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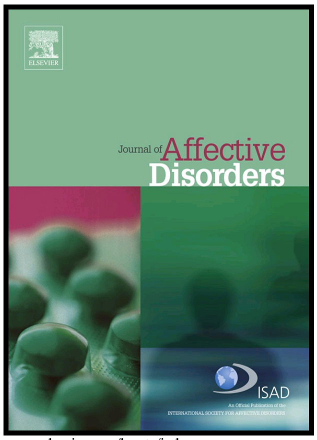

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Persistent leisure-time physical activity in adulthood and use of antidepressants: a follow-up study among twins

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Abstract

Background: To study whether persistent leisure-time physical activity (PA) during adulthood predicts use of antidepressants later in life.

Methods: The Finnish Twin Cohort comprises same-sex twin pairs born before 1958, of whom 11 325 individuals answered PA questions in 1975, 1981 and 1990 at a mean age of 44 years (range 33-60). PA volume over 15-years was used as the predictor of subsequent use of antidepressants. Antidepressant use (measured as number of purchases) for 1995-2004 were collected from the Finnish Social Insurance Institution (KELA) prescription register. Conditional logistic regression was conducted to calculate odds ratios (OR) with 95 % confidence intervals (CI) for the use of antidepressants in pairs discordant for PA (642, including 164 monozygotic (MZ) pairs).

Results: Altogether 229 persons had used at least one prescribed antidepressant during the study period. Active co-twins had a lower risk (unadjusted OR 0.80, 95%CI 0.67-0.95) for using any amount of antidepressants than their inactive co-twins; trends being similar for DZ (0.80, 0.67-0.97) and MZ pairs (0.78, 0.51-1.17). The lowest odds ratio (0.51, 0.26-0.98) was seen among MZ pairs after adjusting for BMI, smoking and binge drinking. The point estimates were similar but non-significant for long-term antidepressant use (4+ purchases equivalent to 12 months use).

Limitations: Self-reported physical activity and low number of discordant MZ pairs.

Discussion: Use of antidepressants was less common among physically active co-twins even when shared childhood experiences and genetic background were controlled for. Physical activity in midlife may therefore be important in preventing mild depression later in life.

Keywords

physical activity; inactivity; depression; antidepressants; twins; genetic; follow-up

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Introduction

Depression is a major cause of sickness leaves and early retirement; it also reduces quality of life and causes high economic costs. In Finland, mood affective disorders were a leading reason for a disability pension in 2013, accounting for 18.9 % of all disability pensions awards and for 23.1 % among women (Finnish Centre for Pensions and The Social Insurance Institution of Finland, 2014). Depression is characterized in the Diagnostic and Statistical Manual of Mental Disorders 5th edition (DSM-V) as the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function (American Psychiatric Association, 2013). According to WHO (2012) recommendations, the treatment options for moderate to severe depression consist of basic psychosocial support which is combined with either antidepressant medication or psychotherapy (WHO, 2012). A recent systematic review on the effect of different treatments for depression concluded that antidepressants or psychotherapy alone are not significantly different from alternative therapies, such as exercise, or active intervention controls (Khan et al., 2012).

Epidemiological studies have shown that physical activity is associated with reduced risk for depressive symptoms and anxiety (Strohle, 2009). Several meta-analyses have been conducted on whether, in randomized controlled trials, physical activity reduces depression (Josefsson et al., 2014; Krogh et al., 2011; Lawlor and Hopker, 2001). The most recent meta-analysis confirms the findings of earlier studies that physical activity has a moderate or large effect on depression and could be recommended as a treatment for depressive subjects (Josefsson et al., 2014). In a study of the relationship between baseline physical activity and future psychotropic medication use (Lahti et al., 2013), physical activity was found to predict decreased risk for using psychotropic medications, the most active participants having the smallest hazard ratios. However, in that study physical activity was measured only once and therefore it does not indicate a long-term physical activity habit. Moreover, in addition to antidepressant medications, the study combined sedatives and sleep medications (N05B and N05C) in the psychotropic medication analysis.

Heritability for participation in physical activity is relatively high (Bouchard et al., 1992; Kujala et al., 2002) while for depression it is low to moderate (Burton et al., 2015; Kendler et al., 2006; Takkinen et al., 2004). Therefore, an association between physical activity and depression may be mediated in part by genetic factors common to both. Genetic and biological factors may also account for interindividual differences in response to therapy, such as exercise, among depressed patients. Twin data offer a unique opportunity for studying the nature of the association between physical activity and depression. By studying outcomes in twin pairs discordant for exposure to physical activity, the possible confounding role of genetic and shared early childhood experiences can be taken into account (Boomsma et al., 2002). Twin pairs nearly always share the same childhood family environment. Dizygotic (DZ) pairs share, on average, half of their segregating genes (like siblings), while monozygotic (MZ) pairs are genetically identical at the sequence level.

The aim of this study was to find out whether persistent leisure-time physical activity during adulthood predicts use of antidepressants (investigated as amount of antidepressant purchases) later in life when shared childhood environment and genetic background are controlled for. In this co-twin control design study, the twin pairs had 15 years of physical activity discordance. We were interested in whether the active co-twins were less likely to use depression medications over a 10-year follow-up period. We expected persistent physical activity to reduce the use of antidepressants.

Methods

Study participants

The Finnish Twin Cohort is a comprehensive national sample of same-sex twin pairs born before 1958 and with both co-twins alive in 1967 (Kaprio and Koskenvuo, 2002). In 1975, a baseline questionnaire was sent to twin pairs with both members alive. At the beginning of prospective follow-up, the total number of twin pairs was 12 069. A second similar questionnaire was sent out to all surviving twin pairs in 1981 (Kaprio and Koskenvuo, 2002). A third questionnaire was sent out in 1990 to all twin individuals aged 33–60 years who had responded to at least one of the earlier questionnaires (Romanov et al., 2003). A total of 11 325 twin individuals had answered the leisure-time physical activity questions in all three questionnaires (1975, 1981 and 1990). Among them were 4 190 complete twin pairs (1 388 MZ, 2 547 DZ and the rest with unknown zygosity). Of these, 642 pairs were discordant for leisure-time physical activity according to the mean metabolic equivalent (MET) index (see below for criteria used to determine discordance in twin pairs). The final study cohort comprised 164 MZ pairs (78 male and 86 female) and 449 DZ pairs (196 male and 253 female), and the remaining 29 pairs (14 male and 15 female) were of uncertain zygosity. In 1990, the mean age of the final study cohort was 44.2 years (SD 7.7, range 33-60) with no sex differences. The study was conducted according to the Declaration of Helsinki. All the participants gave their informed consent before answering the questionnaire.

Physical activity predictor

Physical activity habits were assessed by identical questions in 1975 and 1981 and with slightly different questions in 1990. All three questionnaires enabled calculation of the MET index. On the bases of earlier studies, the physical activity questionnaire data can be considered valid (Kaprio et al., 1978; Kaprio et al., 1987; Kujala et al., 1994; Kujala et al., 1998; Leskinen et al., 2009; Waller et al., 2008). Assessment of the MET index was based on a series of structured questions (Kaprio et al., 1978; Kujala et al., 1998) on leisure-time physical activity (monthly frequency, mean duration and mean intensity of sessions) and physical activity during the journey to and from work. The index was calculated by assigning a MET score to each activity and by calculating the product of that activity: intensity x duration x frequency (Kujala et al., 1998). The MET index was expressed as the sum-score of leisure-time physical activity (PA) MET-hours per day.

To estimate the volume of physical activity during the three baseline years, a mean activity was calculated by summing the MET index values obtained in 1975, 1981 and 1990 and dividing by three. This new mean MET value was then divided into three activity tertiles labelled low (mean MET 0-1.54 MET h/day), medium (1.54-2.92 MET h/day) and high (2.92-26.13 MET h/day). Twin pairs were classified as discordant for physical activity if one co-twin was in the low activity tertile and his/her co-twin in the high activity tertile. A total of 642 twin pairs met this discordance criterion.

Covariates and exclusions

Self-reported social class, smoking status, use of alcohol, body mass index (BMI), and health status in 1990 were used as covariates. Social class was defined by dividing the individuals into three groups by years of education and amount of physical activity at work (Romanov et al., 2003). Smoking status was coded into three categories (never smoked, former smoker and occasional smoker/current (daily) smoker) determined from responses to detailed smoking history questions (Kaprio and Koskenvuo, 1988). Alcohol use was expressed as dichotomous variable of heavy drinking occasions (i.e. consumption of at least six drinks on one occasion) at least monthly (Kaprio et al., 1987; Sipilä et al., 2015). Somatic health status was defined as having/ not having disease diagnosed by a physician, serious injury/illness or permanent work disability, according to self-report items in 1990. Those reporting not having any of the above were classified as healthy (Romanov et al., 2003).

Severity of depressive symptoms at baseline was assessed using the Beck Depression Inventory (BDI) (Beck et al., 1961). The BDI score ranges from 0 to 63, indicating normal mood (BDI 0–9), mild depression (BDI 10–18) and moderate to severe depression (BDI≥19) (Koivumaa-Honkanen et al., 2004). To avoid the effect of depression on physical activity, persons with moderate or severe depression at baseline (n=36 individuals) were excluded from the study. Those for whom the BDI was missing were also excluded (n=48). In total, 78 pairs were excluded owing to one or both co-twins having either no BDI information or BDI ≥ 19.

Antidepressant medication

In this study, the use of antidepressants is measured as number of purchases of antidepressants. The outcome of this study comprised register-based purchases of antidepressant medication (ATC code N06A) during the years 1995-2004. All the persons recorded in the Finnish Social Insurance Institution (KELA) prescription register as purchasing antidepressants were linked with the twin cohort. The prescription registry follow-up was started in 1995, and our linkage covered purchases until the end of year 2004. KELA provides data on the number of purchases of prescribed medications by each citizen and each purchase can cover medication needs for up to three months. A single prescription is valid for 12 months, after which it must be renewed by a physician.

For this study, the medication data were first divided into two classes; individuals with 0 purchases as non-users and those with 1 or more purchases during the study period as users. To study long-term medication use, a secondary analysis was conducted with another binary classification: 0 purchases as non-users and those with 4 or more medication purchases as long-term users (4 purchases is equivalent to one year's supply). Those in between, i.e. 1-3 purchases (n=101), were not included in the analyses. Occasional purchases were studied using the following two classifications: 0 as non-users, 1 or 2 purchases as occasional users (maximum use 6 months). Persons with 3 or more purchases (n=148) were not included in the analyses. The second occasional class was formed to cover use up to 9 months (1-3 purchases), thereby excluding persons with 4 or more purchases.

Statistical analysis

Use of antidepressants were analysed among the twin pairs discordant PA, excluding those with baseline BDI ≥ 19. Firstly, non-users vs. any users were analysed. Second, information on whether use had become long-term (4+ purchases) was analysed within the PA discordant twin pairs. In the third analysis, the two occasional use classifications were studied. Conditional logistic regression was conducted to calculate within pair odds ratios (OR) and 95 % confidence intervals (CI).

All analyses were first performed without any adjustments, as age and sex were already accounted for in the design (same sex twin pairs). Next, the covariates were added to the model individually and, finally, in the variables were added to the full model. Analyses were first performed for all pairs (includes DZ, MZ and pairs with uncertain zygosity) and then for MZ and DZ pairs separately. The paper concentrates on the pairwise analyses, as the design of the study is a co-twin control design; however, the basic analyses were also performed for twins as individuals using age- and sex-adjusted logistic regression with clustering of data within pairs.. All analyses were conducted using StataIC version 14.

Results

During the study period 1995-2004, 229 of the 1 284 twin individuals comprising the physical activity discordant pairs had used at least one prescribed antidepressant, 128 were long-term users (4+ purchases) and 81 had made one or two purchases. Twenty-two individuals had used medication throughout the 10-year period, as they had made a minimum of 40 purchases. The mean number of purchases among all 1 284 individuals was 2.3 and the median 0, while among those who had made at least one purchase the respective numbers were 12.4 and 5. Table 1 shows the baseline characteristics of all 642 pairs according to their PA status. At the baseline in 1990, the inactive co-twins had slightly higher BMI and reported more frequent binge drinking episodes than their active co-twins. Seventy-eight pairs were discarded as one or both twins in these pairs had missing BDI data or had BDI values ≥ 19, leaving 564 pairs for the further analyses (144 MZ and 395 DZ pairs).

The basic logistic regression analysis across the eligible sample (n=1 200 individuals with BDI <19) yielded an age- and sex-adjusted odds ratio of 0.83 (95 % CI 0.72-0.96) for any antidepressant user among the active compared to inactive individuals. Pairwise analysis with conditional logistic regression showed that the active co-twins were less likely (0.80, 95 % CI 0.67-0.95) to use antidepressants than their inactive co-twins. Similar trends were seen for DZ (0.80, 95 % CI 0.67-0.97) and MZ (0.78, 95 % CI 0.51-1.17) pairs. Heterogeneity by zygosity was tested and the results of the model, after adjusting for BMI, revealed a significant difference (p=0.001) between the DZ and MZ pairs. The results of the BMI-adjusted model for any antidepressants remained similar for all pairs and for the DZ pairs, while the odds ratio was even lower, but marginally non-significant, for the MZ pairs (OR 0.57, 95 % CI 0.32-1.00). The lowest odds ratio (OR 0.51, 95 % CI 0.26-0.98) was observed for the MZ pairs in the fully adjusted model (BMI, smoking and binge drinking in 1990). Other adjustments are shown in Table 2. Health status and social class were also used as covariates, but as they did not affect the results they are not shown in the tables or in the results section.

When long-term antidepressant use (4+ prescribed antidepressant purchases) was analysed, no significant differences were seen between the inactive and active co-twins, and the point estimates were weaker than in the prior analysis. The unadjusted OR for all the active co-twins was 0.84 (95 % CI 0.66-1.06). The zygosity-specific and adjusted results can be seen in Table 2.

The analyses of the first classification of the occasional use of antidepressants (one or two purchases over 10 years) showed that the active co-twins had lower odds ratios for medication use among all pairs (0.65, 0.48-0.87) and DZ pairs (0.63, 0.45-0.88) compared to their inactive co-twins. The results did not change when adjusted (Table 2). In the analyses of the MZ pairs, no statistically significant differences were seen between the inactive and active co-twins. The analyses of the second classification of occasional use (1-3 purchases) revealed that the point estimates were weaker than in the first occasional use analyses and statistically significant results were observed only among all pairs in the basic and BMI90-adjusted model, as shown in table 2.

Of the 564 PA discordant pairs with DBI < 19, 139 pairs were also discordant for antidepressant use during the follow-up period (1995-2004). Of the 139 twin pairs discordant for both physical activity and antidepressant use, the inactive twins in 85 pairs used antidepressants while their active co-twins did not. The opposite was true for 54 pairs (exact symmetry test p=0.011). The respective numbers for the DZ pairs were 70 and 45 (p=0.025), and for the MZ pairs 15 and 9 (p=0.308). Comparison of the mean MET values according to use of antidepressants showed that individuals who were non-users had been physically active on average for 2.95 MET h/day across the 15-year baseline period, while the corresponding value for those who had used antidepressants was 2.52 MET h/day (adjusted Wald test, p=0.008).

Discussion

The results of this study showed that the use of antidepressants among physically active twins was less frequent than among their inactive co-twins. These results were most evident among the DZ twin pairs, but some outcomes were also observed among the MZ twin pairs. The lowest odds ratio was seen among MZ pairs after adjusting for confounders. Thus, some of the associations remained after controlling for the effect of shared childhood environmental and genetic factors giving evidence for the causal nature of the protective association. The association was strongest when the analysis included the co-twins who were only occasional antidepressant users. However, weaker and statistically non-significant differences were found when users with more than four purchases were compared to non-users. This result indicates that physical activity might be associated with less severe depression, as proxied by occasional antidepressant use, but not with more severe depressive symptoms, as implied by a requirement for more frequent and long-term medication use.

This study is in line with a previous Finnish study in which physical activity was associated with decreased risk for using psychotropic medications (Lahti et al., 2013). However, the study did not control for familial influences, physical activity was measured only once, and both sedatives and sleep medications (N05B and N05C) were included in addition to antidepressants. Our study, in turn, used data on purchases of prescribed antidepressants (ATC code N06A) only, and included information on long-term baseline physical activity. To our knowledge no studies on the association between physical activity and depression medication use among twins have been conducted. Although, a study by De Moor et al.

2008 found no difference within discordant MZ twin pairs when looking at depressive symptoms; the more active twin did not display fewer depressive symptoms than the less active co-twin (De Moor et al., 2008). While in our study, some of the the associations remained among the MZ pairs.

The results suggest that physical activity in midlife may be important in the prevention of relatively mild depression. Our results are in line with a recent meta-analysis by Josefsson et al. (2014) which also concluded that physical activity could be recommended for mildly and moderately depressed individuals. However, according to another meta-analysis, exercise may also be effective for clinically depressed people (Rethorst et al., 2009). Our study showed no differences between inactive and active co-twins when long-term antidepressant use was studied, indicating that physical activity is unlikely to prevent the onset of more severe depression. A formal trial would be needed to ascertain whether people with more severe depressive symptoms could benefit from physical activity as part of therapy. However, the point estimates of the odds ratios were similar in these analyses as in the main analysis, but statistically significant differences were not observed.

Many different mechanisms have been proposed to explain the effect of exercise on mental health. As summarized by Josefsson et al. (2014), these mechanisms include biological, neurological and physiological changes as well as psychological and psychosocial aspects. Many of the neurobiological mechanisms of physical activity are suggested to be similar to those of antidepressants (Wegner et al., 2014). Physical activity has also been reported to have many other health benefits over traditional treatments (Josefsson et al., 2014). Exercise reduces depression via a neurobiological mechanism that includes increased noradrenaline levels, decreased stress hormone cortisol levels and changes in hippocampal neurogenesis (Rethorst et al., 2009; Wegner et al., 2014) such as increase in b-endorphins, vascular endothelial growth factor, brain-derived neurotrophic factor and serotonin (Ernst et al., 2006). As both genes and physical activity may have an influence on many of the mechanisms and different health aspects (such as decreased stress, reduced anxiety, weight management and chronic diseases) suggested to be underlying the occurrence of depression, studying MZ pairs discordant for physical activity adjusts for the sequence level genetic mechanisms. However, the mechanisms through which physical activity induces a reduction in depressive symptoms are still not well understood and thus warrant further investigation.

Study strengths and limitations

One of the strengths of this study was that physical activity was measured at three baseline time points (1975, 1981 and 1990). This allowed us to use persistent leisure-time physical activity during adulthood as the predictor. Data on antidepressant purchases can be considered a valid and reliable method of indicating the presence of a depressive disorder, as to be able to purchase antidepressants, and therefore to use antidepressants, they have to be prescribed by a physician. However, we do not know if medications prescribed for diagnosed depression were not in fact purchased and/or used. We also have no data on those who were depressed, but did not seek treatment, i.e. did not consult a physician. A further strength of our study was the relatively large number of discordant twin pairs; of the 4 190 twin pairs 15% (642 pairs) were discordant for physical activity. However, the overall and relative number of discordant MZ pairs was smaller (4% of all pairs), which limited the power of the MZ pair analyses. This may explain why the analyses among MZ pairs did not show many significant results.

The use of self-reported physical activity data can be considered a limitation of this study. However, objective measurements of physical activity did not exist at the time when our baseline questionnaires were used. The physical activity questions used in 1975 and 1981 have shown high correlations with subsequent questionnaires and physical activity data obtained by interviews (Waller et al., 2008). In other prospective studies using the entire twin cohort, a low activity metabolic equivalent (MET) index has been shown to be a predictor of mortality, type 2 diabetes, coronary heart disease and hospitalization (Kaprio et al., 2000; Kujala et al., 1998; Kujala et al., 1999; Kujala et al., 2000; Kujala et al., 2002; Waller et al., 2010). A further limitation of the study is that we do not have information about diagnoses of severe psychiatric disorders and use of medication for these at the 1990 baseline, and therefore these individuals could not be excluded from the study. However, we had information about severity of depression symptoms as assessed with the BDI in 1990, and we were able to exclude from the analyses all subjects who had moderate or severe depression (BDI≥19). While we also had information about life satisfaction (LS) in 1990, high BDI was chosen as the sole exclusion criterion as it can be considered to bear a closer relation to depression and we did not want to reduce the number of observations further. When LS was used as a covariate in the basic model, the results did not markedly change (OR for having at least one medication was 0.82, 95 % CI 0.69-0.98). The BDI information was available only for the last baseline year (1990) and hence we are unaware of earlier depressive symptoms and whether they had affected participants' earlier physical activity ability. However, physical activity was assessed at the three baseline years, and can thus be considered to be a long-term health habit regardless of possible earlier depressive symptoms.

Conclusion

Use of antidepressants was less frequent among the active co-twins also when shared childhood experiences and genetic background were controlled for. We conclude that physical activity in midlife can buffer against mild depressive symptoms later in life.

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Table 1. Subject characteristics for 642 pairs discordant for long-term physical activity between 1975 and 1990.

	Inactive co-twins	Active co-twins	p
All pairs			
meanMET 1975-1990, mean h/day ± SD	0.97 ± 0.4	4.77 ± 2.2	< 0.001[a]
MET 1990, mean h/day ± SD	1.05 ± 0.9	5.95 ± 4.1	< 0.001[a]
BMI 1990, mean kg/m^2 ± SD	24.9 ± 4.0	24.2 ± 3.4	< 0.001[a]
Current smoker, n (%)	161 (26.3%)	139 (22.7%)	0.15[b]
Alcohol; heavy drinking in 1990, n yes (%)	183 (29.1%)	146 (23.2%)	0.004[b]
Social class, n blue-collar (%)	295 (48.4%)	259 (42.5%)	0.031[b]
Healthy in 1990, n (%)	276 (45.3%)	269 (44.1%)	0.70[b]
BDI in 1990, mean ± SD	5.54 ± 5.9	4.76 ± 5.1	0.008[a]
BDI ≥19, n (%)	20 (3.4%)	14 (2.4%)	0.05[b]
DZ pairs (n=449 pairs)			
meanMET 1975-1990, mean h/day ± SD	0.96 ± 0.4	4.91 ± 2.2	< 0.001[a]
MET 1990, mean h/day ± SD	1.03 ± 0.9	6.10 ± 4.3	< 0.001[a]
BMI 1990, mean kg/m^2 ± SD	25.1 ± 4.2	24.2 ± 3.3	< 0.001[a]
Current smoker, n (%)	109 (25.7%)	87 (20.5%)	0.15[b]
Alcohol; heavy drinking in 1990, n yes (%)	128 (29.1%)	99 (22.5%)	0.008[b]
Social class, n blue-collar (%)	204 (47.8%)	187 43.8%)	0.03 [b]
Healthy in 1990, n (%)	195 (45.7%)	198 (46.4%)	0.88 [b]
BDI in 1990, mean ± SD	5.53 ± 5.9	4.65 ± 5.0	0.02[a]
BDI ≥19, n (%)	12 (2.9%)	10 (2.4%)	0.04[b]
MZ pairs (n=164 pairs)			
meanMET 1975-1990, mean h/day ± SD	1.01 ± 0.4	4.4 ± 1.8	< 0.001[a]
MET 1990, mean h/day ± SD	1.13 ± 0.9	5.66 ± 3.7	< 0.001[a]
BMI 1990, mean kg/m^2 ± SD	24.57 ± 3.5	24.05 ± 3.5	0.007[a]
Current smoker, n (%)	44 (27.7%)	46 (28.9%)	0.66[b]
Alcohol; heavy drinking in 1990, n yes (%)	42 (25.9%)	39 (24.1%)	0.74[b]
Social class, n blue-collar (%)	77 (49.7%)	60 (38.7)	0.11[b]
Healthy in 1990, n (%)	86 (55.5%)	93 (60.0%)	0.44[b]
BDI in 1990, mean ± SD	5.51 ± 5.7	5.14 ± 5.5	0.46[a]
BDI ≥19, n (%)	6 (4.0%)	4 (2.6%)	0.53[b]

[a] according to paired ttest
[b] according to exact symmetry test, including all categories in that variable

Table 2. Conditional logistic regression for 564 physical activity discordant twin pairs for antidepressant use during a period of 1995 – 2004.[a, b]

	basic	**BMI90 adj.**	**smoking status 90 adj.**	**heavy drinking 90**	**full model [c]**
Any antidepressant use [d]	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**	**OR (95% CI)**
All	0.80 (0.67-0.95)	0.79 (0.66-0.94)	0.84 (0.70-1.00)	0.82 (0.69-0.98)	0.84 (0.70-1.00)
DZ	0.80 (0.67-0.97)	0.81 (0.69-0.98)	0.85 (0.70-1.04)	0.83 (0.69-1.01)	0.87 (0.71-1.06)
MZ	0.78 (0.51-1.17)	0.57 (0.32-1.00)	0.68 (0.41-1.13)	0.77 (0.50-1.17)	0.51 (0.26-0.98)
Long-term antidepressant use [e]					
All	0.83 (0.66-1.04)	0.83 (0.66-1.05)	0.88 (0.69-1.12)	0.84 (0.67-1.07)	0.89 (0.69-1.16)
DZ	0.84 (0.65-1.08)	0.85 (0.66-1.10)	0.88 (0.68-1.15)	0.86 (0.66-1.12)	0.91 (0.68-1.20)
MZ	0.79 (0.45-1.38)	0.57 (0.25-1.30)	0.63 (0.28-1.44)	0.77 (0.43-1.37)	0.58 (0.14-2.46)
Occasional antidepressant use, class one (1-2 purchases) [f]					
All	0.65 (0.48-0.87)	0.62 (0.45-0.85)	0.64 (0.45-0.89)	0.66 (0.48-0.90)	0.62 (0.43-0.88)
DZ	0.63 (0.45-0.88)	0.63 (0.45-0.88)	0.64 (0.44-0.93)	0.65 (0.46-0.93)	0.65 (0.44-0.96)
MZ	0.71 (0.35-1.41)	0.57 (0.25-1.30)	0.71 (0.30-1.65)	0.71 (0.35-1.41)	Not estimable [g]
Occasional antidepressant use, class two (1-3 purchases) [h]					
All	0.76 (0.57-0.98)	0.74 (0.57-0.96)	0.77 (0.58-1.02)	0.79 (0.61-1.03)	0.77 (0.58-1.03)
DZ	0.76 (0.57-1.01)	0.76 (0.57-1.01)	0.79 (0.58-1.07)	0.80 (0.60-1.07)	0.82 (0.59-1.12)
MZ	0.76 (0.41-1.39)	0.58 (0.26-1.29)	0.77 (0.39-1.52)	0.76 (0.41-1.40)	0.70 (0.30-1.65)

[a] reference group in all analyses are inactive co-twins, result is for active co-twins

[b] Maximum number of pairs included in the analyses was 564 pairs, as BDI was missing or BDI was ≥ 19 for at least one member of 78 pairs.

[c] Full model includes all previous adjusting variables

[d] Analyses compares non-users to any user (205 individuals at least one purchase during 10 years).

[e] Analyses compares non-users to long-term users (113 individuals with 4+ purchases), analyses do not include persons who had 1-3 purchases.

[f] Analyses compares non-users to occasional users (74 individuals with 1-2 purchases), analyses do not include persons who had 3 or more purchases.

[g] Not estimable due to low N.

[h] Analyses compares non-users to second occasional user class (92 individuals with 1-3 purchases), analyses do not include persons who had 4 or more purchases.

Highlights

- use of antidepressants was less frequent among physically active than inactive
- some associations remained after controlling for genetic background
- physical activity in midlife can be important for preventing mild depression