



King's Research Portal

DOI:

[10.1016/j.psychres.2018.08.083](https://doi.org/10.1016/j.psychres.2018.08.083)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Kouidrat, Y., Amad, A., Stubbs, B., Louhou, R., Renard, N., Diouf, M., Lalau, J.-D., & Loas, G. (2018). Disordered eating behaviors as a potential obesogenic factor in schizophrenia. *Psychiatry Research*. Advance online publication. <https://doi.org/10.1016/j.psychres.2018.08.083>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Accepted Manuscript

Disordered eating behaviors as a potential obesogenic factor in schizophrenia

Youssef Kouidrat , Ali Amad , Brendon Stubbs , Rufin Louhou ,
Nathalie Renard , Momar Diouf , Jean-Daniel Lalau ,
Gwenole Loas

PII: S0165-1781(17)31441-5
DOI: <https://doi.org/10.1016/j.psychres.2018.08.083>
Reference: PSY 11677



To appear in: *Psychiatry Research*

Received date: 2 August 2017
Revised date: 17 August 2018
Accepted date: 24 August 2018

Please cite this article as: Youssef Kouidrat , Ali Amad , Brendon Stubbs , Rufin Louhou , Nathalie Renard , Momar Diouf , Jean-Daniel Lalau , Gwenole Loas , Disordered eating behaviors as a potential obesogenic factor in schizophrenia, *Psychiatry Research* (2018), doi: <https://doi.org/10.1016/j.psychres.2018.08.083>

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Highlights

- Schizophrenia is associated to high levels of obesity and metabolic disorders.
- High rates of disordered eating behaviors may affect schizophrenia patients.
- The contribution of disordered eating behaviors to an adverse cardiometabolic health appears important in this population.
- More research is needed to help clarify the relationships between eating behaviors and weight-related outcomes in schizophrenia.

ACCEPTED MANUSCRIPT

Disordered eating behaviors as a potential obesogenic factor in schizophrenia

Authors: Youssef Kouidrat^{a,b,c} ; Ali Amad^d ; Brendon Stubbs^{b,e,f} ; Rufin Louhou^a ; Nathalie Renard^c ; Momar Diouf^c ; Jean-Daniel Lalau^c and Gwenole Loas^g .

Affiliations:

^a Department of Nutrition, Maritime Hospital of Berck, AP-HP, 62600 Berck, France.

^b Department of Psychological Medicine, Institute of Psychiatry, King's College London, London, UK.

^c Department of Endocrinology, University of Picardie-Jules Verne, Amiens, France.

^d Psychiatry Department, Univ Lille Nord de France, CHRU de Lille, F-59000 Lille, France.

^e Physiotherapy Department, South London and Maudsley NHS Foundation Trust, Denmark Hill, London SE5 8AZ, United Kingdom

^f Health Service and Population Research Department, Institute of Psychiatry, King's College London, London, United Kingdom

^g Department of Psychiatry, Erasme Hospital, ULB, 1070 Brussels, Belgium.

Address for correspondence: Dr Youssef Kouidrat, Department of Nutrition, Maritime Hospital, AP-HP, 62600 Berck, France. Email: youssef.kouidrat@gmail.com

Tel: 00 33 3 21 89 27 27 Fax: 00 33 3 21 89 27 77

ABSTRACT

Whilst people with schizophrenia have high levels of obesity and metabolic disease, our understanding of their eating behaviors is still limited. Our aim was to evaluate the relationships between eating behavior and clinical data in schizophrenia. A cross-sectional study including 66 schizophrenia outpatients compared to 81 healthy controls was undertaken. Eating behavior was assessed using the shortened 21-item version of the Three-Factor Eating Questionnaire (TFEQ-R21). The patients had a mean of 44±11 years; a mean BMI of 30.3±8 kg/m² (vs 24±3.3 kg/m² for controls) and a mean duration of illness of 7.2±6 years. All mean TFEQ scores were significantly higher in patients (indicating poorer eating behaviors) compared to controls after adjustment for age and sex, BMI and smoking status. Among

patients, mean TFEQ scores were not significantly different between men and women samples. The “cognitive restraint” factor was significantly higher in schizophrenia patients with a BMI < 25 than in the group of overweight patients with a BMI > 25. Our findings suggest that disordered eating behaviors affect schizophrenia patients regardless of gender or duration of disease compared to controls. More research is needed to help clarify the relationships between eating behaviors and weight-related outcomes in schizophrenia.

Key words: Schizophrenia; eating behaviors; eating disorders; obesity; antipsychotics; cardiometabolic disorders.

1. INTRODUCTION

People with schizophrenia exhibit a 2-3 increased level of obesity, metabolic syndrome, diabetes, and cardiovascular disease compared to the general population (Vancampfort et al., 2016). Causes for these increased rates are multifactorial and include several unhealthy lifestyle factors (poor diet, low levels of physical activity, substances abuse, high rates of smoking), antipsychotic medications side effects and genetic predisposition (De Hert et al., 2012; Gardner-Sood et al., 2015; Kouidrat et al., 2013; Malan-Müller et al., 2016; Stubbs et al., 2016).

Eating behaviour and eating disorders (EDs) may correspond to an additional factor that could be crucial in the development of cardiometabolic disorders in patients with schizophrenia (Ward et al., 2015). In the general population, EDs have been associated with profound physical and psychosocial morbidity, obesity, diabetes and an elevated mortality risk (Klump et al., 2009; Treasure et al., 2010); (Hudson et al., 2010). Despite growing interest in weight gain and metabolic disorders in schizophrenia patients, evaluation of their eating behaviour remain underexplored (Kouidrat et al., 2014). However, a previous systematic review identified that people with schizophrenia typically have poor dietary habits (Dipasquale et al., 2013), although very few studies have used a validated outcome measures

to consider nutrition intake or specifically focused on EDs (Kouidrat et al., 2014). Thus, there is a need for studies using validated measures to investigate eating behaviour and EDs in people with schizophrenia, such as the Three-Factor Eating Questionnaire (TFEQ), a widely used scale to measure human eating behaviour (Cappelleri et al., 2009). Current evidence observed in patients and in animal models indicate that antipsychotics lead to a degree of modification in food habits and due to the hyperphagic effects, linked to lack of satiation and increased appetite (Blouin et al., 2008; Fernø et al., 2011). Additionally, certain antipsychotics such as clozapine and olanzapine have been indicated to increase risk of ED symptomology (Brömel et al., 1998; Gebhardt et al., 2007). A previous study among people with schizophrenia found that patients treated with atypical antipsychotics exhibit increased uncontrolled eating, compared to individuals treated with conventional antipsychotics (Sentissi et al., 2009). Another descriptive study indicated that over half of the 40 patients with schizophrenia and a BMI greater than or equal to 28 exhibit binge eating symptomology (Khazaal et al., 2006).

Given that EDs may represent a key factor in the development of cardiometabolic disorders in schizophrenia, it is important to identify the possible EDs symptomology of this population so that effective interventions can be developed. Thus, this study aimed to assess eating behaviors, clinical and biological data of a sample of schizophrenia patients compared to values of healthy controls.

2. METHODS

2.1 Study design and participants

The present cross-sectional study meets the standards of the Declaration of Helsinki and the local ethic committee approved the study protocol. All study participants provided informed consent. Sixty-six consecutive outpatients with schizophrenia or schizoaffective disorder established using the Structured Clinical Interview for DSM-IV, were recruited via clinical referral within a large community from the psychiatric department of Amiens University Hospital (Amiens, France). Patients were compared to 81 healthy controls who were recruited from advertisements at the local university and in the local community. All participants were aged between 18 and 70 years.

Exclusion criteria for both patients and controls were a diagnosis of diabetes mellitus, alcohol or substance abuse, mental retardation, or a history of neurological disorders by reviewing medical files. Individuals were also excluded if they presented poor proficiency in French and if they were unable or unwilling to provide their written informed consent. Both, schizophrenia patients and controls were examined by an experienced endocrinologist (YK). Healthy volunteers were excluded if they presented any psychiatric history or a significant medical illness.

2.2 Eating behavior assessment

Eating behavior was assessed by using the shortened 21-item version of the Three-Factor Eating Questionnaire (TFEQ-R21) (Cappelleri et al., 2009; Karlsson et al., 2000). The TFEQ is a self-assessment scale used widely in studies of eating behavior in overweight and normal weight individuals (Bohrer et al., 2015). For patients who could not read well, the TFEQ-R21 questionnaires were read to them. In case of difficulty, they were allowed to ask the researcher for clarification. The interview was conducted by a TFEQ-trained psychologist, psychiatrist, or dietician.

The questionnaire consists of 21 items and covered the following 3 aspects of eating motivation: cognitive restraint (6 items investigating the conscious mechanisms for restraining food intake to control body weight), emotional eating (6 items investigating overeating behaviour in relationship to negative mood states), and uncontrolled eating (9 items exploring the tendency to lose control over eating when feeling hungry or when exposed to external stimuli). Each factor score ranges from 0 to 100. Higher scores indicate higher levels of the factor. In another words, it is a measure of eating behaviours and cognitions that are consistently associated with disordered eating in general population and may represent a risk factor for development of overweight (Fairburn and Harrison, 2003).

2.3 Demographic, clinical and biological variables

General health data and anthropometric measures were collected. For schizophrenia patients, a complete medical history with detailed information on duration of schizophrenia, current smoking status, associated cardiovascular risk factors, pharmacological treatment and other relevant medical conditions was collected. Anthropometric measurements (weight, height and abdominal circumference) were recorded, and BMI was calculated. Blood pressure was measured using a wrist blood pressure monitor after at least 10 min of rest in a sitting position. Blood fasting glucose, haemoglobin A1C, creatinine, cholesterol, and triglycerides levels were obtained by standard laboratory procedures on blood samples obtained by venipuncture after a 12-h overnight fast.

2.4 Statistical analysis

Frequencies and descriptive statistics were generated using SAS® software (version 9.2, SAS Institute Inc., Cary, NC). Data are presented as means \pm standard deviation or number and percent. Differences in clinical characteristics were compared between patients and controls using the Student/Welch or Wilcoxon's *t*-test for quantitative data and χ^2 or Fisher test for qualitative data. Associations between the different clinical variables and

medication were computed by using Spearman correlation analyses. Eating behaviors scores were compared between patients and controls with the Student/Welch's *t*-test and by multiple linear regression analysis for adjustment of sex, age, BMI, and smoking status. Differences in eating behavior scores were calculated with a confidence interval. Due to small sample size and/or departure from normality, eating behavior scores between patients and controls were compared within gender strata using Wilcoxon rank sum test. For adjusted analyses, we used MANOVA with gender, age, BMI (>25 vs. ≤ 25), smoking status and group (schizophrenia vs. control) as independent variables, the three eating variables as dependent variables we evaluated the interaction between group and gender and the interaction between BMI and group.

3. RESULTS

3.1 Participants

The characteristics of the participants are presented in **Table 1**. A total of 66 patients and 81 healthy controls were included. Forty-three of the patients were male (65%). In the overall sample, mean age was 44±11 years; with a mean BMI of 30.3±8.2 kg/m² and a mean duration of disease of 7.2±6 years. The smoking rate reached 70% in the patient sample. Patients were older and had a higher BMI compared to controls (24±3.3 kg/m²). Almost all patients were taking antipsychotics with 38%, 30%, and 25% of the patients taking respectively first generation, second-generation antipsychotics or both. About 40% used antidepressants and nearly 84% were under anxiolytics treatment.

3.2 Eating behavior assessment

Mean TFEQ scores in the two groups are presented in **Table 2**. The correlations between age, disease duration, medication use and TFEQ score in the patient sample were not statistically significant. On the three domain scores reported according to gender (male, female), all mean scores (restraint, uncontrolled and emotional eating) were higher in

schizophrenia patients compared to controls indicating an increased risk of developing an eating disorder.

In agreement with these findings, all the following comparisons were adjusted for age and sex, BMI and smoking status. In the control group, women had significantly higher scores for “cognitive restraint” and “emotional eating”. In contrast, in the patients group, mean scores were not significantly different between men and women samples. The exception was for “emotional eating”, in which men patients had a higher mean score. In addition, the “cognitive restraint” score was higher in schizophrenia patients with a BMI ≤ 25 than in the group of overweight patients with a BMI >25 (respectively, 64.3 ± 15 and 54.3 ± 18 ; Satterthwaite DF=46.3; $t=2.35$; $P =0.02$). This difference significantly persisted after adjustment, within patients and controls (**Table 3**). No association has been found between BMI and TFEQ scores among controls.

4. DISCUSSION

In the current study, we found that schizophrenia patients had higher TFEQ scores on the three factors compared to controls, which remained evident after controlling for sex, age, BMI and smoking status. Interestingly, various types of EDs including binge eating disorder (BED) and night eating syndrome (NES), have been described in schizophrenia (Kouidrat et al., 2014; Palmese et al., 2011). In a recent review, the prevalence of eating disorders has been found higher in schizophrenia patients than in the general population (Kouidrat et al., 2014). Our research together with the wider literature suggests that eating disorders are equally evident in men as well as women with schizophrenia, which is in contrast of the general population where females are typically more effected (Kouidrat et al., 2014). However, since TFEQ is not specific to any eating disorder, our findings should be taken with caution.

The present results are in line with those of Sentissi et al. 2009, who assessed the

eating behaviour among 153 schizophrenia patients. This study also did not find any difference according to sex but the uncontrolled eating and emotional eating scores increased significantly according to the BMI (Sentissi et al., 2009). Among their sample, the uncontrolled eating score among individuals treated with second-generation antipsychotics ($n = 93$) was significantly higher than patients treated with conventional antipsychotics ($n = 27$) (Sentissi et al., 2009). In contrast, in our study, no correlation was found between medication use or duration of disease and the TFEQ score. Using the Eating Attitudes Test, Fawzi et al. found a higher prevalence of disordered eating in 50 antipsychotic naive schizophrenia patients than in the control group (30% vs 12%, $P = 0.027$), suggesting that disordered eating may represent a feature of schizophrenia regardless of medication use such as antipsychotics (Fawzi and Fawzi, 2012). Indeed, the effects of antipsychotic medication switching as a strategy for reducing metabolic problems in people with schizophrenia, did not provide clear evidence for better outcomes (Mukundan et al., 2010).

In our sample, a high mean BMI and high TFEQ scores may indicate a more susceptibility to BED, which is in agreement with our previous work, demonstrating that BED can frequently affect schizophrenia patients with a prevalence of approximately 10% (Kouidrat et al., 2014). Several studies have demonstrated that patients with BED tend to have higher scores on cognitive restraint, uncontrolled eating, and emotional eating compared with individuals without BED (Bas et al., 2008; Crow et al., 2002; de Zwaan et al., 2003). However, we do not use specific scale to assess BED in this study. Thus, we must be cautious in interpreting this result. Additionally, we did not observe any differences in TFEQ scores according to medication or disease duration, which is in agreement with the results of recent studies (Davison, 2013; Sentissi et al., 2009).

Finally, schizophrenia patients with a normal weight ($BMI < 25$) exhibited higher cognitive restraint score than the group of overweight patients ($BMI > 25$). This significant

relation indicates that a high cognitive restraint score may allow successful weight maintenance or, may represent in certain cases a factor for anorexia syndrome (Kouidrat et al., 2014). Interestingly, increased cognitive restraint score was associated with more weight lost (Urbanek et al., 2015) and better weight loss maintenance (Westenhoefer et al., 2013), suggesting that strategies that target cognitive restraint may be important in preventing and treating obesity.

Study results should be interpreted in the context of certain limitations. Indeed, this is a cross-sectional study, with a sample constituted of established schizophrenia patients. However, our findings support the utilization of the TFEQ-R21 in this population of patients, and the effective of patients and controls allowed us to perform a robust analysis of the relationship between eating behaviour and the clinical characteristics in patients with schizophrenia. The pathophysiology of EDs remains unclear in schizophrenia (Foulon, 2003). Several factors may explain the high prevalence of disordered eating behaviours in schizophrenia patients including mood disorders, stress, sleep disturbance, socioeconomic difficulties and side effects of psychotropic medications (Lundgren et al., 2010). Indeed, several psychiatric medications including antipsychotics, antidepressants or mood stabilizers may influence eating behaviour and weight gain (Davison, 2013; Gebhardt et al., 2007).

We did not include patients with diabetes in our study. However, disordered eating behaviours may affect around 40% of people with type 2 diabetes (García-Mayor and García-Soidán, 2016). The co-occurrence of both medical entities may lead to an impairment of glycemic control and an increased risk of vascular complications. Given that schizophrenia patients exhibit a 2-3 increased rate of diabetes compared to the general population (Vancampfort et al., 2016), patients with diabetes may represent a subgroup in need.

Nevertheless, our study mainly highlights the fact that disordered eating behaviors are

frequent among schizophrenia patients. Thus, our findings corroborate that the assessment of eating behaviour in schizophrenia is important, since eating disorders are closely related to weight gain and cardiometabolic disorders (Kouidrat et al., 2014). Management of EDs may emphasize programs including exercise, diet, psycho-behavioral and pharmacological approaches (Kouidrat et al., 2015; Stubbs et al., 2016). Lifestyle intervention with healthy diet (such as Mediterranean diet) has been associated with better quality of life, psychiatric symptoms and cardiometabolic outcomes in a large cohort of 4470 participants living in North America (Veronese et al., 2016). Furthermore a randomized controlled study found that cognitive and behavioral treatment was effective on binge eating symptomatology and weight loss in patients suffering from weight gain associated with antipsychotic treatment (Khazaal et al., 2007). Given that, we should sensitize patients, their families and caregivers, to improve screening and management of disordered eating behaviors in schizophrenia (Kouidrat et al., 2016).

In conclusion, our results show that the TFEQ-R21 is a useful tool for assessing eating behavior in patients at high risk of eating disorders. More prospective research is needed to help clarify the relationships between eating behaviors and weight-related outcomes that may exist among schizophrenia patients.

REFERENCES

- Bas, M., Bozan, N., Cigerim, N., 2008. Dieting, dietary restraint, and binge eating disorder among overweight adolescents in Turkey. *Adolescence* 43, 635–648.
- Blouin, M., Tremblay, A., Jalbert, M.-E., Venables, H., Bouchard, R.-H., Roy, M.-A., et al., 2008. Adiposity and eating behaviors in patients under second generation antipsychotics. *Obesity (Silver Spring)* 16, 1780–1787. <https://doi.org/10.1038/oby.2008.277>
- Bohrer, B.K., Forbush, K.T., Hunt, T.K., 2015. Are common measures of dietary restraint and disinhibited eating reliable and valid in obese persons? *Appetite* 87, 344–351. <https://doi.org/10.1016/j.appet.2014.12.226>
- Brömel, T., Blum, W.F., Ziegler, A., Schulz, E., Bender, M., Fleischhaker, C., et al., 1998. Serum leptin levels increase rapidly after initiation of clozapine therapy. *Mol. Psychiatry* 3, 76–80.
- Cappelleri, J.C., Bushmakin, A.G., Gerber, R.A., Leidy, N.K., Sexton, C.C., Lowe, M.R., et al., 2009. Psychometric analysis of the Three-Factor Eating Questionnaire-R21: results from a large diverse sample of obese and non-obese participants. *Int J Obes (Lond)* 33, 611–620. <https://doi.org/10.1038/ijo.2009.74>
- Crow, S.J., Stewart Agras, W., Halmi, K., Mitchell, J.E., Kraemer, H.C., 2002. Full syndromal versus subthreshold anorexia nervosa, bulimia nervosa, and binge eating disorder: a multicenter study. *Int J Eat Disord* 32, 309–318. <https://doi.org/10.1002/eat.10088>
- Davison, K.M., 2013. The relationships among psychiatric medications, eating behaviors, and weight. *Eat Behav* 14, 187–191. <https://doi.org/10.1016/j.eatbeh.2013.01.001>
- De Hert, M., Detraux, J., van Winkel, R., Yu, W., Correll, C.U., 2012. Metabolic and cardiovascular adverse effects associated with antipsychotic drugs. *Nat Rev Endocrinol* 8, 114–126. <https://doi.org/10.1038/nrendo.2011.156>
- de Zwaan, M., Mitchell, J.E., Howell, L.M., Monson, N., Swan-Kremeier, L., Crosby, R.D., et al., 2003. Characteristics of morbidly obese patients before gastric bypass surgery. *Compr Psychiatry* 44, 428–434. [https://doi.org/10.1016/S0010-440X\(03\)00092-0](https://doi.org/10.1016/S0010-440X(03)00092-0)
- Dipasquale, S., Pariante, C.M., Dazzan, P., Aguglia, E., McGuire, P., Mondelli, V., 2013. The dietary pattern of patients with schizophrenia: a systematic review. *J Psychiatr Res* 47, 197–207. <https://doi.org/10.1016/j.jpsychires.2012.10.005>
- Fairburn, C.G., Harrison, P.J., 2003. Eating disorders. *Lancet* 361, 407–416. [https://doi.org/10.1016/S0140-6736\(03\)12378-1](https://doi.org/10.1016/S0140-6736(03)12378-1)
- Fawzi, M.H., Fawzi, M.M., 2012. Disordered eating attitudes in Egyptian antipsychotic naive patients with schizophrenia. *Compr Psychiatry* 53, 259–268. <https://doi.org/10.1016/j.comppsy.2011.04.064>
- Fernø, J., Varela, L., Skrede, S., Vázquez, M.J., Nogueiras, R., Diéguez, C., et al., 2011. Olanzapine-induced hyperphagia and weight gain associate with orexigenic hypothalamic neuropeptide signaling without concomitant AMPK phosphorylation. *PLoS ONE* 6, e20571. <https://doi.org/10.1371/journal.pone.0020571>
- Foulon, C., 2003. [Schizophrenia and eating disorders]. *Encephale* 29, 463–466.
- García-Mayor, R.V., García-Soidán, F.J., 2016. Eating disorders in type 2 diabetic people: Brief review. *Diabetes Metab Syndr*. <https://doi.org/10.1016/j.dsx.2016.08.004>
- Gardner-Sood, P., Lally, J., Smith, S., Atakan, Z., Ismail, K., Greenwood, K.E., et al., IMPaCT team, 2015. Cardiovascular risk factors and metabolic syndrome in people with established psychotic illnesses: baseline data from the IMPaCT randomized controlled trial. *Psychol Med* 45, 2619–2629. <https://doi.org/10.1017/S0033291715000562>

- Gebhardt, S., Haberhausen, M., Krieg, J.-C., Remschmidt, H., Heinzl-Gutenbrunner, M., Hebebrand, J., et al., 2007. Clozapine/olanzapine-induced recurrence or deterioration of binge eating-related eating disorders. *J Neural Transm (Vienna)* 114, 1091–1095. <https://doi.org/10.1007/s00702-007-0663-2>
- Hudson, J.I., Lalonde, J.K., Coit, C.E., Tsuang, M.T., McElroy, S.L., Crow, S.J., et al., 2010. Longitudinal study of the diagnosis of components of the metabolic syndrome in individuals with binge-eating disorder. *Am J Clin Nutr* 91, 1568–1573. <https://doi.org/10.3945/ajcn.2010.29203>
- Karlsson, J., Persson, L.O., Sjöström, L., Sullivan, M., 2000. Psychometric properties and factor structure of the Three-Factor Eating Questionnaire (TFEQ) in obese men and women. Results from the Swedish Obese Subjects (SOS) study. *Int. J. Obes. Relat. Metab. Disord.* 24, 1715–1725.
- Khazaal, Y., Frésard, E., Borgeat, F., Zullino, D., 2006. Binge eating symptomatology in overweight and obese patients with schizophrenia: a case control study. *Ann Gen Psychiatry* 5, 15. <https://doi.org/10.1186/1744-859X-5-15>
- Khazaal, Y., Fresard, E., Rabia, S., Chatton, A., Rothen, S., Pomini, V., et al., 2007. Cognitive behavioural therapy for weight gain associated with antipsychotic drugs. *Schizophr. Res.* 91, 169–177. <https://doi.org/10.1016/j.schres.2006.12.025>
- Klump, K.L., Bulik, C.M., Kaye, W.H., Treasure, J., Tyson, E., 2009. Academy for eating disorders position paper: eating disorders are serious mental illnesses. *Int J Eat Disord* 42, 97–103. <https://doi.org/10.1002/eat.20589>
- Koudrat, Y., Amad, A., De Hert, M., 2015. Emerging Drugs and Indications for Cardio-Metabolic Disorders in People with Severe Mental Illness. *Curr. Pharm. Des.* 21, 3317–3324.
- Koudrat, Y., Amad, A., Desailoud, R., Diouf, M., Fertout, E., Scoury, D., et al., 2013. Increased advanced glycation end-products (AGEs) assessed by skin autofluorescence in schizophrenia. *J Psychiatr Res* 47, 1044–1048. <https://doi.org/10.1016/j.jpsychires.2013.03.016>
- Koudrat, Y., Amad, A., Lalau, J.-D., Loas, G., 2014. Eating disorders in schizophrenia: implications for research and management. *Schizophr Res Treatment* 2014, 791573. <https://doi.org/10.1155/2014/791573>
- Koudrat, Y., Amad, A., Renard, N., Corneille, F., Lalau, J.-D., Loas, G., 2016. [Management of eating disorders in schizophrenia]. *Soins Psychiatr* 39–43. <https://doi.org/10.1016/j.spsy.2015.04.011>
- Lundgren, J.D., Rempfer, M.V., Brown, C.E., Goetz, J., Hamera, E., 2010. The prevalence of night eating syndrome and binge eating disorder among overweight and obese individuals with serious mental illness. *Psychiatry Res* 175, 233–236. <https://doi.org/10.1016/j.psychres.2008.10.027>
- Malan-Müller, S., Kilian, S., van den Heuvel, L.L., Bardien, S., Asmal, L., Warnich, L., et al., 2016. A systematic review of genetic variants associated with metabolic syndrome in patients with schizophrenia. *Schizophr. Res.* 170, 1–17. <https://doi.org/10.1016/j.schres.2015.11.011>
- Mukundan, A., Faulkner, G., Cohn, T., Remington, G., 2010. Antipsychotic switching for people with schizophrenia who have neuroleptic-induced weight or metabolic problems. *Cochrane Database Syst Rev* CD006629. <https://doi.org/10.1002/14651858.CD006629.pub2>
- Palmese, L.B., DeGeorge, P.C., Ratliff, J.C., Srihari, V.H., Wexler, B.E., Krystal, A.D., et al., 2011. Insomnia is frequent in schizophrenia and associated with night eating and obesity. *Schizophr. Res.* 133, 238–243. <https://doi.org/10.1016/j.schres.2011.07.030>
- Sentissi, O., Viala, A., Bourdel, M.C., Kaminski, F., Bellisle, F., Olié, J.P., et al., 2009.

- Impact of antipsychotic treatments on the motivation to eat: preliminary results in 153 schizophrenic patients. *Int Clin Psychopharmacol* 24, 257–264. <https://doi.org/10.1097/YIC.0b013e32832b6bf6>
- Stubbs, B., Firth, J., Berry, A., Schuch, F.B., Rosenbaum, S., Gaughran, F., et al., 2016. How much physical activity do people with schizophrenia engage in? A systematic review, comparative meta-analysis and meta-regression. *Schizophr. Res.* 176, 431–440. <https://doi.org/10.1016/j.schres.2016.05.017>
- Treasure, J., Claudino, A.M., Zucker, N., 2010. Eating disorders. *Lancet* 375, 583–593. [https://doi.org/10.1016/S0140-6736\(09\)61748-7](https://doi.org/10.1016/S0140-6736(09)61748-7)
- Urbanek, J.K., Metzgar, C.J., Hsiao, P.Y., Piehowski, K.E., Nickols-Richardson, S.M., 2015. Increase in cognitive eating restraint predicts weight loss and change in other anthropometric measurements in overweight/obese premenopausal women. *Appetite* 87, 244–250. <https://doi.org/10.1016/j.appet.2014.12.230>
- Vancampfort, D., Correll, C.U., Galling, B., Probst, M., De Hert, M., Ward, P.B., et al., 2016. Diabetes mellitus in people with schizophrenia, bipolar disorder and major depressive disorder: a systematic review and large scale meta-analysis. *World Psychiatry* 15, 166–174. <https://doi.org/10.1002/wps.20309>
- Veronese, N., Stubbs, B., Noale, M., Solmi, M., Luchini, C., Maggi, S., 2016. Adherence to the Mediterranean diet is associated with better quality of life: data from the Osteoarthritis Initiative. *Am. J. Clin. Nutr.* <https://doi.org/10.3945/ajcn.116.136390>
- Ward, M.C., White, D.T., Druss, B.G., 2015. A meta-review of lifestyle interventions for cardiovascular risk factors in the general medical population: lessons for individuals with serious mental illness. *J Clin Psychiatry* 76, e477-486. <https://doi.org/10.4088/JCP.13r08657>
- Westenhoefer, J., Engel, D., Holst, C., Lorenz, J., Peacock, M., Stubbs, et al., 2013. Cognitive and weight-related correlates of flexible and rigid restrained eating behaviour. *Eat Behav* 14, 69–72. <https://doi.org/10.1016/j.eatbeh.2012.10.015>

Table 1: Characteristics of schizophrenia patients and controls

| Variables | Patients | Controls | <i>t</i> or χ^2 – Statistic test | <i>P</i> -value |
|---------------------------|-----------|-----------|---------------------------------------|-----------------|
| N | 66 | 81 | | |
| Age (years) | 44±11 | 32±14 | <i>t</i> = -5.71 | <0.0001 |
| Sex (M/F) | 43/23 | 24/57 | χ^2 = 18.5 | <0.0001 |
| BMI, kg/ m ² | 30.3±8.2 | 24±3.3 | <i>t</i> = -6.34 | <0.0001 |
| Current smoker n, (%) | 44 (67%) | 23 (28%) | χ^2 = 21.5 | <0.0001 |
| Disease duration, years | 7.20 ±6 | - | | - |
| Biology | | | | |
| Serum creatinine (mg/l) | 7.7±1.4 | - | | - |
| Fasting glucose (g/l) | 0.90±0.3 | - | | - |
| HbA1C (%) | 5.4±0.4 | - | | - |
| Total cholesterol (g/l) | 1.87±0.41 | - | | - |
| Triglycerides (g/l) | 1.71±1.23 | - | | - |
| Medication use (%) | | | | |
| Antipsychotics | 93 | - | | - |
| FGA/SGA/both | 38/30/25 | | | |
| Antidepressants | 40 | - | | - |
| Anxiolytics | 84 | - | | - |
| Hypnotics | 60 | - | | - |
| TFEQ score | | | | |
| Cognitive restraint (CR) | 57.5±17.7 | 34.6±21.2 | <i>t</i> = -7.01 | <0.0001 |
| Uncontrolled eating (UE) | 57.5±16.9 | 35±21.1 | <i>t</i> = -7.01 | <0.0001 |
| Emotional eating (EE) | 69.1±29.5 | 41.4±27.2 | <i>t</i> = -5.91 | <0.0001 |

Values are mean ± SD

FGA: first generation antipsychotic, SGA: second-generation antipsychotic

Table 2: Eating behavior assessed by the TFEQ in patients and controls

| TFEQ Score | Patients | | <i>P</i> -value* | Controls | | <i>P</i> -value* |
|---|------------------------|--------------------------|-------------------------------------|------------------------|--------------------------|--|
| | Men (<i>n</i> =43) | Women (<i>n</i> =23) | | Men (<i>n</i> =24) | Women (<i>n</i> =57) | |
| CR | 60.2±15.8 | 52.4±20 | <i>W</i> =384 <i>p</i> =0.1359 | 27.1±19.9 | 37.8±21 | <i>W</i> =877.5 <i>p</i> =0.0453 |
| UE | 58.7±16.7 | 55.1±17.3 | <i>W</i> =441.5 <i>p</i> =0.4784 | 29.5±20.5 | 37.3±21.1 | <i>W</i> =840.5 <i>p</i> =0.1061 |
| EE | 76.2±26.8 | 55.8±30.3 | <i>W</i> =291.5 <i>p</i> =0.0058 | 27.3±26.3 | 47.4±25.5 | <i>W</i> =877.5 <i>p</i> =0.0020 |
| Difference in scores between Patients and Controls after adjustment | | | | | | <i>t</i> -statistic; <i>P</i> -value** |
| CR | 27.6 [18.7-36.6] | | | | | <i>t</i> =6.18; <i>p</i> <0.0001 |
| UE | 27.3 [18.6-35.9] | | | | | <i>t</i> =6.29; <i>p</i> <0.0001 |
| EE | 27.6 [18.7-36.6] | | | | | <i>t</i> =6.18; <i>p</i> <0.0001 |

Values are mean ± SD, NS: not significant

CR: Cognitive restraint, UE: Uncontrolled eating, EE: Emotional eating

*Wilcoxon *W*-test of Patients versus controls.

**Multiple linear regression analysis for adjustment of sex, age, BMI and smoking status.

Table 3: Difference in scores between BMI \leq 25 vs. BMI $>$ 25 after adjustment, within patients and controls

| TFEQ Score | Patients | Controls | MANOVA <i>P</i> -value for interaction between BMI and group |
|------------|------------------|-------------------|--|
| CR | 8.8 [-4.5;22.2] | -11.9 [-24.6;0.7] | Wilk's Lamda=0.936 <i>F</i> (3, 137)=3.12; <i>P</i> =0.0280 |
| UE | 5.8 [-7.6;19.2] | 2.2 [-10.5;14.9] | |
| EE | 5.2 [-14.0;24.3] | 1.6 [-16.6;19.7] | |

ACCEPTED MANUSCRIPT