Physical Activity, Sedentary Index, and Mental Disorders in the SUN Cohort Study

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ABSTRACT

SANCHEZ-VILLEGAS, A., I. ARA, F. GUILLÉN-GRIMA, M. BES-RASTROLLO, J. J. VARO-CENARRUZABEITIA, and M. A. MARTÍNEZ-GONZÁLEZ. Physical Activity, Sedentary Index, and Mental Disorders in the SUN Cohort Study. *Med. Sci. Sports Exerc.*, Vol. 40, No. 5, pp. 827–834, 2008. **Purpose:** There is evidence to suggest a beneficial effect of physical activity on several mental disorders. **Methods:** The study aim was to assess the association between low physical activity during leisure time (or sedentary lifestyles) and the incidence of mental disorders in 10,381 participants, from a Spanish dynamic prospective cohort of university graduates followed up for 6 yr (the SUN study). The baseline assessment included a validated questionnaire on physical activity during leisure-time and sedentary activities. A subject was classified as an incident case of mental disorder if he or she reported a physician diagnosis of depression, anxiety or stress, and/or the use of antidepressant medication or tranquilizers in at least one of the follow-up questionnaires. **Results:** The odds ratios (OR) and 95% confidence intervals (CI) of a mental disorder for successive levels of leisure-time physical activity were 1 (reference), 1.00 (0.81, 1.23), 0.99 (0.81, 1.21), 0.72 (0.58, 0.89), and 0.81 (0.65, 1.00) (P for trend: < 0.01). The OR for subjects who spent more than 42 $h \cdot wk^{-1}$ watching television and/or using the computer was 1.31 (95% CI = 1.01, 1.68) as compared with those spending less than 10.5 $h \cdot wk^{-1}$. **Conclusion:** Our findings suggest a joint association of leisure-time physical activity and sedentary behavior on the incidence of mental disorders. **Key Words:** EXERCISE, INACTIVITY, DEPRESSION, ANXIETY, EPIDEMIOLOGIC STUDY

BASIC SCIENCES

Mental health problems are a public health burden, decreasing the quality of life and resulting in important health care costs (31,34). For instance, the Global Burden of Disease study reported that depression was the leading cause of life of years lived with disability worldwide, and the third-leading cause of disability-adjusted life years in developed countries (17).

Although the beneficial effect of physical activity on chronic disorders such as cardiovascular disease, diabetes, or obesity has been widely proven (5,14), the association between physical activity and mental disease has been less studied. Moreover, the majority of the results are based on patients, and there is a scarcity of studies conducted in large samples of healthy subjects at baseline. There is some evidence to suggest that physical activity has a beneficial effect and alleviates symptoms of mood disturbances (4) and of several mental disorders such as mild and moderate depression (16), anxiety (9), stress (2,15), and bipolar disorder (24). In addition, some clinical trials have explored the dose–response relationship between physical activity and mental disorders (9). There are currently insufficient data to support the idea that a minimum amount of physical activity should be reached to ensure that physical activity results in an effective treatment that helps to alleviate the symptoms of mental disorders (8). However, it seems that once a sufficient level of physical activity is achieved the response and remission rates can be comparable to other depression treatments such as medication or cognitive behavioral therapy (8). Consequently, the amount more than the frequency of physical activity seems to be a stronger determinant of its therapeutic effect on mental problems (8,29).

The studies based on initially healthy populations have suggested a preventive role of physical activity on mental disorders. However, most of the available evidence is based only in cross-sectional analyses (9). The cross-sectional design has the inherent limitation that the direction of the association can not be ascertained. This methodological limitation can be solved with the use of longitudinal

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analyses. Thus, several cohort studies have analyzed the association between physical activity and mental disorders reporting a protective effect for physical activity (6,9–11, 13,25,33,38).

On the other hand, the relationship between sedentary lifestyles and mental conditions has been even less studied. Recently, an inverse association between physical inactivity and mental health was found in men and women (11) concluding that relative increases in cardiovascular fitness are cross-sectionally associated with lower depressive symptomatology and greater emotional well-being. However, longitudinal assessments relating sedentary lifestyles with the incidence of mental disorders are scarce.

The main aim of our study was to assess the association between physical activity during leisure time and sedentary lifestyles on the incidence of mental disorders in a dynamic prospective cohort study of university graduates in Spain. Furthermore, we sought to provide data to address whether a graded dose–response between leisure-time physical activity and mental disorders was present.

METHODS

The SUN study is a multipurpose, dynamic cohort based on university graduates in Spain. Information is collected using self-administered questionnaires sent by postal mail every 2 yr (19,27). The recruitment of participants started in December 1999 and is permanently ongoing. Up to April 2007, data from 17,419 participants were coded and prepared to be analyzed. Participants recruited > 6 yr ago (5360) were able to answer to the baseline (Q0), the 2-yr (Q2), the 4-yr (Q4), and the 6-yr (Q6) follow-up questionnaires. Among them, 1627 are currently undergoing the process of completing their 6-yr follow-up questionnaire, or we confirmed their death. Only other 236 participants can be definitively classified as lost to follow-up after 6-yr follow-up, because they have not returned their Q6 after five mailings. The other 3497 members of the cohort successfully returned their Q6 and completed a ≥ 6-yr follow-up period. The number of participants retained for the 4-yr follow-up (they returned Q2 and Q4 but not Q6) and only for the 2-yr follow-up (they returned Q2) were 4890 and 4245, respectively. Only 4787 had responded exclusively Q0. The overall follow-up rate was approximately 90%.

Participants without follow-up, those who reported extremely low or high values for total energy intake (less than 600 kcal·d^{-1} in men and 400 kcal·d^{-1} in women, or more than 4200 kcal·d^{-1} in men and 3500 kcal·d^{-1} in women), those who were users of either antidepressant or tranquilizer medication at baseline, and subjects with a self-reported physician-diagnosed depression, bipolar disorder, anxiety, or stress at baseline were excluded. Finally, data from 10,381 participants remained available for the analysis.

The study was approved by the human research ethical committee at the University of Navarra. Voluntary completion of the first questionnaire was considered to imply informed consent.

Exposure Assessment. The baseline assessment (Q0) included a physical activity questionnaire collecting information about 17 activities. To quantify the volume of activity during leisure time, an activity metabolic equivalent (MET) index was computed by assigning a multiple of resting metabolic rate (MET score) to each activity (1), and the time spent in each of the activities was multiplied by the MET score specific to each activity, and then summed over all activities to obtain a value of overall weekly MET-hours.

Finally, the continuous variable was categorized into five groups (≤ 3.27, 3.28–9.54, 9.55–18.92, 18.93–32.94, and ≥ 32.95 MET·h·wk^{-1}).

Leisure-time physical activity estimated with the questionnaire was previously validated by our group using a triaxial accelerometer as the gold standard. Physical activity during leisure time (estimated as MET-hours per week) derived from the questionnaire moderately correlated with kilocalories per day assessed through the accelerometer (Spearman's rho = 0.507, 95% confidence interval (CI) 0.232, 0.707, $P < 0.001$) (18).

A sedentary index was built considering the hours per week spent by the subjects watching television and/or using the computer. The information about the number of hours a day spent watching television or using the computer for both a typical day during the week and for a typical day during the weekend was collected. A weighted mean (5 × typical weekday + 2 × typical weekend) was calculated. The sedentary index thus computed was also significantly (inversely) correlated with the objectively measured energy expenditure value (accelerometer) in the validation substudy ($P = 0.007$) (18). The strongest correlation ($r = -0.58$, $P < 0.001$) was found in the validation substudy for the ratio of sedentary activity to leisure-time physical activity (18).

For the present analysis, the sedentary index was categorized into five groups (< 10.5 h·wk^{-1}, 10.5–17.49 h·wk^{-1}, 17.5–27.99 h·wk^{-1}, 28–41.99 h·wk^{-1}, and ≥ 42 h·wk^{-1}).

Covariate Assessment. Energy and alcohol intakes were ascertained through a semiquantitative food frequency questionnaire (136 food items) previously validated in Spain (21). Q0 also included other questions (totaling 46 items for men and 54 items for women). Sociodemographic (e.g., gender, age, and marital status), anthropometric (e.g., weight and height), lifestyle- and health-related habits (e.g., smoking status), and medical history variables (e.g., prevalence of chronic diseases and medication use) were collected. Participants were classified as having cardiovascular disease at baseline if they reported at least one of the following conditions: myocardial infarction, stroke, atrial fibrillation, paroxysmal tachycardia, coronary artery bypass grafting or other revascularization procedures, heart failure, aortic aneurism, pulmonary embolism, or peripheral venous thrombosis. We considered a participant to present a respiratory disease if he or she reported a medical diagnosis of asthma or emphysema. Moreover, information

TABLE 1. Characteristics of the participants of the SUN cohort study according to their physical activity during leisure time.

	Physical Activity During Leisure Time (MET·h·wk^{-1})				
	≤ 3.27 (*N* = 2283)	3.28–9.54 (*N* = 1865)	9.55–18.92 (*N* = 2073)	18.93–32.94 (*N* = 2075)	≥ 32.95 (*N* = 2085)
Median (MET·h·wk^{-1})	0.5	6.4	13.7	24.8	46.3
Sedentary index (h·wk^{-1})†	28.0	26.6	26.6	26.6	25.9
Age (yr)	41.8 (11.0)	43.9 (11.6)	43.3 (11.8)	44.0 (12.2)	42.4 (12.0)
Body mass index (kg·m^{-2})	23.2 (3.6)	23.8 (3.6)	23.7 (3.3)	23.5 (3.3)	23.4 (3.1)
Alcohol intake (g·d^{-1})	5.9 (9.9)	6.9 (11.3)	6.8 (10.2)	7.4 (11.0)	8.1 (11.9)
Energy intake (kcal·d^{-1})	2381.3 (824.6)	2366.4 (780.2)	2390.7 (705.6)	2453.3 (702.0)	2614.7 (889.8)
Smoking status (%)					
Current smoker	31.2	24.4	22.1	21.0	17.2
Ex-smoker	25.6	30.4	28.5	30.3	28.6
Women (%)	67.4	58.9	56.4	53.5	43.0
Married (%)	50.6	56.7	52.0	52.0	46.8
Severe diseases (%)					
Cancer	3.0	2.8	2.7	3.4	3.6
Cardiovascular	2.9	3.6	4.4	4.2	4.0
Ulcer	4.3	4.5	4.8	4.8	4.6
Arthritis	1.8	2.4	2.3	2.1	1.2
Respiratory	6.0	6.7	6.2	6.1	6.8

Values are means and standard deviations (SD) unless otherwise stated. † Sedentary index defined as the sum of hours per week spent on watching television and using the computer.

regarding cancer, rheumatoid arthritis, and ulcer was also collected in Q0.

Outcome Assessment. Any participant, initially free of depression and of antidepressant treatment, who positively responded to the following question in Q2, Q4, or Q6: *Have you ever been diagnosed of depression by a health professional?* was classified as an incident case of depression. The same criteria were applied for bipolar disorder, anxiety, and stress. Self-reported physician diagnosis of depression has been validated in our cohort using the Structured Clinical Interview for DSM-IV (SCID-I) as the gold standard. Sixty-two subjects with a self-reported physician diagnosis of depression and 42 subjects without the diagnosis were included in the validation study. The percentage of confirmed depression was 74.2%; the 95% CI was 63.3, 85.1. The percentage of confirmed nondepression was 81.1%; 95% CI was 69.1, 92.9 (submitted article). Any participant initially free of depression and of antidepressant treatment who reported the habitual use of antidepressant drugs in Q2, Q4, or Q6, was also classified as an incident case of depression. Any participant initially free of a diagnosis of anxiety who reported the habitual use of tranquilizers in Q2, Q4, or Q6 was also classified as an incident case of anxiety. A subject was classified as an incident case of mental disorder if he or she reported a physician diagnosis of depression, anxiety or stress, and/or habitual use of antidepressant medication or tranquilizers in Q2, Q4, or Q6.

Statistical Analysis. Nonconditional logistic regression models were fit to assess the relationship between physical activity (categorized in five successive categories) during leisure time or the sedentary index and the incidence of depression, anxiety, or mental disorder (one of the following conditions: depression, bipolar disorder, anxiety, or stress) in our cohort. Odds ratios (OR) and their 95% CI were calculated considering the lowest level of physical activity and the lowest level of the sedentary index as the reference categories. Tests of linear trend across increasing groups were conducted by assigning the medians to each category and treating the levels of physical activity and sedentary index as continuous variables. Potential confounders included in the multivariate models were gender, age (continuous), employment status (employed/unemployed), body mass index (< 25, 25–29.9, and ≥ 30 kg·m^{-2}), marital status (married, no married), smoking (never, past and current smokers), presence of any severe disease at baseline (cancer, cardiovascular, respiratory, arthritis or gastroduodenal ulcer), alcohol intake (g·d^{-1}), and total energy intake (kcal·d^{-1}).

To ascertain the effect of the joint exposure to low levels of leisure-time physical activity and high levels of the sedentary index, participants with the lowest baseline physical activity levels (below the median < 13.8 MET·h·wk^{-1}) and with the highest level of the sedentary index (above the median ≥ 22.4 h·wk^{-1}) were considered as the reference

TABLE 2. Association between baseline physical activity during leisure time and the risk of mental disorder in the SUN study.

	Physical Activity During Leisure Time (MET·h·wk^{-1})					
	≤ 3.27 (*N* = 2283)	3.28–9.54 (*N* = 1865)	9.55–18.92 (*N* = 2073)	18.93–32.94 (*N* = 2075)	≥ 32.95 (*N* = 2085)	*P* for Trend
Median (MET·h·wk^{-1})	0.5	6.4	13.7	24.8	46.3	
Number of cases	235	184	199	149	156	
Model 1 (OR; 95% CI)	1 (ref)	0.97; 0.79, 1.19	0.96; 0.79, 1.18	0.71; 0.57, 0.88	0.79; 0.64, 0.98	< 0.01
Model 2 (OR; 95% CI)	1 (ref)	1.00; 0.81, 1.23	0.99; 0.81, 1.21	0.72; 0.58, 0.89	0.81; 0.65, 1.00	< 0.01

OR, odds ratio; CI, confidence interval. Risk of mental disorder was defined as self-reported physician diagnosis of depression, bipolar disorder, anxiety or stress, or use of antidepressant medication or tranquilizers reported in Q2, Q4, or Q6. Model 1: Adjusted for age (yr) and gender. Model 2: Additionally adjusted for energy intake (kcal·d^{-1}), smoking (never, smoker, ex-smoker, missing), marital status (married, not married, missing), arthritis, ulcer, and cancer in Q0.

TABLE 3. Association between baseline sedentary index and the risk of mental disorder in the SUN study.

	Sedentary Index					
	< 10.5 (*N* = 1450)	10.5–17.49 (*N* = 1477)	17.5–27.99 (*N* = 1925)	28–41.99 (*N* = 1615)	≥ 42 (*N* = 1524)	*P* for Trend
Median ($h \cdot wk^{-1}$)	7.7	14.0	21.7	34.3	51.8	
Number of cases	123	128	168	135	152	
Model 1 (OR; 95% CI)	1 (ref)	1.07; 0.82, 1.38	1.10; 0.86, 1.40	1.09; 0.85, 1.41	1.35; 1.05, 1.74	0.02
Model 2 (OR; 95% CI)	1 (ref)	1.06; 0.82, 1.38	1.08; 0.85, 1.38	1.07; 0.83, 1.39	1.31; 1.01, 1.68	0.04

OR, odds ratio; CI, confidence interval. Mental disorder was defined as self-reported physician diagnosis of depression, bipolar disorder, anxiety or stress, or use of antidepressant medication or tranquilizers reported in Q2, Q4, or Q6. Sedentary index was defined as the sum of hours per week spent on watching television and using the computer. Model 1: Adjusted for age (yr) and gender. Model 2: Additionally adjusted for energy intake ($kcal \cdot d^{-1}$), smoking (never, smoker, ex-smoker, missing), marital status (married, not married, missing), arthritis, ulcer, and cancer in Q0.

category, and they were compared with the other three categories created by combining both exposures.

All *P* values presented are two tailed; $P < 0.05$ was considered statistically significant.

RESULTS

Table 1 shows the main characteristics of the participants according to the levels of physical activity during leisure time. Physical activity level was lower among women, current smokers, and married subjects. On the other hand, participants with the highest level of physical activity also showed the highest alcohol and total energy intake.

We identified 923 cases of mental disorders (418 of them were depression cases, and 731 were anxiety cases with some of the cases belonging to both categories) during the 6-yr period of follow-up.

Table 2 shows the association between leisure-time physical activity and the risk of mental disorder in the cohort. The multivariate-adjusted OR and 95% CI for a mental disorder for successive levels of physical activity during leisure time were 1 (reference), 1.00 (0.81, 1.23), 0.99 (0.81, 1.21), 0.72 (0.58, 0.89), and 0.81 (0.65, 1.00). Moreover, the linear trend for physical activity across successive categories of exposure was statistically significant (*P* for trend: < 0.01). Taking into account the fact that an excess of physical activity may also produce some negative psychological effects (3), the analysis was repeated after excluding those subjects with a leisure-time physical activity level above the 95th percentile ($61.6\ MET \cdot h \cdot wk^{-1}$). The results for the highest category of physical activity did not change substantially: OR = 0.79 (0.63, 1.00).

To avoid a possible reverse causation (i.e., people who are subclinically depressed or anxious have reduced activity), we repeated the analysis excluding those cases of mental disorders reported in Q2 ($N = 538$). The OR for the forth and fifth category of leisure-time physical activity were 0.48 (0.34, 0.68) and 0.69 (0.50, 0.94) respectively.

Opposite results were found for the sedentary lifestyle analyses (restricted to 7991 subjects with available information on sedentary activities) (Table 3). Subjects with the highest level of the sedentary index showed an increased risk of mental disorder. The OR for subjects who spent more than 42 $h \cdot wk^{-1}$ watching television or using the computer was 1.31 (95% CI = 1.01, 1.68) as compared with those spending less than 10.5 $h \cdot wk^{-1}$. Moreover, a direct dose–response relationship between sedentary lifestyles and the incidence of mental disorders was found (*P* for trend = 0.04). All these results were not materially affected by further adjustment for employment status, body mass index, alcohol intake, or prevalent cardiovascular or respiratory disease in Q0.

The relationship between the joint exposure to both levels of physical activity during leisure time and sedentary lifestyles with the risk of mental disorders is shown in Table 4. Those subjects with a physical activity level above the median (≥ 13.8 $MET \cdot h \cdot wk^{-1}$) showed a relative risk reduction of suffering a mental disorder of approximately 25% irrespective of their reported level of the sedentary index (OR = 0.76; 95% CI = 0.61, 0.95 for those with a high sedentary index and OR = 0.75; 95% CI = 0.60, 0.93 for those with a low sedentary index).

Figure 1 shows the OR and 95% CI for a diagnosis of anxiety according to the levels of physical activity during leisure time and the levels of the sedentary index. Those subjects with a level of physical activity during leisure time higher than 18.93 $MET \cdot h \cdot wk^{-1}$ showed a decreased risk of receiving an anxiety diagnosis compared with those with the lowest level of physical activity (OR = 0.67; 95% CI = 0.52, 0.85 for those subjects with a physical activity level

TABLE 4. Joint association between the incidence of mental disorder and both baseline physical activity and the sedentary index.

	Physical Activity Below the Median < 13.8 $MET \cdot h \cdot wk^{-1}$		Physical Activity Above the Median ≥ 13.8 $MET \cdot h \cdot wk^{-1}$	
	Sedentary Index Above the Median ≥ 22.4 $h \cdot wk^{-1}$	Sedentary Index Below the Median < 22.4 $h \cdot wk^{-1}$	Sedentary Index Above the Median ≥ 22.4 $h \cdot wk^{-1}$	Sedentary Index Below the Median < 22.4 $h \cdot wk^{-1}$
Number of cases	218	184	143	161
Model 1 (OR; 95% CI)	1 (ref)	0.83; 0.68, 1.03	0.75; 0.60, 0.94	0.73; 0.51, 0.91
Model 2 (OR; 95% CI)	1 (ref)	0.85; 0.69, 1.05	0.76; 0.61, 0.95	0.75; 0.60, 0.93

OR, odds ratio; CI, confidence interval. Mental disorder was defined as self-reported physician diagnosis of depression, bipolar disorder, anxiety or stress, or use of antidepressant medication or tranquilizers reported in Q2, Q4, or Q6. Sedentary index was defined as the sum of hours per week spent on watching television and using the computer. Model 1: Adjusted for age (yr) and gender. Model 2: Additionally adjusted for energy intake ($kcal \cdot d^{-1}$), smoking (never, smoker, ex-smoker, missing), marital status (married, not married, missing), arthritis, ulcer, and cancer in Q0.

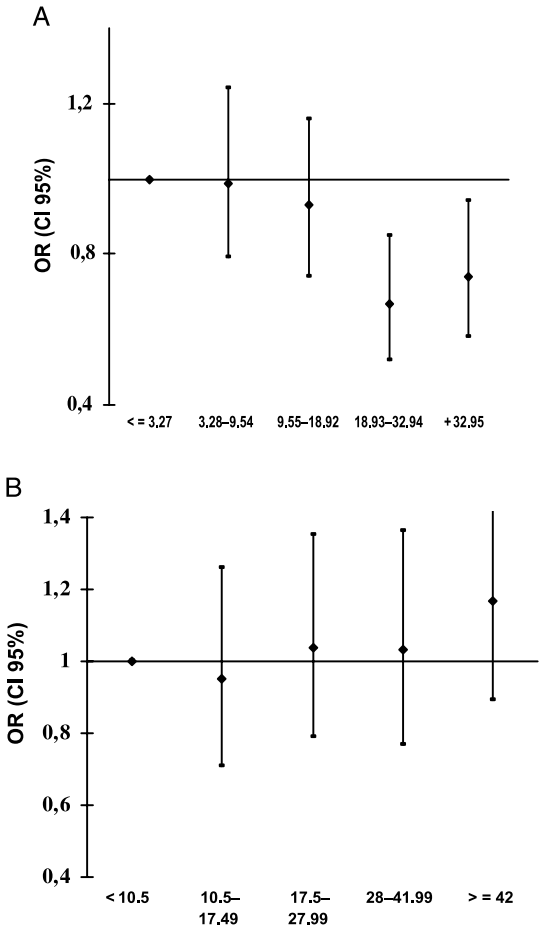

FIGURE 1—Multivariate OR (95% CI) of anxiety according to levels of physical activity during leisure time (*A*) and the sedentary index (*B*) in the SUN study. Multivariate OR = odds ratio adjusted for age, gender, energy intake (kcal·d^{-1}), smoking (never, smoker, ex-smoker, missing), marital status (married, not married, missing), arthritis, ulcer, and cancer in Q0. Anxiety was defined as physician diagnosis of anxiety or use of tranquilizer medication reported in Q2, Q4, or Q6. Sedentary index was defined as the sum of hours per week spent on watching television and using the computer.

between 18.93 and 32.94 MET·h·wk^{-1} and OR = 0.74; 95% CI = 0.58, 0.94 for those subjects with a level of activity higher than 32.94 MET·h·wk^{-1}) (P for trend = < 0.01). However, we did not find a statistically significant association between the sedentary index and anxiety risk (P for trend = 0.17).

When depression incidence was analyzed, no significant associations were found for physical activity during leisure time (OR for the highest category of physical activity = 0.90; 95% CI = 0.65, 1.23; P for trend = 0.30) or for sedentary lifestyles (OR for the highest level of the sedentary index = 1.35; 95% CI = 0.94, 1.94; P for trend = 0.27).

DISCUSSION

Despite the growing body of evidence suggesting that physical activity might reduce the risk of mental disorders, limited longitudinal data assessing the relationship between physical activity during leisure time and the incidence of mental disorders can be found in the literature. The findings of the present study support the previous notion that participants with higher levels of physical activity per week during their leisure time had a reduced risk of mental disorders compared with less active individuals. Additionally, those subjects with maximum levels of sedentary habits (more than 42 h·wk^{-1}) showed a 31% increased risk for developing mental disorder compared with those individuals with lesser time devoted to sedentary activities (< 10.5 h·wk^{-1}). As a result of this, an interesting joint association between the incidence of mental disorder and both baseline physical activity and sedentary lifestyles was identified in our cohort.

Data from the National Health and Nutrition Examination Survey (NHANES I) including 7000 subjects ages 25–74 found that people who reported little or no physical activity in their leisure time were more likely to exhibit more symptoms of depression (10). Moreover, several reviews have concluded that physical activity is associated with a reduction in depressive or anxiety symptoms (9,26). However, these reviews included many cross-sectional studies from which the nature of the association could not be determined.

Longitudinal epidemiologic studies have produced conflicting results. In a study of approximately 10,000 male Harvard University alumni, physical activity was shown to reduce the likelihood of developing physician-diagnosed depression (25). Brown et al. (2005) also reported a relationship between increasing physical activity and decreasing depressive symptoms in middle-aged women (6). Moreover, Goodwin et al. (2003) found that in a representative sample of adults in the United States, this association persisted independently of differences in sociodemographic characteristics (13). In contrast, Wiles et al. (2007) observed that heavy-intensity leisure-time physical activity was associated with only a small reduction in the likelihood of common mental disorder over a 5-yr period, while no evidence for an association over the long term (10 yr) was found in middle-aged men of their study, concluding that no evidence to support a long-term dose–response effect or association was found (37). The authors did not exclude the possibility that final results can be influenced by the fact that no repeated measurements of leisure-time physical activity were made. The fact that changes in physical activity and leisure physical activity behaviors during the follow-up (from active to nonactive, and vice versa) can considerably influence the OR of several mental disorders (38) strengthens the authors' concerns. In our study, the significant inverse linear trend between physical activity during leisure time and the risk of mental disorders may indicate that an inverse dose–response relationship between both variables was found, suggesting that increasing the levels of physical activity during leisure time may contribute to lower the incidence of mental disorders.

Interestingly, our results were not materially affected by further adjustment for body mass index, alcohol intake, or cardiovascular/respiratory prevalent disease. Moreover, the observed associations do not seem to be related to an early undetected mental disease that could cause reverse causality, because when we excluded the cases reported in the first follow-up questionnaire, the physical activity estimations improved substantially.

Recently, it has been published that the "public health dose" of physical activity (the equivalent to public health recommendations: 17.5 $kcal \cdot kg^{-1} \cdot wk^{-1}$) produced a positive effect on the treatment of depression, whereas a low dose of physical activity (i.e., 7 $kcal \cdot kg^{-1} \cdot wk^{-1}$) did not produce the same positive effect (8). Nevertheless, experimental studies can only determine the short-term effects of an intervention. Data from our study points toward the same direction as those groups with lower physical activity levels during leisure time (< 19 $MET \cdot h \cdot wk^{-1}$) did not show any marked reduction in the risk of developing mental disorders, while those groups with highest levels of physical activity (> 19 $MET \cdot h \cdot wk^{-1}$) lowered their risk in a relative range of 19–28%, suggesting that a sufficient level of physical activity (frequency, duration, and intensity) might be needed to obtain the beneficial effect that physical activity during leisure time may exert on the incidence of mental disorders.

Several hypotheses have been proposed to describe the beneficial effects of physical activity on mental health. Specific mechanisms could be related to antiinflammatory and neurochemical effects of physical activity. The large amounts of encephalins and endorphins secreted during exercise (12,22) can be a potentially important pathway. Exercise of sufficient intensity and duration has been demonstrated to increase circulating beta-endorphin levels. However, the exact mechanism that may explain how physical activity helps to stimulate healthy several brain processes still remain not fully understood. Several prospective analyses have also suggested that physical activity influences the central dopaminergic, noradrenergic, and serotonergic systems presumably exerting therapeutic effects on the patient (7,23). Other authors have suggested improvements in some psychosocial parameters such as body image, self-esteem, self-efficacy, or self-worth, and a decrease in social isolation as a result of a greater recreational physical activity (32). Thus, social relations could constitute an intervening variable between physical activity and mental disorders (33,35).

One of the main strengths of this cohort study is the collection of detailed data on leisure-time physical activity (17 activities based on the validated SUN questionnaire). This contrasts with previous studies in which information on leisure-time physical activity was collected, often using a single question (10,28,36). In our study, based on the activities reported by the participants, METs were computed as a proxy measurement of the amount of physical activity. The use of METs enabled us to discriminate among subgroups of the population characterized by their different intensity of leisure-time physical exercise. As a result, we found that groups with intermediate or moderate physical activity levels) had only a minor reduction in their relative risk for developing mental disorders. Conversely, those groups with the highest levels of physical activity ($MET \cdot h \cdot wk^{-1}$) showed a clear reduction in their relative risk for receiving a medical diagnosis of a mental disorder.

Although an inverse cross-sectional association between inactivity and mental health was recently published (11), to the best of our knowledge this is the first prospective study to evaluate the association between sedentary habits (using a sedentary index that includes hours per week spent watching television or using the computer) and the risk of develop mental disorders after a follow-up, and one of the few epidemiological studies to asses the dose–response relationship between both physical activity and sedentary behavior and mental disorders in adults. We acknowledge that one limitation of our study is that the SUN cohort is not representative of the general population, because it consists exclusively of university graduates of Spain. A higher educational level has been reported to be associated with a higher prevalence of leisure-time physical activity in Europe (20). It is possible that the effect of physical activity on mental disorders maybe modified by educational levels. If this were true, our results could not be extrapolated to segments of the population with lower educational attainments. However, to our knowledge, there is no available evidence showing that literacy levels may modify the effect of leisure-time physical on mental disorders.

Consistent with prior observational studies (11,13) that studied the association between sedentary behavior and several mental disorders, our results showed a clear graded relationship between our sedentary index and the relative risk of developing mental disorder. Subjects with the highest level of sedentary behavior showed an increased risk of mental disorder (31%) compared with more active individuals. Interestingly, in some of the mental disorders included in the study (i.e., anxiety), it is possible that physical activity levels but not sedentary behavior had a more determinant role in the incidence of this disorders, as it is shown by fact that anxiety on its own only showed a significant trend with physical activity levels but not with sedentary levels after adjusting for several confounding factors.

Thus, in our view, one of the most interesting findings of the study is the joint association between activity and the levels of sedentary behavior on the incidence of mental disorders. It is possible to perceive that when data related to physical activity levels below the median are selected, the sedentary index lower than the median indicates a lowered incidence of mental disease (15%), suggesting that among those with lower physical activity levels, a sedentary lifestyle might have an important

role in the incidence of mental disorder. However, when physical activity levels above the median are selected, sedentary behaviors seem not to be so critical, showing again that once a sufficient level of physical activity is reached, sedentary habits might be not so decisive. To our knowledge, no previous study has found this type of association.

In summary, data from our study are consistent with and extend previous findings by showing a joint association between physical activity and sedentary behavior on the incidence of mental disorders. This association persisted independently of differences in age, gender, energy intake, smoking status, marital status, arthritis, ulcer, and cancer. Replication of these findings is necessary, and future studies are needed to directly address the mechanisms to explain these associations.

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