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Lifetime occupational and leisure time physical activity and risk of Parkinson's disease

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ABSTRACT

Introduction: While regular exercise has been shown to alleviate the motor symptoms of Parkinson's disease (PD), it remains unclear whether a physically active lifestyle may prevent PD.
Methods: To examine physical activities across the lifespan and risk of PD, we relied on data from a population-based case-control study that enrolled 357 incident PD cases and 341 controls. We assessed physical activity levels via self-report of (1) overall physical activity (PA) over 4 age periods; (2) competitive sports; and (3) occupational histories.
Results: PD risks were lower comparing the overall PA highest quartile (moderate to vigorous activities ≥180 metabolic equivalent task-hours/week (MET-h/wk)) with the lowest quartile (<47.8 MET-h/wk) in age-period 18–24 years (adjusted odds ratio (OR) 0.64, 95% confidence interval (CI) 0.40–1.02), and 45–64 years (OR 0.50, 95%CI 0.31–0.83) but not in age-period 25–44. Individuals who consistently engaged in overall PA at high levels (before age 65 years) had a 51% lower PD risk than those with low levels. Also, having participated in competitive sports prior to age 25 was inversely associated with PD (OR 0.53, 95% CI 0.31–0.91 for high level versus never). There was no association for measures of occupational physical activity though.
Conclusion: The long prodromal stage of PD makes it difficult to conclude whether insidious disease leads to a reduction of physical activity years before motor symptom onset and PD diagnosis. However, sports activities and high levels of overall PA in youth appear protective unless they are markers for biologic or genetic factors that lower PD risk.

1. Introduction

Parkinson's disease (PD) is characterized by progressive motor and non-motor impairments leading to disability, a considerable decline in health related quality of life, and a large financial and caretaker burden in aging societies. Many clinical trials have shown beneficial effects of exercise therapies in people with PD as summarized in meta-analyses; for example, two recent meta-analyses found that aerobic exercise or physical therapy improved motor scores based on the Unified Parkinson's disease rating scale (UPDRS), as well as balance and gait compared with no intervention [1,2]. Even though there is some evidence from animal experiments and PD intervention studies that intensive physical exercise induces neuroplasticity in the nigrostriatal dopaminergic system [3–6], less is known about the role lifetime physical activity may play for PD risk.

Some cohort studies (Supplementary Table 1) have suggested that those physically inactive or reporting prolonged daily TV viewing are more likely to develop PD [7–12]. However, many of these cohort studies relied on self-report of physical activity levels or recorded activity patterns at baseline only [11,12], accrued small numbers of incident PD cases or followed populations with a lifestyle different from the general population [10,11]. In addition, most previous studies focused on leisure time activities while only two considered work related activities [8,10]. Activities at work and during leisure time likely entail very different physical demands, in terms of intensity, frequency and duration, and are known to affect all-cause mortality and cardiovascular disease differently [13,14]. Our aim here is to examine whether the type and/or the timing of

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physical activity throughout adulthood affects risk of PD.

2. Methods

Data collection and procedures described in this study have been approved by the University of California, Los Angeles (UCLA), Institutional Review Board for human subjects, and written informed consent has been obtained from all participants.

2.1. Study population

We conducted a population-based case-control study in largely agricultural counties in Central California. Details of the study have been provided elsewhere [15]. Briefly, we enrolled recently diagnosed PD patients (within 3 years of diagnosis) between 1998 and 2007, residing in Fresno, Kern, or Tulare counties, who at recruitment had lived in California for 5 years or more. Potential cases and controls were contacted by mail, by telephone, or both with eligibility criteria including: (1) being at least 35 years of age; (2) not too ill to participate; (3) currently living in one of the three designated counties; (4) having lived in California for five years or more; and (5) having PD for cases.

Of the 1167 PD patients who responded to invitations, we excluded 604 who had their initial PD diagnosis 3 years prior to contact or did not fulfill the above inclusion criteria. Of the 563 eligible cases, 90 were too ill to be examined, moved or died prior to exam. The remaining eligible cases were examined by movement disorder specialists from UCLA to confirm PD diagnoses while 94 did not meet published criteria for idiopathic PD [16], an additional 13 were reclassified as not having idiopathic PD during our follow-up study [17], and 6 withdrew between examination and interview. Of the remaining 360 cases, 357 provided complete information on physical activity.

Population controls 65 years or older were first identified from Medicare lists (in 2001). Later, due to implementation of the Health Insurance Portability and Accountability Act (HIPPA), we recruited around 70% of controls of all ages from residential parcel tax assessor records in the tri-county area. Of the 1212 potential controls, 457 were ineligible, and 409 declined participation due to illness or moving; a total of 341 individuals provided complete information on physical activity.

2.2. Assessment of physical activity

Trained interviewers blinded to case/control status conducted structured telephone interviews to obtain demographic and physical activity information, including self-report of (1) overall physical activity level across four age periods; (2) history of participation in competitive sports; and (3) occupational histories to create a job exposure matrix (JEM) and estimate occupational physical activity.

2.2.1. Overall physical activity

Participants were asked to report average number of days per week and average number of hours per day during which they performed mild, moderate, or vigorous physical activity at work and leisure time, during 4 periods of adulthood: 18–24, 25–44, 45–64, and ≥65 years. Definitions and examples for intensity of activities were provided during interview. To account for both the effects of duration and intensity, we assigned metabolic-equivalent (MET) values to the activity intensities (vigorous activities as 8 and moderate activities as 4) [18] and created a cumulative physical activity measure — MET-hour per week (MET-h/wk) at each age period. Previous studies suggested that only moderate to vigorous activities were associated with PD risk and no effect was observed for mild activities [7,8]; therefore we set “mild” activities to a MET value of zero to maximize the specificity of the physical activity measures. We also calculated the sum of the MET-hour per week for every year of adulthood before index date (PD onset in cases, interview date in controls) and divided by the total number of adult years to derive the average lifetime activity score.

2.2.2. Competitive sports history

If a participant reported ever having engaged in competitive sports, we collected information about type of sports, and ages at which they started and stopped. For every type of sport, a MET value was assigned according to published standard equivalents [19]. We then multiplied the MET value with the reported years for each sport, and summed those to derive cumulative sports measures (MET-year).

2.2.3. Occupational history

Participants were asked to report job titles, tasks, companies, industries, and duration (years) and frequency (hours per week) for all jobs in which they had worked for 6-months or more throughout their lifetime. We created a JEM to estimate occupational physical activity by coding information about jobs and industries based on the Integrated Public Use Microdata Series (IPUMS-USA) 2000 Occupation Code System [20], and assigned MET value to each job code [21]. We first multiplied the MET value with the reported years in each job, and summed those to derive cumulative occupational physical activity measures, and then calculated an average lifetime score by dividing the cumulative score by the total number of working years.

2.3. Statistical analyses

Logistic regression analysis were performed using SAS software version 9.3 (SAS Institute, Inc., Cary, North Carolina), with adjustment for age (continuous), gender, race (white, non-white), education (<12 years, 12 years, >12 years), smoking status (never, past, or current smoker), having a 1st degree family member with PD (yes, no), residential pesticide exposures (ever or never exposed) [22] and pesticide exposure estimates previously derived from a JEM (never, low, median or high exposure) [23]. We reported odds ratio (OR), 95% confidence intervals (95%CI), and p-values for trend based on the median of each exposure category.

We categorized the physical activity scores into quartiles based on the distribution of average lifetime MET scores in controls: <47.8, 47.8–93.0, 93.0–180.0, ≥180.0 MET-h/wk. Participants who never performed moderate and/or vigorous physical activities and those who fell in the 1st quartile of the MET distribution were considered less active and formed our reference group. Furthermore, we examined whether changes in overall physical activity over lifetime until age 64 were associated with PD risk. For each age period, participants were categorized as having high or low activity based on the overall median (93.0 MET-h/wk). We compared those who reported a consistently high activity, and those who reported either low-high or high-low trajectories to those who reported consistently low activity throughout life. For occupational physical activity measures, we categorized cumulative (MET-year) and average (MET) scores into quartiles based on the control distribution in each age period, and for cumulative sport activity scores, we considered those who never participated in any strenuous sport as reference and examined age periods specific tertiles (MET-year). We also included all three measures in the same model to mutually adjust for the different types of activity.

In sensitivity analyses we stratified by gender or excluded subjects with a PD diagnosis prior to age 60. Examining occupational physical activity, we also excluded participants with high occupational pesticide exposures, because we previously found pesticide

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