Exercise training and fat metabolism after menopause: implications for improved metabolic flexibility in aging

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A GREATER RELIANCE ON FATTY acids for fuel, along with the ability to conserve and replenish muscle glycogen, offered a distinct survival advantage, as it allowed our Paleolithic ancestors to work (i.e., hunt and gather) longer and more often (3). Unfortunately for women today, the triple burden of menopause, an age-related loss in functional reserve (maximum O$_2$ uptake/resting metabolic rate) (2), and the modern-day lifestyle alters the efficient use of lipid-derived energy sources, which then has important consequences to the maintenance of metabolic flexibility (the ability to switch efficiently to a greater reliance on fat oxidation during fasting or prolonged exercise) and insulin sensitivity in older age. A study by Johnson and colleagues (8) published in this current issue of the Journal of Applied Physiology, describes the benefits of endurance training to improved lipid metabolism (i.e., mobilization, reesterification, and oxidation) in middle-aged post-menopausal women ($N = 10$). The authors observed that, despite a lower overall capacity for total lipid oxidation during exercise (relative to younger women), 12 wk of endurance training (300 min/wk at 65% peak O$_2$ uptake) resulted in an enhanced work-related ability to mobilize and oxidize free fatty acids (FFA). Following the training period, FFA reesterification was minimized during exercise performed at the same absolute intensity as pretraining, thereby enabling greater FFA oxidation. The authors conclude that older women can adapt in this regard, although probably not to the same extent as younger women having a higher work capacity.

These studies have several important strengths. The first is the determination of fuel utilization under working, rather than resting, conditions. This is an important aspect of the experimental design, since human beings are intended to be physically active, and physical activity accelerates turnover of stored triglycerides and glycogen. Thus the study of lipid kinetics during actual exercise provides a more physiological picture of our complex metabolic machinery and a more sensitive measure of assessing it (5). A second strength is the examination of lipid kinetics after menopause. This is of great significance to understanding the aging process in women, since this is a vulnerable time with regard to one’s susceptibility to dysregulated lipid metabolism. Johnson, et al. (8), cite the dearth of information on the impact of estrogen withdrawal on FFA mobilization, reesterification, and oxidation. Finally, the post-training exercise trials were set at both a similar absolute and relative work load in relation to the pretrial work load. The authors observed training-related improvements in FFA mobilization and oxidation only during exercise at the same absolute output as pretraining; thus they may have avoided a possible shift toward carbohydrate oxidation with a similar relative load (but higher absolute load) in these postmenopausal women. While the absolute vs. relative intensity issue is not new, it remains an important factor as we begin to fine-tune exercise prescriptions to address specific health concerns across the life span.

The implications of improvements in metabolic flexibility after menopause may be complicated by two important menopausal cofactors: excess abdominal adiposity, and high circulating FFA concentrations. These issues are further complicated in the presence of multitissue (muscle, adipocyte, and liver) insulin resistance. This is particularly complicated in those who have had a sedentary lifestyle, as well as aging-related β-cell deficiency, resulting in an inadequate insulin secretory response. These common factors associated with aging and menopause may alter the way a subject responds to regular exercise. I am certain not to be the only one confused by the observation that high levels of stored triglycerides exist both in trained endurance athletes (6) who are insulin sensitive and in sedentary obese people with insulin resistance (10). This metabolic paradox suggests different lipid kinetics with regular sustained work activity vs. sustained inactivity (9).

If prolonged sedentary living can be considered the underlying agent in this round-about of metabolic pathophysiology in aging, then 100,000 yr of evolution, as well as modern science (1, 7), suggests that regular exercise can correct defects in the bioenergetic capacity of the mitochondria, thereby improving lipid metabolism, metabolic flexibility, and insulin sensitivity. The dose of exercise necessary to elicit such improvements in older age, however, is not clear, especially as daily energy expenditure among the entire population continues to decline. Both Johnson et al. (8) and previous work from my laboratory (4) required rather large training volumes to observe improvements in lipid metabolism. Such intensive regimens may not be sustainable by older people in the absence of the structure provided by a formal training program. Scientific findings in the laboratory are often difficult to translate into sound public health practice.

A comparison of findings between Johnson et al. (8) and previous work from my laboratory in older women needs to be interpreted with caution (4, 11). There are important methodological differences between these studies, some of which are mentioned briefly in their paper. We studied lipid metabolism under resting conditions using insulin stimulation, and, as stated previously, studies that make these same assessments under working (i.e., exercising) conditions provide a more physiological picture of metabolic regulation. Furthermore, we performed our studies after a 12-h fast, rather than 3–4 h postmeal, which clearly would impact the permissiveness of fuel availability on fat oxidation. The shorter fast is associated with...
with higher insulin levels and the possibility of continuing gastrointestinal absorption. Future studies of postexercise meal timing and composition on fat metabolism may offer additional insight to lipid kinetics during exercise. Our findings of blunted FFA reesterification were specific to older women with excess abdominal adiposity, who had fat oxidation levels similar to their leaner counterparts. Finally, the female study subjects in our earlier work were, on average, nearly 20 yr older, with an average peak \( \text{O}_2 \) uptake that was \(~20\%\) lower than those studied in Dr. Brooks’ laboratory. Clearly, the problematic issue of reduced functional reserve in late middle-age is an even greater problem among septuagenarians.

In any case, increasing aging demographics alone encourages further work in the area of work-related lipid kinetics and metabolic flexibility as they relate to the maintenance of metabolic health with advancing age. Clearly, what was once a survival advantage to our ancient ancestors (i.e., the propensity to store and conserve fuel) creates what is now a major public health problem. The extent to which biomarkers of susceptibility to metabolic dysregulation can be identified early in life (before the onset of clinical symptoms of obesity and insulin resistance) enhances our ability to then use exercise where it is most effective: as a preventive, rather than as a rehabilitative, strategy.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES