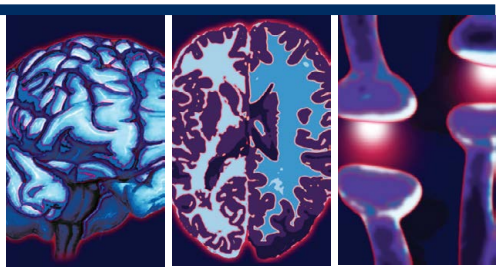

Metabolic syndrome and depression are not correlated: results from a community sample exploring the unique and common correlates for the two diseases

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ABSTRACT

Aim:

More and more studies are suggesting evidence for the comorbidity of cardiovascular disease and depressive disorders, yet the mechanism is obscure. Our study aimed to identify correlates common and unique to metabolic syndrome and depression, in order to clarify the relationship between the two diseases in terms of their taxonomy and potential overlapping mechanisms.

Methods:

Data from a large-scale community sample of 30-year-old or older residents of a Taiwanese city (*N*=11,258) were analyzed to compare sociodemographic and lifestyle factors between four groups: metabolic syndrome only, depression only, comorbid condition, and no disease. The metabolic syndrome was defined by using the standards published by National Health Promotion Administration and the depression was assessed by using the Mental Health Inventory-5.

Results:

Results showed that prevalence rates of metabolic syndrome and depression were 14% and 16.5%, respectively, whilst a low, <3%, comorbidity rate was found. Education level and weekly exercise frequency were common factors to both metabolic syndrome and depression individually, but their directionality was different. Personal income was a unique factor to metabolic syndrome, while age, sex, and drinking habits were so for depression.

Conclusion:

Our findings implied that metabolic syndrome and depression may not have direct relationship in terms of diagnostic taxonomy. However, social environment and personal lifestyle habits may be common factors connecting the two diseases. Thus, maintaining preferable lifestyle habits is the key to both physiological and psychological health.

Keywords

Metabolic syndrome, Depression, Comorbidity, Correlates

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Introduction

Cardiovascular disease (CVD) and major depressive disorder (MDD) are two major diseases that cause the most severe functional impairment in the twenty-first century [1]. This is especially important for countries with high income: of all deaths due to physical disability, the leading cause was MDD, implicated in 9% of them, and the second-place cause was CVD, at 6% [2]. These statistics indicate that CVD and MDD are currently very important topics in public health.

Individuals with metabolic syndrome (MS) are a high-risk group for CVD because both diseases share a cluster of factors and symptoms, such as central obesity, hypertension, high-density lipoprotein (HDL) deficiency, hyperglycemia, and hypertriglyceridemia [3]. In addition to physical problems, researchers have recently suggested that a proportion of MS patients also suffer from mental illness. This is not surprising because people with diabetes [4] or CVD [5] were reported to have high comorbidity with MDD. Those who with MS may have MDD due to obesity affecting their psychological health [6]. Nevertheless, one recent meta-analysis study showed that MDD and MS have a bidirectional relationship, meaning that MDD may cause MS and vice versa [7]. The relationship of the two diseases appears to be intertwined and complicated. Although depressive symptoms are not equal to, but an important precursor of [8], MDD, the term "depression" is used in this article to represent a general concept that mixes both depressive symptoms and MDD wherever necessary.

In order to further understand the mechanisms behind the comorbidity of MS and depression, it is crucial to distinguish common and unique risk factors for both diseases. However, the risk factors involved in MS and depression are extensive, and encompass physiological, psychological, and socio-environmental factors in various aspects. A massive and representative sample covering all kinds of information is necessary for performing statistical comparisons to ensure sufficient statistical power and unbiased generalizability. Accordingly, our study collected extensive information in terms of both physiological and psychological variables from a large-scale and representative community sample. Using this information, we identify the common and unique factors for MS and depression to gain a preliminary understanding of the possible pathological mechanism behind the comorbidity and to provide a reference for future public health prevention and intervention strategies.

Methods

■ Study population

Our study performed analysis based on data from the Landseed Cohort established by Taiwan Landseed Hospital from 2005. Participants were selected from residents over 30 year's old living in Pingzhen City, Taiwan. According to Household Registration Office, the total population of Pingzhen City over 30 years old numbered about 128,659 in 2013, accounting for 0.85% of the same age population in Taiwan. Through probability-proportional-to-size sampling, Landseed Hospital invited 15,000 residents over 30 years old in Pingzhen City to participate free physical health examinations every two to three years. Meanwhile, participants also completed a questionnaire regarding their family medical history, personal medical history, medication history, mental status, quality of life, diet, exercise habits, etc. We combined the three time points of examination data to focus on factors related to MS and depression, thus including a total of 11,258 individuals in our analysis. Our study design was examined and approved by the Institutional Review Board of Landseed Hospital.

Measurements

■ Metabolic syndrome

The diagnostic standard for MS used in our study was based on WHO standards and modified by the Taiwan Health Promotion Administration for Taiwanese population. Briefly, individuals having three or more items of the following five are diagnosed with MS: (1) Central obesity (waist circumference ≥ 90 cm (male) or ≥ 80 cm (female)); (2) High blood pressure (SBP ≥ 130 mmHg or DBP ≥ 85 mmHg); (3) Fasting glucose ≥ 100 mg/dl; (4) Low HDL-C (<40 mg/dl (male) or <50 mg/dl (female)); and (5) Triglycerides ≥ 150 mg/dl.

■ Depressive symptoms

The presence of depressive symptoms in the participants was assessed using the 5-item Mental Health Inventory, MHI-5, extracted from the SF-36 Health Survey. The inventory requires respondents to reply each question (e.g., "How

much of the time have you felt downhearted and blue?") on six-point Likert scale of the past month. Questions 3 and 5 were reverse scored, giving a total score of between 5 and 30, with higher scores representing more depressive symptoms. Recent studies have shown that the MHI-5 is a recommended screening tool for mood disorders [9] and has good reliability [10]. The Cronbach's alpha of MHI-5 in the present study was 0.83. To increase the specificity of MHI-5, our study transformed the original score to a standardized score distributed between 0 and 100; individuals with a score higher than the threshold of 90 were determined to have a high risk of depression and therefore categorized as depressed group.

■ Control variables and lifestyle factors

The basic demographic variables and lifestyle factors included in our study were: age, education level, marital status, personal monthly income, smoking, alcohol use, betel nut chewing and other habits, current work load, and weekly exercise time.

■ Statistical Analyses

We estimate the point prevalence and comorbidity rates of MS and depression. The comorbidity rate was estimated in terms of bidirectional comorbidity rate [11]. In addition, we identified common factors between MS and depression and unique factors to each through logistic regression modeling. By comparing patients with MS only, patients with depression only, and patients with both diseases with patients with neither disease, a given factors was considered a common factor if the odds ratio (OR) significantly deviated from 1 in both MS only and depression only groups, or in the comorbid group. Otherwise, the factor was considered a unique factor if its OR significantly deviated from 1 only in MS only group or only in depression only group. The Hosmer-Lemeshow test was used to examine how well model fit the data for each logistic regression model. The variance inflation factor (VIF) was calculated as a diagnostic index to test multicollinearity in multiple regression models. A mean VIF lower than 10 suggested multicollinearity did not substantially affect model estimates.

Results

Among the 11,258 community residents over 30 years old included in our study, age was normally distributed, with about one third (32.65%) of the residents aged between 50 and 59 years old (Table 1). More females (55.62%) received the health examination than males. Approximately 20% of participants had an education level of elementary school, which is lower than the average of the Taiwanese population. The majority of the participants (87.06%) were married. More than half (57.01%) of the residents had a monthly personal income less than 30,000 NTD (approximately 950 USD). Among the five MS criteria, central obesity was met by the most individuals (39.03%), while HDL deficiency was met by the fewest (16.41%). In total, 14.01% of the population fit the criteria for a diagnosis of MS.

The proportion of total residents who met the criteria for depression was 16.52% in our study. Individuals diagnosable with both MS and depression accounted for 2.9%, and the proportion with neither was 70.96%. Table 2 showed three models with MS only, depression only, and comorbid condition were regressed on 10 potential factors in terms of age, sex, educational level, marital status, personal income, cigarette use, alcohol use, betel nut use, activity, and frequency of exercise. The Hosmer-Lemeshow goodness-of-fit test for MS only (χ^2 = 9.25, p = 0.352), depression only (χ^2 = 16.92, p = 0.129), and comorbid condition (χ^2 = 20.11, p = 0.083) models showed all models fit the data. The VIFs of all independent variables for the three models were all less than 10, indicating that the relationships among the independent variables were not too high to affect model estimates. In Table 2, personal income was a unique factor related to MS: middle income (monthly income of 50-75 thousand NTD) was a protective factor against MS (OR = 0.6, 95% CI = 0.4-0.8). On the other hand, age, gender, and drinking habits were unique factors related to depression. Higher age conferred a relatively higher risk, and females were at a higher risk than males (OR = 1.3, 95% CI = 1.1-1.6); however, individuals who abstained from alcohol exhibited a significant protective effect (OR = 0.6, 95% CI = 0.4-0.9) against depression compared with individuals who had never used alcohol. Notably, education level and weekly exercise time were related to both MS and depression, yet with opposite directional effects. Low education level was a risk factor for MS (OR = 2.4, 95% CI = 1.1-5.4), but a protective factor against depression (OR = 0.5, 95% CI = 0.3-0.9). Regular exercise (4-7 times per week) was a protective factor against MS (OR = 0.7, 95% CI = 0.6-0.9), but a risk factor

Table 1: Distribution of socio-demographic characteristics and metabolic syndrome-related factors (N=11258).

	n	%
Age		
30-39	1301	11.56
40-49	2752	24.44
50-59	3676	32.65
60-69	1870	16.61
≥70	1484	13.18
Sex		
Male	4996	44.38
Female	6262	55.62
Educational level		
Graduate	236	2.10
Undergraduate	2232	19.83
Senior high	3355	29.80
Junior high	1882	10.50
Elementary	2315	20.56
Under elementary	769	6.83
Marital status		
Married	9801	87.06
Unmarried	486	4.32
Separated	36	0.32
Divorced	276	2.45
Widowed	435	3.86
Others	6	0.05
Personal income (10,000 NTD/month)		
<30	6418	57.01
30-50	1695	15.06
50-75	1018	9.04
75-100	707	6.28
100-180	230	2.04
>180	53	0.47
Central obesity (waist circum.; m. ≥ 90 cm; f. ≥ 80cm)	4394	39.03
Blood pressure (SBP ≥ 130 mmHg or DBP ≥ 85 mmHg)	1856	16.49
HDL-C (male <40 mg/dl; female <50 mg/dl)	1848	16.41
Fasting glucose (≥ 100 mg/dl)	2086	18.53
Triglyceride (≥ 150 mg/dl)	2916	25.90
Meets metabolic syndrome criteria	1577	14.01

for depression (OR = 1.2, 95% CI = 1.1-1.4). These two variables did not show significance in the analysis of comorbidity group.

Discussion

In this over-30-years-old community sample, both MS (14%) and depression (16.5%) were prevalent, yet residents with comorbid condition for the two diseases accounted for less than 3%. Although the prevalence rate of MS was generally higher with age, the estimated prevalence in our sample is not higher than those obtained from general population in Western countries (~33%) [12,13] or in Asian countries (10-30%) [14]. It is also a lower estimate when compared with large-scale surveys from Taiwan (25.5%) [15] or from China (25%) [16]. This variation in results may be caused by differences in diagnostic standards between studies. Another possible reason may be that our study collected information through community health examinations, and those participants able to go outdoors and undergo examinations are likely relatively healthy individuals. For depression, the estimated point prevalence in this study (16.6%) is consistent with a recent American study [17]. This similarity implies that, unlike many past studies used a standardized score of 70 as their cutoff point and obtained a prevalence rate of about 33% [18], using a standardized score of 90 from the MHI-5 may prevent the prevalence estimation from a high false positive rate.

It is interesting to note that a low number of individuals in the comorbid group and no factor significantly linked to the comorbidity condition. This result might have meant insufficient statistical power, but it could simply indicate the lack of a direct relationship between MS and depression. This is in line with one large-scale community study which showed no correlations between depression-related disorders and the mutant allele of the *apoE2* gene [19], implying that MS and depression disorders lack a common genetic background. However, non-genetic factors in terms of education level and weekly exercise frequency may affect the two diseases simultaneously. Nevertheless, the direction of the effect of these two factors on MS and depression were opposite. Individuals with higher education might possess comparatively deeper health knowledge and plan for regular health-promoting activities well, which both decrease the risk for MS [20]. On the other hand, individuals with higher education usually encounter more work-related pressures, a phenomenon that increases the risk for depressive disorders [21]. In our study, the group with under-elementary education included mostly elderly individuals, most of who were retired and thus experience less work-related pressure: this is a likely reason why fewer symptoms of depressive disorders were discovered. It is even possible that the elderly individuals were reluctant to express deep emotion due to Chinese cultural tendencies [22], which caused the appearance of a protective effect in our results.

Individuals who performed exercise 4-7 times per week reduced their risk of MS by one-third, yet excessive exercise did not confer a protective

Table 2: Multiple logistic regression analyses.

	Metabolic syndrome only				Depression only				Comorbid condition			
	n	%	OR	95% CI	n	%	OR	95% CI	n	%	OR	95% CI
Age												
30-49	214	13.6	1.0	—	242	11.9	1.0	—	35	10.7	1.0	—
50-59	422	26.7	1.2	0.6-2.4	616	30.4	**1.6***	**1.1-2.3**	86	26.2	1.5	0.6-4.3
60-69	552	35.0	2.0	0.9-4.0	677	33.4	**2.1***	**1.5-3.4**	127	38.7	2.6	0.9-7.9
≥70	390	24.7	1.7	0.8-3.1	494	24.4	**2.1***	**1.2-3.2**	80	24.4	2.3	0.8-7.5
Sex												
Male	828	52.5	1.0	—	1005	49.5	1.0	—	147	44.8	1.0	—
Female	750	47.5	1.2	0.9-1.4	1024	50.5	**1.3***	**1.1-1.6**	181	55.2	1.2	0.9-1.6
Educational level												
Undergraduate or higher	243	15.9	1.0	—	343	17.2	1.0	—	44	13.8	1.0	—
Senior high	401	26.1	1.2	0.5-2.8	590	29.6	0.8	0.5-1.3	98	30.5	1.2	0.5-2.7
Junior high	301	19.6	1.4	0.7-3.0	408	20.5	0.8	0.5-1.3	70	21.8	1.3	0.5-3.2
Elementary	426	27.8	1.4	0.7-3.1	530	26.6	0.8	0.5-1.4	84	26.2	1.3	0.5-3.2
Under elementary	163	10.6	**2.4***	**1.1-5.4**	121	6.1	**0.5***	**0.3-0.9**	25	7.8	1.4	0.5-3.8
Marital status												
Unmarried	1399	89.1	1.0	—	1830	90.5	1.0	—	302	92.1	1.0	—
Married	46	2.9	1.1	0.5-1.4	51	2.5	0.9	0.6-1.7	6	1.8	0.9	0.6-2.1
Other [a]	124	7.9	1.0	0.4-2.9	141	6.9	0.9	0.6-3.0	20	6.0	1.0	0.4-6.7
Personal income (10,000 NTD/month)												
<30	1010	70.7	1.0	—	1256	66.6	1.0	—	206	67.8	1.0	—
30-50	168	11.8	0.8	0.6-1.1	267	14.2	0.9	0.8-1.2	39	12.8	0.8	0.5-1.1
50-75	95	6.7	**0.6***	**0.4-0.8**	151	8.0	0.8	0.6-1.1	20	6.6	0.5	0.3-0.8
75-100	93	6.5	0.9	0.6-1.4	123	6.5	0.8	0.6-1.1	21	6.9	1.0	0.6-1.7
100-180	40	2.8	1.3	0.7-2.4	56	3.0	1.5	0.9-2.3	11	3.6	1.6	0.9-3.1
>180	13	0.9	1.3	0.4-4.0	13	0.7	1.4	0.6-3.4	3	1.0	1.4	0.4-5.2
Cigarette use												
Never use	1227	77.8	1.0	—	1559	76.9	1.0	—	236	72.2	1.0	—
Abstained	100	6.3	1.1	0.7-1.5	141	7.0	1.0	0.8-1.3	23	7.0	0.8	0.5-1.3
Currently use	250	15.9	1.2	0.9-1.6	327	16.1	0.9	0.7-1.1	68	20.8	0.9	0.6-1.4
Alcohol use												
Never use	1377	87.6	1.0	—	1797	88.7	1.0	—	273	83.5	1.0	—
Abstained	39	2.5	1.3	0.7-2.3	43	2.1	**0.6***	**0.4-0.9**	12	3.7	0.9	0.5-2.1
Currently use	156	9.9	1.2	0.8-1.5	185	9.1	0.9	0.7-1.2	42	12.8	1.2	0.8-1.7
Betel nut use												
Never use	1461	92.6	1.0	—	1912	94.2	1.0	—	294	89.6	1.0	—
Abstained	62	3.9	1.4	0.8-2.3	62	3.1	0.9	0.6-1.5	17	5.2	1.7	0.9-3.2
Currently use	55	3.5	1.3	0.6-2.5	55	2.7	1.1	0.6-1.8	17	5.2	1.5	0.7-3.4
Activity												
Mild	888	85.7	1.0	—	1093	84.6	1.0	—	176	86.3	1.0	—
Moderate	87	8.4	0.7	0.5-1.1	134	10.4	1.1	0.8-1.4	16	7.8	0.7	0.5-1.1
Heavy	27	2.6	0.9	0.5-1.8	42	3.3	0.8	0.5-1.3	6	2.9	0.9	0.4-1.9
Extreme heavy	31	3.0	1.5	0.7-3.1	23	1.8	1.3	0.7-2.3	6	2.9	1.1	0.4-2.7
Frequency of exercise (times/week)												
<3	412	42.0	1.0	—	496	35.7	1.0	—	92	40.2	1.0	—
4-7	540	55.1	**0.7***	**0.6-0.9**	857	61.7	**1.2***	**1.1-1.4**	129	56.3	0.8	0.6-1.1
8+	28	2.9	1.2	0.7-2.2	37	2.7	1.1	0.7-1.7	8	3.5	1.6	0.9-3.1

[a]Including separated, divorced, and widowed. *p<0.05

effect, compared with those who did less than 3 times per week. These results imply that the effect of exercise on MS may not be a linear or dose-response relationship, but rather that both too much and too little exercise are harmful to the metabolism of adults [23]. The relationship between insufficient exercise and MS has been indicated in many studies [24]. However, the exact mechanism that related excessive exercise to MS is still unclear. It is possible that obese individuals forced themselves to exercise heavily after realizing their high risk for various

diseases. Interestingly, our study discovered that individuals who exercised 4-7 times per week had a 20% higher risk of having depression compared with those who did less than 3 times per week. Some previous studies have suggested that exercise helps to reduce risk for depressive disorders. This discrepancy may due to the different definition of exercise between studies where many studies used high-intensity exercise or aerobic exercise as a measure [25], which is not a requirement in the present study.

Our study found that moderate personal income was a unique protective factor against having MS. In Taiwan, a certain proportion of the middle-class population is civil servants, who live rather regular lives and do not regularly consume high-fat or high-salt foods and therefore have a low risk of MS. Low-income population lack social resources and social capital, which increases their risk for MS. High-income population do benefit from abundant social resources; however, long working hours, lack of time for exercise, and unhealthy lifestyles can lead to the occurrence of MS.

The unique factors for depression in this study were age, gender and drinking habits, which are consistent with the results of previous studies. The heightened risk for depressive disorders that old age and female gender has intercultural consistency [26]. However, unlike previous findings [27], our study found that the risk of depression is lower in individuals who had quit drinking compared with individuals who never drink. Few past studies have commented on the risk of depression in individuals who quit drinking. One potential cause is that people who successfully quit drinking develop strong personal motivation and positive attitude, and enjoy great support from society [28], which are all protective factors against depressive disorders.

When interpreting the results of our study, one needs to consider the following limitations. First, the relationship between factors and diseases may not be causal because they were analyzed cross-sectionally in this study. Second, our study combined data at three time points; some individuals may be duplicated in the overall dataset. Third, the self-reported weekly exercise frequency may retain large variance in the intensity of exercise performed, and a high frequency may not necessarily represent a large amount of exercise. Fourth, our results can only reflect the situation of a subpopulation of residents of Taoyuan County, and may not be generalizable to the populations of other regions.

Conclusions

The low comorbidity rate of and lack common factors between MS and depression imply that the two diseases have no direct relationship. However, education level and weekly exercise frequency had opposite effects on the two diseases, suggesting that social environment and lifestyle may be factors connecting them. In addition, the variable of social economic status had a unique relationship with MS, and those factors uniquely affecting depression were variables related to demography and lifestyle.

Funding

This work was supported in part by the collaborative projects between Chung Shan Medical University and Landseed Hospital (CSMU-LSH-101-02 and CSMU-LSH-102-01) awarded to Dr. Hao-Jan Yang.

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