Time after time: biological factors in the course of recurrent depression
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Obesity

2.1 The ‘weight’ of recurrent depression: a comparison between recurrent depressed individuals and the Dutch population.

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Both depression and obesity share similar risk factors and are mutually associated. Among obese people, depression is one of the most common psychiatric disorders. Studies in persons seeking treatment for mood disorders like depression indicate that obesity and overweight are common problems in these groups. It has also been suggested that obesity and depression might be different manifestations of the same disease.

Although most publications regarding the association between major depressive disorder (MDD) and obesity corroborate each other, the literature on the relation between obesity and the recurrent type of MDD (MDD-R; having had at least 2 major depressive episodes) is limited and equivocal. Most studies on depression and obesity did not distinguish between single and recurrent episodes. However, this distinction may be important because depression is increasingly considered a chronic recurrent disorder with various levels of interepisodic functioning, and evidence is growing that the recurrent type (MDD-R) is a distinct one.

Most studies on the relation between depression and obesity did not control for antidepressant (AD) medication use, although a substantial part (20-60%) of the recurrently depressed patients use ADs for lengthy periods of time. Recently, Patten et al. reported in this journal an association between AD use and obesity incidence in their longitudinal analysis on a large community sample followed over a 10-year period. However, Patten et al. did not distinguish between single and recurrent episodes either. Our study, albeit a cross-sectional one, elaborates on their findings by focussing on the relation between obesity and MDD-R and the association between long-term use of ADs and obesity.

MDD-R patients participated in the DELTA study. To be eligible for this study, they had to meet the following criteria: (a) at least 2 major depressive episodes in the past 5 years (DSM-IV), (b) current remission status, according to DSM-IV criteria, for longer than 10 weeks and no longer than 2 years before, and (c) Hamilton Rating Scale for Depression of <10. At 2 years, follow-up assessment anthropomorphometric parameters were collected of 134 subjects. The protocol was approved by the ethics review committees. Reference data of BMI, waist-to-hip ratio and waist circumference were derived from the cross-sectional monitoring project on risk factors for chronic diseases (MORGEN project), a large population-based study of time trends on obesity prevalence rates. To adjust for differences in age and gender distribution between the reference and patient groups, we used for each sex the proportions of people constituting a specific age cohort in the total Dutch population as weights in the calculation of both the reference group and patient group anthropometric parameters for each sex.
a method resembling direct standardization. All subjects had their weight (in kilograms), height, waist and hip (in centimetres) measured by trained staff.

To assess relapse/recurrence, the Structured Clinical Interview for DSM-I V (SCID-I) was used. In the DELTA study, use of ADs was recorded but not controlled by the investigators for obvious ethical reasons. Every 3 months during the 2-year study, information on AD (type and dosage) over the previous month had been monitored using the Trimbos/IMTA Self-Report Questionnaire for Cost Associated with Psychiatric Illness which covers a maximum recall period of 1 month. Regarding the use of ADs, two groups were distinguished: those who used ADs throughout the entire 2-year study period \( (n = 46) \) and those who did not use ADs continuously, but intermittently \( (n = 49) \) or not at all \( (n = 39) \). Differences between these groups in BMI, waist circumference and waist-to-hip ratio were tested stratified by gender.

Standardized prevalence rates of (abdominal) overweight and obesity in recurrent depression patients and the reference group are shown in table 1. Overweight and obesity occurred more often in patients with recurrent depression than in the reference group, although statistical significance was reached in women only (74% of this sample). The extent of the differences was also larger for women (medium effect sizes in terms of Cohen’s \( h \)).

<p>| Table 1. Prevalence rates of (abdominal) overweight and obesity in recurrent depression patients and the general population |
|---------------------------------|----------------|----------------|----------------|-------|----------------|-----------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Recurrent depression</th>
<th>General population</th>
<th>Difference</th>
<th>( p )</th>
<th>95% CI</th>
<th>Cohen’s ( h )</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Men</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI ( \geq 25 \text{ kg/m}^2 ))</td>
<td>62.2</td>
<td>46.5</td>
<td>15.7</td>
<td>0.152</td>
<td>-5.8-37.1</td>
<td>0.32</td>
</tr>
<tr>
<td>Obesity (BMI ( \geq 30 \text{ kg/m}^2 ))</td>
<td>16.4</td>
<td>8.5</td>
<td>7.9</td>
<td>0.408</td>
<td>-10.8-26.5</td>
<td>0.24</td>
</tr>
<tr>
<td>Abdominal overweight (WC ( \geq 94 \text{ cm} ))</td>
<td>53.9</td>
<td>35.9</td>
<td>17.9</td>
<td>0.083</td>
<td>-23.7-38.3</td>
<td>0.36</td>
</tr>
<tr>
<td>Abdominal obesity (WC ( \geq 102 \text{ cm} ))</td>
<td>24.4</td>
<td>15.0</td>
<td>9.5</td>
<td>0.359</td>
<td>-10.7-29.6</td>
<td>0.24</td>
</tr>
<tr>
<td><strong>Women</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overweight (BMI ( \geq 25 \text{ kg/m}^2 ))</td>
<td>55.6</td>
<td>35.7</td>
<td>19.9</td>
<td>0.002</td>
<td>7.6-32.4</td>
<td>0.40</td>
</tr>
<tr>
<td>Obesity (BMI ( \geq 30 \text{ kg/m}^2 ))</td>
<td>28.0</td>
<td>9.7</td>
<td>18.3</td>
<td>0.002</td>
<td>7.1-29.5</td>
<td>0.48</td>
</tr>
</tbody>
</table>

Table is continued on the next page >
Abdominal overweight (WC ≥80 cm) | 70.3 | 44.1 | 26.2 | <0.001 | 14.5-37.9 | 0.54

Abdominal obesity (WC ≥88 cm) | 40.6 | 21.3 | 19.3 | 0.002 | 7.1-31.6 | 0.42

**Abbreviations** - WC = Waist circumference; CI = confidence interval; Cohen’s $h = 2\arcsin(\sqrt{p1}) - 2\arcsin(\sqrt{p2})$; small $h = 0.20$, medium $h = 0.50$, large $h = 0.80$.

$a$ Direct standardization to the age distribution in the Netherlands.


Within the MDD-R patient group, serotonin-selective reuptake inhibitors (SSRIs) were the most commonly used type of AD (73.3% of the men and 84.6% of the women) among the continuous AD users. Compared with SSRIs, other types of ADs used (e.g. tricyclic ADs) did not have a significant impact on the anthropometric measures. AD use was related to anthropometric measures. The mean AD equivalent correlated positively with both waist circumference ($r = 0.239$, $p = 0.006$) and waist-to-hip ratio ($r = 0.252$, $p = 0.004$), but not with BMI. In addition, mean waist circumference and waist-to-hip ratio scores were consistently higher amongst the continuous AD users compared to intermittent and non AD users. The mean waist circumference for non-users was 85.5 cm versus intermittent users with 87.7 cm versus continuous users with 94.5 cm ($F_{2, 122} = 4.95$, $p = 0.009$). The mean waist-to-hip ratio for non-users was 0.82 versus intermittent users with 0.84 versus continuous users with 0.87 ($F_{2, 122} = 6.08$, $p = 0.003$).

These results in our MDD-R sample are comparable to those of other studies in first episode or combined first episode MDD-R depressive patient samples. To our knowledge, this is the first study that examines this relation in recurrently depressed patients. Importantly, our patients were not in a depressive relapse per se (did not meet full DSM-IV-R criteria for MDD) at the time of assessment. Comparisons were adjusted for age and sex differences; however, we cannot rule out that the patient and reference groups are different in other characteristics that may account for the differences in anthropomorphic characteristics. However, this is also a drawback of all other studies.

Patients using ADs continuously, mostly SSRIs, show significantly more (abdominal) overweight and obesity than those using them intermittently or not at all. Compared with SSRIs, other types of ADs used (e.g. tricyclic ADs) did not have a significant impact on the anthropometric measures. We did find, however, a small association between AD equivalent dosage and waist circumference and waist-to-hip ratio. Patten et al. concluded that a major depressive...
episode does not appear to increase the risk of obesity, although the results were limited by
the self-report of height and weight, but they did find an association between AD use and
obesity incidence. This association was, like in our study, found for SSRIs and venlafaxine.
One explanation for these findings is that physicians may specifically select these medications
for use in patients they believe to be most at risk of weight gain. As such, those exposed to SSRIs
may represent a group at higher risk of obesity for reasons other than their AD medications. If,
on the other hand, ADs act as risk factors for obesity, this is of great concern given the increase
in the number of patients who receive AD treatment.

In general, a better understanding of the relationship between obesity and depression, i.e. un-
derstanding the beneficial and adverse effect of psychotropics on appetite, eating behaviour,
body weight and metabolism \(^{18}\), should improve our ability to prevent and treat both obesity and
depression. Thereby, ideally person-tailored interventions can be developed, including effective
non-pharmaceutical preventive strategies for recurrent depression \(^{9, 19, 20, 21}\) and extra physical
activities with - as added benefit - protection against AD-induced weight gain.

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References


