Effects of physical activity and exercise on experimentally-induced mammary carcinogenesis

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Summary

Physical activity is defined as skeletal muscle contraction resulting in a quantifiable expenditure of energy, whereas exercise is a specific type of physical activity in which planned, structured, and repetitive bodily movement is done to improve or maintain one or more components of physical fitness. The focus of laboratory studies of the physical activity-breast cancer hypothesis has been on evaluating how various types of physical activity including exercise affect the process of mammary carcinogenesis. A key objective has been the evaluation of the characteristics of physical activity, i.e. intensity, duration, and frequency, required to confer protection against experimentally-induced breast cancer. The results of those studies indicate that exercise rather than physical activity can exert a greater inhibitory effect against experimentally-induced breast cancer, and that the duration of exercise may not be as important as its intensity. This finding differs from evidence that other health benefits attributed to physical activity are proportional to the total amount of activity rather than the manner in which it is obtained. In this review criteria are defined for categorizing laboratory studies into those that investigated the effects of physical activity versus exercise on experimentally-induced mammary carcinogenesis, and the literature is reinterpreted in this context.

Introduction

The evidence that physical activity affects the risk for cancer has been reviewed extensively [1-4]. In those analyses it has been repeatedly noted that reports of the relationship between physical activity and breast cancer risk have been inconsistent, and the strength of observed associations has been weak. This pattern of inconsistency has been reported both in human population studies and in laboratory investigations in which defined models were used. Nonetheless, in the overall analysis the available evidence indicates that physically active lifestyle patterns can be identified that are associated with reduced breast cancer risk.

While the inconsistencies in the epidemiologic evidence may be accounted for by a host of factors many of which cannot be readily identified [5-7], an analysis of the differences reported among laboratory experiments, in which most
variables are controlled, provides potentially important insights about the relationship between physical activity and breast cancer. That research suggests that simply increasing physical activity is not in itself sufficient to reduce breast cancer risk [8]. Rather, it appears that the intensity of physical activity may be critical to whether a particular type of activity confers protection against experimentally-induced breast carcinogenesis [9-11]. A second observation emerging from laboratory experiments is that a number of intervening factors, particularly those associated with either diet composition or the energy equilibrium of the host, are likely to modify the effect of physical activity on the carcinogenic process [4,12]. Identification of these factors and the mechanisms by which they act could potentially be the most important area for additional research. A third point indicated by previous laboratory work, is that there are not patently right or wrong animal models for physical activity research, but rather that the use of specific models allows different aspects of the physical activity cancer hypothesis to be evaluated [9].

Definitions of physical activity and exercise

Physical activity is defined as skeletal muscle contraction that results in a quantifiable expenditure of energy [13]. Physical activity is closely related to, but distinct from, exercise and physical fitness [13]. Exercise is a subset of physical activity defined as “planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness” [13]. Physical fitness is “a set of attributes that relate to the ability of an organism to perform physical activity” [13]. There are three primary components of exercise that can be varied and that may have different effects relative to carcinogenesis. They are the intensity (work-rate), the duration (length per activity bout), and the frequency (times per week) of the activity(s) performed. Other attributes of exercise also can be considered and are reviewed in [6,7].

Rationale for using animal models to investigate physical activity-breast cancer hypotheses

Currently, there are no established surrogate intermediate biomarkers for breast carcinogenesis that can be used to facilitate the rapid testing of physical activity-breast cancer hypotheses in human populations [14]. Also, there are currently no markers for the level of physical activity or physical fitness that is associated with protection against breast cancer and that can be used in research with humans [1-4,6,7]. Consequently, while there is little disagreement that the most definitive tests of physical activity-breast cancer hypotheses are those conducted in human subjects, population based studies that take many years to complete will be prohibitively expensive until such markers become available. On the other hand, laboratory experiments in which animal models are used have the potential: to identify the characteristics of physical activity or exercise that are most likely to be critical to cancer prevention in humans; to define mechanisms and markers of those mechanisms that would allow monitoring of disease progression in human populations over a short time frame; to identify physical activity or fitness related biomarkers of the “cancer-protected state”; and to identify potentially confounding variables, for example dietary factors, that could actually mask the protective effects of physical activity if their existence were unrecognized.

Animal models for physical activity and exercise

An analysis of the literature indicates that there have been three primary approaches to increasing the physical activity of laboratory animals [15-19]. They are: free access to an activity wheel, swimming, or running animals in a motor-driven activity wheel or rotating drum, or on a treadmill. The following classification of these approaches