

**BIPOLAR DISORDER & COMORBID TYPE II DIABETES:
RAMIFICATIONS OF UNSTABLE INSULIN LEVELS**

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Abstract

The human body literally “runs” on glucose. Blood Insulin levels were the primary hormonal players in regulating concentrations of both extra- and intracellular glucose in the maintenance of somatic homeostasis and metabolism. As to the broad actions of glucose, most body systems were involved with this small, polar compound in some way including nutritionally, physiologically, osmotically (osmolarity), and metabolically. Furthermore, acting over all neurological pathways, glucose was the absolute required form of nutrition for nerve cells. It follows that fluctuations of glucose concentrations both inside and outside each cell had a considerable impact on behavior. The symptoms and genetics of Type II Diabetes and Bipolar Disorder were intermingled multidimensionally--congruent with the effects of almost tidal concentrations of glucose. The comorbid relationship of Type II Diabetes and Bipolar Disorder has been studied epidemiologically by researchers and clinicians. The interplay of the comorbid conditions of Bipolar Disorder and Type II Diabetes could be applied to patients in both the diagnostic and therapeutic phases of treatment. It is recommended in this work that all patients that were diagnosed with Bipolar Disorder have a complete medical workup to diagnose common conditions—especially the comorbid presence of Type II Diabetes.

Key Words: Bipolar Disorder, Type II Diabetes, Glucose Metabolism; Insulin Secretion; Insulin Resistance.

Introduction

Type II Diabetes was a disease of advanced societies and complex cultures. It was a “disease of plenty” --an adult ailment of over-nutrition and obesity. According to epidemiological results published by the Centers for Disease Prevention [1], the following estimates were given for the morbidity of Type II Diabetes in the United States (2011):

- Prevalence of Diabetes: 25.8 million or 8.3% of population.
- Incidence of Type II Diabetes: 1.9 million new cases diagnosed.
- Prevalence of pre-Diabetes (Metabolic Syndrome): 79 million people.
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Furthermore, the United States has the highest lifetime rate of Bipolar Disorder at 4.4% [2]. The elevated occurrence of delayed diagnosis and misdiagnosis of Bipolar Disorder may explain why incidence (new cases) and enumerating the amount of existing cases in the USA population (prevalence) cannot be expressed accurately—therefore in this study the term “lifetime rate” was used instead.

In many cases, there was misdiagnosis of mental illness in the Diabetic patient by public officials (mostly law enforcement) or even surprisingly by medical workers. According to a previous publication by the authors of this manuscript, bipolar individuals were often subject to criminal treatment and jailed when what was actually needed was crisis intervention and medical treatment [3]. Police needed to be trained to distinguish between mental illness and conditions related to Diabetes. However, with today’s simple blood glucose testing monitors with small fingerprick or distal arm sampling, there may be a tentative diagnosis of Diabetes made ‘on the street’. It could subsequently follow that after these routine tests at the crisis scene that the patient was a Diabetic and had no mental disorder after all.

Bipolar Disorder & Risk of Diabetes

Mental illness was diagnosed as a *primary risk factor, but not a cause* for Metabolic Syndrome and Type II Diabetes [4]. Furthermore, Metabolic Syndrome and obesity were commonly comorbid with Bipolar Disorder [5]. This relationship was on par with the risk of a genetically-based family history of Diabetes--genetic errors serving as risk factors in the functions of glucose metabolism. In glucose metabolism, insulin serves an anabolic function as cellular “fuel” whereas glycogen serves a catabolic function serving as stored glucose [6]. Hypertension, overweight/obesity, and some forms of mental illness were the primary risk factors for Type II Diabetes. The transformation of Metabolic Syndrome into frank Type II Diabetes decreased with a healthy diet and proper exercise program—both served a “protective function” against insulin resistance [4].

Excluding the use or influence of psychoactive drugs, *a comorbid relationship exists between Bipolar Disorder and Type II Diabetes*. Increased comorbidity of Diabetes (or metabolic syndrome) with bipolar illness *predates* initiation of the use of psychoactive medicines [4]. Therefore pharmacotherapy with these psychoactive medications was not the cause of the increased incidence and prevalence of Diabetes or metabolic syndrome [4].

Review of the Literature

Due to the elevated internal and external stressors in severe mental illness, increased cortisol is secreted by the adrenal cortex and was evident in the bloodstream (hypercortisolemia). Subsequent psychiatric treatment, especially pharmacological intervention, lowers stressors often countering this effect by promoting decreased body cortisol [7].

Modern therapy with Lithium was the “gold standard” medication for the treatment of Bipolar Disorder [8]--the most efficacious, inexpensive, and available chemical—usually in the

pharmaceutical form 'Lithium carbonate'. The *in vitro* effects of Lithium in laboratory animal models at levels analogous to human therapeutic treatment levels were studied acting as mood stabilizers in models of Bipolar Disorder [9]. In this study, dose dependent Lithium levels stimulated cultures of insulin-producing β -Cells extracted from rat pancreatic islets. Results showed that insulin production in response to Lithium treatment was clearly dependent on significantly increased β -Cell replication and subsequently augmented insulin secretion. There appeared to be a relationship between Lithium levels and increased insulin secretion (*in vitro*) which possibly resulted in the hypoglycemia that served as a "protective effect" against the hyperglycemia which was characteristic of Type II Diabetes. This relationship may help explain the lack of hard data for determining the prevalence of *comorbid* Diabetes and Bipolar Disorder. Typically, increased incidence of Type II Diabetes was mostly due to decreased secretion of insulin by the β -cells of the Islet of Langerhans in the pancreas and/or the development of insulin resistance by the somatic cells. Several risk factors for Type II Diabetes and Lithium metabolism, due to unstable blood insulin levels were given in Figure 1. In addition, Figure 1 presents therapeutic choices for the treatment of Bipolar Disorder as per the National Institute for Health and Clinical Excellence [10]. Several cogent metabolic relationships of Bipolar Disorder, insulin secretion, insulin resistance, and cortisol interactions were given in Figure 2. [11,12]. In Figure 2, key interrelationships of Metabolic Syndrome, including the propensity for cardiovascular disease, were given in this schema of Type II Diabetes and Bipolar Disorder [12,13].

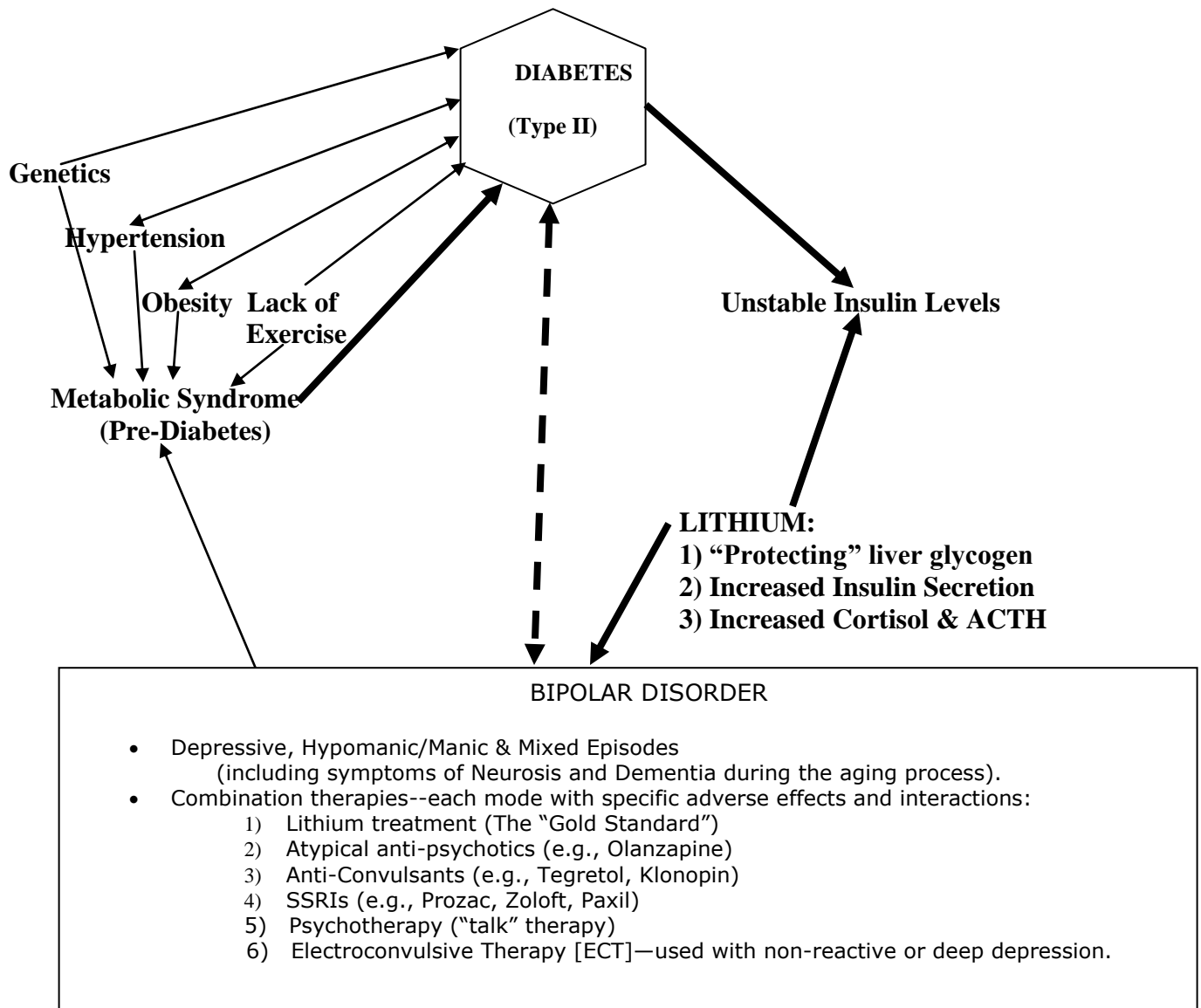


Figure 1: BIPOLAR DISORDER & DIABETES

(Note: Negative behavioral changes can occur in uncontrolled or poorly-controlled diabetes irrespective of the presence of a concurrent mental illness.)

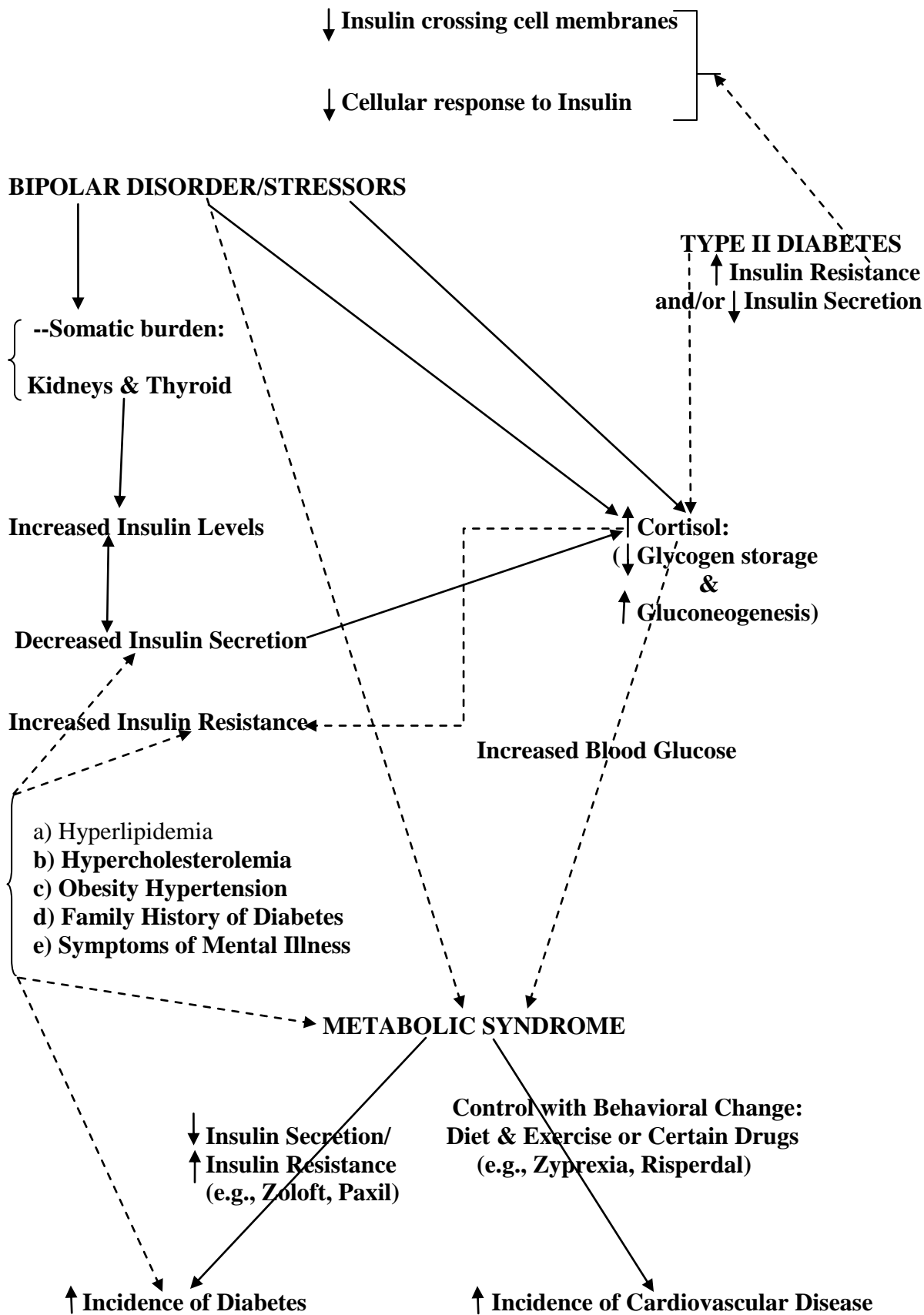


Figure 2: INTERACTIONS OF BIPOLAR DISORDER WITH TYPE II DIABETES AND METABOLIC SYNDROME

Conclusions

Bipolar Disorder, Metabolic Syndrome, and Type II Diabetes were intertwined at many levels of glucose metabolism, insulin resistance, and as stored glucose as glycogen in liver and muscle tissues [6]. Blood and cellular glucose, insulin levels and resistance, and stored glycogen act on the body's neuronal nutrition, metabolically, physiologically, psychologically, and behaviorally. Bipolar Disorder stands as a tough illness to diagnosis and may present only the first incidence of 'frank mania' as to a definitive diagnosis. Furthermore, epidemiological trends in the relationship of Type II Diabetes and Bipolar Disorder were evident as to morbidity, mortality, socioeconomic status, and social-cultural factors. The presence of Type II Diabetes, Metabolic Syndrome, and Bipolar Disorder as comorbid conditions should be tested in the diagnostic medical workup, blood work, and the treatment planning for each case of Bipolar Disorder that was diagnosed (Figure 1). According to Freeman [14, p.1): "All people diagnosed with Bipolar Disorder should immediately have a comprehensive physical exam to check for the presence of common comorbid conditions, especially Diabetes." Furthermore, a diabetic individual could be misdiagnosed and mistreated for a mental illness by law enforcement, medical workers, even mental health practitioners when presenting with hypomania, mania, or depression (or a mixed disorder)—the common clinical signs of Bipolar Disorder.

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