



Review:

Psychosocial and Biological Factors Contributing to Body Weight Gain in Schizophrenia

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Abstract: Overweight and obesity are frequently reported to be a significant issue in schizophrenia resulting in the inherent complications of these disorders. Body weight gain also commonly results from treatment with the most tolerable and efficacious pharmacological treatments, second-generation antipsychotics. However there are numerous other factors that contribute to increased body mass in individuals with schizophrenia prior to the initiation of treatment. With prior research indicating that individuals with schizophrenia have higher rates of overweight and obesity before treatment. Therefore this article provides a review of pertinent issues associated with body weight gain in schizophrenia in an attempt to delineate the impact of both the disease and treatment upon body weight gain. The results of the review indicate that body weight gain in schizophrenia occurs from both psychosocial and biological factors that are further compounded by antipsychotic treatment. The article concludes with recommendations for future research.

Key Words: Body weight gain; Psychosocial factors; Biological factors; Schizophrenia; Overweight; Obesity

Introduction:

The relationship between schizophrenia and increased body weight was identified prior to the advent of the first antipsychotics to treat the disease.[1] This association was first described in the early 1900's in the writings of Emil Kraepelin on the disorder then termed 'dementia praecox'; the first nomenclature of schizophrenia symptomology.[1]

Epidemiologically it is also evident that individuals who suffer from schizophrenia have higher rates of overweight and obesity in comparison to the general population.[2,3] A study conducted by Thakore and colleagues [4] found that both drug-naive and drug-free patients with schizophrenia had higher BMI's and waist to hip ratios than age and sex matched controls.

After the introduction of the first conventional antipsychotic chlorpromazine, in the 1950's body weight gain (BWG) as a side effect of treatment was reported.[1] However BWG was not viewed as one of the most detrimental side effects due to conventional antipsychotics having other serious side effects, such as extrapyramidal symptoms, and inducing significantly less BWG than second generation antipsychotics (SGA).

Although SGA have superior tolerability and efficacy in comparison to conventional neuroleptic treatment [5] they commonly induce clinically significant BWG.[6] That is an increase

in body weight that is $\geq 7\%$ of the individual's body weight at the initiation of treatment.[6]

Even though the challenge of increased body mass of individuals with schizophrenia proportionate to the general population has been identified for more than a century; there is relatively scarce literature on the issue relative to the scope and consequences of the problem. In regards to SGA-induced BWG there has been a plethora of research. The issue of BWG in schizophrenia is complex and multi-faceted resulting not only from treatment but also from the disease itself in addition to the social and cultural environment. Therefore this article attempts to further clarify the means by which BWG occurs in schizophrenia.

The Genesis of Body Weight Gain & the Consequences

An increase in body mass or BWG generally results from a caloric intake that is higher than the expended energy rate. Energy is expended through the basal metabolic rate, thermogenesis and physical activity.[3] BWG as a result of SGA treatment is thought to result from the same genesis as BWG generally. Within the general population it has been found that even fidgeting combined with exercises of daily living excluding physical activity is enough to provide sedentary individuals with a protective barrier against obesity.[7]

An increase in body weight can result in overweight and obesity and the inherent complications of these disorders. Namely, metabolic syndromes such as type II diabetes, cardiovascular disease, hypotension and some forms of cancer.[3] In addition to the physical toll of overweight and obesity these disorders also incur a psychological toll. Reducing self-esteem and body image and leading to greater social deprivation than what the patient is already experiencing due to schizophrenia symptomology.[3]

Innate Nature of Schizophrenia

One of the most obvious causal mechanisms that may predispose individuals with schizophrenia to body weight changes is the innate nature of the illness. Specifically the cognitive impairment that results from psychosis and the motivational impact of negative symptomology such as flattened affect may induce poor lifestyle choices.[3,8] That is unhealthy dietary choices, substance use / abuse and decreased levels of physical activity. These symptoms also promote social isolation leading to fewer opportunities for activity and thus reduced energy expenditure.

Environmental Mechanisms

In recent times there has been a proliferation in the number of individuals in the general population suffering from overweight and obesity.[3] This increase is thought to have resulted from the influence of an obesogenic environment evident in industrialised societies. That is an immense increase in access to high calorie convenience food coupled with reduced opportunities for physical activity due to labour saving devices, sedentary occupations and inactive past times.

Furthermore social deprivation and exclusion are thought to be a causal mechanism that can contribute to the onset of schizophrenia as well as being maintained through the nature of the illness [9]. A component of social deprivation is socio-economic status (SES); which directly affects body weight by mediating the availability of healthy food choices along with knowledge of healthy lifestyle factors. Therefore it is not surprising that this increase in overweight and obesity is also apparent in individuals suffering from schizophrenia.

Dietary Preferences

Although there is not a great deal of research on the diets of individuals with schizophrenia the existing evidence indicates an exaggerated predilection for a diet of palatable foodstuffs.[2] Palatable foods are those that induce cravings for consumption (i.e. lollies); and when consumed evoke pleasure and positive affective states. As oppose to non-palatable foods such as broccoli. Specifically individuals with schizophrenia have preference for a diet high in convenience foods that are high in saturated fat and carbohydrates and low in fibre, such as that provided by fruit and vegetables.[3]

Furthermore there is strong correlational evidence to suggest that a diet high in sugar and saturated fat produces poorer illness outcomes in individuals suffering from schizophrenia.[10] Whereas the consumption of pulses resulted in better illness outcomes; that is less hospitalisations and less social impairment.[10] Thus individuals in developing nations consuming a non-westernised diet and without access to convenience foodstuffs fair better than individuals with schizophrenia in industrialised countries.[2,10]

Inherent Metabolic Disadvantage

Metabolic syndrome is a group of disorders consisting of obesity, glucose intolerance, insulin resistance and dyslipidaemias that are highly related to the occurrence of type II diabetes mellitus and cardiovascular disease.[4] It has also been suggested that individuals that are suffering from schizophrenia have an inherent metabolic disadvantage that predisposes them to the onset of metabolic syndromes.[2] Additionally it is known that individuals with schizophrenia have increased rates of metabolic syndromes above that of the general population.

That is the metabolic disadvantage does not just result from SGA treatment as reports of glucose problems in patients with schizophrenia were recorded prior to the advent of neuroleptic treatments.[4] Elman, Borsook and Lukas [2] have tentatively proposed that obesity in schizophrenia may partly result from glucose metabolism issues that are evident in individuals with schizophrenia. An inverse relationship to what is currently conceptualised.

For example the higher rates of type II diabetes mellitus maybe a function of the disease and not the treatment.[2,4] Empirical research has found that first-degree relatives of individuals with schizophrenia who do not have schizophrenia themselves have higher rates of type II diabetes than the general population [4], thus indicating a possible genetic relationship between schizophrenia and type II diabetes. In fact, current evidence suggests inherent abnormalities of insulin signalling pathway in schizophrenia.[11]

In addition another factor that is implicated in the aetiology of schizophrenia is Insulin-like Growth Factor 1 (IGF-1). IGF-1 is so named due to its similarity to insulin. According to the

neurodevelopmental model of schizophrenia deficits of IGF-1 affect prenatal and postnatal development acting as a pathogenesis for schizophrenia.[12] A deficit IGF-1 has also been implicated in insulin resistance.[13] This is further supported through recent studies that have found lower levels of IGF-1 in drug naive individuals with schizophrenia in comparison to age and sex matched controls.[12,13]

Furthermore it has been demonstrated that obesity has a very strong heritable component with 45-85% of the variation in BMI is estimated to be accounted for by genetics.[14] This is similar to the aetiological contribution of genetics to schizophrenia.[8]

Neurological Reward & Inhibition Mechanisms

Neurological and neuroanatomical abnormalities beyond the effect of SGA therapy have been implicated in driving the desire for sweet and fatty foodstuffs in schizophrenia through reward and inhibition mechanisms. Specifically neuroanatomical abnormalities have been identified in the reward and reinforcement circuits in patients with schizophrenia through neuroimaging, preclinical and clinical studies.[2] In particular, a hyperfunctional state of the mesolimbic dopaminergic system in schizophrenia may cause motivational reward system insensitivity to palatable food.[2]

This reward deficiency is further highlighted by the clinical symptomology of the illness namely; anhedonia, flattened affect and avolition as well as being reflected in the high co-morbidity for substance abuse disorders.[2] The neurological abnormalities coupled with these symptoms induce a reward deficit that requires higher levels of stimulation; sweeter, fattier foodstuffs in large quantities in order to satisfy the desire or craving.

It is thought that the same reward and inhibition mechanisms that drive the desire to seek and consume drugs and alcohol in substance use disorders also mediate the desire to seek and consume palatable foodstuff. As it has been found that palatable foods activate the dopaminergic reward system; in addition it is also evident that chronic consumption of sweet and fatty foods can alter the dopaminergic reward system.[2,15] This alteration results in the individual becoming susceptible to over eating and food addiction; through conditioning processes.

Furthermore both palatable foods and drugs are known to increase the release of endogenous opiates.[2,15] Although there are limited human studies, the chronic consumption of palatable food sources can result in neuroadaptations in the opioid receptors resulting in opioid dependence. Further driving the desire to seek and consume unhealthy foodstuffs.

This desire to seek and consume palatable food is further exacerbated by the ability of the individual to utilise control mechanisms. Studies with both obese and drug-addicted individuals have indicated increased prefrontal cortex activation and decreased performance on a cognitive task in response to food stimuli and drug stimuli, respectively.[2,14] This hypo-functionality of the prefrontal cortex results in inhibitory control thus leading to over eating or the consumption of drugs. In addition recently Volkow and colleagues [15] have found that addiction not only impacts upon the dopaminergic reward circuits but is also involved in conditioning or the forming of habits, motivation as well as executive functioning.

SGA Induced BWG

With regards to antipsychotic-induced BWG in schizophrenia, the neurological mechanisms through which SGA treatment results in weight gain are yet to be fully elucidated.[16] It is thought that SGA-induced BWG results primarily from an increase in appetite.[3,16] However it is also postulated that a decrease in energy expenditure may also contribute to SGA-induced BWG.[3]

That is SGA's are known to induce appetite in individuals with schizophrenia; specifically an appetite for unhealthy foodstuffs.

[3] This cumulatively impacts upon their already existing predilection for palatable foodstuffs and their predisposition to metabolic syndromes. This further induces neurological and neuroanatomical changes in individuals with schizophrenia which may result in food addiction.

In regards to reduced energy expenditure a common side effect of SGA treatment is sedation. This sedation may result in a lack of participation in physical activity further contributing to weight gain.[3]

Discussion:

From the above review it is apparent that there are numerous factors beyond treatment with SGA that induce BWG in some individuals with schizophrenia. There is substantial evidence that individuals' with schizophrenia are already predisposed to making poor food choices through the social and cultural environment and the symptomology of the disease.

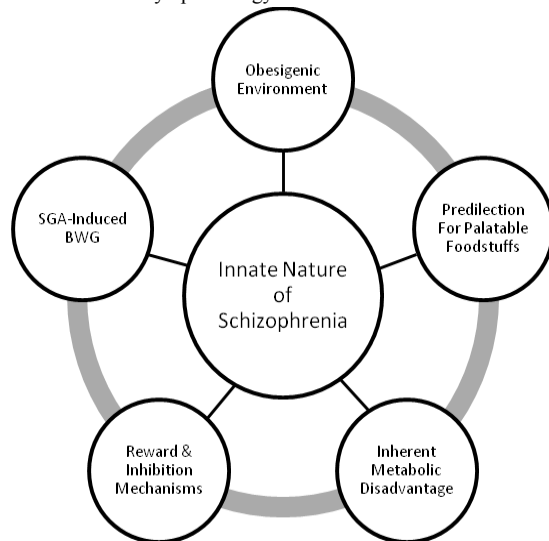


Figure 1: The Cumulative Process of BWG in Schizophrenia

This figure depicts the multiple factors that can result in BWG in schizophrenia, each of these factors either emanates from or interacts with the innate nature of schizophrenia resulting in a cumulative process of BWG

This is further exacerbated by neuroanatomical abnormalities evident in some individuals in schizophrenia that result in a reward deficient and a lack of executive functioning. Thus through this deficit and conditioning processes individuals become vulnerable to food addiction. This further strengthens the predilection for palatable foodstuffs. The effect of a diet of sugary and fatty foodstuffs is further compounded by the inherent metabolic disadvantage in some individuals with schizophrenia. These pre-existing factors are further compounded by SGA treatment resulting in greater amounts of BWG. The components of this cumulative process of weight gain are illustrated in figure 1 above.

Although there is strong empirical and theoretical evidence that each of these factors can contribute to BWG for some individuals with schizophrenia. It remains less clear as to which individuals are predisposed to BWG through each of the above factors. In addition the hypothesized cumulative nature of BWG in schizophrenia needs to be tested.

Furthermore future research should also investigate the diets of individuals with schizophrenia specifically; trying to ascertain individual and illness differences between individuals with poor and 'good' food choices. Such endeavours could both highlight those that are at an increased risk of BWG as well as inform lifestyle interventions.

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