 and 27 month old rats in soleus, plantaris or diaphragm mass when normalized by body weight . It is important to point out that Rabon and this study used the same F344BNF1/NIA hybrid rats. Taken together results suggest that larger weight-bearing muscles atrophy to a greater extent than smaller limb muscles and respiratory muscles. The data also gives farther documentation that skeletal muscle function declines with advancing age.

One of the dysfunctions experienced by the elderly is diminished exercise intolerance. Exercise intolerance is associated with strength decrements. It is plausible that strength decrements may somehow be related to the effects of ROS. Cell death is also believed to be the result of ROS intolerance. Researchers have not actually proven that ROS initiate skeletal muscle cell, but many have documented the effects of ROS on SR function. The present data showed that the SR Ca^{2+} pump of animal skeletal muscle was no more susceptible to the effects of ROS than was that of adult rats. ROS, speicifcally HOCl, depressed the rates of Ca^{2+} uptake and release in both 12 and 27 month old rats. The present data show that while HOCl depressed Ca^{2+} uptake, the magnitude of effect was similar in both groups. On the other hand, the ROS H_2O_2 stimulated greater Ca^{2+} release in the aged animals. This suggests that the release channel, as opposed to the Ca^{2+} pump, may be more susceptible to ROS effects.

Alterations in SR Ca^{2+} uptake and release can have affects on whole muscle function by (1) a reduction in uptake will cause a decline in the rate of relaxation of skeletal muscle (shown by others) and (2) a decrease in release will reduce the activation of contractile apparatus leading to reduced force output (shown by others). Conceivably changes in SR function with aging could lead to decrease force and diminished exercise capacity. Although this may be an attractive hypothesis, it awaits conformation.

If any alterations have occurred then the SR will face problems in maintaining Ca^{2+} homeostasis within the cell. Damage to the SR will have other implication to the entire skeletal muscle system. Also, the method of exposure to H_2O_2, direct or transient, appears to induce either an increase (Favero, 1995) or a depression (Brotto, 1996) in Ca^{2+} release, respectively.

CONCLUSIONS

In conclusion, it appears that ROS cause adverse effects on Ca^{2+} homeostasis of aged muscle and presents some minor damage to adult SR. Specifically, the Ca^{2+} release channel seems to be susceptible to the deleterious effects of ROS. These changes in SR function may lead to decreased force in older adults in which exercise intolerance may very well be heighten.

SUGGESTIONS FOR FURTHER RESEARCH

Like other studies, this study has shown that reactive oxygen species alters Ca^{2+} homeostasis of SR skeletal muscle. However, present research has not been successful in formalizing an relationship between altered Ca^{2+} homeostasis and cell injury which may lead to cell death. This void may be do to the lack of affordable methodology for measuring ROS. This study also documented that aged skeletal muscle is no more susceptible to ROS damage than younger skeletal muscle. Though for some apparent reason, aged skeletal muscle has a impaired defense against these scavengers. One possibility may be the role of anti-oxidants such as, vitamin E and C which have been found to provide some level of defense. Unfortunately, long-term consequences of vitamin supplementation will cause toxicity in the body in large quantities. Research should focus on at what stage of life should supplementation begin to increase ones chance of reducing cellular damage. But the question which remains, is at what point in life does the most damage occurs. And what is the cause-effect relationship of exercise on ROS production besides exercise utilizing more oxygen producing ROS. Controversial still remains on the free radical theory of aging because no one has yet to proving its validity. However, numerous studies have shown that healthy active lifestyles can slow down the aging process.