Brain and Cognition 97 (2015) 32–39

Contents lists available at ScienceDirect

Brain and Cognition

journal homepage: www.elsevier.com/locate/b&c

Domain dependent associations between cognitive functioning and regular voluntary exercise behavior

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ARTICLE INFO

Article history:
Accepted 2 April 2015
Available online 24 May 2015

Keywords:
Exercise
Physical activity
Neurocognition
Cognitive aging
Computerized Neurocognitive Battery

ABSTRACT

Regular exercise has often been suggested to have beneficial effects on cognition, but empirical findings are mixed because of heterogeneity in sample composition (age and sex); the cognitive domain being investigated; the definition and reliability of exercise behavior measures; and study design (e.g., observational versus experimental). Our aim was to scrutinize the domain specificity of exercise effects on cognition, while controlling for the other sources of heterogeneity.

In a population based sample consisting of 472 males and 668 females (aged 10–86 years old) we administered the Computerized Neurocognitive Battery (CNB), which provided accuracy and speed measures of abstraction and mental flexibility, attention, working memory, memory (verbal, face, and spatial), language and nonverbal reasoning, spatial ability, emotion identification, emotion- and age differentiation, sensorimotor speed, and motor speed. Using univariate and multivariate regression models, CNB scores were associated with participants' average energy expenditure per week (weekly METhours), which were derived from a questionnaire on voluntary regular leisure time exercise behavior.

Univariate models yielded generally positive associations between weekly METhours and cognitive accuracy and speed, but multivariate modeling demonstrated that direct relations were small and centered around zero. The largest and only significant effect size ($\beta = 0.11$, $p < 0.001$) was on the continuous performance test, which measures attention.

Our results suggest that in the base population, any chronic effects of voluntary regular leisure time exercise on cognition are limited. Only a relation between exercise and attention inspires confidence.

1. Introduction

Regular exercise has often been suggested to have beneficial effects on cognitive performance, but empirical findings do not always support this suggestion. As a result, the effectiveness of regular exercise behavior as a means to improve cognitive performance remains a subject of debate, not only among scientists, but also among policy makers. When published findings are summarized, associations between exercise behavior and cognitive performance appear positive on average, but vary considerably in strength (Fedewa & Ahn, 2011; Hindin & Zelinski, 2012; Ploughman, 2008; Singh, Uijtdewilligen, Twisk, van Mechelen, & Chinapaw, 2012; Taras, 2005; Trudeau & Shephard, 2008; Verburgh, Konigs, Scherder, & Oosterlaan, 2014). The literature provides four major sources of heterogeneity among study outcomes, the first concerning sample constitution (Singh et al., 2012). Study samples have differed greatly with respect to age, while the association strength between exercise behavior and cognitive performance is considered to differ between children, adolescents and adults (Hillman, Castelli, & Buck, 2005; Tomporowski, Davis, Miller, & Naglieri, 2008; but see Verburgh et al., 2014).

In childhood and adolescence exercise may influence the (rapid and specific) brain changes that take place during development, while in the elderly exercise may prevent (slow or general) deterioration of the brain during aging (Churchill et al., 2002; Fabel & Kempermann, 2008; Greenwood & Parasuraman, 2010; Hillman, Erickson, & Kramer, 2008; Kraft, 2012; Yuki et al., 2012).

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http://dx.doi.org/10.1016/j.bandc.2015.04.001
0278-2626/

Furthermore, rates of cognitive decline differ across sexes, which has been linked to the loss of estrogen (Kramer, Erickson, & Colcombe, 2006). Sex may be regarded as a source of heterogeneity in itself as the associations between exercise behavior and cognitive measures in samples consisting of a majority of women tend to be larger than in samples consisting of relatively many men (Colcombe & Kramer, 2003). A second major source of heterogeneity amongst study outcomes concerns the cognitive domain being measured. Recent studies (Colcombe & Kramer, 2003) suggest that cognitive functions are differently susceptible to exercise; executive functions may be more sensitive to exercise than, for example, long-term memory. Empirically however, little is known about how effects of exercise vary across cognitive domains, let alone about how these effects differ in their dependencies on age and sex. Many studies have focused on global cognitive measures, and outcomes thereof, such as academic achievement. This is unfortunate because they do not inform about the sensitivity of specific cognitive functions (Tomporowski et al., 2008). The present study is unique, in that we measured in a single, population representative sample cognitive performance across a wide range of well-defined, specific cognitive domains. The battery we used, the web-based Computerized Neurocognitive Battery (CNB), consists of 17 cognitive tests, and provides measures of accuracy as well as speed in the following cognitive domains: abstraction and mental flexibility, attention, working memory, memory (verbal, face, and spatial), language and nonverbal reasoning, spatial ability, emotion identification, emotion- and age differentiation, sensorimotor speed, and motor speed. Individual differences in these domains are substantially heritable and demonstrate genetic linkage (Almasy et al., 2008). Scores on the CNB are reliable and compare well to scores on traditional pen-and-paper tests in healthy samples as well as in clinical samples (e.g. schizophrenia patents, Gur, Ragland, Moberg, Bilker, et al., 2001; Gur, Ragland, Moberg, Turner, et al., 2001). While initially constructing the test battery, tests were selected from neuroimaging studies that showed selective activation of specific brain systems in the magnetic resonance imaging (MRI) scanner (Gur et al., 2010). Recently, the CNB tests adapted for administration in the MRI scanner replicated the brain areas that are activated by the CNB's cognitive domains. More specifically, the executive tests activated mainly frontal areas, memory tests involved anterior medial temporal regions, and a test measuring emotion identification activated temporo-limbic regions (Roalf et al., 2014).

A third source of heterogeneity amongst previous results, the definition and reliability of exercise behavior measures, has been discussed extensively in the literature. Studies have varied greatly in the conceptualization of exercise behavior, the broadest conceptualization being the inclusion of all forms of physical activity (i.e. every activity increasing energy expenditure above basal metabolic rate). However, self-reported physical activity corresponds poorly with actual physical activity (Prince et al., 2008). In addition, the idea that common, low intensity forms of physical activity will be sufficient to induce cognitive effects has been questioned; exercise likely needs to be carried out at a moderate to vigorous intensity to have effect on cognitive functioning (Colcombe & Kramer, 2003; Fedewa & Ahn, 2011; Hindin & Zelinski, 2012). It is recommended to focus on relatively vigorous activities, especially leisure time exercise activities: recall is relatively easy and quite accurate as these activities are self-initiated and often clearly defined in time. Indeed, voluntary regular leisure time exercise behavior demonstrated excellent test–retest reliability (de Moor, Boomsma, Stubbe, Willemsen, & de Geus, 2008; Stubbe, de Moor, Boomsma, & de Geus, 2007). In the present study, we will focus on this narrow but well-defined behavior, also because it is often the main target of health-promoting exercise interventions (Kahn et al., 2002).

A fourth source of heterogeneity concerns study design. This is an important source to recognize, because study designs are differently suited to estimate effects of physical activity. In experimental and clinical intervention studies the focus is usually on mean effects as a result of intervention, while the focus of observational studies lies on individual differences in voluntary behavior and on dose–response relationships. Furthermore, intervention studies – experimental studies included – have varied widely in their definition of intervention. In addition, not all intervention studies have been truly experimental; clinical intervention is often performed in non-random samples (Singh et al., 2012; Tomporowski et al., 2008). Another distinction concerns studies investigating the effects of acute physical exercise, and studies that investigate the effects of chronic physical exercise (Verburgh et al., 2014). In the first, the focus is on (short-term) cognitive enhancement right after a single bout of exercise, typically within less than an hour. In the latter, the focus is on (long-term) cognitive enhancement as the result of regular exercise over longer periods, typically weeks or months. Although there is ample evidence for beneficial effects of acute physical exercise (Verburgh et al., 2014), studies into the effects of chronic physical exercise are scarce, hence the call for more research.

The general objective of the present study is to investigate the chronic dose–response association between voluntary regular leisure time exercise behavior and cognitive performance across a wide range of cognitive domains, while controlling for other sources of heterogeneity. To this end, we first examine whether leisure time exercise associated with accuracy and speed scores, exploring whether and how these associations vary across domains. Next, we explore whether, how, and to what extent these associations vary when accounting for differences in age and sex. We end with a general discussion, in which the results of the present population-based observational study are compared with results from previous (high quality) intervention studies, which typically involve clinical-control designs.

2. Material and methods

2.1. Participants

The subject sample consisted of 472 males and 668 females from the Netherlands Twin Register (NTR) recruited from all over the Netherlands (Boomsma et al., 2006; van Beijsterveldt et al., 2013; Willemsen et al., 2013). The majority ($n = 1110$) was comprised of twin pairs and their family members (parents, children, siblings, and spouses) who volunteered in NTR projects. The rest ($n = 30$) was comprised of undergraduate students who piloted in these projects. The participants ranged in age from 10 to 86 years old (mean = 37.73, $SD = 20.86$, see Fig. 1).

2.2. Procedure

Studies and procedures were approved by the Medical Ethics Review Committee of the VU Medical Center Amsterdam and the Central Committee on Research Involving Human Subjects. The twins and their family members were approached by mail. In case of a positive response, a structured telephone call followed, which was informative about possible exclusion criteria (epilepsy, paralysis). The students were recruited at the university through flyers. They signed up themselves. Data collection took place either at home ($n = 536$) or in a laboratory (VU University Amsterdam, University Medical Center Utrecht, Amsterdam Medical Center, $n = 604$).

Cognitive performance was assessed on a 15 inch Macbook laptop, using the web-based Computerized Neurocognitive