Chapter 165
Schizophrenia and the Metabolic Syndrome

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165.1 Introduction

It has been well known for at least 2 decades that schizophrenia is associated with excess mortality, premature death, and increased standard mortality from both natural and unnatural causes (Allebeck 1989). Patients with schizophrenia are at high risk of death from unnatural causes such as suicides and accidents; however, unnatural causes do not account for even half of the excess mortality. It is increasingly recognized that patients with schizophrenia are at increased risk for natural causes of death, primarily life-shortening illnesses (Marder et al. 2004). Epidemiological data have for decades evinced that natural causes afflict patients with schizophrenia much earlier than they do people in the general population. In fact, one meta-analysis concluded that at least 60% of the excess mortality in patients with schizophrenia is attributable to physical illness (Brown 1997). This well-received study also found that only 28% of the excess mortality is attributable to suicide and only 12% to accidents, leaving even more room than initially expected for the contribution of illness. Individuals with schizophrenia have been shown to die younger from a variety of cardiovascular, infectious, gastrointestinal, respiratory, urogenital, and metabolic conditions. It is not clear if there is a common contributing pathological factor that underlies these epidemiological correlations. Probably the best candidate for such a unifying factor is the metabolic syndrome, a cluster of commonly comorbid metabolic derangements that tend to exacerbate one another and tend to afflict individuals with schizophrenia. It is not clear why the metabolic syndrome is relatively prevalent in populations with schizophrenia, but taken together, various points of evidence regarding this association are beginning to elucidate how the two are related and what can be done in regard to prevention.

Most medical professionals do not think of the metabolic syndrome when they hear the word schizophrenia. Schizophrenia is a psychiatric diagnosis that is characterized by abnormalities in the perception or expression of reality. It can present in different ways but commonly manifests as auditory hallucinations, paranoid or bizarre delusions, or disorganized speech and thinking. The impairment in sensory gating, emotional inhibition, and the organization of complex behaviors cause individuals with schizophrenia to have significant impairments in social and occupational abilities. Onset of symptoms typically occurs in young adulthood with between 0.4% and 0.6% of the worldwide population affected (Bhugra 2006). It has become clear that the psychological symptoms are accompanied by a variety of somatic symptoms and health issues. In a study of over 168,000 affected

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Table 165.1 The key features of schizophrenia

Thought	Hallucinations, delusions, paranoid ideation, bizarre thinking
Behavior	Disorganized speech, emotional outbursts, social and occupational dysfunction, long term unemployment, homelessness, poverty
Causes	Both genetic and environmental, high heritability, stress, prenatal stress, drug abuse, social disadvantage
Brain physiology	Increased dopamine activity in the mesolimbic pathway, hypometabolic states in the prefrontal and temporal cortices and hippocampus
Comorbid conditions	Major depression, anxiety disorders, metabolic disorders, substance abuse

The key features of schizophrenia with selected aspects

patients in Sweden, schizophrenia was associated with an average life expectancy of approximately 80–85% of that of the general population (Hannerz et al. 2001). It is currently thought that a large proportion of this excess mortality can be attributed to metabolic disease.

Before the explicit ties to the metabolic syndrome were made, it was noted by epidemiologists that cardiovascular disease plays a large role in the premature deaths of schizophrenic patients. It was estimated that cardiovascular disease was responsible for as much as 50% of the excess mortality (Osby et al. 2000). Moreover, nearly 20% of deaths in schizophrenia can be attributed to ischemic heart disease, the most common cause of death in both sexes (Newman and Bland 1991). Today it is thought that even though there may be many contributing factors to cardiovascular disease in schizophrenia (such as cardiac arrhythmia and toxic cardiomyopathy), the major contributing factors may be metabolic disturbances – shared, common comorbidities in cardiovascular disease and schizophrenia. Since this realization, it has been well documented that individuals with schizophrenia are markedly susceptible to a specific group of metabolic disturbances that tend to present together in human and animal populations as the metabolic syndrome. It is thought that susceptibility to metabolic disease may be due to many different aspects common to schizophrenia, the most probable include inactive lifestyle, poor dietary choices, severe stress, and the side effects of psychotropic medications (Wirshing and Meyer 2003) (Table 165.1).

165.2 The Metabolic Syndrome in Schizophrenia

The metabolic syndrome has been a significant construct in the field of cardiology and endocrinology for at least 2 decades, but has become of interest to a variety of different fields in the last decade because of the ongoing, worldwide epidemic of obesity and diabetes. The metabolic syndrome is comprised of a group of clinical features that include atherogenic dyslipidemia (low high density lipoprotein (HDL) and elevated fasting triglycerides), hypertension, increased abdominal or visceral adiposity, and impaired fasting glucose or diabetes mellitus (Expert Panel on Detection 2001) (Table 165.2).

In 2005, the Adult Treatment Panel III of the National Cholesterol Education Program defined diagnosis as the presence of three or more of the five states listed in Table 165.3. The International Diabetes Federation, the European Group for the Study of Insulin Resistance, the World Health Organization, and others have each identified unique sets of diagnostic criteria. This disparity in diagnostic definition has created some concern and confusion; however, all three systems are relatively similar. There is broad overlap between the definitions, especially those of the World Health Organization and National Cholesterol Education Program. These similarities led researchers to find that, using data from the third National Health and Nutrition Examination Survey, NCEP and WHO criteria led to identical diagnoses for a group of 8,608 subjects in 86.2% of subjects. Not surprisingly,

Table 165.2 The key features of the metabolic syndrome

Obesity	Increased total body fat, abdominal or central fat distribution, increased visceral fat
Insulin resistance	Hyperinsulinemia
Dyslipidemia	Hypertriglyceridemia, decreased HDL cholesterol, increased LDL cholesterol
Impaired glucose tolerance	Type 2 diabetes mellitus
Hypertension	High or deranged blood pressure

The defining disorders of the metabolic syndrome and their components

Table 165.3 Criteria for the metabolic syndrome

Increased waist circumference	>102 cm in men, >88 cm in women
Elevated triglycerides	>150 mg/dl or 1.7 mmol/l
Decreased HDL cholesterol	<40 mg/dl in men, <50 mg/dl in women
Blood pressure	>130/85 mgHg or active treatment for hypertension
Fasting glucose	>110 mg/dl or active treatment for hyperglycemia

The National Cholesterol Education Program's criteria for diagnosis of the metabolic syndrome and their defining measures. Three of the five risk factors must be present for a diagnosis

differences in susceptibility to individual features caused the prevalence estimates between the two definitions to differ for some subpopulations, including sex and race (Ford and Giles 2003). It is not known if schizophrenia is another subpopulation whose prevalence might be affected arbitrarily by differences in susceptibility to certain features over others, although it is certainly possible.

The metabolic syndrome is highly prevalent in the general population. Based on the estimates derived from the third National Health and Nutrition Examination Survey it is thought that around 47 million people in the US meet the diagnostic criteria (Ford and Giles 2003). The age-adjusted prevalence in the US is 23.7% with the lowest prevalence of 6.7% for individuals between the ages of 20 and 29 and the highest prevalence of 43.5% for individuals aged 60 and higher. Both schizophrenia and a closely related psychiatric illness, schizoaffective disorder, are associated with a drastically increased risk for the metabolic syndrome and together have an age-adjusted prevalence of 42.6% for males and 48.5% for females (Cohn et al. 2004). Ethnicity as a predictor persists even after controlling for age, BMI, and socioeconomic status. For instance, Hispanics have the highest age adjusted prevalence of 31.9%. The age adjusted prevalence for schizophrenia is thought to be above 40%, significantly higher than the highest prevalence by ethnicity (Cohn et al. 2004).

McEvoy et al. (2005) confirmed in a large and well-controlled study that the metabolic syndrome is much more prevalent in patients with schizophrenia than among individuals from the general population, even after controlling for body mass and a variety of demographic variables. The order of the significance of this finding persuaded researchers to state that schizophrenia patients may represent a patient population with one of the highest metabolic syndrome prevalence rates of the major patient groups studied today. This study also showed that female patients with schizophrenia may constitute one of the subpopulations most vulnerable to central obesity and type 2 diabetes mellitus. Despite this and other fine studies in this area, there is no consensus about the prevalence of the metabolic syndrome in schizophrenia, in it subsets, or in associated psychotic disorders. It will be very informative to have the cross-sectional, longitudinal, and component feature data, and this may be available in a more reliable form in the near future.

The etiology of the metabolic syndrome, like that of schizophrenia, is still mysterious and controversial. There are a large number of secondary factors, aside from the key features, that are closely associated with the metabolic syndrome (Ryan and Thakore 2002), see Table 165.4. A review of these by Hansen (1999) identifies a wide assortment including: autonomic neuropathy, altered adipose tissue

Table 165.4 Secondary associations with the metabolic syndrome

Adipose tissue abnormalities: hyperleptinemia, altered lipoprotein lipase activity
Alcohol consumption
Pituitary adrenal abnormalities: hypercoritisolemia, impaired glucocorticoid receptor function
Reduced physical activity
Reduced ability to cope with stress, elevated stress hormone levels
Genetic predisposition, high heritability
Smoking
Increased food intake: hyperphagia, increased dietary fat content
Sex hormone abnormalities

A brief list of some of the secondary abnormalities associated with the diagnosis of the metabolic syndrome

physiology, difficulty coping with stress, excess alcohol consumption, hypercortisolemia, hyperphagia, impaired glucocorticoid receptor function, increased dietary fat content, reduced growth hormone, reduced physical activity, sex hormone abnormalities, and smoking. Factor analyses of the key and secondary features suggest that there is no unifying etiological feature (Zimmet et al. 1999). Many of these features are known to be quite commonplace in schizophrenia (Ryan and Thakore 2002). There has been very little research though, on whether populations of nonschizophrenic individuals with the metabolic syndrome exhibit symptoms particular to schizophrenia.

Individuals with schizophrenia may have increased risk for the metabolic syndrome because of patterns of unhealthy lifestyle choices common to schizophrenia and other psychotic disorders. Heavy alcohol (Mortensen and Juel 1993) and cigarette (Masterson and O'Shea 1984) use, along with poor diet, high fat consumption, lack of exercise and low physical activity (Brown et al. 1999) are all strongly associated with schizophrenia and have been for decades. These lifestyle factors are also powerful risk factors for the metabolic syndrome. It is clear that there is an increased need for lifestyle therapy intervention in this population. Diminishing substance abuse and increasing physical activity have long been treatment goals in schizophrenia therapy designed to ameliorate the psychological symptoms and improve mood. Now it is obvious that these goals will do more for this population than previously appreciated because they will also help to treat the metabolic symptoms.

It is becoming clear that the high prevalence of the metabolic syndrome in schizophrenia is due to more than just the behavioral propensities of patients or the antipsychotic drugs that the majority of patients have been prescribed. Several family history studies, and even decades old historical studies have found weighty, positive associations between schizophrenia and diabetes. Studies have also shown that first episode drug-naïve patients have an increased prevalence of central obesity, impaired fasting glucose, and insulin resistance suggesting that metabolic disturbances may be an inherent genetic component of the schizophrenia phenotype (de Leon and Diaz 2007; Spelman et al. 2007). Some well controlled studies have even shown that diabetes is more common in patients not taking antipsychotics than in those that were receiving them (Mukherjee et al. 1996). This represented powerful evidence suggesting that the association between schizophrenia and the metabolic syndrome is due to more than just the commonly accepted environmental influences. Some recent articles have even stated explicitly that there is evidence indicating that, "patients with schizophrenia might have an inherent predisposition towards the metabolic syndrome in a similar manner seen with certain ethnic groups" (McEvoy et al. 2005). In fact, genes responsible for schizophrenia and the metabolic syndrome seem to transmit together across generations. There is an increased frequency of the metabolic syndrome in the nonschizophrenic relatives of patients with schizophrenia (Mukherjee et al. 1989). Also, many of the individual facets of the metabolic syndrome have been closely tied to first episode or drug naïve schizophrenia as Table 165.5 demonstrates.

Table 165.5 Metabolic disorders and schizophrenia

Cardiovascular disease	Kendrick (1996); Davidson (2002) Ryan and Thakore (2002)
Insulin resistance	Felker et al. (1996); Ryan and Thakore (2002); Ristow (2004)
HPA axis up-regulation	Walker et al. (1996); Walker and Diforio (1997)
Metabolic syndrome	Ryan and Thakore (2002); Heiskanen et al. (2003)
Obesity	Allison et al. (1999); Davidson (2002)

A list of some of the features of the metabolic syndrome that have been associated with drug naïve or first episode schizophrenia

165.3 Schizophrenia and Diabetes

Studies indicate that diabetes mellitus may be twice as prevalent in schizophrenia (14%) as it is in the general population (7%) (Dixon et al. 2000). Additionally, impaired glucose tolerance and insulin resistance are also more common (Jeste et al. 1996). It is still not clear to what extent schizophrenia and diabetes present comorbidly because of shared genetic backgrounds, or if they are associated environmentally through weight gain. Prior to the onset of schizophrenia, there is not strong evidence for preexisting obesity (Weiser et al. 2004), an observation which provides some support for the latter assumption given that susceptibility of children and adults to the metabolic syndrome increases with worsening obesity. This does not necessarily detract from the significance of genetic contribution though, especially since individuals with schizophrenia are more likely to have obese parents. Furthermore, some studies have shown that even though there may not be a predisposition towards obesity prior to onset, it seems there is a prodromal predisposition for visceral adiposity (Zhang et al. 2004). It is possible that this inclination becomes fully expressed as obesity and diabetes after onset due to epigenetic factors, lifestyle, medications or interactions between all three.

The number of published prevalence studies of the metabolic syndrome in schizophrenia patients is not large, but it documents that the association is probably larger than the association between schizophrenia and diabetes mellitus (Heiskanen et al. 2003; Basu et al. 2004). Why this might be is unclear. The association between diabetes mellitus and schizophrenia has come under scrutiny recently because of new data associating atypical antipsychotics (also known as second generation antipsychotics) with new onset diabetes and the dangerous state of diabetic ketoacidosis (American Diabetes Association et al. 2004). Atypical antipsychotics have been known to work well to alleviate the symptoms of schizophrenia, and other forms of psychosis, but have received negative attention in the literature because of the significant weight gain liabilities associated with certain drugs (Meyer 2001).

165.4 Antipsychotic Medications

Atypical antipsychotics have been immensely effective in treating schizophrenia. Ironically though, they have been implicated in greatly accelerating the progression of the metabolic syndrome. More specifically, they have been heavily associated with cardiac irregularities, dyslipidemia, glucose intolerance, and weight gain (Ryan and Thakore 2002). The proportion of patients on antipsychotics with the metabolic syndrome ranges between 20% and 60% and in most cases is double the prevalence in the general population (De Hert et al. 2006; Haupt 2006). The evidence is the strongest for clozapine and olanzapine (Shirzadi and Ghaemi 2006) and suggestive but weaker for other antipsychotics (Newcomer and Haupt 2006).

It has been difficult for researchers to come to conclusions about the adverse effects of antipsychotics without the much needed randomized, controlled trials with prospective designs. Prior antipsychotic treatment and other medications confound the findings of many of the studies. Recent studies done with first episode schizophrenia avoided some of these confounds because all of the participants were drug naïve and had no prior antipsychotic prescription. One such study, using historic data, found that even though there was no difference in prevalence of the metabolic syndrome between first episode schizophrenics from 15–20 years ago compared with first episode moderns, the incidence of the metabolic syndrome was three times higher in the modern group that took atypical antipsychotics compared to the historic group that took first-generation antipsychotics (Hert et al. 2008). A number of findings have reinforced the consensus that first generation antipsychotics were far less likely to lead to metabolic complications. Another first episode study compared individual medications and showed that the test groups receiving olanzapine had the highest prevalence of the metabolic syndrome at 20–25%, followed by risperidone at 9–24% and finally haloperidol at 0–3% (Saddichha et al. 2008). Other studies have identified clozapine as being among the worst of these agents.

There are still many unknowns in this arena but fortunately there are also some thoughtful articles aimed at educating health professionals about what is known. The American Diabetes Association published a consensus paper on antipsychotic drugs and metabolic outcome that provides clear and helpful guidelines for health monitoring and medication selection for patients needing atypical antipsychotic drugs (American Diabetes Association et al. 2004). Despite many strong findings, it is important to point out that the influence of antipsychotic drugs comprises only a piece of this puzzle. As stated earlier, metabolic abnormalities have consistently been associated with schizophrenia even before the era of antipsychotic medications (Raphael 1921; Homel et al. 2002).

165.5 Schizophrenia and Cardiovascular Disease

As stated earlier, cardiovascular disease is one of the primary causes of morbidity and mortality in patients with schizophrenia (Meyer and Nasrallah 2003). Patients are known to commonly exhibit several different markers for cardiovascular risk. Both individuals treated with atypical antipsychotics and those who are drug free have a high propensity for platelet aggregation differences which makes them more likely to produce thrombus. Thrombus production is crucial during wound healing but overproduction can lead to life-threatening pathology including myocardial infarction. Exactly why and how this increased platelet aggregation occurs is unclear. Other unhealthy cardiac features that are associated with schizophrenia include: abnormal heart variation, prolonged phase of cardiac depolarization, decreased variations in cardiac rate, high sinus rhythm resting heart rate, long periodicity of endogenous ultradian rhythm of heart rate, and others. Interestingly, most of these features were abnormal in both individuals treated with antipsychotic drugs and those that were never treated. These findings lead one to conclude that there are multiple sources of evidence for abnormal autonomic control of heart rate, each of them related to cardiovascular risk, and many of them particular to the condition of schizophrenia specifically because they seem to be independent of the effects of antipsychotic medication.

The autonomic basis for these cardiovascular effects may be related to the extreme liability of both the sympathetic and parasympathetic divisions of the autonomic nervous system in untreated schizophrenia. It has been found that treatment with antipsychotic drugs actually has the effect of normalizing these swift autonomic swings. Such major autonomic dysregulation in untreated individuals could be inextricably tied to the development of the metabolic syndrome for several reasons including the following three: insulin is known to stimulate sympathetic activity, habitually elevated

Table 165.6 Therapeutic intervention for the metabolic syndrome

Obesity	Behavior modification, caloric restriction, regular exercise
Atherogenic diet	Reduce trans fats, saturated fats, dietary cholesterol and total fat
Cigarette smoking	Complete smoking cessation
Low HDL	Advise adding fibrate or nicotinic acid to diet
Hypertension	Lifestyle therapy, advise antihypertensive drugs
High LDL	Advise LDL cholesterol lowering drugs
Elevated glucose	Lifestyle therapy, advise hypoglycemic agents
Physical inactivity	Sixty minutes of moderate-intensity exercise daily
Prothrombotic state	Advise low-dose aspirin therapy

A very brief summary of clinical recommendations for individual facets of the metabolic syndrome

levels of sympathetic activity induce insulin resistance in skeletal muscle, increased sympathetic tone is associated with obesity and visceral fat deposition. The autonomic dysregulation may also lead to risk factors for the metabolic syndrome via a separate route. Chronic arousal of the sympathetic branch of the autonomic nervous system causes upregulation in the hypothalamic-pituitary-adrenal axis which in turn increases levels of circulating cortisol. Chronically elevated cortisol levels, a major finding in schizophrenia, influence and accelerate, at multiple etiologic stages, insulin resistance, abdominal obesity and dyslipidemia. An article by Rosmond and Bjorntorp (2000) provides compelling support for the wealth of evidence tying autonomic and hypothalamic-pituitary-adrenal axis dysregulation to risk factors for the metabolic syndrome.

Physician efficacy in moderating lifestyle risk factors for cardiovascular disease such as physical activity, diet and smoking can be very low even in healthy populations. Due to their psychological symptoms such as high levels of emotion and low capacity for inhibition, influencing lifestyle factors is probably more difficult in populations of patients with psychiatric histories, especially ones with schizophrenia. This makes it even more important to treat the other risk factors: hyperlipidemia, obesity, and glucose intolerance. In other words, because patients with schizophrenia can be relatively resistant to lifestyle therapy, the medications and the role of the prescribing physician are of upmost importance. There are a daunting number of antihypertensive, hypoglycemic, and cholesterol lowering drugs to keep track of, each with multiple contraindications and implications for medication evaluation. Table 165.6 summarizes some of the major therapeutic interventions for individual features of the metabolic syndrome, including behavioral goals and medications. These are forms of intervention that any medical professional treating schizophrenia should be aware of.

165.6 Applications to Other Areas of Health and Disease

It is clear that patients with schizophrenia are susceptible to a variety of medical illnesses and that these are responsible for a large proportion of the excess mortality observed. A large proportion of these disturbances map on neatly to the various features of the metabolic syndrome. It is not obvious whether the metabolic disorders are an integral part of schizophrenia or whether both are caused by a third, unidentified mechanism. The close association probably has at least a small genetic foundation and is further exacerbated by unhealthy lifestyle choices and the commonly prescribed antipsychotics. The existence of serious metabolic disease in schizophrenia has major implications for public health. It is very important that mental health professionals are made cognizant of the metabolic issues in patients with schizophrenia and instructed in how to address them proactively. Serious efforts should

be made to instruct and educate psychologists and psychiatrists to investigate, recognize, and actively monitor metabolic conditions in their patients with schizophrenia as well as readily refer these patients to primary care physicians. It is also important to increase awareness among psychiatrists of the fact that these conditions can be iatrogenically exacerbated during antipsychotic therapy.

A great deal of evidence suggests that the existence of the metabolic syndrome in schizophrenia, as in other populations, is contingent upon a high fat diet and living in a Westernized culture (Thakore et al. 2002). The metabolic syndrome is reaching pandemic proportions worldwide and this is thought to be closely related to the absence of physical exercise and abundant and cheap supply of calorie dense foods. Another chapter in this book, "Nutrition, Behavior and the Developmental Origins of the Metabolic Syndrome," discusses how immoderate eating habits and reductions in physical activity have the capacity to greatly exacerbate metabolic disturbances in humans from Westernized cultures. Now that we no longer forage throughout the day for lean meats, fruit and vegetables we are susceptible to obesity and metabolic disease, just like laboratory animals that are caged and fed ad libitum. Many of the topics highlighted by that chapter, including the Westernization of diet, the genetic associations between different metabolic abnormalities, the discussion of "thrifty genotypes" and the influences of epigenetic programming may also be relevant to the present discussion.

There are several well refined animal models of schizophrenia. Most of these induce schizophrenic symptoms in rats or mice by using the same cues thought largely responsible for inducing schizophrenia in humans stress and hypercortisolemia. Rats that are stressed, either prenatally or postnatally, exhibit many of the fundamental symptoms of schizophrenia including impulsivity, habituation deficits, sensory gating deficiencies and reduced hippocampal size. There is truly a paucity of research on the metabolic abnormalities in these animals and the present literature on schizophrenia and the metabolic syndrome has all but ignored this model. Researching the metabolic features of the animal models of schizophrenia should be far less expensive and easier to control and manipulate than many of the current studies looking at these features in humans. Of course, further studies with people are urgently needed as well though, and an emphasis should be placed on drug-naïve, longitudinal designs.

Comprehensive reviews in clinical endocrinology have established that, as our population ages, the metabolic syndrome will be an increasingly important concern. The incidence of schizophrenia does not increase with advancing age yet very little is known about the incidence of the metabolic syndrome in aging individuals with a past diagnosis of schizophrenia. As this chapter has illustrated, we know a good deal but there are still many unknowns. The formulation of treatment standards for the metabolic syndrome remains a highly contentious topic even in individuals without schizophrenia. Increasing the efficacy of lifestyle therapy, decreasing the metabolic disturbances associated with antipsychotics and disentangling people from their genetic propensities for schizophrenia and the metabolic syndrome all remain formidable and complicated problems for the future. It is clear; however, that the careful monitoring of metabolic health in patients with schizophrenia, especially those on atypical antipsychotics, could help markedly in early detection and prevention of the metabolic syndrome.

Summary Points

- Schizophrenia is a life-shortening illness with excess mortality attributable to increased frequency of specific natural and unnatural causes.
- Schizophrenia carries increased risk of a variety of metabolic disorders.
- High visceral fat, type 2 diabetes mellitus and cardiovascular disorders occur with increased frequency in schizophrenia.

- Unhealthy lifestyle, poor diet and lack of exercise probably contribute to the metabolic syndrome and metabolic abnormalities in schizophrenia.
- An inherent susceptibility to stress and elevated levels of cortisol probably exacerbate both psychiatric and metabolic disturbances.
- Atypical, or second generation, antipsychotics have been largely implicated in the onset of obesity, diabetes mellitus and the exaggeration of metabolic complications.
- New findings in this literature have important implications for public health and the treatment of schizophrenia.

Definitions

Antipsychotics: Medications used to treat schizophrenia or other psychotic conditions often manipulating dopamine function to decrease hallucinations, delusions, and other symptoms. Also referred to as neuroleptic drugs.
Dyslipidimia: A disruption of the levels of lipids in the blood. In western societies, most dyslipidemias are hyperlipidemias; an elevation of lipids often due to diet, lifestyle or prolonged elevations of insulin.
Glucose tolerance: The ability of the body to adapt to a relatively large dose of glucose. This ability is usually diminished in diabetics and is used to diagnose diabetes mellitus. A fasting subject ingests around 75 g of glucose and blood glucose is measured at intervals. In diabetics the concentration is higher and takes longer to return to baseline value.
Hypercortisolemia: A state marked by elevated levels of circulating cortisol, an essential glucocorticoid steroid hormone, the major hormone secreted by the adrenal glands.
Hyperglycemia: A complex metabolic condition characterized by high levels of blood glucose in the circulation, usually a result of insufficient or ineffective insulin production in either type 1 or type 2 diabetes mellitus.
Hyperphagia: An abnormal appetite or increased consumption of food, often associated with abnormalities in the hypothalamus.
Hypertension: High blood pressure or force of blood on the vessel walls of the arteries.
Hypothalamic-Pituitary-Adrenal axis: This is a neuroendocrine system in the body responsible for regulating stress physiology. Brain areas that sense threat, signal the hypothalamus which communicates hormonally to the pituitary which in turn signals the adrenal glands to secrete adrenaline and cortisol.
Insulin resistance: A condition in which cells, especially those comprising muscle, fat and liver tissue, fail to be properly receptive to the messages of the hormone insulin. Because insulin promotes the extraction of glucose from the blood, allowing cells to meet their metabolic needs, insulin resistance is associated with elevated levels of blood glucose.
Metabolic syndrome: A combination of metabolic disorders that commonly present together and increase the risk of developing diabetes and cardiovascular disease.
Schizophrenia: A group of psychotic disorders characterized by impairments in sensory gating, emotional inhibition and the organization of complex behaviors.
Visceral fat: The accumulation of fat around the internal organs of the torso. It is associated with the "apple shape," belly fat, central obesity and a high waist to hip ratio.

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