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Habitual physical activity and the risk for depressive and anxiety disorders among older men and women

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ABSTRACT

Background: Regular physical activity is generally associated with psychological well-being, although there are relatively few prospective studies in older adults. We investigated habitual physical activity as a risk factor for *de novo* depressive and anxiety disorders in older men and women from the general population.

Methods: In this nested case-control study, subjects aged 60 years or more were identified from randomly selected cohorts being followed prospectively in the Geelong Osteoporosis Study. Cases were individuals with incident depressive or anxiety disorders, diagnosed using the Structured Clinical Interview for DSM-IV-TR (SCID-I/NP); controls had no history of these disorders. Habitual physical activity, measured using a validated questionnaire, and other exposures were documented at baseline, approximately four years prior to psychiatric interviews. Those with depressive or anxiety disorders that pre-dated baseline were excluded.

Results: Of 547 eligible subjects, 14 developed *de novo* depressive or anxiety disorders and were classified as cases; 533 controls remained free of disease. Physical activity was protective against the likelihood of depressive and anxiety disorders; OR = 0.55 (95% CI 0.32–0.94), p = 0.03; each standard deviation increase in the transformed physical activity score was associated with an approximate halving in the likelihood of developing depressive or anxiety disorders. Leisure-time physical activity contributed substantially to the overall physical activity score. Age, gender, smoking, alcohol consumption, weight and socioeconomic status did not substantially confound the association.

Conclusion: This study provides evidence consistent with the notion that higher levels of habitual physical activity are protective against the subsequent risk of development of *de novo* depressive and anxiety disorders.

Key words: anxiety, depression, epidemiology, physical activity, risk factors

Introduction

The adverse impacts that modern sedentary lifestyles have on physical health are recognized as contributing to today's high rates of chronic diseases (Booth *et al.*, 2000). While physical activity is generally regarded as beneficial for mental health, definitive data examining exercise prospectively in terms of risk reduction are lacking. Most studies of physical activity are conducted in already depressed individuals, where a clear therapeutic effect of exercise is documented (Conn, 2010). Cross-sectional studies are unable to shed light on causality, and intervention studies are likely to suffer validity issues relating to inadequate blinding. Positive treatment studies also do not linearly equate to evidence of risk reduction in currently well individuals. Prospective observational studies have yielded inconsistent findings, with some (Farmer *et al.*, 1988; Paffenbarger *et al.*, 1994; Morgan and Bath, 1998; Lampinen *et al.*, 2000; Wyshak, 2001; Strawbridge *et al.*, 2002; van Gool *et al.*, 2003; Brown *et al.*, 2005; Wise *et al.*, 2006; Wiles *et al.*, 2007; Sanchez-Villegas *et al.*, 2008), but not all (Weyerer 1992; Cooper-Patrick *et al.*, 1997; Kritz-Silverstein, *et al.*, 2001), reporting a protective effect of physical activity on psychiatric well-being.

Depression in older adults is common (Williams *et al.*, 2010) and differs in many ways from early

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onset depression (Janssen *et al.*, 2006), yet relatively few prospective studies have investigated physical activity as a risk factor in this age-group (Morgan and Bath 1998; Lampinen *et al.*, 2000; Kritz-Silverstein *et al.*, 2001; Strawbridge *et al.*, 2002). In this epidemiological study, we aimed to investigate habitual physical activity as a risk factor for incident depressive and anxiety disorders in men and women aged 60 years or more, recruited from the general population.

Methods

Subjects

This case-control study is nested within the Geelong Osteoporosis Study (GOS), a large prospective, population-based study initially designed to investigate the epidemiology of osteoporosis in Australia and subsequently expanded to examine mental health. A listing on the compulsory Australian Commonwealth electoral roll for the region known as the Barwon Statistical Division fulfilled the inclusion criterion for the GOS. Death, inability to provide informed consent and contact failure formed the basis for exclusion (Pasco *et al.*, 2000). From 1114 men and women, aged at least 60 years, who attended the study centre and completed questionnaires during the period 2000–2006 (designated "baseline" for this analysis), 680 agreed to a psychiatric interview approximately four years later at follow-up (median period of follow-up 4.1 years, interquartile range, IQR, 3.5–4.7 years). Thirty-four were excluded because questions concerning physical activity were incomplete and a further 99 excluded because they had experienced depressive or anxiety disorders prior to baseline. Thus, 547 were included in this analysis. The study was approved by the Human Research Ethics Committee at Barwon Health. All participants provided informed, written consent.

Data

The Structured Clinical Interview for DSM-IV-TR Research Version, Non-patient edition (SCID-I/NP) was used to identify cases with a lifetime history of depressive and/or anxiety disorders at endpoint, and to determine the age of onset. Individuals with depression or anxiety that pre-dated baseline were excluded; cases were identified as those who met DSM-IV-TR criteria for a depressive or anxiety disorder during the period of follow-up.. Controls had no history of depressive and anxiety disorders. Trained personnel conducted psychiatric interviews. We decided *a priori* to pool depression and anxiety disorders to ensure that the study was adequately powered.

The exposure of interest – habitual physical activity – was assessed at baseline interview using a validated questionnaire designed for the elderly and for use in epidemiological studies (Voorrips *et al.*, 1991). Subjects reported participation in habitual physical activity throughout the prior year, including household activities, sporting activities and other physically active leisure-time activities. Items relating to household activities had four to five possible ratings ranging from very active to inactive; those relating to sport and other activities included details on type of activity, intensity, hours per week and period of the year in which the activity occurred. Details of scoring have been described previously (Voorrips *et al.*, 1991). An overall physical activity score was obtained by combining scores for activities from the household, sporting and leisure domains. Other lifestyle exposures such as smoking, alcohol consumption and medication use were documented by self-report at the baseline visit. Tobacco smoking was recognized if practiced currently and regularly, alcohol use was recognized if average consumption exceeded two standard drinks per day, and socioeconomic status (SES) was ascertained using the Socio-Economic Index For Areas (SEIFA) values based on census data from the Australian Bureau of Statistics. SEIFA values were used to derive an Index of Relative Social Disadvantage (IRSD) that was categorized into quintiles of IRSD for the study region. Quintiles 1 and 2 (most disadvantaged), and 4 and 5 (least disadvantaged) were collapsed because of small numbers to create three categories of SES, namely low (most disadvantaged), medium and high. Employment status referred to both paid and unpaid work, undertaken full-time, part-time or casually; marital status also included de-facto relationships. Mobility was documented by self-report, with those reporting "little walking outside home, but prepares meals and does very light housework or equivalent" or "sits in chair or lies in bed most of the time, walks independently from bed to chair to toilet but requires assistance for greater movement" classified as having poor mobility. A history of cancer was self-reported. Body weight and height were measured and body mass index (BMI) calculated as weight/height^2 (kg/m^2).

Statistical analysis

Standard statistics were used to compare characteristics of cases and controls, and characteristics of individuals in each tertile of physical activity scores. Physical activity scores were categorized into tertiles for descriptive purposes and to determine the kappa

Table 1. Subject characteristics are listed for cases (depressive and anxiety disorders) and controls (no history of depression or anxiety). Data are shown as median (IQR), mean (±SD) or n (%)

	CASES (N = 14)	CONTROLS (N = 533)	p-VALUE
Men	6 (43%)	298 (56%)	0.3
Age (yr)	69 (65–80)	72 (66–78)	0.8
Weight (kg)	74.9 (±12.3)	76.3 (±14.3)	0.7
Height (cm)	167 (±11)	166 (±10)	0.8
BMI (kg/m^2)	27 (±4)	28 (±4)	0.6
Smokers	1 (7%)	30 (6%)	0.6
Alcohol (>2 drinks/day)	3 (21%)	121 (23%)	0.9
SES			0.3
low	4 (29%)	223 (42%)	
medium	5 (36%)	96 (18%)	
high	5 (36%)	214 (40%)	
Employed	2 (14%)	87 (16%)	0.9
Married/de-facto	10 (71%)	402 (75%)	0.8

BMI = body mass index; SES = socioeconomic status

statistic (κ) for measuring the agreement between overall physical activity scores and those associated with leisure-time activities. The distribution of physical activity scores was skewed, but was normalized by square root transformation, and expressed in standard deviation units for regression analysis. Logistic regression modeling was used to determine the association between habitual physical activity and the likelihood for developing a subsequent depressive or anxiety disorder. Age, anthropometry, smoking, alcohol use and SES were tested in the models as potential confounders and effect modifiers. Statistical analyses were performed using Stata (release 9.0, StatCorp, College Station, TX) and Minitab (version 15; Minitab, State College, PA).

Results

Characteristics of cases and controls are presented in Table 1. There were no differences in age, anthropometry, smoking, alcohol consumption, SES, or employment and marital status between cases and controls. The median overall physical activity score was lower for cases than for controls (median (IQR): 10.7 (5.2–17.3) *vs* 15.2 (10.0–22.1), p = 0.03). Characteristics of individuals in each tertile of physical activity are shown in Table 2. The proportion of men progressively increased, and the proportion of those employed progressively decreased, with each increase in the level of physical activity; individuals in the lowest tertile had greater BMI, while there were fewer married individuals in the medium tertile; no other differences were detected. The distribution of cases and controls in the low, medium and high physical activity tertiles for cases were: 4.4% (95% CI 1.4–7.4) *vs* 2.2% (95% CI 0.07–4.3) *vs* 1.1% (95% CI 0.0–2.6); and for controls: 95.6% (95% CI 92.6–98.6) *vs* 97.8% (95% CI 95.7–99.9) *vs* 98.9% (95% CI 97.4–100.0), respectively. The percentage of cases across tertiles of physical activity and percentage of controls across tertiles of physical activity are shown in Figure 1. In contrast to a

Table 2. Subject characteristics categorized into tertiles of physical activity scores described as low (physical activity score 1.00–7.13), medium (score 7.14–8.24) and high (score 8.25–16.36). Data are shown as median (IQR), mean (±SD) or n (%)

	LOW (N = 182)	MEDIUM (N = 183)	HIGH (N = 182)	p-VALUE
Men	89 (49%)	98 (54%)	117 (64%)	0.01
Age (yr)	72 (66–78)	72 (66–77)	72 (66–77)	0.7
Weight (kg)	78.1 (±16.0)	75.1 (±14.0)	75.6 (±12.4)	0.1
Height (cm)	166 (±10)	166 (±10)	167 (±9)	0.2
BMI (kg/m^2)	28 (±5)	27 (±4)	27 (±4)	0.006
Smokers	8 (4%)	14 (8%)	9 (5%)	0.4
Alcohol (>2 drinks/day)	36 (20%)	40 (22%)	48 (26%)	0.3
SES				0.5
low	74 (41%)	75 (41%)	78 (43%)	
medium	27 (15%)	37 (20%)	37 (20%)	
high	81 (45%)	71 (39%)	67 (37%)	
Employed	38 (21%)	30 (16%)	21 (12%)	0.05
Married/de-facto	146 (80%)	122 (67%)	144 (79%)	0.004

BMI = body mass index; SES = socioeconomic status.

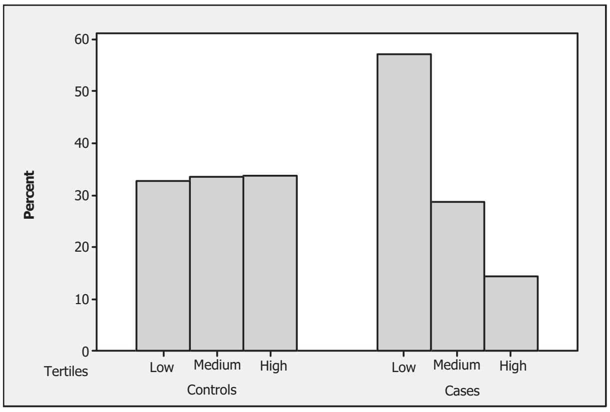

Figure 1. Percentage of cases and percentage of controls in each level of physical activity categorized into tertiles described as low (physical activity score 1.00–7.13), medium (score 7.14–8.24) and high (score 8.25–16.36).

relatively even distribution of controls across the tertiles, more of the cases clustered in the low tertile, with sequentially fewer in the medium and high tertiles.

Overall, physical activity was protective against the likelihood of depressive and anxiety disorders; OR = 0.55 (95% CI 0.32–0.94), $p = 0.03$; thus, each standard deviation increase in the transformed physical activity score was associated with an approximate halving in the likelihood of developing depressive or anxiety disorders during the ensuing four-year period. None of the variables listed in Table 1 confounded this association. There were 12 individuals with poor mobility and they occurred in the control group only. Exclusion of individuals with poor mobility did not impact on the relationship between physical activity score and the development of depressive and anxiety disorders; OR = 0.56 (95%CI 0.34–0.91), $p = 0.02$. Seventy-one individuals had a history of cancer (an example of a physical illness that may not have been captured by poor mobility), but there were no differences in prevalence between cases and controls (n (%): 1 (7%) *vs* 70 (13%), $p = 0.9$) nor between tertiles of physical activity (low 28 (15%) vs 22 (12%) vs 21 (12%), $p = 0.5$). Cancer did not confound the association between physical activity and depressive or anxiety disorders.

Leisure-time physical activity contributed 80.7% to the overall physical activity score, whereas those associated with household and sporting activities contributed 9.6% and 9.7%, respectively. The distribution pattern of individuals into tertiles of scores for leisure-time activities was similar to the overall scores, with 82.6% agreement ($\kappa = 0.7$). A similar pattern was not observed for scores from household or sporting activities. The median leisure-time physical activity score was lower among cases than controls (median (IQR): 7.8 (3.7–14.0) *vs* 12.2 (7.2–18.2), $p = 0.05$). Leisure-time physical activity score was also protective against the likelihood of depressive and anxiety disorders; OR = 0.59 (95% CI 0.36–0.96), $p = 0.04$. None of the variables in Table 1 were identified as confounders. The likelihood of incident depressive and anxiety disorders was not associated with the household activity or sport activity scores.

Discussion

This study provides longitudinal evidence that physical activity is protective against the development of *de novo* depressive and anxiety disorders in the elderly. Further analysis suggests that leisure-time physical activity contributes substantially to this association. The potential for differential recall bias, often considered a major limitation for case-control studies, has been diminished by nesting the study within a larger prospective cohort study. It should be emphasized that physical activity levels had been documented and scored before the onset of depressive and anxiety disorders. However, as these disorders can impact on habitual physical activity, the possibility of reverse causality cannot be excluded. Although individuals with prior depression or anxiety were excluded, those with sub-clinical depression or anxiety at baseline remained unrecognized.

Similar findings have been reported from previous studies. A prospective study involving U.S. adults aged 50–94 years observed that physical activity reduced the risk of incident depression at five-year follow up (Strawbridge *et al.*, 2002). Another Australian study, which examined the dose-response relationship between physical activity and depressive symptoms in middle-aged women, reported a clear inverse relationship between the two variables (Brown *et al.*, 2005). Lower levels of physical activity in childhood have been associated with an increased risk of adult depression (Jacka *et al.*, 2008).

Data from U.S. adults aged 25–74 years showed that low physical activity during leisure time was a risk factor for depressive symptoms eight years later (Farmer *et al.*, 1988) and, for middle-aged men in the U.K., high-intensity leisure-time physical activity was associated with a small reduction in common mental disorders over five years (Wiles *et al.*, 2007). In a study that followed Spanish university graduates over a six-year period, an increase in physical activity during leisure time was found to contribute to a lower incidence of mental disorders (Sanchez-Villegas *et al.*, 2008). Our results also suggest that leisure-time physical activity is an important component of patterns of physical activity for protection against the development of common mental disorders.

In a community-based sample of 1536 individuals in Bavaria, an inverse relationship between physical activity and depressive disorders was observed cross-sectionally, but not prospectively (Weyerer, 1992). A likely explanation is that of reverse causality, inasmuch as depression and anxiety impact on the motivation to pursue physical activity. It is possible that, although we excluded subjects for whom the onset of depressive or anxiety disorders predated the physical activity assessment, their responses may have been biased among those with subclinical disorders. A recent study involving twins from the Netherlands Twin Register showed that, although lower levels of regular exercise were associated with greater levels of anxious and depressive symptoms, there was no evidence to support a causal role of exercise in protecting against anxious and depressive symptoms (de Moor *et al.*, 2008). These authors suggested that an apparent association observed between the protective effects of exercise and depressive and anxiety symptoms was explained by common genetic factors.

By contrast, however, controlled intervention studies have consistently shown that physical activity programs are beneficial for patients with both depression and anxiety. In a 12-week study of depressed outpatients, running was of equivalent benefit to psychotherapy, with patients showing significant improvements measured on the symptoms checklist 90 (Greist *et al.*, 1979). Physical activity programs also appear to have therapeutic effects on mood in non-clinical populations of non-depressed individuals (Lennox *et al.*, 1990). A meta-analysis of treatment versus control comparisons yielded a standardized mean effect size of 0.372 among 38 supervised physical activity studies and 0.522 among 22 that were unsupervised (Conn, 2010).

There are several psychosocial advantages to engaging in leisure-time physical activity. Exercise as part of a productive routine and activity scheduling has been shown to be useful in depression management (Cuijpers *et al.*, 2007). Group activities are likely to increase social interaction, and the development of physical skills may improve self-esteem, improve body image and impart a sense of achievement, as well as fostering a sense of self efficacy (Cuijpers *et al.*, 2008). Outdoor activities may also increase casual exposure to sunlight, guarding against vitamin D deficiency that underlies affective disorders (Berk *et al.*, 2007; 2008) and has been implicated as a risk factor for depression (Berk *et al.*, 2007).

A number of physiological mechanisms have been implicated in the putative role for physical activity in modulating psychological well-being. Data from animal models suggest that acute and chronic physical activity increases the availability of the monamine neurotransmitters, specifically serotonin (Greenwood *et al.*, 2005) and noradrenaline (Dishman *et al.*, 2000), which is consistent with their positive effects on mood. Chronic physical activity attenuates the body's reaction to stress by blunting the hypothalamic-pituitary-adrenal axis response (Stranahan *et al.*, 2008), while increasing the levels of neurotrophins, such as brain-derived neurotrophic factor (van Praag, 2008). Additionally, exercise may ameliorate the detrimental effects of a poor quality diet on neurotrophins and oxidative stress (Molteni *et al.*, 2004; Jacka *et al.*, 2010).

Biomarkers of both oxidative stress and inflammation are consistently associated with depression (Maes *et al.*, 2010). Intensive exercise generates reactive oxygen species (Sachdev and Davies, 2008) and inflammatory cytokines (Kramer and Goodyear, 2007) that can acutely cause muscle cell damage, muscle fatigue, soreness and inflammation. However, chronic or habitual exercise has been shown to improve antioxidant defenses (Carlsohn *et al.*, 2008) and blunt the inflammatory response (Kramer and Goodyear, 2007).

We acknowledge some limitations in our study. Inconsistencies in the pattern of physical activity over time may have resulted in misclassification of exposure status, attenuating the association. The possible confounding by co-morbid disease and cognitive impairment was not addressed, as subjects were not clinically screened for all potential physical and neurological illnesses. It should be noted, however, that exclusion of individuals with poor mobility, which might reflect physical illness and inability to participate in physical activities, did not attenuate the relationship between physical activity and depressive and anxiety disorders. In recognition that cancer may represent a physical illness not necessarily characterized by poor mobility at baseline, cancer was investigated, but excluded, as a confounder in this dataset. Data from two independent studies (van Gool *et al.*, 2003; Brown *et al.*, 2005) showed that the protective effects of physical activity on incident depression were independent of baseline physical disease status. Moreover, although confounding by genetic factors that influence both physical activity and the common mental disorders is possible (de Moor *et al.*, 2008), this was not addressed, as it was outside the scope of this study. It is possible that other components of leisure-time physical activity such as social engagement may have contributed to the beneficial effects of exercise. However, we found that neither marital status nor employment status confounded the relationship. While the inverse relationship observed between employment rates and physical activity likely reflects restricted leisure time for exercise among employed individuals, employment status was not associated with depressive and anxiety disorders.

In conclusion, our data support extant literature that espouses the mental health benefits of physical activity. The therapeutic effects of exercise in the treatment of depression are established (Berk, 2007; Ng *et al.*, 2007; Conn, 2010) Extending this, the results of this study would suggest that exercise is a viable lifestyle candidate for the primary prevention of high prevalence mental health disorders, with clear benefits in a range of other common health issues. However, further research investigating the effects of both vigorous and habitual physical activity and the contributions of different types of physical activity are required before physical activity can be unequivocally recognized as a modifiable risk factor for the primary prevention of depression and anxiety in older adults.

Conflict of interest declaration

M. Berk has received Grant/Research Support from the Stanley Medical Research Foundation, MBF, NHMRC, BeyondBlue, Geelong Medical Research Foundation, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Organon, Novartis, Mayne Pharma, Servier and Astra Zeneca. He has been a paid consultant for Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen Cilag, Lundbeck and Pfizer and a paid speaker for Astra Zeneca, Bristol Myers Squibb, Eli Lilly, Glaxo SmithKline, Janssen Cilag, Lundbeck, Merck, Organon, Pfizer, Sanofi Synthelabo, Solvay and Wyeth.

Description of authors' roles

J. A. Pasco was involved in the conception and design of the study, analysis and interpretation of data and drafting of the paper. In addition, she had full access to the data and takes responsibility for the integrity of the data and the accuracy of the data analysis. L. J. Williams and F. N. Jacka were involved in study conception and design, and critical revision of the paper for important intellectual content. M. J. Henry was involved in study conception and design, analysis and interpretation of data, and critical revision of the paper for important intellectual content. C. E. Coulson and S. L. Brennan undertook data acquisition and were involved in critical revision of the paper for important intellectual content. E. Leslie, G. C. Nicholson and M. A. Kotowicz were involved in study design and critical revision of the paper for important intellectual content. M. Berk was involved in study conception and design, interpretation of data, drafting of the paper, and critical revision for important intellectual content. All authors gave final approval of the paper for publication.

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