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Which biopsychosocial variables contribute to more weight gain in depressed persons?

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ABSTRACT

Depression appears to be associated with weight gain. Little is known about whether this association is independent of, or partly due to, several biopsychosocial variables. This study aims to investigate which biopsychosocial variables contribute to weight gain over a 4-year period in persons with major depressive disorder (MDD) or high depressive symptoms. Data from 1658 adults who participated in the Netherlands Study of Depression and Anxiety were used. Baseline depression was measured with a DSM-IV based psychiatric interview and with a depressive symptom measure. Four year weight gain was classified as stable weight (within 5% gain or loss) versus weight gain (> 5% gain). Twenty-one baseline psychological, lifestyle and biological variables and antidepressant use were considered as potential contributing variables. In sociodemographic adjusted models, MDD and depressive symptoms were associated with subsequent weight gain. None of the biopsychosocial variables or antidepressants was associated with weight gain, thus did not contribute to the observed increased weight gain risk in depression, except for alcohol intake and TCA use. Future research should explore other potential factors that may be responsible for the increased risk for subsequent weight gain in depression, e.g. unhealthy dietary patterns or eating styles, or underlying intrinsic factors such as genetics.

1. Introduction

Depression and obesity are associated, and their link appears to be bidirectional (De Wit et al., 2010; Luppino et al., 2010; Faith et al., 2011). Persons experiencing major depressive disorder (MDD) and depressive symptoms have shown to subsequently gain weight (Forman-Hoffman et al., 2007; Patten et al., 2009; Koster et al., 2010; Singh et al., 2014). Multiple pathways related to psychological, physical or biological variables could contribute to the observed weight gain and obesity in depression, however few have been systematically investigated.

A small number of reviews have attempted to clarify why and how depression and obesity are related by examining the role of different biopsychosocial variables as contributing variables (Markowitz et al., 2008; Preiss et al., 2013; Rossetti et al., 2014). These reviews were narrative in nature, only included cross-sectional studies and/or did not study weight gain but only incidence of obesity. Studying weight gain over time as opposed to body mass index (BMI) at one time point has several advantages. It can show the dynamic relationship between depression and weight gain, and weight gain is a more sensitive measure as compared to developing obesity. Also, using substantial weight change categories (i.e. comparing weight gain to stable weight), as was also done in earlier studies (Forman-Hoffman et al., 2007; Koster et al., 2010), is relevant from a clinical perspective. Gaining insight into which biopsychosocial variables contribute to weight gain in depression may help us to improve our understanding of how intervention strategies can prevent this negative consequence of depression.

Psychological vulnerabilities may contribute to weight gain and development of obesity in depressed persons. Persons with depressive disorders tend to experience more cognitive reactivity responses like hopelessness, aggression and rumination, anxiety sensitivity and worry, as opposed to psychiatrically healthy controls (Hong, 2007; Naragon-Gainey, 2010; Drost et al., 2012). They also experience feelings of limited mastery (Papageorgiou et al., 2015). Cognitive reactivity is the ease at which negative thinking patterns are reactivated through minor triggers, and is depicted as general negative thoughts. One previous

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study found cross-sectional associations between lower self-efficacy, strongly related to mastery, and higher body weight in depressed participants (Linde et al., 2004). We recently showed associations between higher cognitive reactivity and a high BMI in persons with current depression and anxiety disorder as compared to healthy controls (Paans et al., 2016). Markowitz et al. (2008) suggested there to be an indirect pathway from specific weight-related negative thoughts, associated to the psychological vulnerabilities we measure, to a worse self-care and subsequently a higher BMI. However, to date, no other studies have directly investigated whether these psychological vulnerabilities may contribute to the increased subsequent weight gain risk in depression.

Depression has also repeatedly been related to more unhealthy lifestyle aspects such as smoking, increased alcohol intake and less physical activity (Van Gool et al., 2007). These lifestyle aspects are also related to obesity and weight gain (Filozof et al., 2004; World Health Organisation (WHO), 2004; Ruotsalainen et al., 2015; Traversy and Chaput, 2015). Furthermore, biological dysregulations might also contribute to weight gain in depression. It is known that MDD is associated with dysregulation in several immuno-metabolic processes such as autonomic nervous system dysregulation, HPA-axis dysfunction and inflammation (Markowitz et al., 2008; Penninx et al., 2013). These dysregulations have also been linked to obesity and food intake (Hotamisligil, 2006; Messina et al., 2013). While several narrative reviews have already recognized these biological factors as possible contributing variables explaining how depression and obesity are related (Markowitz et al., 2008; Rossetti et al., 2014; Singh, 2014), no previous studies have directly analyzed whether the association between depression and weight gain is (partly) due to these factors.

Alternatively, it is also possible that, as opposed to biopsychosocial external factors, the antidepressant treatment of MDD links depression to weight gain. Earlier studies have observed subsequent weight change in persons using antidepressants (Fava, 2000), while another study did not find an independent effect of antidepressant use on weight change (Gibson-Smith et al., 2016). Since the associations between antidepressant use and weight change remain unclear, we also considered treatment with antidepressants as a potential contributing variable.

A few studies have found associations between psychological vulnerabilities, lifestyle and biological variables, antidepressant use, and weight gain. However the evidence for the extent to which these are relevantly contributing is weak and inconclusive. Shedding more light on variables contributing to the association between depression and weight gain is important, since changes in weight can lead to overweight and obesity, which have serious health consequences such as cardiovascular diseases and diabetes (Field et al., 2004). Also, more insight into these contributing variables can possibly help to tailor useful treatment strategies for depressed persons to prevent subsequent weight gain. Therefore, the aim of this 4-year prospective study is to examine which biopsychosocial factors and antidepressant use contribute to the observed increased weight gain in persons with MDD or high depressive symptoms as compared to healthy controls and those with low depressive symptoms.

2. Methods

2.1. Study sample

Data from the Netherlands Study of Depression and Anxiety (NESDA), an ongoing cohort study of people with depression and anxiety disorders and healthy controls were used. In order to represent diverse settings and developmental stages of psychopathology, 2981 adults (18–65 year) from the community (19%), general practice (54%) and specialized mental health care (27%) were included at baseline. Exclusion criteria were a primary clinical diagnosis of psychotic disorder, obsessive-compulsive disorder, bipolar disorder, or severe substance abuse disorder, and insufficient command of the Dutch language. The research protocol was approved by the Ethical Committees of the contributing universities and all participants provided written informed consent. A detailed description of the NESDA study design can be found elsewhere (Penninx et al., 2008). Between September 2004 and February 2007, all participants underwent a baseline assessment containing an extended face-to-face interview conducted by a trained research assistant, which included a standardized diagnostic psychiatric interview (Composite International Diagnostic Interview (CIDI) version 2.1,(Wittchen, 1994)) and self-report questionnaires.

For the current study, we selected participants with a diagnosis of current or remitted MDD along with controls with no history of depressive or anxiety disorders at baseline (n = 2605), excluding those with a pure anxiety disorder (n = 373) and of whom data on psychiatric disorders was inconclusive (n = 3). We also excluded participants with no weight data (n = 689), women who were pregnant (n = 43) and persons with self-reported hyperthyroidism (n = 15) at baseline or at 4-year follow-up. In addition, we excluded participants who experienced > 5% weight loss over four years (n = 200), since it can be expected that this group has a different pathology (Lamers et al., 2012), leaving 1658 participants for the main analyses. The excluded participants were significantly younger ($p < 0.05$), more often female ($p < 0.001$), had followed less years of education ($p < 0.05$), had higher depressive symptom scores (Inventory of Depressive Symptoms, $p < 0.001$), and had more often a diagnosis of depressive disorder at baseline ($p < 0.05$).

2.2. Depression measurements

At baseline, presence of a DSM-IV depressive disorder (MDD, dysthymia) was established using the Composite Interview Diagnostic Instrument (CIDI, version 2.1 (Wittchen, 1994)). The current sample included 655 participants with a current diagnosis (i.e. within the past 6 months), 530 participants with a remitted diagnosis, and 473 control participants (i.e. no lifetime history of psychiatric disorders). Severity of depressive symptoms in the past week was assessed with the 30-item Inventory of Depressive Symptomatology - Self Report (IDS-SR, range 0 to 84 (Rush et al., 1996)).

2.3. 4-year weight change

Height and weight were measured at baseline and 4-year follow-up by a trained research assistant. BMI was calculated as weight kilograms divided by height squared in meters (kg/m^2). As in earlier studies (Forman-Hoffman et al., 2007; Koster et al., 2010; Gibson-Smith et al., 2016), we operationalized weight change based on > 5% change in weight over a 4-year period from baseline weight. Weight change was classified as: weight stable (within 5% weight loss or gain) and weight gain (> 5% weight gain).

2.4. Psychological vulnerabilities

Cognitive reactivity was measured by the Leiden Index of Depression Sensitivity-Revised (LEIDS-R, values range from 0 to 20 or 0 to 24 (Van der Does, 2002; Williams et al., 2007)). The LEIDS-R questionnaire assesses the extent in which dysfunctional cognitions are triggered during normal mood variations, three subscales (hopelessness/suicidality, aggression and rumination) were included. Anxiety sensitivity was measured by the Anxiety Sensitivity Index (ASI, values range from 0 to 64 (Reiss et al., 1986)), assessing the sensitivity to sensations of fear. Worrying was operationalized using the Penn-State Worry Index (PSWQ, values range from 16 to 80), examining the extent to which persons worry frequently and extensively (Meyer et al., 1990). The amount of feelings of mastery was assessed through the Pearlin Mastery Scale (values range from 5 to 25 (Pearlin and Schooler, 1978)). All psychological vulnerabilities were measured at baseline, and were based on self-report questionnaires.

2.5. Lifestyle factors

Baseline lifestyle factors contained smoking, alcohol use and physical activity. Smoking was operationalized by number of cigarettes per day. Alcohol use was expressed in number of drinks per week. Physical activity was examined using the International Physical Activity Questionnaire (Craig et al., 2003) and expressed as overall energy expenditure in Metabolic Equivalent Total (MET in hours/week).

2.6. Indicators of physiological (stress-) systems

We included baseline biomarkers of pathophysiological systems consisting of the autonomic nervous system, inflammation, leptin and cortisol levels. Autonomic nervous system measurements were recorded with a "Vrije Universiteit Ambulatory Monitoring System" (VU-AMS), a lightweight portable device that records ECGs and changes in thorax impedance (impedance cardiography [ICG]) from a six-electrode configuration, which was worn for an average of 90 min during the baseline interview (Licht et al., 2012). From the VU-AMS recordings, heart rate (HR), respiratory sinus arrhythmia (RSA) and pre-ejection period (PEP) could be computed, as indicators of sympathetic and parasympathetic nervous system activity. For the inflammation markers and leptin levels, morning fasting blood samples were obtained and frozen at −80 °C. Circulating plasma levels of tumor necrosis factor-alpha (TNF-α), c-reactive protein (CRP) and interleukin-6 (IL-6) were used as markers of inflammation. These measurements were assessed with high sensitivity enzyme-linked immunosorbent assays, as described earlier (Vogelzangs et al., 2012). Leptin concentrations were measured in ethylenediaminetetraacetic acid (EDTA) plasma using an enzyme-linked immunosorbent assay (Milaneschi et al., 2012). To examine HPA-axis functioning, subjects were instructed to collect saliva samples at home on a regular (preferably working) day at awakening, and 30, 45 and 60 min later, and in the evening (Vreeburg et al., 2009). We calculated the cortisol awakening curve (area under the curve with respect to the ground; AUCg), an estimate of the total cortisol secretion over the first hour after awakening (Pruessner et al., 2003), as well as evening cortisol levels by averaging two evening values (22:00 and 23:00).

2.7. Antidepressant treatment

Antidepressant use was assessed at baseline by asking participants to bring the packaging from all medications used in the previous month. These were classified according to the Anatomical Therapeutic Chemical (ATC) classification (World Health Organisation (WHO), 2014). Antidepressants were grouped according to type and/or suspected effect on weight gain into the following three groups: tricyclic antidepressants (TCA's) (ATC code: N06AA), selective serotonin reuptake inhibitors (SSRIs) (ATC code: N06AB), and other antidepressants, 92% of which were mirtazapine (ATC code: N06AX11) and venlafaxine (ATC code: N06AX16), along with ATC codes N06AF, N06AG, and other N06AX. For all antidepressants a derived daily dose (DDD) was calculated by dividing the subject's daily dose used by the defined daily dose recommended by the World Health Organisation (WHO) (2014).

2.8. Covariates

Covariates were selected a priori based on findings based on other studies. Age, sex, years of education and baseline weight were assessed during the interview and included as potentially confounding variables.

2.9. Statistical analyses

Baseline sample characteristics were described as means and standard deviations, or percentages. For non-normally distributed variables the median and interquartile range were calculated. We first tested whether several depression indicators (i.e. current depressive disorder and remitted depressive disorder versus healthy controls, and depressive symptom severity; together referred to as depression) were associated with weight gain (as opposed to stable weight) using logistic regression analyses (Fig. 1, pathway c). Only the associations of depression indicators that remained significantly related with weight gain after adjustment for sociodemographic covariates were included in the subsequent statistical mediation analyses.

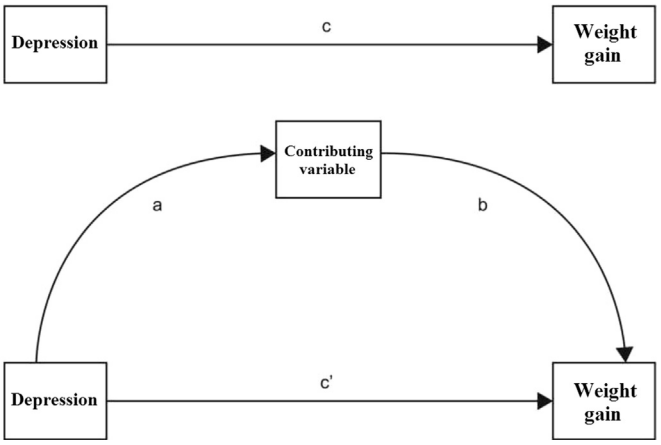

Fig. 1. Illustration of the total effect of depression on weight gain (c) and a statistical mediation design where depression is associated with weight gain directly (c′) and indirectly (a × b) through a contributing variable.

To examine whether the associations between depression and 4-year weight gain appeared to be independent of, or appeared to be (partly) due to, 21 biopsychosocial variables and baseline antidepressant use, analyses according to the Hayes statistical mediation model were performed (Hayes, 2012). This model was chosen because the goal of this study to understand how and why depression and weight gain are associated. Also, since depression and the potential contributing variables are in general associated, this statistical mediation model seemed the best choice (Kraemer et al., 2001). Values of all biopsychosocial and antidepressant use variables were standardized to create comparable effect sizes. For skewed variables, the natural logarithm was taken before standardizing. Weight gain over 4 years was considered as a categorical outcome variable (weight stable vs. weight gain), and analyses were done using both MDD versus healthy controls, and depressive symptom severity separately as independent variables. We applied statistical mediation analyses to test I) the associations between depression and potential contributing biopsychosocial variables (pathway a in Fig. 1); II) the associations between the contributing variables and weight gain (pathway b in Fig. 1); III) the direct associations between depression and weight gain, corrected for a × b (pathway c′ in Fig. 1); and IV) the indirect associations between depression and weight gain through the contributing variables (pathway a × b). Analyses were performed using the Hayes SPSS 'process' macro, which allows the use of dichotomous outcomes and estimates the indirect associations of the independent variable on the dependent variable through the contributing variables (Hayes, 2012). This method uses bootstrap resampling procedures, in which participants are randomly selected, with replacement, from the original sample. For each bootstrap sample the model is estimated and the parameters saved. The indirect association is deemed significant if the 95% bootstrap percentile confidence interval did not include zero. Number of bootstraps were set at 5000. Contributing variables were entered into the model separately first. Thereafter, variables found to be successfully contributing to the relationship between depression and weight gain at the previous analyses will be entered into a final "multiple mediation model". All analyses were adjusted for age, sex, years of education and baseline weight.

All analyses were conducted using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). A p-value of 0.05 was considered statistically significant.

Table 1
Baseline sample characteristics per four-years weight change categories across patients and controls (N = 1658).

Sociodemographic variables	4-year weight stable (n = 1075)	4-year weight gain (n = 583)
Age (years), mean (SD)	44.6 (12.6)	38.5 (12.9)
Sex (% female)	63.2	66.7
Years of education	12.6 (3.2)	12.2 (3.1)
Psychiatric variables and course		
Depressive symptoms (IDS), mean (SD)	19.0 (13.7)	22.2 (14.6)
< 80% of the time depressive symptoms (%)[a]	41.4	51.1
≥ of 80% of the time depressive symptoms (%)[a]	10.2	14.9
Diagnosis status		
Controls (%)	30.9	24.2
Remitted depressive disorder, %)	34.7	26.9
Current depressive disorder (%)	34.4	48.9
Antidepressant use (% yes)	24.4	24.5
No antidepressant use, stable[a]	21.7	30.7
Started antidepressant use[a]	5.3	9.2
Stopped antidepressant use[a]	11.3	11.5
Chronic antidepressant use[a]	21.1	19.0
TCA derived daily dose, mean (SD)	0.02 (0.17)	0.02 (0.16)
SSRI derived daily dose, mean (SD)	0.22 (0.62)	0.27 (0.65)
Other antidepressants derived daily dose, mean (SD)	0.06 (0.31)	0.06 (0.33)
Weight		
Baseline weight, mean (SD)	76.6 (15.8)	74.7(16.7)
Body Mass Index (kg/m^2), mean (SD)	25.5 (4.7)	24.8 (5.0)
4-year weight change, mean (SD)	0.3 (2.1)	7.9 (4.3)
Psychological vulnerabilities		
Hopelessness, median (IQR)	3.0 (1.0–6.3)	4.0 (2.0–8.0)
Aggression/hostility, median (IQR)	3.0 (1.0–6.0)	4.0 (2.0–7.0)
Rumination, mean (SD)	8.8 (5.2)	9.6 (5.4)
Anxiety sensitivity, median (IQR)	26.0 (21.0–33.0)	27.0 (22.0–35.0)
Worry, mean (SD)	29.3 (12.0)	31.4 (12.1)
Mastery, mean (SD)	17.7 (4.5)	17.1 (4.7)
Lifestyle factors		
Alcohol (drinks/week), median (IQR)	3.7 (0.4–8.7)	5.8 (0.2–8.2)
Smoking (cigarettes/day), median (IQR)	10 (5.0–20.0)	10 (5.0–20.0)
Physical activity (MET-minutes/week), median (IQR)	2784 (1398.0–5001.0)	3058 (1371.8–5486.3)
Biological factors and physiological stress systems		
Heart rate, mean (SD)	71.2 (9.7)	72.0 (9.2)
Respiratory sinus arrhythmia, median (IQR)	36.5 (26.2–50.7)	42.9 (29.8–59.7)
Pre-ejection period, mean (SD)	120.4 (18.4)	120.7 (17.2)
C-reactive protein (mg/l), median (IQR)	1.1 (0.5–2.9)	1.1 (0.5–2.9)
Interleukin-6 (pg/l), median (IQR)	0.9 (0.5–1.3)	0.8 (0.5–1.2)
Tumor necrosis factor-alpha (pg/ml), median (IQR)	0.8 (0.6–1.1)	0.8 (0.6–1.1)
Leptin (μg/l), median (IQR)	10.9 (5.1–19.3)	11.3 (4.7–20.1)
Cortisol awakening curve (AUCg; nmol/l/h), mean (SD)	18.9 (6.7)	19.4 (7.6)
Evening cortisol, median (IQR)	4.9 (3.4–6.6)	4.7 (3.4–6.5)

SD = standard deviation; IDS = Inventory of Depressive Symptoms; IQR = Interquartile range; TCA: Tricyclic antidepressants; SSRI: Selective serotonin reuptake inhibitors. Hopelessness, Aggression & Rumination subscales: Leiden Index of Depression Sensitivity-Revised; Anxiety sensitivity: Anxiety Sensitivity Index; Worry: Penn State Worry Questionnaire; Mastery: Pearlin Mastery Scale; Smoking: numbers of cigarettes per day; Alcohol use: amount of drinks per week, sum score; Physical activity: total minutes per day; AUCg: area under the morning curve with respect to the ground. Weight stable is defined as within 5% weight loss or gain over a 4-year period from starting weight. Weight gain is defined as > 5% gain in weight over a 4-year period from starting weight.

[a] Only for the patient group, over a period of four years.

3. Results

Table 1 shows the distribution of baseline study characteristics per weight change group (total n = 1658, weight stable n = 1075, weight gain n = 583). The mean age of the total study sample at baseline was 42.3 years (SD = 13.0), 64.4% was female and the participants had followed on average 12.5 years of education (SD = 3.2). The weight stable group contained relatively more healthy controls as opposed to the weight gain group (Table 1). The mean BMI of the weight stable group was 25.5 (SD = 4.7), and they gained on average 0.3 kg (SD = 2.1) over 4-years. The weight gain group had a mean BMI of 24.8 (SD = 5.0), and gained on average 7.9 kg (SD = 4.3).

3.1. Associations between depression and subsequent weight gain (c)

Compared to healthy controls, patients with a current depressive disorder, but not those with a remitted depressive disorder, were significantly more likely to gain > 5% of their body weight over a 4-year period (Table 2). After adjustment for age, sex, years of education and baseline weight, this association remained significant (odds ratio (OR) 1.92, 95% confidence interval (CI) 1.48–2.50). Comparable associations were found for depressive symptom severity and weight change; after adjustment for confounding variables, there was a significant relationship between higher depressive symptoms and 4-year weight gain (OR 1.26, 95% CI 1.14–1.41).

3.2. Associations between depression and contributing variables (a)

Table 3, column I shows the associations between current MDD and each of the included potential contributing variables. As expected, almost all of the associations between MDD and the biopsychosocial variables and baseline antidepressant use were significant. Those with a current depressive disorder showed more and higher psychological vulnerabilities (hopelessness, aggression, rumination, anxiety sensitiv-

Table 2
Logistic regression analysis with Major Depressive Disorder (MDD; baseline) and Inventory of Depressive Symptomatology (IDS; baseline) as independent variables and 4-year weight change categories (weight stable n = 1075; weight gain n = 583) as dependent variable.

	4-year Weight gain[a]	
	Crude OR (95% CI)	Fully adjusted OR[b] (95% CI)
Analysis 1		
Depression status		
Healthy controls (N = 473)	1.00 (reference)	1.00 (reference)
Remitted MDD (N = 530)	0.99 (0.76–1.30)	1.10 (0.83–1.46)
Current MDD (N = 655)	**1.81 (1.41–2.33)****	**1.92 (1.48–2.50)****
Analysis 2		
Depression severity		
IDS score[c]	**1.24 (1.12–1.37)****	**1.26 (1.14–1.41)****

Abbreviations: OR, odds ratio.
* $p < 0.01$.
** $p < 0.001$.
[a] The reference category is weight stable.
[b] Adjusted for age, gender, years of education and baseline weight.
[c] Results are presented per standard deviation (SD) increase in IDS score.

ity and worry), smoked a higher number of cigarettes, showed a longer basal PEP (indicative of decreased SNS activity), higher cortisol levels, and higher baseline TCA, SSRI and other antidepressant derived daily doses, as compared to healthy controls (column I, Table 3). They also showed lower mastery, less alcohol intake and lower basal RSA (indicative of decreased PNS activity). Findings were similar for depressive symptom severity as independent variable, with addition of associations with higher leptin levels and less physical activity (column I, Supplementary Table 1), but now no associations with cortisol levels were apparent.

3.3. Associations between contributing variables and subsequent weight change (b)

From all the potential contributing variables investigated in the study, only alcohol intake was significantly associated with weight gain: those with higher alcohol intake were significantly less likely to gain weight during a 4-year period (column II, Table 3; column II, Supplementary Table 1). Contrary to our expectations, none of the other potential contributing variables turned out to be significantly associated with weight gain.

3.4. Role of contributing variables in the association between depression and weight gain (c′ and a × b)

The direct associations of current depressive disorder on 4-year weight gain remained significant after adding all potential biopsychosocial variables and baseline antidepressant use to the model separately (column III, Table 3). The indirect associations of depression on weight gain through these contributing variables was not significant in any of

Table 3
Statistical mediation analyses with separate contributing variables between current Major Depressive Disorder (yes/no; T0) and weight gain (T0–T4) via standardized psychological, lifestyle and biological variables (T0) controlling for T0 weight based on 5000 bootstrap resamples (N = 1128).

Separate mediators	I. Association between MDD and contributing variable (a) B (SE)	II. Association between contributing variable and weight gain (b) B (SE)	III. Direct association between MDD and weight gain (c′) B (SE)	IV. Indirect association between MDD and weight gain (a × b)	
				B (SE)	95% CI
Psychological vulnerabilities					
(ln) Hopelessness	1.38 (0.05)***	0.11 (0.08)	0.48 (0.18)**	0.16 (0.12)	[−0.07; 0.38]
(ln) Aggression	0.87 (0.06)***	0.01 (0.07)	0.63 (0.15)***	0.01 (0.06)	[−0.11; 0.15]
Rumination	1.40 (0.05)***	−0.001 (0.08)	0.64 (0.18)***	−0.001 (0.12)	[−0.24; 0.22]
(ln) Anxiety Sensitivity	1.10 (0.05)***	0.03 (0.07)	0.59 (0.16)***	0.03 (0.08)	[−0.14; 0.21]
Worry	1.48 (0.05)***	−0.03 (0.09)	0.68 (0.19)***	−0.04 (0.13)	[−0.30; 0.21]
Mastery	−1.38 (0.05)***	−0.02 (0.08)	0.60 (0.18)**	0.03 (0.01)	[−0.20; 0.25]
Lifestyle factors					
(ln) Smoking	0.31 (0.06)***	0.08 (0.07)	0.69 (0.14)***	0.03 (0.02)	[−0.01; 0.07]
(ln) Alcohol use	−0.18 (0.06)**	−0.17 (0.07)*	0.60 (0.14)***	0.01 (0.01)	[0.01; 0.08]*
(ln) Physical activity	−0.21 (0.06)	0.02 (0.07)	0.64 (0.14)***	0.001(0.01)	[−0.02; 0.04]
Biological factors and physiological stress systems					
Heart Rate	−0.09 (0.06)	−0.13 (0.07)	0.67 (0.14)***	0.01 (0.01)	[−0.002; 0.01]
(ln) Respiratory Sinus Arrhythmia	−0.14 (0.05)*	0.064 (0.06)	0.68 (0.14)***	−0.01 (0.01)	[−0.04; 0.01]
Pre-Ejection Period	0.14 (0.06)**	0.04 (0.07)	0.66 (0.14)***	0.01 (0.01)	[−0.01; 0.04]
(ln)CRP	0.05 (0.06)	−0.04 (0.07)	0.65 (0.14)***	−0.002 (0.01)	[−0.02; 0.004]
(ln) Interleukin-6	0.06 (0.06)	0.06 (0.07)	0.65 (0.14)***	0.004 (0.01)	[−0.003; 0.03]
(ln) TNF-α	0.01 (0.06)	−0.03 (0.07)	0.67 (0.14)***	−0.003 (0.01)	[−0.01; 0.01]
(ln) Leptin	−0.03 (0.04)	−0.01 (0.11)	0.61 (0.14)***	0.003 (0.01)	[−0.01; 0.02]
AUCg (nmol/l/h)	0.20 (0.07)**	0.08 (0.09)	0.44 (0.16)**	0.02 (0.02)	[−0.01; 0.06]
(ln) Evening cortisol	0.21 (0.07)*	0.04 (0.08)	0.52 (0.16)**	0.01 (0.02)	[−0.02; 0.05]
Psychiatric variables					
TCA use (baseline)	0.13 (0.04)**	−0.25 (0.13)	0.68 (0.14)***	−0.03 (0.13)	[−0.43; −0.003]*
SSRI use (baseline)	0.66 (0.05)***	0.01 (0.06)	0.64 (0.14)***	0.01 (0.04)	[−0.07; 0.09]
Other antidepressants use (baseline)	0.40 (0.06)***	0.06 (0.06)	0.63 (0.14)***	0.03 (0.03)	[−0.02; 0.07]

Hopelessness, Aggression & Rumination subscales: Leiden Index of Depression Sensitivity-Revised; Anxiety sensitivity: Anxiety Sensitivity Index; Worry: Penn State Worry Questionnaire; Mastery: Pearlin Mastery Scale; Smoking: numbers of cigarettes per day; Alcohol use: amount of drinks per week, sum score; Physical activity: total minutes per day; CRP, C-reactive protein; TNF-α; Tumor necrosis factor alpha, AUCg: area under the morning curve with respect to the ground, TCA: Tricyclic antidepressants; SSRI: Selective serotonin reuptake inhibitors; All antidepressant use: Derived Daily Dose.
Analyses are controlled for age, gender, years of education and baseline weight. ln = natural logarithm transformation.
* $p < 0.05$.
** $p < 0.01$.
*** $p < 0.001$.

the models (column IV, Table 3), except for the model with alcohol intake. Also, even though the direct association between TCA use and weight gain (b-path) was not significant, the significant indirect effect indicates a small negative effect of TCA use. Besides these two small effects, the associations between current depressive disorder and weight gain seems to be independent of almost all of the biopsychosocial variables or baseline antidepressant use. These findings were almost consistent in the models with depressive symptom severity (column III and IV, Supplementary Table 1).

3.5. Depression course and treatment trajectory

Since, except alcohol intake and TCA use, none of the biopsychosocial variables or baseline antidepressant use contributed to the observed weight gain in depression, we decided on performing post-hoc analyses to investigate whether then the change in depression and treatment trajectories between baseline and 4-year follow up, as opposed to baseline characteristics, could contribute to the depression - weight gain association. To study whether depression course characteristics could identify those individuals who showed more weight gain, we included 4-year course of depressive symptom severity as measured by the Life Chart Interview (LCI), which is described in more detail elsewhere (Lyketsos et al., 1994; Beekman et al., 2002; Penninx et al., 2011). We made three 4-year depression course categories (healthy controls, baseline current MDD but no chronic course, baseline current MDD with chronic course (> 80% of the time depressive symptoms)). We also included 4-year change in antidepressant use, with 5 categories (no antidepressant use because healthy control; current patients with no antidepressant use over 4-year; started antidepressant use; stopped antidepressant use; and continuous antidepressant use). Separate multinomial logistic regression analyses were done with 4-year depression course, or change in antidepressant use categories as independent variables, and 4-year weight gain as outcome. The control group was used as reference category in both analyses. Multinomial logistic regression analyses showed that both MDD patients with and without a chronic course trajectory had a significantly higher odds of gaining weight than healthy controls (Table 4). In addition, compared to healthy controls, MDD patients who never used antidepressants during 4-year follow-up, as well as MDD patients who started using antidepressants at some point during 4-year follow up, had a significantly higher odds of gaining weight (Table 4). So, overall, also differences in course or treatment trajectories did not further differentiate in weight gain patterns over time.

Table 4
Logistic regression analysis with 4-year course trajectory of depression and antidepressant use as independent variables and 4-year weight gain (weight stable n = 686; weight gain n = 415) as outcome.

	4-year Weight gain (> 5%)[a]	
	Crude OR (95% CI)	Fully adjusted OR[b] (95% CI)
Analysis 1[c] (N = 1101)		
Healthy controls	1.00 (reference)	1.00 (reference)
Current MDD, non-chronic	**1.76 (1.35 – 2.29)***	**1.83 (1.39 – 2.42)***
Current MDD, chronic	**2.09 (1.41 – 3.10)***	**2.35 (1.56 – 3.55)***
Analysis 2[d] (N = 1277)		
Healthy controls, no antidepressant use	1.00 (reference)	1.00 (reference)
Current MDD, no antidepressant use over 4-year	**1.94 (1.44–2.61)***	**2.02 (1.48–2.74)***
Current MDD, started antidepressant use	**2.36 (1.48–3.76)***	**2.50 (1.54–4.06)***
Current MDD, stopped antidepressant use	1.40 (0.95–2.07)	1.43 (0.96–2.15)
Current MDD, continuous antidepressant use	1.23 (0.89–1.70)	1.41 (1.00–1.97)

Abbreviations: MDD, major depressive disorder; OR, odds ratio.
* $p < 0.001$.
[a] The reference category is weight stable.
[b] Adjusted for age, gender, years of education and baseline weight.
[c] Chronic is defined as experiencing ≥80% of the time depressive symptoms over 4 years.
[d] Change in antidepressant use over 4 years.

4. Discussion

In this large-scale, prospective cohort study, we found a robust association of both current MDD as well as depressive symptoms with 4-year weight gain. This association was almost independent of the large range of psychological, lifestyle and biological variables and antidepressant use included in this study. Depressed participants showed lower alcohol intake, and where thereby more likely to gain weight over 4-year. Also, there seems to be a small indirect effect of TCA use, causing a small reduction of the direct association between depression and weight gain, although the effect has little overall impact. None of the other nineteen potential contributing baseline variables had an association with subsequent weight gain and therefore were not logical contributing factors to the observed increased risk in weight gain among depressed persons. The 4-year depressive symptoms or antidepressant use patterns did neither further differentiate the subsequent 4-year weight gain in depressed persons.

An explanation for not finding more significant contributing variables could be that there are other variables are involved, not tested in this study due to absence of data. For example, research has suggested that dietary intake and psychological eating styles can influence both depression and weight change. Several studies showed associations between elevated depressive symptoms and more emotional eating and binge eating (Drapeau et al., 2003; Konttinen et al., 2010; Skinner et al., 2012), as well as between MDD and binge eating disorder, and unhealthy dietary patterns (Grilo et al., 2009; McNaughton et al., 2007; Lai et al., 2014). Also, it can be possible that not general negative thoughts, but only specific weight related negative thoughts are contributing to weight gain in depression (Markowitz et al., 2008). Alternatively, the comorbidity of depression and weight gain could be caused by the same underlying variables, that we did not measure. Several genes may be candidates for being an underlying variable, as indicated by a recent large, genome-wide study (Hyde et al., 2016). Results of this genome-wide study showed there to be evidence for overlap between the genetic bases of depression and both overweight and obesity.

Our results also show that the 4-year course of depression does not predict the depression- weight gain association. Both the chronic and the non-chronic group showed significant associations with weight gain, the results do indicate that weight gain tended to be higher in the chronic group, although this was not significant. Furthermore, both patients who never used antidepressant medication during the 4-years and patients who started using antidepressants had higher odds of gaining weight compared to healthy controls. No association with weight gain was found for patients who were on antidepressants during the full four years. This would imply that the effect of antidepressant treatment on weight as reported in prior trials may be a rather acute short-term phenomenon, but is not visible over an extended period of time. Indeed one review of Cassano and Fava (2004) found that when looking at the relative long term (> 6 months) effects of SSRI's versus placebo, patients who used SSRI's gained the same amount of body weight as control groups. However, another systematic review found effects of different types of antidepressants on weight gain both during the acute face (≤8 weeks) and on the longer term (Fava, 2000). Alternatively, an earlier study of our group of Gibson-Smith et al. (2016) found no independent 2-year effect of antidepressant use on

weight gain after adding depression status to the analysis. More research on the long term effects of antidepressant use over multiple years is needed to draw firm conclusions.

The strengths of this study were the large dataset, and the fact that we had detailed depression characteristics for our sample, including DSM-based depression diagnosis as well as depressive symptom severity measurements. Also weight was measured by a trained interviewer rather than using self-reported weight, and we included a broad range of potential contributing variables. However, some limitations should be taken into account. First, we measured depression and biopsychosocial variables both at baseline, since no data was available of all biopsychosocial variables at a time point between baseline and outcome. Thereby we did not truly analyze the temporal relationships between depression, contributing variables and weight gain over time (Kraemer et al., 2001). Second, no information was available on food intake or psychological eating styles, while literature shows that these variables are also associated with both depression and weight change.

This is the first large-scale cohort study that investigated the role of a broad range of different psychological, lifestyle and biological variables, psychiatric course and antidepressant use in the association between depression and prospective weight change. We confirmed the relationship of depressive disorder and depressive symptoms with 4-year weight gain, and showed that this robust relationship was not dependent of several biopsychosocial and antidepressant use variables, with the exception of alcohol intake and TCA use. Depression course trajectories and antidepressant medication use over the 4-year neither did further differentiate weight gain in depressed persons. Further research should focus on the question whether the depression - weight gain association is caused by other underlying factors. Solving this puzzle can have huge impact on the prevention of weight gain, and subsequent weight-related diseases and disorders, in patients with depression.

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Conflicts of interest

None.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.psychres.2017.04.044.

References

Beekman, A.T.F., Geerlings, S., Deeg, D., Smit, J., Schoever, R., De Beurs, E., Braam, A., Penninx, B.W.J.H., van Tilburg, W., 2002. The natural history of late-life depression. Arch. Gen. Psychiatry 59, 605–611.

Cassano, P., Fava, M., 2004. Tolerability issues during long-term treatment with antidepressants. Ann. Clin. Psychiatry 16, 15–25.

Craig, C.L., Marshall, A.L., Sjöström, M., Bauman, A.E., Booth, M.L., Ainsworth, B.E., Pratt, M., Ekelund, U., Yngve, A., Sallis, J.F., Oja, P., 2003. International physical activity questionnaire: 12-country reliability and validity. Med. Sci. Sports Exerc. 35, 1381–1395. http://dx.doi.org/10.1249/01.MSS.0000078924.61453.FB.

De Wit, L., Luppino, F., van Straten, A., Penninx, B., Zitman, F., Cuijpers, P., 2010. Depression and obesity: a meta-analysis of community-based studies. Psychiatry Res. 178, 230–235. http://dx.doi.org/10.1016/j.psychres.2009.04.015.

Drapeau, V., Provencher, V., Lemieux, S., Després, J.-P., Bouchard, C., Tremblay, A., 2003. Do 6-y changes in eating behaviors predict changes in body weight? Results from the Québec Family Study. Int. J. Obes. 27, 808–814. http://dx.doi.org/10.1038/sj.ijo.0802303.

Drost, J., Van der Does, A.J.W., Antypa, N., Zitman, F.G., Van Dyck, R., Spinhoven, P., 2012. General, specific and unique cognitive factors involved in anxiety and depressive disorders. Cogn. Ther. Res. 36, 621–633. http://dx.doi.org/10.1007/s10608-011-9401-z.

Faith, M.S., Butryn, M., Wadden, T., Fabricatore, A., Nguyen, A.M., Heymsfield, S.B., 2011. Evidence for prospective associations among depression and obesity in population-based studies. Obes. Rev. 12, 438–453. http://dx.doi.org/10.1111/j.1467-789X.2010.00843.x.

Fava, M., 2000. Weight gain and antidepressants. J. Clin. Psychiatry 61, 37–41 (doi: 10926053).

Field, A.E., Manson, J.E., Laird, N., Williamson, D.F., Willett, W.C., Colditz, G.A., 2004. Weight cycling and the risk of developing type 2 diabetes among adult women in the United States. Obes. Res. 12, 267–274. http://dx.doi.org/10.1038/oby.2004.34.

Filozof, C., Fernández Pinilla, M.C., Fernández-Cruz, A., 2004. Smoking cessation and weight gain. Obes. Rev. 5, 95–103. http://dx.doi.org/10.1111/j.1467-789X.2004.00131.x.

Forman-Hoffman, V.L., Yankey, J.W., Hillis, S.L., Wallace, R.B., Wolinsky, F.D., 2007. Weight and depressive symptoms in older adults: direction of influence? J. Gerontol. B Psychol. Sci. Soc. Sci. 62, S43–S51.

Gibson-Smith, D., Bot, M., Milaneschi, Y., Twisk, J.W., Visser, M., Brouwer, I.A., Penninx, B.W.J.H., 2016. Major depressive disorder, antidepressant use, and subsequent 2-year weight change patterns in the netherlands study of depression and anxiety. J. Clin. Psychiatry 77, e144–e151. http://dx.doi.org/10.4088/JCP.14m09658.

Grilo, C.M., White, M.A., Masheb, R.M., 2009. DSM-IV psychiatric disorder comorbidity and its correlates in binge eating disorder. Int. J. Eat. Disord. 42, 228–234. http://dx.doi.org/10.1002/eat.20599.

Hayes, A.F., 2012. PROCESS: a versatile computational tool for observed variable mediation, moderation, and conditional process modeling. White Pap. 1–39 (doi: 978-1-60918-230-4).

Hong, R.Y., 2007. Worry and rumination: differential associations with anxious and depressive symptoms and coping behavior. Behav. Res. Ther. 45, 277–290. http://dx.doi.org/10.1016/j.brat.2006.03.006.

Hotamisligil, G.S., 2006. Inflammation and metabolic disorders. Nature 444, 860–867. http://dx.doi.org/10.1038/nature05485.

Hyde, C.L., Nagle, M.W., Tian, C., Chen, X., Paciga, S.A., Wendland, J.R., Tung, J.Y., Hinds, D.A., Perlis, R.H., Winslow, A.R., 2016. Identification of 15 genetic loci associated with risk of major depression in individuals of European descent. Nat. Genet. 1–9. http://dx.doi.org/10.1038/ng.3623.

Konttinen, H., Silventoinen, K., Sarlio-Lahteenkorva, S., Mannisto, S., Haukkala, A., 2010. Emotional eating and physical activity self-efficacy as pathways in the association between depressive symptoms and adiposity indicators. Am. J. Clin. Nutr. 92, 1031–1039. http://dx.doi.org/10.3945/ajcn.2010.29732.

Koster, A., Van Gool, C., Kempen, G., Penninx, B.W.J.H., Lee, J., Rubin, S., Tylavsky, F., Yaffe, K., Newman, A., Harris, T., Pahor, M., Ayonayon, H., van Eijk, J.T.M., Kritchevsky, S., 2010. Late-life depressed mood and weight change contribute to the risk of each other. Am. J. Geriatr. Psychiatry 18, 236–244. http://dx.doi.org/10.1111/j.1532-5415.2011.03416.x.

Kraemer, H.C., Stice, E., Kazdin, A., Offord, D., Kupfer, D., 2001. How do risk factors work together? Mediators, moderators, and independent, overlapping, and proxy risk factors. Am. J. Psychiatry 158, 848–856.

Lai, J., Hiles, S., Bisquera, A., Hure, A.J., McEvoy, M., Attia, J., 2014. A systematic review and meta-analysis of dietary patterns and depression in community-dwelling adults. Am. J. Clin. Nutr. 99, 181–197. http://dx.doi.org/10.3945/ajcn.113.069880.Am.

Lamers, F., Burstein, M., He, J.P., Avenevoli, S., Angst, J., Merikangas, K.R., 2012. Structure of major depressive disorder in adolescents and adults in the US general population. Br. J. Psychiatry 201, 143–150. http://dx.doi.org/10.1192/bjp.bp.111.098079.

Licht, C.M.M., Penninx, B.W.J.H., de Geus, E.J.C., 2012. Effects of antidepressants, but not psychopathology, on cardiac sympathetic control: a longitudinal study. Neuropsychopharmacology 37, 2487–2495. http://dx.doi.org/10.1038/npp.2012.107.

Linde, J.A., Jeffery, R.W., Levy, R.L., Sherwood, N.E., Utter, J., Pronk, N.P., Boyle, R.G., 2004. Binge eating disorder, weight control self-efficacy, and depression in overweight men and women. Int. J. Obes. Relat. Metab. Disord. 28, 418–425. http://dx.doi.org/10.1038/sj.ijo.0802570.

Luppino, F.S., de Wit, L.M., Bouvy, P.F., Stijnen, T., Cuijpers, P., Penninx, B.W.J.H., Zitman, F., 2010. Overweight, obesity, and depression. Arch. Gen. Psychiatry 67, 220–229.

Lyketsos, C.G., Nestadt, G., Cwi, J., Heithoff, K., et al., 1994. The life chart interview: a standardized method to describe the course of psychopathology. Int. J. Methods Psychiatr. Res.

Markowitz, S., Friedman, M., Arent, S.M., 2008. Understanding the relation between obesity and depression: causal mechanisms and implications for treatment. Clin. Psychol. Sci. Pract. 15, 1–20.

McNaughton, S.A., Mishra, G.D., Stephen, A.M., Wadsworth, M.E.J., 2007. Dietary patterns throughout adult life are associated with body mass index, waist circumference, blood pressure, and red cell folate. J. Nutr. 137, 99–105.

Messina, G., De Luca, V., Viggiano, A., Ascione, A., Iannaccone, T., Chieffi, S., Monda, M., 2013. Review article autonomic nervous system in the control of energy balance and body weight: personal contributions. Neurol. Res. Int. 2013, 1–5.

Meyer, T.J., Miller, M.L., Metzger, R.L., Borkovec, T.D., 1990. Development and validation of the penn state worry questionnaire. Behav. Res. Ther. 28, 487–495. http://dx.doi.org/10.1016/0005-7967(90)90135-6.

Milaneschi, Y., Simonsick, E.M., Vogelzangs, N., Elsa, S., Yaffe, K., Harris, T.B., Tolea, M.I., 2012. Leptin, abdominal obesity and onset of depression in older men and women. J. Clin. Psychiatry 73, 1205–1211. http://dx.doi.org/10.4088/JCP.11m07552.Leptin.

Naragon-Gainey, K., 2010. Meta-analysis of the relations of anxiety sensitivity to the depressive and anxiety disorders. Psychol. Bull. 136, 128–150. http://dx.doi.org/10.

1037/a0018055.
Paans, N.P.G., Bot, M., Gibson-Smith, D., Van der Does, W., Spinhoven, P., Brouwer, I., Visser, M., Penninx, B.W.J.H., 2016. The association between personality traits, cognitive reactivity and body mass index is dependent on depressive and/or anxiety status. J. Psychosom. Res. 89, 26–31. http://dx.doi.org/10.1016/j.jpsychores.2016.07.013.
Papageorgiou, K., Vermeulen, K.M., Schroevers, M.J., Stiggelbout, A.M., Buskens, E., Krabbe, P.F.M., van den Heuvel, E., Ranchor, A.V., 2015. Do individuals with and without depression value depression differently? And if so, why? Qual. Life Res. 24, 2565–2575. http://dx.doi.org/10.1007/s11136-015-1018-3.
Patten, S.B., Williams, J.V.A., Lavorato, D.H., Brown, L., McLaren, L., Eliasziw, M., 2009. Major depression, antidepressant medication and the risk of obesity. Psychother. Psychosom. 78, 182–186. http://dx.doi.org/10.1159/000209349.
Pearlin, L., Schooler, C., 1978. The structure of coping. J. Health Soc. Behav. 19, 2–21.
Penninx, B.W.J.H., Milaneschi, Y., Lamers, F., Vogelzangs, N., 2013. Understanding the somatic consequences of depression: biological mechanisms and the role of depression symptom profile. BMC Med. 11, 129. http://dx.doi.org/10.1186/1741-7015-11-129.
Penninx, B.W.J.H., Beekman, A.T.F., Smit, J.H., Zitman, F.G., Nolen, W.A., Spinhoven, P., Cuijpers, P., de Jong, P., van Marwijk, H.W.J., Assendelft, W.J.J., van der Meer, K., 2008. The Netherlands study of depression and anxiety (NESDA): rationale, objectives and methods. Int. J. Methods Psychiatr. Res. 17, 121–140. http://dx.doi.org/10.1002/mpr.
Penninx, B.W.J.H., Nolen, W.A., Lamers, F., Zitman, F.G., Smit, J.H., Spinhoven, P., Cuijpers, P., De Jong, P.J., Van Marwijk, H.W.J., Der Meer, K., Van, Verhaak, P., Laurant, M.G.H., De Graaf, R., Hoogendijk, W.J., Der Wee, N., Van, Ormel, J., Van Dyck, R., Beekman, A.T.F., 2011. Two-year course of depressive and anxiety disorders: results from the Netherlands study of depression and anxiety (NESDA). J. Affect. Disord. 133, 76–85. http://dx.doi.org/10.1016/j.jad.2011.03.027.
Preiss, K., Brennan, L., Clarke, D., 2013. A systematic review of variables associated with the relationship between obesity and depression. Obes. Rev. 14, 906–918. http://dx.doi.org/10.1111/obr.12052.
Pruessner, J.C., Kirschbaum, C., Meinlschmid, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28, 916–931. http://dx.doi.org/10.1016/S0306-4530(02)00108-7.
Reiss, S., Peterson, R.A., Gursky, D.M., Mcnally, R.J., 1986. Anxiety sensitivity, anxiety frequency and the prediction of fearfulness. Behav. Res. Ther. 24, 1–8.
Rossetti, C., Halfon, O., Boutrel, B., 2014. Controversies about a common etiology for eating and mood disorders. Front. Psychol. 5, 1–19. http://dx.doi.org/10.3389/fpsyg.2014.01205.
Ruotsalainen, H., Kyngäs, H., Tammelin, T., Kääriäinen, M., 2015. Systematic review of physical activity and exercise interventions on body mass indices, subsequent physical activity and psychological symptoms in overweight and obese adolescents. J. Adv. Nurs. 71, 2461–2477. http://dx.doi.org/10.1111/jan.12696.
Rush, J., Gullion, C., Basco, M., Jarrett, R., Trivedi, M., 1996. The inventory of depressive symptomatology (IDS): psychometric properties. Psychol. Med. 26, 447–486.
Singh, G., Jackson, C.A., Dobson, A., Mishra, G.D., 2014. Bidirectional association between weight change and depression in mid-aged women: a population-based longitudinal study. Int. J. Obes. (Lond.). 38, 591–596. http://dx.doi.org/10.1038/ijo.2013.127.
Singh, M., 2014. Mood, food, and obesity. Front. Psychol. 5, 1–20. http://dx.doi.org/10.3389/fpsyg.2014.00925.
Skinner, H.H., Haines, J., Austin, S.B., Field, A.E., 2012. A prospective study of overeating, binge eating, and depressive symptoms among adolescent and young adult women. J. Adolesc. Health 50, 478–483. http://dx.doi.org/10.1016/j.jadohealth.2011.10.002.
Traversy, G., Chaput, J.-P., 2015. Alcohol consumption and obesity: an update. Curr. Obes. Rep. 4, 122–130. http://dx.doi.org/10.1007/s13679-014-0129-4.
Van der Does, W., 2002. Cognitive reactivity to sad mood: structure and validity of a new measure. Behav. Res. Ther. 40, 105–120.
Van Gool, C.H., Kempen, G.I.J.M., Bosma, H., van Boxtel, M.P.J., Jolles, J., van Eijk, J.T.M., 2007. Associations between lifestyle and depressed mood: longitudinal results from the Maastricht aging study. Am. J. Public Health 97, 887–894. http://dx.doi.org/10.2105/AJPH.2004.053199.
Vogelzangs, N., Duivis, H.E., Beekman, A.T.F., Kluft, C., Neuteboom, J., Hoogendijk, W., Smit, J.H., de Jonge, P., Penninx, B.W.J.H., 2012. Association of depressive disorders, depression characteristics and antidepressant medication with inflammation. Transl. Psychiatry 2, 1–9. http://dx.doi.org/10.1038/tp.2012.8.
Vreeburg, S.A., Kruijtzer, B.P., van Pelt, J., van Dyck, R., DeRijk, R.H., Hoogendijk, W.J.G., Smit, J.H., Zitman, F.G., Penninx, B.W.J.H., 2009. Associations between sociodemographic, sampling and health factors and various salivary cortisol indicators in a large sample without psychopathology. Psychoneuroendocrinology 34, 1109–1120. http://dx.doi.org/10.1016/j.psyneuen.2009.04.024.
Williams, J.M.G., Van der Does, A.J.W., Barnhofer, T., Crane, C., Segal, Z.S., 2007. Cognitive reactivity, suicidal ideation and future fluency: preliminary investigation of a differential activation theory of hopelessness/suicidality. Cogn. Ther. Res. 32, 83–104. http://dx.doi.org/10.1007/s10608-006-9105-y.
Wittchen, H., 1994. Reliability and validity studies of the who-composite international diagnostic interview (CIDI): a critical review. J. Psychiatr. Res. 28, 57–84.
World Health Organisation (WHO), 2004. Global Stategy on Diet, Physical Activity and Health [WWW Document]. Geneva. URL 〈http://books.google.de/books?Hl=de&lr=&id=u32pBrXlEWEC&oi=fnd&pg=PR7&ots=d9TgDLfKDG&sig=aCtFPcT_mKSwlDPdZyj3ClKlGqg〉.
World Health Organisation (WHO), 2014. WHO Collaboration Centre for Drug Statistics Methodology. World Health Organisation (WHO) [WWW Document]. Available at: //〈www.whocc.no/〉.