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Leisure time physical activity and its relation to psychiatric comorbidities in depression. Findings from Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study.

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Abbreviations: BDI (-21), Beck Depression Inventory; BMI, Body Mass Index; CVD, cardiovascular disease; DM, diabetes mellitus; DS, depressive symptoms; FDMSA-study, Finnish Depression and Metabolic Syndrome in Adults- study; GAD, generalized anxiety disorder; HPA-axis , hypothalamic-pituitary-adrenal -axis; LTPA, leisure-time physical activity; M.I.N.I., Mini-International Neuropsychiatric Interview; OCD, obsessive-compulsive disorder; PA, physical activity; SD, standard deviation; US, United States; vs, versus

ABSTRACT

Purpose: The study aim was to examine association between leisure time physical activity (LTPA) and psychiatric comorbidities among people with depression.

Methods: Total 447 patients aged 35 years and older suffering from depressive symptoms (DS) and who were confirmed depression positive participated this study. The study was conducted between 2008 and 2011 in municipalities within Central Finland Hospital District. DS were determined with Beck Depression Inventory (BDI-21) with cutoff score ≥ 10 and psychiatric diagnoses were confirmed by Mini-International Neuropsychiatric Interview (M.I.N.I.). LTPA, other diseases as well as use of antidepressant were captured by self-reported questionnaire. Participants also took part in physical examination. The associations between LTPA and psychiatric comorbidities were analyzed using generalized linear models.

Results: LTPA level was not related to number of psychiatric comorbidities (after adjustment for age, gender, BMI, BDI and use of antidepressant $p=0.24$) among depressed patients. The higher levels of LTPA were linearly associated with lower cardiovascular diseases ($p=0.036$) and obesity ($p=0.006$) as well as fewer DS ($p<0.001$) among depressed patients.

Limitations: Possibility of LTPA level overestimation and study results generalizability to younger persons.

Conclusions: According to this study, LTPA level is not associated with psychiatric comorbidities among depressed patients in Finnish adult population. However, our results showed that the higher the LTPA level was, the less the participants suffered from depressive symptoms. In addition, higher levels of physical activity were associated with fewer heart diseases and obesity outlining the importance of overall health-care and health promotion although other forms of treatment are also needed.

Keywords: Depression, leisure time physical activity, psychiatric comorbidities

Introduction:

Depression is one of the most disability causing illnesses in the world (Whiteford et al., 2013) and its economical and individual burden are huge. Depression is often associated with one or more other psychiatric disorder and together they can impact one's life dramatically. Over 70 % of depression diagnosed patients have at least one other psychiatric comorbidity (Kessler et al., 2003). Patient suffering from mental illnesses has over two-fold higher risk of early death compare to people in general and their life expectancy is ten years shorter (Walker et al., 2015). Depression together with psychiatric comorbidities are found to increase the sensation of pain and decrease one's performance and quality of life (Bair et al., 2008). Depression is also associated with increased risk of many somatic diseases such as obesity, diabetes and cardiovascular diseases (Penninx et al., 2013).

According to recent knowledge leisure time physical activity (LTPA) is useful for treating and preventing depression. Physical activity reduces depressive symptoms (DS) in people with mental illness (Rosenbaum et al, 2014) and physically active individuals have lower risk for depression in the future compared to in-active ones (Mammen and Faulkner, 2013; Schuch et al., 2018). According to review of Mammen and Faulkner (2013) any physical activity (PA) level, including low levels (e.g., walking <150 minutes/weeks), may prevent for future depression. Recent large United States (US) nationwide study (Chekroud et al., 2018) has revealed that physical exercised and physically active individuals had nearly 43% fewer poor mental health days than those who not in the past month. The relationship between PA and depression is also bidirectional, increased PA can reduce depressive symptoms as well as depression itself can reduce PA (Sieverdes et al., 2012).

As depression is often associated with multiple psychiatric comorbidities (Kessler et al., 2003), it is still largely unknown whether or how amount of LTPA is related to psychiatric comorbidities among depressive patients. Depression by itself and particularly with additional psychiatric comorbidities is not only individual misery but huge societal burden (Mrazek et al., 2014; Sobocki et al., 2006) and therefore it is sensible to figure out means and factors to resolve or at least reduce these negative effects of illness. Most of the previous studies investigating the relationship between depression and LTPA have not took psychiatric comorbidity into account or psychiatric comorbidities are excluded. Thus, the main aim of this study as a part of Finnish Depression and Metabolic Syndrome Study (FDMSA) is to explore the relationship between LTPA and psychiatric comorbidities among depressive diagnosed patients.

Materials and methods:

Participants

The study data were drawn from the Finnish Depression and Metabolic Syndrome in Adults (FDMSA) study which was conducted between 2008 and 2011 in municipalities within Central Finland Hospital District with catchment area of 274 000 inhabitants. The population of this study were enrolled from 35 years of age or older patients (n=730) with depressive symptoms determined with Beck Depression Inventory (BDI-21) with cutoff score ≥ 10 . Participants were self-referred or referred by general practitioners to depression nurse case managers and who's psychiatric diagnoses were confirmed by diagnosis structured interview (M.I.N.I.) conducted by depression nurse case managers. Total 447 patients received a diagnosis of depression. The Ethics Committee of the Central Finland Hospital District approved the study protocol prior to the commencement of the study. All participants signed an informed written consent.

Data sources

All participants filled out a standard self-administered questionnaire containing questions about previously diagnosed somatic disorders, use of antidepressant, smoking habits, number of alcohol doses per week and leisure time physical activity (LTPA). Data on participants' socio-economical background such as years of education, marital and employment status were also collected via questionnaire. Participants also took part on physical examination during the study visit. The physical examination included measurements of participants' weight and height during the study visit. Weight and height were measured in light clothing and was accurate to the nearest 0.5 cm and 0.1 kg, respectively. The body mass index (BMI) was defined as person's weight (body mass) divided by the square of the height. Obesity were defined when $BMI \geq 30$ (World Health Organization, 2018).

LTPA was assessed by asking: "How often do you do physical activity at least for half an hour so that you are out of breath and sweating?" Answers were classified into three levels: low (twice per month or less), moderate (once or twice per week), or high (three times per week or more). In previous studies self-assessed LTPA has shown a high correlation with physical fitness as measured by maximal oxygen uptake (Aires et al., 2003).

The severity of depressive symptoms (DS) was captured using the 21-item Beck Depression Inventory (BDI-21) (Beck et al., 1961), which was completed by the participants. The cut-off point was set to ≥ 10 (Koponen et al., 2015). The psychiatric diagnosis and number of other psychiatric comorbidities were confirmed and obtained with a diagnostic Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al., 1998) delivered by trained study nurse.

Statistical methods

The results were presented as means with standard deviations (SD) or as counts with percentages. Statistical significance for the unadjusted analyses of linearity across the LTPA categories were evaluated using the Cochran-Armitage test, Cuzick test and analysis of variance with an appropriate contrast. Adjusted analyses of linearity (orthogonal polynomial) were evaluated using generalized linear models (e.g. analysis of co-variance, regression models and logistic models) with appropriate distribution and link function. Models included age, gender, years of education, marital status, comorbid diseases and household income as covariates. In the case of violation of the assumptions (e.g. non-normality), a bootstrap-type method was used (10 000 replications) to estimate standard errors. The normality of variables was evaluated by the Shapiro-Wilk W test. All analyses were performed using STATA 14.1.

Results:

Table 1 shows the socio-demographic and clinical characteristics of the participants according to LTPA levels. BMI ($p=0.005$) and depressive symptoms ($p<0.001$), and further proportion of subjects with cardiovascular diseases ($p=0.036$) and obesity ($p=0.006$) decreased linearly across increasing LTPA categories. Although antidepressant was used by 68% ($n=305$) of participants, there were no linear association between the LTPA level and use of antidepressant ($p=0.53$), nor with other clinical or socio-demographic characteristics either (Table 1).

The prevalence of psychiatric comorbidities among all depressed participants ($n=447$) were as follow: generalized anxiety disorder (GAD) 56%, suicidal 49%, panic disorder 25%, social phobia 16%, alcohol abuse or dependence 15%, hypomania 12%, agoraphobia 6%, posttraumatic stress reaction 6%, obsessive-compulsive disorder (OCD) 6%, bulimia or anorexia 2% and psychosis 2% (Table 2). Only one-fifth (23%) of the participants had no psychiatric comorbidity. More than one third (38%)

of the participants had one comorbidity, 22% had two and 17% had at least three psychiatric comorbidities. Participants with one or more psychiatric comorbidities were younger (50 years vs. 53 years) and smoked more often (34% vs. 23%, $p=0.023$) than those without psychiatric comorbidities. Instead there were no difference in gender, BMI or educational years among participants with or without psychiatric comorbidities.

The statistical analysis revealed that LTPA level was not related to number of psychiatric comorbidities ($p=0.24$). In addition, there was no significant linear relationship between the prevalence of psychiatric comorbidities and physical active level after adjusting the results for age, gender, BMI, BDI score and use of antidepressant (Table 2).

Discussion:

Main findings and study implications

Our findings suggested that LTPA is not associated with psychiatric comorbidities in patients with depressive symptoms. However, as in line with some earlier findings (Barengo et al., 2017; Korniloff et al., 2010) our study showed that LTPA had positive association with such health-related factors as DS obesity and CVD in depressive patients. This is important, since it has been shown in recent review that people with severe mental illness with low LTPA has increased risk of cardiovascular disease and premature mortality (Vancampfort et al. 2017).

Because PA, in general, has positive effect on mental health, it would be expected that these positive effects of PA are reflected on psychiatric comorbidities as well. Although, for example Bartley et al. (2013) have concluded in their meta-analysis that current evidence does not support the use of aerobic exercise as an effective treatment for anxiety disorders as compared to other treatment. In our study, the majority of study participants suffered from GAD (56%) and as PA seems to be useful in depression it may have lesser impact on depression with anxiety disorder (Bartley et al., 2013). This could be one reason why LTPA does not seem to have positive association with psychiatric comorbidities in this study.

There are also neurobiological changes associated with depression e.g. in hypothalamic-pituitary-adrenal (HPA)- axis homeostasis, neurotransmitters, neurogenesis and inflammatory markers where PA could work as a “scaffolding” factor that support amelioration processes (Archer et al., 2014). Again, neurotic disorders might “purely” associate more with “mind” than “body”. This could also

explain, at least partly, why positive health effects of PA associated more clearly with pure depression but not depression with additional psychiatric disorders and that PA can reduce depressive symptoms but not necessarily psychiatric comorbidities.

Recent study of Chekroud et al. (2018) has also revealed that while physical exercise is in general useful for mental health, more exercise is not always better and that the optimal amount lies between 30-60 min per day three to five times a week. As depression itself can reduce PA (Sieverdes et al., 2012), neurotic disorders might force one to move more and therefore neutralize depression's effects on PA. This phenomenon might be reflected in our study also because we were not able to catch those who exercise "more". Nor we did not use objective PA measurement instead of subjective assessment nor we didn't know what kind of PA lifestyle each participant had before the study due to cross-sectional study design. This may have affected these results also.

With these study findings without more extensive investigation we cannot say what is the relevance of LTPA in depression in terms of psychiatric comorbidities. While these findings can increase and widen our knowledge about factors related to depression, it also raises questions about methods and tools which are suitable in prevention and treatment of illness. As PA has many health benefits in depression its suitability as treatment method to reduce psychiatric comorbidities associated with depression are arguable. Therefore, further research and more knowledge from the underlying factors behind these study findings are needed.

Strengths and limitations

The main strength of this study is the use of diagnostic interview (M.I.N.I.) to confirm depression and psychiatric comorbidities. Another strength of this study is national representative study population with catchment area of 274 000 inhabitants. **Main limitation lies on the self-reported LTPA which may be prone to overestimation by participants. Although, a self-reported questionnaire has proven to be a valid and reliable method to measure PA in cross-sectional studies (Aires et al., 2003) and in this study design we were not trying to estimate exact amount and intensity of PA instead of crude LTPA level categorization. Moreover, generalization of study results to younger persons cannot be done due to study population of 35 and older in this study. Also, generalizability to other countries might be questionable as in Finnish society social equity is in a very high level and for example physical education and health promotion as well as health services are well organized compared to many other countries.**

Conclusion(s):

LTPA level was not associated with psychiatric comorbidities among depressive diagnosed patients. This may suggest a different pathophysiology in depression and anxiety disorders as the level of LTPA was inversely associated with depressive symptoms. However, higher levels of physical activity associated with fewer heart diseases and obesity highlights the importance of LTPA promotion in the treatment of comorbid depression although other forms of treatment for comorbid anxiety disorders are also needed.

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Conflict of interest

The authors declare that they have no conflict of interest.

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Table 1. Depressed patients' socio-demographic and clinical characteristics at baseline.

Variables	Total N=447	Leisure time physical activity			P-value*
		Low N=111	Moderate N=185	High N=151	
Female, n (%)	312 (70)	82 (74)	129 (70)	101 (67)	0.23
Age, years (SD)	51 (10)	49 (9)	52 (10)	51 (10)	0.055
BMI, mean (SD)	28.0 (5.9)	28.9 (6.3)	28.4 (6.0)	26.9 (5.2)	0.005
Obesity, (BMI \geq 30), n (%)	143 (32)	43 (39)	65 (35)	35 (23)	0.006
Education years (SD)	11.0 (3.0)	11.0 (2.9)	11.2 (3.1)	10.8 (3.1)	0.50
Married or cohabited, n (%)	266 (60)	68 (61)	103 (56)	95 (66)	0.23
Employment status, n (%)					0.28
Employed	202 (45)	55 (50)	84 (45)	63 (42)	
Unemployed	113 (25)	32 (29)	41 (22)	40 (26)	
Student	11 (2)	4 (4)	4 (2)	3 (2)	
Retired	121 (27)	20 (18)	56 (30)	45 (30)	
Smoking, n (%)	142 (32)	47 (42)	49 (26)	46 (30)	0.067
Alcohol, doses per week, n (%)					0.99
None	95 (21)	25 (23)	35 (19)	35 (23)	
1-5	251 (56)	62 (56)	109 (59)	80 (53)	
6-9	41 (9)	6 (5)	19 (10)	16 (11)	
\geq 10	60 (13)	18 (16)	22 (12)	20 (13)	
BDI score, mean (SD)	23.4 (8.2)	25.4 (8.6)	23.4 (8.2)	22.0 (7.7)	<0.001
Antidepressant, n (%)	305 (68)	75 (68)	123 (66)	107 (71)	0.53
Disease, n (%)					
Neurological	11 (2)	4 (4)	2 (1)	5 (3)	0.99
Cancer	3 (1)	0 (0)	2 (1)	1 (1)	0.58
CVD	73 (16)	10 (9)	34 (18)	29 (19)	0.036
Rheumatic	15 (3)	4 (4)	9 (5)	2 (1)	0.25
Lung	42 (9)	10 (9)	12 (6)	20 (13)	0.18
DM	64 (14)	18 (16)	23 (12)	23 (15)	0.90

*p for linearity across the LTPA categories

BDI beck depression inventory, CVD cardiovascular disease, DM diabetes mellitus

Table 2. Psychiatric comorbidities among depressed patients according to leisure-time physical activity level at baseline.

Variables	Total N=447	<u>Leisure time physical activity</u>			P for linearity*
		Low N=111	Moderate N=185	High N=151	
GAD, n (%)	250 (56)	68 (61)	101 (54)	81 (54)	0.62
Suicidal, n (%)	218 (49)	60 (54)	86 (46)	72 (48)	0.97
Panic disorder, n (%)	111 (25)	26 (23)	46 (25)	39 (26)	0.24
Alcohol abuse or dependence, n (%)	65 (15)	17 (15)	25 (14)	23 (15)	0.93
Social phobia, n (%)	71 (16)	20 (18)	30 (16)	21 (14)	0.83
Hypomania, n (%)	55 (12)	16 (14)	17 (9)	22 (15)	0.57
Posttraumatic stress reaction, n (%)	27 (6)	9 (8)	13 (7)	5 (3)	0.41
Agoraphobia, n (%)	28 (6)	9 (8)	9 (5)	10 (7)	0.84
OCD, n (%)	26 (6)	8 (7)	7 (4)	11 (7)	0.45
Bulimia or anorexia, n (%)	11 (2)	7 (6)	1 (1)	3 (2)	0.68
Psychosis, n (%)	7 (2)	3 (3)	2 (1)	2 (1)	0.69
Number of psychiatric comorbidities, mean (SD)	1.5 (1.3)	1.6 (1.4)	1.4 (1.2)	1.4 (1.2)	0.24
Number, n (%)					
0	102 (23)	23 (21)	44 (24)	35 (23)	
1	169 (38)	37 (33)	77 (42)	55 (36)	
2	99 (22)	28 (25)	38 (21)	33 (22)	
>=3	77 (17)	23 (21)	26 (14)	28 (19)	

* p for linearity across the LTPA categories, adjusted for gender, age, BMI, BDI and use of antidepressant.

GAD generalized anxiety disorder, OCD obsessive-compulsive disorder

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