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Biopsychosocial pathways linking subjective socioeconomic disadvantage to glycemic control in youths with type I diabetes

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ABSTRACT

Older adolescent and young adults (OAYA) with type 1 diabetes (T1D) living in contexts of socio-economic disadvantage (SED) suffer disproportionately from poor glycemic control and related health complications. Although SED may convey a variety of risks, it may exacerbate diabetes-related stress levels, which in turn may account for observed disparities in health outcomes. The primary goal of the present study was to investigate the relationship between subjective SED, diabetes-related perceived stress, and diurnal cortisol secretion in urban OAYA with T1D. A secondary goal was to determine if cortisol was related to measures of blood glucose (HbA1c and mean blood glucose). Analyses were conducted among OAYA ages 17–20 years ($n = 61$) affected by T1D, who provided daily saliva samples for four days, measures of glycemic control (i.e., HbA1c and mean blood glucose assessed via Continuous Glucose Monitor), and completed psychosocial questionnaires. We found that subjective SED was associated with a flatter diurnal cortisol rhythm via diabetes-related stress. Flattened cortisol rhythm was, in turn, associated with higher levels of HbA1c, but not with mean blood glucose assessed via Continuous Glucose Monitor. These results represent some of the first empirical evidence on how distal social factors (i.e., subjective SED) and proximal psychological processes (diabetes-related perceived stress) are connected to condition-relevant biological mechanisms (i.e., elevated HbA1c), via broad biological pathways implicated in health (i.e., flatter cortisol slope).

1. Introduction

Older adolescents and young adults (OAYA) with type 1 diabetes (T1D) are more likely to experience adverse health status than either younger children or older adults, marking this as a high risk developmental period (Wood et al., 2013). Furthermore, OAYA with chronic poor metabolic control are more likely to come from disadvantaged groups such as those of lower socioeconomic status, those who hold public insurance, single-parent headed households, and members of minority groups (Harris et al., 1999; Wang et al., 2011). African-American OAYA in particular have been found to be at significantly higher risk for problems with treatment adherence and metabolic control (Palta et al., 1997; Wang et al., 2011) and also for post-diagnostic diabetic ketoacidosis (DKA) admissions (Frey et al., 2007). Such outcomes may be accounted for by a clustering of risk factors among minority OAYA. These include higher numbers of single-parent families where parents must juggle diabetes care with multiple other demands and have fewer resources for supervising adolescents' diabetes care (Beyers et al., 2003). Social disadvantage is also a marker for other community factors that may play a role in poor diabetes management, such as lack of access to healthy foods in neighborhood stores (Kipke et al., 2007).

One plausible explanation for disparities in health outcomes in OAYA with T1D living under conditions of socioeconomic disadvantage (SED) is increased psychological stress, the feeling of strain that emerges when an individual appraises environmental threats as taxing and unmanageable. The relationship between SED and higher levels of stress is well established in general population samples (Baum et al., 1999). Further, individuals affected by chronic conditions such as diabetes face unique stressors, such as the need to engage in daily management of a complex self-care regimen, coping with fluctuations in blood glucose levels that result in physical symptoms (e.g., fatigue and trouble concentrating), and facing stigma associated with their condition (Delamater et al., 1987; Chao et al., 2015). Some of these challenges, such as fitting in with

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peers, are particularly salient during adolescence and young adulthood, which may explain why OAYA with T1D, despite their more advanced diabetes management skills and disease knowledge, display poorer glycemic control than younger children (Thomas et al., 1997). Diabetes-related stressors have been shown to be even more common in the context of SED (Mühlhauser et al., 1998), likely because of the additional burden associated with material resources scarcity and the exposure to negative social experiences (e.g., discrimination based on social class). It is thus plausible that perceived stress could act as a psychological intermediary between SED and disparities in diabetes-related health (Viner et al., 1996; Lloyd et al., 1999). Evidence to support the possibility that stress can explain the relationship between SED in OAYA with T1D and poorer glycemic control also comes from research among individuals affected by other chronic conditions. For example, among youth with asthma, perceived stress has been shown to account for the detrimental effect of SED on asthma-relevant immunological mechanisms (Chen et al., 2003; Chen et al., 2006). Such studies also indicate that psychological stress may be associated with worse disease progression among high SED individuals with asthma.

In the current study we tested whether perceived diabetes-related stress acts as an intermediate psychological factor connecting SED to diurnal cortisol secretion. Disruptions in the hypothalamic pituitary adrenal (HPA) axis are associated with increased risk of infectious disease and inflammatory diseases, including type 2 diabetes (T2D) (Schoorlemmer et al., 2009; Nefs et al., 2015). In T2D, cells are compromised in their ability to properly respond to insulin, a condition known as insulin resistance. Insulin resistance, in turn, leads to high levels of blood glucose. In T1D, pancreatic islet beta-cells, which are responsible for the synthesis and release of insulin, are attacked and destroyed by the immune system, leading to extremely low or absent levels of endogenous insulin. Cortisol, the end product of the HPA axis, contributes to gluconeogenesis, hinders peripheral glucose uptake, and thus offsets the effects of insulin. Because cortisol is not only responsive to metabolic challenges (e.g., fasting, illness), but also psychological stressors, it is plausible that increased cortisol secretion is a direct pathway through which stress impairs glucose control (Barglow et al., 1984; Mazziotti et al., 2011) in persons with T1D. Cortisol secretion follows a diurnal rhythm, with higher levels at awakening followed by a gradual decline throughout the day. Cortisol slope corresponds to the rate of decline of cortisol throughout the day. Broadly, a flatter cortisol slope is indicative of sustained levels of cortisol during waking hours and is a stronger predictor of poor health outcomes (Matthews et al., 2006; Kumari et al., 2011) than other diurnal cortisol parameters, such as the cortisol awakening response (CAR).

Previous studies showed that exogenous disruptions of the cortisol diurnal pattern (Plat et al., 1999) as well as stress-related increases in cortisol secretion (Rosmond et al., 1998) lead to glucose metabolism abnormalities typical of people affected by T2D. Further, among T2D subjects, elevated cortisol is related to diabetes complications (Chiodini et al., 2007). Lastly, recent work has also shown that a flatter diurnal cortisol slope (less "healthy") was prospectively associated with T2D onset (Hackett et al., 2015). Taken together, these findings suggest that stress can have downstream effects on glucose metabolism through disruptions of diurnal cortisol rhythm (e.g., via a flatter diurnal cortisol slope).

In T1D subjects, cortisol levels are higher compared to matched control groups (Radetti et al., 1994) and, because cortisol acts in opposition to exogenous insulin, elevated cortisol is related to impaired glycemic control (Couch, 1992). Psychological stress, which activates the HPA axis (Miller et al., 2007), is also associated with poor glycemic control (Aikens et al., 1992; Goldston et al., 1995; Viner et al., 1996; Lloyd et al., 1999) (for similar findings in non-human animals, see Radahmadi et al., 2006). Despite these complementary lines of evidence, empirical support in favor of diurnal cortisol fluctuations as a mechanism for the link between diabetes-related psychological stress and impaired glycemic control among T1D patients is lacking. Further, studies that have established the relationship between psychological stress and increased blood glucose levels (Kramer et al., 2000) have not demonstrated that cortisol dysregulation is the mechanism through which this occurs.

In the current study, we tested two hypotheses concerning the effects of psychological stress on the HPA activity of OAYA with T1D. First, we hypothesized that high-SED OAYA would report more diabetes-related stress, which in turn would predict a flatter diurnal cortisol slope (i.e., higher SED → higher diabetes-related stress → flatter diurnal cortisol slope). Second, we investigated whether cortisol dysregulation resulting from SED and psychological stress would influence critical markers of health among people with diabetes such as glycemic control. Two measures of glycemic control were implemented, HbA1c and mean blood glucose assessed via Continuous Glucose Monitor (CGM). Thus, we tested whether cortisol disruption (i.e., flatter cortisol slope) resulting from SED and diabetes-related stress would be ultimately associated with higher levels of glycemic control (i.e., higher SED → higher diabetes-related stress → flatter diurnal cortisol slope → poorer glycemic control).

Table 1
Descriptive Statistics.

Descriptive variables	M or%	SD
Female	32.8%	–
Ethnicity		–
African American/Black	45.9%	–
White	45.9%	–
Other	8.2%	–
Education (some college)	16.4%	–
Age	18.30	0.99
Employed	49.2%	–
Living with Parents	86.9%	–
Diabetes insulin regimen		–
Mixed short and intermediate acting via injection	9.8%	–
BBT via injection	77.0%	–
Insulin Pump	13.1%	–
BMI	23.22	3.30
Diabetes Duration (years)	7.29	4.36
SSED	0.60	0.58
DSQ	1.97	0.60
Cortisol (ng/mL)	4.42	1.86
HbA1c (%)	9.58	2.22
Blood Glucose from CGM (mg/dL)	208.85	55.13

Note: BBT = Basal Bolus Therapy, BMI = Body Mass Index, DSQ = Diabetes Stress Questionnaire, CGM = Continuous Glucose Monitor.

2. Methods

2.1. Participants

A total of 68 OAYA between the ages of 17 and 20 and affected by type 1 diabetes (i.e., diagnosed for at least 6 months) took part in the current study. Of the larger sample of 68 OAYA, sixty-six provided saliva samples for cortisol analyses. Among these 66 individuals, five reported endocrine disorders other than diabetes and were therefore excluded for analyses concerning diurnal cortisol secretion. Thus, the final sample comprised sixty-one OAYA (32.8% female, 54.1% non-black, age, $M = 18.30$ years, $SD = 0.99$ years, see Table 1 for detailed descriptive statistics). All procedures were subject to review and prior approval by the Institutional Review Board at Wayne State University.