# Weight Changes in Patients Admitted to a Specialised Ward with Profound, Refractory Obsessive-Compulsive Disorder (OCD).

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## Abstract

**Introduction:** South West London and St George’s Mental Health Trust treats patients with profoundly severe Obsessive Compulsive Disorder (OCD). Previous study noted high numbers of individuals had raised blood lipids1. The weight of patients throughout their admission was monitored, to identify prescribing patterns which may contribute to this.

**Aims and Hypothesis:** Examine any relationship between prescription of specific drugs and weight gain amongst patients with profound, refractory OCD.

 **Methods:** 217 patients admitted into the National Inpatient Unit for OCD between 2009 -2016. Demographic data, Body Mass Index (BMI) at the beginning and end of the inpatient stay, and main drugs prescribed were recorded.

**Results:** 217 patients were included in the study. On admission average age was 40 years. And YBOCS was 35.6 representing profoundly severe OCD. The average reduction in YBOCS was 11.99 (CI 10.8-13.18). 31.5% of patients were prescribed sertraline and 5.1% refused to take an SRI. 73.6% of patients received dopamine blocking drugs. The mean BMI on admission was 26.24 and on discharge was 26.89. Patient’s weight gain was not related to medication and no drug regime was implicated in the weight gain.

**Conclusion:** Patients gained weight following admission, weight changes are not related to any specific drug.

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## Introduction

**Obsessive Compulsive Disorder (OCD)**

Obsessive-compulsive disorder (OCD) is a common psychiatric illness, with a lifetime prevalence of 1.9-3%2. Symptoms of OCD include obsessions and compulsions, which can cause significant functional impairment and distress3. Obsessions are recurring unwanted thoughts, images, or impulses that enter the mind despite attempts to resist3. The main themes of obsession often include contamination, aggression (thoughts of self-harm or harm to others), infection, and mortality (commonly surrounding sex or religion)4. Compulsions are acts, images or thoughts which are designed to reduce or prevent the risk of harm arising from the obsessive thought. For example, a person with contamination obsessions may have excessive handwashing compulsions. There are many theories surrounding the cause of OCD. Some suggest there might be genetic links, as relatives of patients with OCD are three times more likely to develop the condition compared to the rest of the population4.

**Treatments**

Guidance on the treatment of OCD was first published by the National Institute for Health and Clinical Excellence (NICE) in 2005. These recommend people with OCD initially either receive a course of psychological treatment involving graded exposure and self-imposed response prevention (ERP) or treatment with a serotonin reuptake inhibiting drug. ERP requires trained therapists who use graded ERP in order to encourage patients to ‘face their fears’ and let the obsessive thoughts occur without neutralising them by carrying out the compulsions5. Serotonin reuptake Inhibitors (SRIs) are antidepressants which comprise selective serotonin reuptake inhibitors and Clomipramine (a non-selective serotonin reuptake inhibiting drug). They cause increased levels of the neurotransmitter Serotonin in the brain. Although shown to be effective in the treatment of OCD, the dosage required is higher than that typically used in depression5.Most patients with OCD respond to treatment with SRIs or ERP but some are refractory. In such cases, the patient can be switched to an alternative SRI first but if neither ERP nor two trials of SRI medication are effective, the most frequent next step is to introduce a dopamine blocking drug6.

**Background**

The National Inpatient Unit for OCD based at South West London and St George’s Mental Health NHS Trust has been treating patients with profound refractory and disabling OCD for over 30 years2.  The current inpatient service began in 1985, and it has become apparent that patients have been increasingly more likely to be overweight when admitted. A study carried out by the National OCD service showed that 48 (49.0%) of the 98 patients with profound OCD admitted to the unit were overweight. The mean BMI for those patients was 30±6 and 42% of patients had evidence of high blood cholesterol2. There is also a suggestion that patients with a low BMI may have a poorer prognosis6.

This mirrors the increasing rate of obesity in the general population. The prevalence of obesity among adults in England rose from 14.9% in 1993 to 26.9% in 2015; an increase of 8% over 12 years7. It was noted that during the inpatient stay, many patients gained weight. The weight gain may have health implications for patients, particularly as research findings suggest that inpatients treated for OCD were likely to have raised blood lipids1. Increased blood lipids are concerning, as it can indicate dyslipidaemia. This is a metabolic disorder that can lead to increased cardiovascular and metabolic risks of strokes, heart attacks and type 2 diabetes.

In light of this finding, it was decided that the weight of patients should be monitored throughout their admission and that a number of preventative measures to reduce weight gain should be employed. These included staff producing and distributing booklets on healthy living as well as promoting exercise and healthy eating. A dietician regularly visited the ward advising patients on healthy eating. Despite these interventions, a pattern of excess weight gain was still observed.

## Literature Review

Clinically the classification of weight is based on the [body mass index](http://topics.sciencedirect.com/topics/page/Body_mass_index) ([BMI](http://topics.sciencedirect.com/topics/page/Body_mass_index)). Normal healthy BMI is defined as between 18.5 and 24.9. Patients with a BMI from 25 to 29.9 are classified as overweight, and from 30 to 39.9 as obese. Patients with a BMI above 40 are designated morbidly obese9.

**Weight Changes in Psychiatric Patients**

There are well-documented differences in body weight amongst patients with psychotic disorders and the general population, as a result of long-term treatment with [antipsychotic drugs](http://topics.sciencedirect.com/topics/page/Antipsychotic). According to a study looking at the effects of psychiatric medications on 226 outpatients, patients with psychotic disorders had four times more clinically relevant [adiposity](http://topics.sciencedirect.com/topics/page/Adipose_tissue) than the general population12.  This study also showed that there was no difference in the BMI of patients treated for less than two years versus patients treated for longer, suggesting that weight gain due to antipsychotics occurs mainly during the first two years of treatment and then plateaus12.

A majority of psychiatric medications are known to produce weight gain and lead to obesity in some patients8. This weight gain is sometimes accompanied by [increased appetite](http://topics.sciencedirect.com/topics/page/Polyphagia) or food craving. Eventually, this results in discontinuation of treatment in a substantial amount of patients even if the treatment is effective9. A prospective study found that during a 6-month treatment course with tricyclic antidepressants 44% of patients on amitriptyline and 70% of those on nortriptyline stopped taking the medication due to excessive weight gain10.

Weight gain is well documented in patients treated with some of the [second-generation antipsychotic](http://topics.sciencedirect.com/topics/page/Atypical_antipsychotic) drugs and also in treatment with some [mood stabilisers](http://topics.sciencedirect.com/topics/page/Mood_stabilizers). Noticeable weight gain frequently occurs during treatment with most [tricyclic antidepressants](http://topics.sciencedirect.com/topics/page/Tricyclic_antidepressants), while only slight to moderate weight gain is associated with orthodox [antipsychotics](http://topics.sciencedirect.com/topics/page/Antipsychotics)9. [Serotonin reuptake inhibitors](http://topics.sciencedirect.com/topics/page/Serotonin_reuptake_inhibitors) have been shown to induce weight loss during the first few weeks, but then lead to weight gain during longer periods of treatment. Several antidepressant and [antipsychotic drugs](http://topics.sciencedirect.com/topics/page/Antipsychotic) have been identified as having no effect on weight9.

**Weight Gain with Antipsychotic Medication**

In a cross-sectional study investigating 51 women experiencing long-term antipsychotic treatment with a variety of antipsychotics, 62% were found to be either overweight (BMI>25) or obese (BMI>30)13. In four other studies reviewed by [Allison and Casey (2001](http://www.sciencedirect.com/science/article/pii/S0022395603000189#BIB2)), 26, 40, and 55% of patients treated with antipsychotics had a BMI of >3014. According to those studies, obesity rates in both men were 31% and women were 37%, three times the rate of the general population.

 The consequences of antipsychotic treatment-induced weight gain on health and mortality rate were estimated based on data from the Framingham Heart Study. Using the assumed weight gain of 12.5 kg, a prediction of an additional 2335 cases of diabetes mellitus, 9456 cases of hypertension, and 662 deaths amongst 100,000 [schizophrenic](http://topics.sciencedirect.com/topics/page/Schizophrenia) patients within 10 years was made15.

**Effects of SRI’s on Weight Gain**

Although there are several studies examining weight gain in long-term patients with major depression, there is a dearth of studies for patients with OCD. One study which looking at weight gain during long-term treatment of Obsessive-Compulsive Disorder, involved 138 patients of which 21 were on Citalopram, 23 on Fluoxetine, 28 Fluvoxamine, 21 paroxetine, and 22 on sertraline. The average change after 30 months was a 2.5% increase in weight compared to baseline measurements. 14.5% of the study sample had significant weight increase (≥7%)16 with women showing greater weight gain. Clomipramine seemed to have the highest weight increase, whereas Fluoxetine and Sertraline had the lowest. A higher proportion of patients on Clomipramine (38.4%) compared to sertraline and fluoxetine (4.5% and 8.7%) were classed as having significant weight increase increase)16. Unlike the tricyclic antidepressant Clomipramine, SSRI’s are thought to induce weight loss rather than gain. There are a number of studies on fluoxetine’s effect on the weight of patients without psychiatric disorders treated for extreme obesity8.

A double-blind placebo-controlled study looked into the effect of fluoxetine on body weight after cessation of smoking in nicotine-dependent, non-depressed subjects. Although during the initial 10-week weight gain was lower in the groups treated with 30mg or 60 mg of fluoxetine, rebound weight gain occurred after discontinuation equalising the effect of fluoxetine 6 months after study entry17.

There are fewer studies examining the effect of other SSRIs on weight. In a study comparing the effect of fluoxetine and paroxetine as antidepressants, weight loss was observed more often in the patients on fluoxetine (12%) than in the paroxetine patients (3%)18. However, weight loss appeared to only occur during the early weeks of treatment and may even be followed by weight gain in some cases19. The SSRI which was most frequently associated with weight gain is Paroxetine20. A study found a significant mean increase in body weight from baseline in patient on paroxetine (3.6%), while patients on sertraline (+1%) or fluoxetine (−0.2%) exhibited no significant change over 26-32 week study period20.

**Effects of Dopamine Blockers on weight gain**

Treatment with antipsychotic medication, of which dopamine blockers are a subtype has often been associated with weight gain. A systematic review of atypical antipsychotics found that they lead to weight gain more often than conventional antipsychotics21. A possible cause could be that atypical antipsychotics interfere with the metabolism of glucose11. Other review studies have suggested that this weight gain is most severe with clozapine and olanzapine, followed by quetiapine, with less weight gain seen with the use of risperidone22.

*Clozapine*

Clozapine is the best documented second-generation atypical antipsychotic when it comes to its impact on weight gain. In a trial considering changes in patient’s weight during the first 10 weeks of treatment with clozapine, a 5.3Kg weight gain versus baseline was found22. Another study found a weight increase of 3.0 kg after 3 months, an average increase of 7.7 kg after 6 months, 3.35 kg after one year, and an increase of 10.4 kg in men and 16.2 kg in women after 3 years of clozapine treatment22. In a prospective longitudinal study extending over 5 years of continuous clozapine treatment, body weight appeared to increase steadily during the first four years by a mean of 11.6kg, before remaining stable23.

*Olanzapine*

Three studies comparing approximately 1700 patients reported the effects of Olanzapine on weight. After 6 weeks there was an increase in weight of 1.88 kg, 4 kg after 8 weeks, and 4.1 kg after 28 weeks22. Another study found a 6.8 kg weight increase after 21 weeks24. During a study looking at the one-year double-blind treatment, 85 patients on olanzapine gained an average of 5.02 kg, whereas patients on haloperidol experienced an average weight reduction of 1.53kg24.

*Risperidone*

Results from most trials suggest some weight gain during treatment with risperidone. One study found an increase of 3.4 kg after 6 weeks, another found and increase of 0.3 kg within patients on a dose of 1 mg, an increase of 1.6 kg in patients on a dose of 16 mg after 8 weeks, and an increase of 2 kg in patients on a mean dose of 12 mg after 12 weeks22. Risperidone has been shown to cause more weight gain in patients compared to haloperidol9. One reported study found no weight gain during risperidone treatment25.

*Quetiapine*

There are several studies documenting an increase in weight during short-term treatment with quetiapine. One study found a weight increase of 5.5 kg during acute treatment with 75–750 mg/d of Quetiapine26. Another found weight gain at the percentage deemed as clinically significant, occurred in 25% of patients receiving high dosages (up to 750 mg/d) and only 16% of patients on low dosages (up to 250 mg/d) and 5% on placebo27.  Research data collected by Astra-Zeneca reported a mean increase in weight of 3.5 kg after 18-26 weeks of treatment with Quetiapine, progressing to an increase of 5.6 kg after one year28.

**Mechanisms of psychiatric pharmacological Weight gain**

*Overeating and Food cravings*

Often, drug-induced weight gain is preceded by a rapid increase in appetite, explicitly for sweet and fatty foods29. It was suggested that if cravings were present in patients who experienced weight gain while on psychiatric medications, then increased food intake was the probable cause of weight gain30. Increased appetite and food yearning are often symptoms of brain diseases affecting the hypothalamus. The same symptoms can be elicited in non-depressed healthy subjects by short-term intake of TCA31. There is some suggestion that drug-induced weight gain might be due to the interference of the drug with the function of specific central nervous feedback systems regulating appetite and food intake, in a similar fashion to psychiatric disorders in some circumstances9.

*Altered resting metabolic rate*

There is a significant proportion of patients who report weight gain despite a subjectively reduced appetite and reportedly reducing food intake for several weeks or months. There is a suggestion that this could be explained by an altered resting metabolic rate. At normal levels of activity, baseline energy turnover can account for as much as 70% of daily energy expenditure, which is much more than the percentage accounted for by physical activity11. Therefore, even small changes in the basal metabolic rate (BMR), if sustained over extended periods of time, may have a considerable impact on body weight and lead to weight gain9.

The idea that an altered BMR could be involved in drug-induced weight gain is supported by findings of a study where a reported reduction of 5–24% of BMR was recorded in 10 patients taking various Tricyclic antidepressants for 2–4 weeks, in comparison to their individual baselines prior to drug treatment. This lead to an increase in weight of 3.5 kg during this study32. Olanzapine-induced weight gain has been shown not to have an association with an altered BMR. Instead in the study involving a small sample of patients with schizophrenia, olanzapine-induced weight gain was associated with an increased caloric intake, without a change in diet composition33.

*Effect on Neurotransmitters involved in control of food intake*

The ability of various Tricyclic Antidepressants to induce weight gain can be explained by their different patterns of stimulation or functional activation of dopamine, noradrenaline, serotonin, and histamine receptors9. Recent discoveries have been made with regards to the serotonergic system, where some receptor subtypes have been shown to promote satiety and induce weight loss in animal studies using selective agonists of the 1A, 1B, 2B, and 2C34.  In light of these findings, the patterns of weight loss observed during the early weeks of treatment with and SSRI is due to their serotoninergic effect, although weight gain taking place during long-term SSRI treatment cannot be explained by this9.

Most models do not account for the ability of receptors to evoke opposite actions on appetite control, depending on the neuroanatomical structure it is acting on9. An example is the regulation of food intake based on dopamine stimulation. In animal studies, local injections of dopamine into lateral hypothalamic areas resulted in a decreased food intake, and dopamine D2-receptor antagonist (sulpiride) had the opposite effect leading to increased food intake. However, in mesolimbic areas dopamine is found to stimulate feeding35. Therefore the effect of alpha-adrenoreceptors on appetite and food intake also depends on the location the neurotransmitter is acting on.

The specific role of histamine-1 receptors in appetite control is not known, but binding studies of psychotropic medications suggest that weight gain in humans is proportional to their ability to block H-1 receptors36.

*Leptin*

Decreases in body fat results in a reduction of leptin, which stimulating food intake9. In obese individuals, there are suggestions of leptin resistance37. This could be caused by a limited capacity of the active transporters able to carry leptin across the blood-brain barrier, due to oversaturation38.

The mechanism of leptin secretion in fat cells suggests that psychotropic drug-induced weight gain might be associated with increased levels of leptin. For some drugs this seems to be the direct cause of weight gain in patients however, in others there is evidence of induced weight gain without affected leptin secretion or only a very subtle increase9.

During acute treatment of schizophrenia with clozapine, the level of leptin in the blood doubled after two weeks of treatment and remained elevated throughout the first 10 weeks. The body weight of those patients increased by a mean of 4.2 kg39. Another study showed an increase in leptin secretion in patients treated with clozapine or olanzapine for four weeks, linked with an increase in weight of 2.3kg and 3.9 kg, respectively. In contrast, patients treated with haloperidol or on no psychotropic drugs at all did not gain any weight and had constant serum levels of leptin40.

In regard to antidepressants and their relationship with serum levels of leptin, during a six-week treatment with either tricyclic medications or paroxetine, body weight increased by 3.5 and 1.0 kg, respectively, while no change occurred in the control group of depressive patients treated without pharmacotherapy. Plasma leptin levels did not change in in the treatment or control groups41. In another 4 week study looking at the effect of mirtazapine treatment for major depression, a very small increase in plasma leptin was reported in in 11 patients compared to baseline measurements, these patients gained an average of 2.4 kg of body weight during the study42.

It also seems that the influence of antidepressants on leptin secretion differs from that of antipsychotics and mood stabilisers. Therefore, this may not merely reflect increased body fat mass, but hint to a different effect of those drugs on leptin regulation.

**Metabolic Syndromes in Psychiatric Patients**

Metabolic syndrome can be defined as a multisystem disorder. The phrase Metabolic syndrome is a term used to describe the collection of metabolic and cardiovascular abnormalities including obesity, hypertension, dyslipidaemia, hyperuricemia, and abnormalities of glucose homoeostasis such as insulin resistance, glucose intolerance, or diabetes mellitus43.All of these conditions are potentially life threatening and can lead to morbidity and sometimes even mortality. Similarly, high triglycerides and low high-density lipoprotein (HDL) are specific blood lipid changes associated with metabolic syndrome43.

Progressively, physical disorders such as obesity, hyperlipidaemia, hypertension, and type 2 diabetes mellitus are becoming significant comorbidities in people with serious mental illnesses, such as schizophrenia. Whether these disorders are part of the disease process itself through increased stress and inflammatory responses, genetic vulnerabilities, or environmental factors, or whether they are as a result of treatment of the disease is still being debated43.

Patients with serious mental illness have an increased prevalence of metabolic syndrome compared to the general population43. The current age-adjusted prevalence of the metabolic syndrome among the general population of U.S. adults is approximately 24%44. In a cross-sectional study, there was a 60% prevalence of metabolic syndrome estimated among 63 schizophrenic outpatients45.

The prevalence of obesity in 89 patients with bipolar disorder was estimated and compared with 445 matched controls from the general population who had participated in a national health survey. They found patients with bipolar disorder were more likely to be overweight or obese, and exhibit central patterns of obesity43. In a follow-up analysis, these investigators found that these patients consumed more sugars and carbohydrates than controls43.

Patients with severe mental illnesses, particularly schizophrenia and chronic mood disorders, have been shown to exhibit a higher prevalence of metabolic syndrome than the general population in several countries43.

**Comorbidities Associated with Psychiatric Illnesses**

Chronic psychiatric disorders are associated with increased morbidity and early mortality as individuals with psychiatric conditions are at an increased risk of physical health problems46. Patients with conditions such as [depression](http://topics.sciencedirect.com/topics/page/Major_depressive_disorder), anxiety disorders and [schizophrenia](http://topics.sciencedirect.com/topics/page/Schizophrenia) have all been shown to be at increased risk of physical illness compared with the general population1.

Many studies have raised significant concerns about the number of avoidable health risks in a population of long-stay psychiatric patients. These risks include high rates of smoking, obesity, central weight distribution and excessive weight gain 46. All of these factors contribute to the high levels of morbidity as they can lead to cardiovascular and metabolic complications.

The standardised mortality ratio of schizophrenic patients compared to the general population is 1.57 (95% CI: 1.53–1.6). Despite the high rate of suicides, natural causes account for 80% of all deaths in schizophrenic patients. An increased mortality of 60% in schizophrenic patients results from diseases that are potentially worsened by weight gain and the resultant health problems47.

**Summary and Aims**

Many studies looking at the effect of SRI’s and antipsychotics on weight gain fail to explore the effects of these medications in patients with severe OCD. It is important that this group of individuals be examined separately, as they often receive SRI’s and antipsychotics under different dosing regimens from other patients on the same medications. Additionally, there seems to be a link between obesity and metabolic syndromes. Patients with OCD have been shown to have higher levels of blood lipids. Obesity and high blood lipid levels are signs of metabolic syndrome and can lead to cardiovascular disease and diabetes. It is essential that we reduce the risk of metabolic syndromes in these patients by looking for any weight changes during admission and examining if there is any relationship between prescription of specific drugs and weight gain amongst these patients.

## Materials and Methods

**Inclusion Criteria**

Patients included in the study were aged 18 years or over, had refractory and profoundly severe OCD symptoms, and were admitted to the unit during the study period. To be eligible for admission to the unit, patients need to have profound OCD with a Yale –Brown Obsessive Compulsive Scale Score of at least 30/40 48. In addition, they had previously been treated with two different SRI drugs at the maximum recommended dosages for a minimum of 3 months each; to have had one of these trials augmented with a recognised augmenting agent (typically a dopamine blocking drug); to have received 2 previous trials of ERP treatment. In addition, there needs to be clear reasons as to why 24-hour care is necessary. This is most commonly due to extreme self-neglect, incontinence, or inability to drink sufficient fluid to maintain health49.

**Sample Population**

 A total of 217 patients admitted into the National Inpatient Unit for OCD between 2009 and 2016 were included in the study.

**Procedure:**

Data was collected using a combination of electronic patient records from RIO, paper records, discharge summaries, discharge medication prescriptions (TTO’s), initial assessments and other relevant clinical documentation. Various demographic data including age and sex; a record of the Body Mass Index (BMI) at the beginning and end of the inpatient stay; the Yale-Brown Obsessive Compulsive scale (Y-BOCs) on admission and discharge, was recorded into the database. BMI values were calculated using measurements from paper or electronic notes if available, otherwise they were calculated using the weights and heights measured during general observations at admission and discharge. These were calculated using the equation BMI= Weight (kg) ÷ Height (m2). This calculation was used to double check any BMI measurements recorded in patient records, to make sure the BMI readings were reliable. Along with this, any information of any SRI’s or dopamine blockers prescribed to the patient during admission and on discharge was also recorded.

**Ethical Approval**

No formal ethical approval was required as data was collected as part of a standard data set routinely required by the commissioners NHS England.

**Materials:**

Statistical Package for the Social Sciences (SPSS) Version 23

RIO Electronic Patient Records

Patient clinical records – Discharge summaries, TTO’s Admission reports, Clinical Letters, Progress reports.

Physical List of Patients admitted 2009 – 2016

Calculator

## Results

Ninety women and one hundred and twenty-seven men were admitted during the study period. Their average age at admission was 40 years (range 19-71 years SD: 13.1). On admission, they had an average YBOCS score of 35.6/40 (range 30-40; SD: 2.9) which represents profoundly severe OCD and during their inpatient stay this reduced by 12.27 points (CI 11.12-13.42) 34.5%, to an average of 23.3 (2-40; SD: 8.3) which represents moderate OCD symptomatology. Most patients were prescribed sertraline (31.3%) with fluoxetine (23.0%) and clomipramine (19.4%) the next most commonly prescribed. Paroxetine (9.7%); Citalopram (7.8%) and Escitalopram (3.2%) were the least frequently prescribed. Despite the severity of their condition, 5.1% of patients refused to take an SRI. Dopamine-blocking drugs were prescribed to 73.6% of patients with the remainder either refusing or having found them not to be of benefit. The most commonly prescribed drugs were aripiprazole (30.9%), quetiapine (13.8%), and risperidone (12.4%).

The mean BMI on admission was 26.2 (SD: 7.1) and on discharge was 26.9 (SD: 6.4). T-Test statistical comparison showed a significant mean change in BMI, which was an increase of 0.64 (SD: 2.5 CI 0.99 - 0.30) (P=0.00) from baseline.

**SRI Estimated Marginal Mean Dependent Variable: BMI Change**

**F=1.547 P= 0.165**

**Table 1. Mean BMI change in Patients Admitted to a Specialised Ward with Profound, Refractory Obsessive-Compulsive Disorder (OCD) according to SRI use.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| SRI | Mean | Standard Error | 95% confidence interval Lower Bound | 95% confidence intervalUpper Bound  |
| No SSRI | -0.458 | 0.67 | -1.78 | 0.87 |
| Clomipramine | -0.32 | 0.35 | -1.00 | 0.37 |
| Sertraline | -1.02 | 0.27 | -1.55 | -0.48 |
| Fluoxetine | -0.32 | 0.33 | -0.96 | 0.33 |
| Paroxetine | -0.76 | 0.48 | -1.71 | 0.19 |
| Citalopram | 0.29 | 0.55 | -0.80 | 1.37 |
| Escitalopram | -1.99 | 0.84 | -3.63 | -0.34 |

There is no significant difference between the mean change in BMI for patients on different SRIs or for those on no SRI.

**Dopamine Estimated Marginal Means Dependent Variable: BMI Change F= 1.02 P=0.41**

**Table 2. Mean BMI change in Patients Admitted to a Specialised Ward with Profound, Refractory Obsessive-Compulsive Disorder (OCD) according to Dopamine Blocker use.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Dopamine Blocker | Mean | Standard Error | 95% confidence interval Lower Bound | 95% confidence intervalUpper Bound  |
| No Dopamine Blocker | -0.26 | 0.30 | -0.85 | 0.33 |
| Risperidone | -0.30 | 0.44 | -1.17 | 0.58 |
| Aripiprazole | -0.98 | 0.28 | -1.53 | -0.43 |
| Quetiapine | -0.98 | 0.41 | -1.78 | -0.18 |
| Olanzapine | -0.06 | 0.78 | -1.62 | 1.49 |
| Other Dopamine Blocker | -0.43 | 0.44 | -1.31 | 0.45 |

There is no significant difference between the mean change in BMI for patients on different Dopamine blockers or for those on no Dopamine blockers.

**Figure 1. BMI at beginning and end of treatment showing that patients in the Underweight, normal and overweight categories seem to put on some weight during their stay whereas those in the obese category and above seem to lose weight.**





## Discussion

Overall, patients admitted with profound refractory OCD seemed to gain weight while admitted. However, it seems that these weight changes were not related to the use of any specific SSRI or dopamine blocker.

Therefore it is important to consider other explanations for weight gain amongst this patient population. Possible explanations aside from drug-induced weight gain, are the effect of altered fat storage and metabolic conditions associated with mental disorders on adiposity. This change in weight may also be due to various factors related to improvement in OCD symptomology. It might be, for example that reducing OCD symptoms lead to an increase in other compulsive behaviours such as binge-eating or general over-eating. Consideration should be given to how disease-related factors can contribute to weight gain, these factors include food craving patterns, eating habits and tenancies caused by the OCD.

**Disease Factors contributing to weight gain In Patients Admitted with OCD**

*Eating Habits*

Food intake is associated with a process of reward and gratification which leads to dopamine production, this in turn activates reward and pleasure centres in the brain50. The link between food intake and the activation of brain reward pathways eventually leads to the reduction or cessation of other signals of satiety and hunger. This leads to overeating and morbid obesity50. This type of behaviour is identical to the ritualistic patterns present in patients with OCD, as carrying out ritualistic compulsions gives the patient positive gratification and releases. Therefore patients with OCD are highly susceptible to obesity, due to their increased association with food intake and dopamine release. Dopamine directly activates reward and pleasure centres, so affects both mood and food intake. Mood disorders are often associated with abnormal eating behaviours e.g. depression and anxiety which are comorbidities of obesity51.

 Overeating and obesity originate from biological factors in a bi-directional manner involving mood and emotions. Emotional eating and altered mood caused by anxiety is often present in OCD and can lead to altered food choice and increased consumption leading to overeating and obesity50. In a study looking at the food intake, significantly higher intakes of fatty, sugary, and salty foods were found in the diets of adults with mood disorders in comparison to the general population52.

Therefore the relationship between altered mood and anxiety in the case of these patients with profound refractory OCD can alter food intake and eating habits. It is important to mention how an inpatient admission may affect this group of patients with heightened anxiety by causing increased levels of anxiety. This may be due to being in a new environment such as the ward, or the stress of new treatment or ERP. This theory could explain why a majority of these patients not only seem to be overweight or obese on admission, but also gain weight while admitted. Additionally, treatment of OCD removes the positive gratification a patient receives while enacting compulsions. Therefore they may seek this gratification from other sources, for example through eating.

*Metabolic conditions altering Lipid levels*

Evidence from previous studies showed that patients admitted with severe chronic OCD had higher levels of blood lipids than those on a general acute psychiatric ward (67% versus 42.2%)1. The same was found in comparison to patients admitted with schizophrenia, were the number of patients with elevated cholesterol levels were found to be 14 out of 38 (16.8%), in comparison to 61 out of 91 patients (67%) in patients with OCD1. A raise in one or more fat proteins in the blood is defined as hyperlipidaemia and is a component of metabolic syndrome. This is in stark contrast as according to a study of adults in the United States, only 17% of adults in the general population have a raised blood lipid level1. It could be that the increased levels of blood lipids and the weight gain can be linked to increased levels of leptin in psychiatric patients. Leptin is synthesised by fat cells and is thought to signal the brain, leading to activation of hypothalamic centres regulating energy homoeostasis. In obese animals, an increase in leptin receptor activity leads to increase in Neuropeptide Y (NPY) concentration resulting in hyperphagia and weight gain53.

 *‘Carbohydrate craving’ Phenomena*

Recently studies exploring emotional factors have examined the relationship between obesity, anxiety, and mood disorders54. Sugar addiction, carbohydrate craving, and emotional eating have been correlated with obesity and being overweight. A strong correlation between obesity, anxiety, and mood disorders was also found 55. Recent research postulates a carbohydrate-craving syndrome, in which carbohydrate intake treats a dysphoric mood state56.

Carbohydrate craving syndrome involves cravings to eat sweets or starchy foods at least four times a week during the afternoon or at night, in conjunction with an unease or generalised dissatisfaction, which is relieved by eating these foods55.

Regulation of eating and energy homoeostasis is controlled by many factors including; hunger and satiety signals, the sense of reward from food, environmental cues, and cognitive factors57. Carbohydrate craving during states of anxiety is due to the ability of carbohydrates to trigger hedonic brain response by activating the endogenous opioid system58. This means that when the individual with anxiety eats highly palatable food it lowers his or her anxiety levels. There is evidence that patients with psychiatric disorders (mood, anxiety and eating disorders) and premenstrual syndrome have greater hedonic response levels to concentrated sucrose solutions (e.g. carbohydrates). This is a stable, innate, and inherited trait that is partially genetic, and is associated with higher hedonic response levels to sweet tastes, which increases the risk of these individuals developing obesity59.

*Eating behaviour in OCD: Binge eating*

Multiple mental disorders like anxiety, depression, and OCD are associated with binge eating60. Binge eating may be triggered by anxiety, but binging can also reduce anxiety and increases reward sensation during and after the period of distress61. Anxiety is triggered in individuals with OCD during the obsessive phase and is reduced or relieved when the individual engages in the compulsive act. While there is a high likelihood that OCD and eating disorders share common pathology, it is yet to establish whether OCD is a risk factor for eating disorders or whether it exists as a consequence of it. One possibility is that the developmental emergence of OCD behaviours in humans predisposes an individual to binge eating even before reaching clinical criteria62. Binge eating is defined by the American Psychiatric Association as the consumption of large amounts of food within a short period of time.

*Dietary Changes*

Findings of the study looking at the relationships between psychiatric medications, eating behaviours, and weight showed a lower proportion of individuals reported weight gain when some dietary restraint was present. This suggests that cognitive dietary restraint could contribute to weight suppression and may help with weight management63. It could be used as part of therapeutic treatment for weight gain amongst patients with profound refractory OCD. Although, another study has suggested that high dietary restraint may have serious implications, as it can create psychological stress by the activation of the hypothalamic-pituitary-adrenal axis, increasing the release of cortisol64. Therefore this method of treatment should be explored further before implementation and must be used in conjunction with advice from dietitians.

*Behavioural Changes*

Behavioural therapy has been shown to improve the outcome of efforts to lose weight, especially in long-term follow-up studies, which showed a return to weight before therapy in participants who did not have continued behaviour intervention9. Behaviour therapy programs are based on individual analysis of eating and physical activity using activity guidelines and specific registers65. Body weight and waist-hip ratio should be monitored regularly from the beginning of treatment by both the patients and staff. Based on this information, individual eating and activity schedules can be designed to guide patients and make them aware of relevant behaviour in order to help them to modify specific points that are agreed upon themselves and the therapist9. Self-reinforcing and self-evaluating techniques can help patients to comply with their individual daily schedules66. This involves long-term pervasive modification of behaviour, such programmes can only be successful if patients can be made aware of the emotional and biological processes associated with eating. These insights must allow them to change basic living and eating habits. An example of a similar behavioural treatment program, whereby 6 schizophrenic patients continuously treated with clozapine or olanzapine underwent a behavioural therapy intervention consisting of 7-9 individual and 16 two-weekly group sessions of cognitive behaviour therapy lead to a reduction in BMI from 29.6 to 25.167. However, it should be taken into consideration that the cognitive impairment and loss of energy associated with many psychiatric disorders, may complicate the success of this approach, and may therefore require additional pharmacological measures9.

*Medications to Aid with weight loss*

One recent study in paediatric patients (aged 12–18 years) showed that the antidiabetic drug metformin may reverse weight gain induced by olanzapine, risperidone, quetiapine, and valproate68. The weight of 19 patients on either of these drugs decreased by a mean of 2.93 kg after 12 weeks of additional treatment with metformin 500 mg three times daily68. However, another earlier study found no effect on the weight of 5 obese patients on long-term treatment with either haloperidol, fluphenazine, trifluoperazine, or risperidone after 8 weeks of additional metformin treatment69. It is thus difficult to gauge whether metformin may be helpful or not.

**Management and prevention of complications as a result of Metabolic Syndrome in patients with profound Refractory OCD**

Medical treatment, along with measures to reduce the risk of developing of cardiovascular and metabolic conditions, is recommended in all obese patients and in patients with more than two risk factors who are overweight or have an increased waist circumference9. Relevant risk factors include; established coronary heart disease, type II diabetes mellitus, cigarette smoking, hypertension, high LDL-cholesterol, low HDL-cholesterol, increased fasting serum glucose and/or a family history of premature coronary heart disease9.

**Limitations of the project:**

There are several limitations to this study. The first limitation of this study is the variation in methods of assessing, calculating and measuring weight gain the patients studied. There were some inaccuracies and discrepancies between measurements of BMI between the paper records and the electronic records found on RIO. This varied based on time and method of measurement. This was most commonly due to the nursing staff and admitting doctor measuring the patient at different times of day and whether the patient was clothed and wearing shoes, and if so, whether the BMI calculation took this into consideration. Many patients with OCD contamination fears had difficulty removing shoes at admission but most improved at discharge and thus the tendency for any error would be a reduced apparent gain in BMI.

The second limitation was the use of BMI itself, which can often be an inaccurate indication of weight and adiposity. BMI does not account for increase muscle mass and can be more inaccurate at representing weight in some ethnicities. Also, fairly large changes in weight do not correspond in similar-sized increases in BMI, for example a patient can have an increase of 3-4 kg and only a small increase in BMI. Alternatively, it could be useful to measure waist to height ratio in future studies as it is a better indicator of central obesity which is a risk factor for metabolic syndromes.

 The third limitation was that there was a range of drug regimes applicable to the patient group in the study. This study was naturalistic, therefore the prescribing of drugs was determined by response, clinician’s preferences and patient’s preferences. As a result of this, only a handful of patients were on some of the drug regimes. This factor made it more difficult to evaluate their contribution to overall weight gain.

**Conclusion**

In conclusion, weight gain in patients with psychiatric conditions has been well documented in many previous studies and a majority have suggested a pharmacological cause for this weight gain. The results from this study show that patients admitted to a specialised ward with profound, refractory Obsessive-Compulsive Disorder gained weight overall and that this could not be attributed to a specific drug regime. There are suggestions that there may be other causes of weight gain in patients besides pharmacological causes. Regardless of the cause of weight gain, these patients should receive appropriate treatment and monitoring throughout their stay to allow clinicians to manage the effects of weight gain on their physical and mental health. Advice from dieticians and other professionals may be helpful in preventing some of this weight gain. Any risk factors of metabolic syndrome should be treated.

It would be beneficial for future studies to explore possible factors causing weight gain in patients admitted with profound refractory Obsessive Compulsive Disorder. For example, looking at the food intake and physical activity levels of these individuals during admission, and monitoring changes in weight.

**Word Count: 6107**

## References

1. Drummond LM, Boschen MJ, Cullimore J, Khan-Hameed A, White S, Ion R. Physical complications of severe, chronic obsessive-compulsive disorder: A comparison with general psychiatric inpatients. General Hospital Psychiatry. 2012 Nov;34(6):618–25.
2. DRUMMOND LM, HAMEED AK, ION R. Physical complications of severe enduring obsessive-compulsive disorder. World Psychiatry. 2011 Jun;10(2):154.
3. NICE. www.nice.org.uk. online: NICE. Obsessive-compulsive disorder and body dysmorphic disorder: Treatment; 2005 Nov 1 [cited 2016 Dec 13]. Available from: https://www.nice.org.uk/guidance/cg31/chapter/introduction.
4. Muenchrath D, Potschisvili H, Lodhia A. Psychiatry P.R.N.: Principles, reality, next steps. Stringer S, Church L, Davison S, editors. New York: Oxford University Press; 2009 Mar 5. 156–7 p. ISBN: 9780199561988.
5. Choices N. NHS Choices. Department of Health. Treatments for OCD; 2016 Oct 3 [cited 2016 Dec 22]. Available from: http://www.nhs.uk/Conditions/Obsessive-compulsive-disorder/Pages/Treatment.aspx.
6. Pallanti S, Quercioli L. Treatment-refractory obsessive-compulsive disorder: Methodological issues, operational definitions and therapeutic lines. Progress in Neuro-Psychopharmacology and Biological Psychiatry. 2006 May;30(3):400–12.
7. 2017 PHE. Public Health England. Online: Public Health England. UK and Ireland prevalence and trends: Public health England obesity knowledge and intelligence team; 2017 [cited 2017 Jan 29]. Available from: https://www.noo.org.uk/NOO\_about\_obesity/adult\_obesity/UK\_prevalence\_and\_trends.
8. Virk S, Schwartz TL, Jindal S, Nihalani N, Jones N. Psychiatric medication induced obesity: An aetiologic review. Obesity Reviews. 2004 Aug;5(3):167–70.
9. Zimmermann U, Kraus T, Himmerich H, Schuld A, Pollmächer T. Epidemiology, implications and mechanisms underlying drug-induced weight gain in psychiatric patients. Journal of Psychiatric Research. 2003 May 1 [cited 2017 Jan 17];37(3):193–220. Available from: http://www.sciencedirect.com/science/article/pii/S0022395603000189 doi: 10.1016/S0022-3956(03)00018-9.
10. Berken GH, Weinstein DO, Stern WC. Weight gain. Journal of Affective Disorders. 1984 Oct;7(2):133–8.
11. http://www.psychiatrist.com/jcp/article/Pages/2002/v63n03/v63n0306.aspx.
12. Silverstone T, Smith G, Goodall E. Prevalence of obesity in patients receiving depot antipsychotics. The British Journal of Psychiatry. 1988 Aug 1;153(2):214–7.
13. Stedman T, Welham J. The distribution of adipose tissue in female in-patients receiving psychotropic drugs. The British Journal of Psychiatry. 1993 Feb 1;162(2):249–50.
14. Allison DB, Casey DE. J Clin psychiatry/Antipsychotic-Induced weight gain: A review of the literature. The Journal of Clinical Psychiatry. 2001 Jun 1 [cited 2017 Jan 18];62(suppl 7):22–31. Available from: http://www.psychiatrist.com/jcp/article/Pages/2001/v62s07/v62s0704.aspx.
15. Fontaine KR, Heo M, Harrigan EP, Shear CL, Lakshminarayanan M, Casey DE, Allison DB. Estimating the consequences of anti-psychotic induced weight gain on health and mortality rate. Psychiatry Research. 2001 Apr;101(3):277–88.
16. Maina G, Albert U, Salvi V, Bogetto F. Weight gain during long-term treatment of obsessive-compulsive disorder. The Journal of Clinical Psychiatry. 2004 Oct 15;65(10):1365–71.
17. Borrelli B, Spring B, Niaura R, Kristeller J, Ockene JK, Keuthen NJ, Harvard. Weight suppression and weight rebound in ex-smokers treated with fluoxetine — northwestern scholars. Journal of Consulting and Clinical Psychology. 1999 [cited 2017 Jan 20];67(1):124–31. Available from: https://www.scholars.northwestern.edu/en/publications/weight-suppression-and-weight-rebound-in-ex-smokers-treated-with- doi: 10.1037/0022-006X.67.1.124.
18. Chouinard G, Saxena B, Bélanger M-C, Ravindran A, Bakish D, Beauclair L, Morris P, Vasavan Nair NP, Manchanda R, Reesal R, Remick R, Colleen O’Neill M. A Canadian multicenter, double-blind study of paroxetine and fluoxetine in major depressive disorder. Journal of Affective Disorders. 1999 Jul;54(1-2):39–48.
19. Sussman N. J Clin psychiatry/review of atypical Antipsychotics and weight gain. The Journal of Clinical Psychiatry. 2001 Jan 9 [cited 2017 Jan 21];62(suppl 23):12–5. Available from: http://www.psychiatrist.com/jcp/article/Pages/2001/v62s23/v62s2302.aspx.
20. Fava M, Judge R, Hoog S, Nilsson M, Koke S. Fluoxetine versus sertraline and paroxetine in major depressive disorder: Changes in weight with long-term treatment. The Journal of clinical psychiatry. 2000 Dec 6 [cited 2017 Jan 21];61(11):863–7. Available from: https://www.ncbi.nlm.nih.gov/pubmed/11105740.
21. Allison DB, Mentore JL, Heo M, Chandler LP, Cappelleri JC, Infante MC, Weiden PJ. Antipsychotic-Induced Weight Gain: A Comprehensive Research Synthesis. American Journal of Psychiatry. 1999 Nov;156(11):1686–96. Available from: http://ajp.psychiatryonline.org/doi/abs/10.1176/ajp.156.11.1686?url\_ver=Z39.88-2003&rfr\_id=ori%3Arid%3Acrossref.org&rfr\_dat=cr\_pub%3Dpubmed.
22. Taylor DM, McAskill R. Atypical antipsychotics and weightgain - a systematic review. Acta Psychiatrica Scandinavica. 2000 Jun;101(6):416–32.
23. Henderson DC. Clozapine, diabetes Mellitus, weight gain, and lipid abnormalities: A Five-Year naturalistic study. American Journal of Psychiatry. 2000 Jun 1;157(6):975–81.
24. Wirshing DA, Wirshing WC, Kysar L, Berisford AM, Goldstein D, Pashdag J, Marder SR. J Clin psychiatry/novel Antipsychotics: Comparison of weight gain liabilities. The Journal of Clinical Psychiatry. 1999 Jun 30 [cited 2017 Jan 22];60(6):358–63. Available from: http://www.psychiatrist.com/jcp/article/Pages/1999/v60n06/v60n0602.aspx doi: 10.4088/JCP.v60n0602.
25. Ganguli R, Brar JS, Ayrton Z. Weight gain over 4 months in schizophrenia patients: A comparison of olanzapine and risperidone. Schizophrenia Research. 2001 Apr;49(3):261–7.
26. Borison RL, Arvanitis LA, Milier BG. The US Seroquel Study Group. ICI 204,636, an atypical antipsychotic: efficacy and safety in a multicenter, placebo-controlled trial in patients with schizophrenia. Journal of Clinical Psychopharmacology. 1996 Apr;16(2):158–69.
27. Small JG. The Seroquel Study Group. Quetiapine in patients with schizophrenia: a high- and low-dose double-blind comparison with placebo. Archives of General Psychiatry. 1997 Jun 1;54(6):549.
28. Gunasekara NS, Spencer CM. Quetiapine. A review of its use in schizophrenia. CNS Drugs. 1998;9(4):325–40.
29. Kazes M, Danion JM, Grangé D, Pradignac A, Simon C, Burrus-Mehl F, Schlienger JL, L. S. Eating behaviour and depression before and after antidepressant treatment: A prospective, naturalistic study. Journal of Affective Disorders. 1994 Mar;30(3):193–207.
30. PAYKEL ES, MUELLER PS, DE LA VERGNE PM. Amitriptyline, weight gain and carbohydrate craving: A side effect. The British Journal of Psychiatry. 1973 Nov 1;123(5):501–7.
31. GARLAND EJ, REMICK RA, ZIS AP. Weight gain with Antidepressants and lithium. Journal of Clinical Psychopharmacology. 1988 Oct;8(5):323–30.
32. Fernstrom MH, Epstein LH, Spiker DG, Kupfer DJ. Resting metabolic rate is reduced in patients treated with antidepressants. Biological Psychiatry. 1985 Jun;20(6):692–5.
33. Gothelf D, Falk B, Singer P, Kairi M, Phillip M, Zigel L, Poraz I, Frishman S, Constantini N, Zalsman G, Weizman A, Apter A. Weight gain associated with increased food intake and low habitual activity levels in male adolescent schizophrenic inpatients treated with Olanzapine. American Journal of Psychiatry. 2002 Jun;159(6):1055–7.
34. De Vry J, Schreiber R. Effects of selected serotonin 5-HT1 and 5-HT2 receptor agonists on feeding behavior: Possible mechanisms of action. Neuroscience & Biobehavioral Reviews. 2000 May;24(3):341–53.
35. Baptista T. Body weight gain induced by antipsychotic drugs: Mechanisms and management. Acta Psychiatrica Scandinavica. 1999 Jul;100(1):3–16.
36. Stahl SM, Muntner N. Stahl’s essential Psychopharmacology: Neuroscientific basis and practical applications. 4th ed. Cambridge: Cambridge University Press; 2013 Apr 11. ISBN: 9781107686465.
37. Kolaczynski JW, Ohannesian JP, Considine RV, Marco CC, Caro JF. Response of leptin to short-term and prolonged overfeeding in humans. The Journal of Clinical Endocrinology & Metabolism. 1996 Nov;81(11):4162–5.
38. Koistinen H. Circulating leptin has saturable transport into intrathecal space in humans. European Journal of Clinical Investigation. 1998 Nov;28(11):894–7.
39. Brömel T, Blum WF, Ziegler A, Schulz E, Bender M, Fleischhaker C, Remschmidt H, Krieg J-C, Hebebrand J. Serum leptin levels increase rapidly after initiation of clozapine therapy. Molecular Psychiatry. 1998 Feb 24;3(1):76–80.
40. Kraus T, Haack M, Schuld A, Hinze-Selch D, Uhr M. Body Weight and Leptin Plasma Levels During Treatment With Antipsychotic Drugs. The American Journal of Psychiatry. 1999 Feb 2;156(2):312–4.
41. Hinze-Selch D. Effects of Antidepressants on weight and on the plasma levels of Leptin, TNF-α and soluble TNF receptors A longitudinal study in patients treated with Amitriptyline or Paroxetine. Neuropsychopharmacology. 2000 Jul;23(1):13–9.
42. Kraus T, Haack M, Schuld A, Hinze-Selch D, Koethe D, Pollmächer T. Body weight, the tumor necrosis factor system, and Leptin production during treatment with Mirtazapine or Venlafaxine. Pharmacopsychiatry. 2002 Nov;35(6):220–5.
43. Toalson P, Ahmed S, Hardy T, Kabinoff G. The metabolic syndrome in patients with severe mental illnesses. 2004 [cited 2017 Jan 23];6(4). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC514841/pdf/i1523-5998-6-4-152.pdf.
44. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults. JAMA. 2002 Jan 16;287(3):356.
45. Kato M, Gonzalez-Blanco M, Sotelo J. Metabolic syndrome in schizophrenia: a pilot study. 156th annual meeting of the American psychiatric association. 56th annual meeting of the American Psychiatric Association. [place unknown]: Cambridge University Press (CUP); 2003 Jul. p. 477–82. (vol. 8, no. 07).
46. Cormac I, Ferriter M, Benning R, Saul C. Physical health and health risk factors in a population of long-stay psychiatric patients. Original papers. 2005 Jan 1 [cited 2017 Jan 23];29(1):18–20. Available from: http://pb.rcpsych.org/content/29/1/18 doi: 10.1192/pb.29.1.18.
47. Harris EC, Barraclough B. Excess mortality of mental disorder. The British Journal of Psychiatry. 1998 Jul 1;173(1):11–53.
48. Drummond LM, Fineberg NA, Heyman I, Kolb PJ, Pillay A, Rani S, Salkovskis P, Veale D. National service for adolescents and adults with severe obsessive-compulsive and body dysmorphic disorders. Psychiatric Bulletin. 2008 Sep 1;32(9):333–6.
49. Harris PM, Drummond LM. Compliance of community teams with specialist service recommendations for obsessive-compulsive and body dysmorphic disorders. BJPsych Bulletin. 2016 May 12;40(5):245–8.
50. Singh M. Mood, food, and obesity. 2014 Sep 1 [cited 2017 Feb 2];5. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4150387/pdf/fpsyg-05-00925.pdf.
51. Novick JS, Stewart JW, Wisniewski SR, Cook IA, Manev R, Nierenberg AA, Rosenbaum JF, Shores-Wilson K, Balasubramani GK, Biggs MM, Zisook S, Rush AJ, Object object. Clinical and demographic features of atypical depression in Outpatients with Major Depressive disorder. The Journal of Clinical Psychiatry. 2005 Aug 15;66(08):1002–11.
52. Davison KM, Kaplan BJ. Food intake and blood cholesterol levels of community-based adults with mood disorders. BMC Psychiatry. 2012 Feb 14;12(1).
53. Harvey BH, Bouwer CD. Neuropharmacology of Paradoxic weight gain with selective serotonin Reuptake inhibitors. Clinical Neuropharmacology. 2000 Mar;23(2):90–7.
54. Corwin RL, Avena NM, Boggiano MM. Feeding and reward: Perspectives from three rat models of binge eating. Physiology & Behavior. 2011 Jul;104(1):87–97.
55. Ventura T, Santander J, Torres R, Contreras AM. Neurobiologic basis of craving for carbohydrates. Nutrition. 2014 Mar;30(3):252–6.
56. Corsica JA, Spring BJ. Carbohydrate craving: A double-blind, placebo-controlled test of the self-medication hypothesis. Eating Behaviors. 2008 Dec;9(4):447–54.
57. Lemmens SG, Martens EA, Born JM, Martens MJ, Westerterp-Plantenga MS. Lack of effect of high-protein vs. High-carbohydrate meal intake on stress-related mood and eating behavior. Nutrition Journal. 2011;10(1):136.
58. Macht M, Mueller J. Immediate effects of chocolate on experimentally induced mood states. Appetite. 2007 Nov;49(3):667–74.
59. Kampov-Polevoy AB, Alterman A, Khalitov E, Garbutt JC. Sweet preference predicts mood altering effect of and impaired control over eating sweet foods. Eating Behaviors. 2006 Aug;7(3):181–7.
60. McElroy S, Phillips K, Keck P. Obsessive compulsive spectrum disorder. The Journal of clinical psychiatry. 1994 Oct 1 [cited 2017 Feb 6];55:33–51. Available from: https://www.ncbi.nlm.nih.gov/pubmed/7961531.
61. Kaye W. Neurobiology of anorexia and bulimia nervosa. Physiology & Behavior. 2008 Apr;94(1):121–35.
62. Freund N, Thompson BS, Norman KJ, Einhorn P, Andersen SL. Developmental emergence of an obsessive-compulsive phenotype and binge behavior in rats. 2015 May 29 [cited 2017 Feb 6];232(17). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4536183/pdf/nihms695318.pdf.
63. Davison KM. The relationships among psychiatric medications, eating behaviors, and weight. Eating Behaviors. 2013 Apr;14(2):187–91.
64. Miller DB, O’Callaghan JP. Neuroendocrine aspects of the response to stress. Metabolism. 2002 Jun;51(6):5–10.
65. Stunkard AJ, Messick S. The three-factor eating questionnaire to measure dietary restraint, disinhibition and hunger. Journal of Psychosomatic Research. 1985 Jan;29(1):71–83.
66. Wadden TA, Foster GD. BEHAVIORAL TREATMENT OF OBESITY. Medical Clinics of North America. 2000 Mar;84(2):441–61.
67. UMBRICHT D, FLURY H, BRIDLER R. Cognitive behavior therapy for weight gain. American Journal of Psychiatry. 2001 Jun;158(6):971.
68. Morrison JA, Cottingham EM, Barton BA. Metformin for weight loss in pediatric patients taking Psychotropic drugs. American Journal of Psychiatry. 2002 Apr;159(4):655–7.
69. Baptista T, Hernandez L, Prieto LA, Boyero EC, de Mendoza S. Metformin in obesity associated with Antipsychotic drug administration. The Journal of Clinical Psychiatry. 2001 Aug 15;62(8):653–5.