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The relation of atypical antipsychotic use and stress with weight in individuals at clinical high-risk for psychosis

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Abstract

Atypical antipsychotics (AT) and stress are related to weight gain in individuals with severe mental illness. This cross-sectional study examines AT use, stressful life events, and baseline weight in a sample of youth at clinical high-risk (CHR) for psychosis. Results showed that dependent and desirable life-events moderated the relationship between AT use and weight after controlling for demographic factors and SSRI antidepressant (AD) use. The relation of AD and weight was explored as a secondary analysis and showed no relation between AD use and weight. Further, stress did not moderate the relationship between AD medication and weight after controlling for antipsychotic use. Results suggest that stress exposure may exacerbate the relationship between ATs and increased weight in CHR populations. Findings have implications for the development of interventions to address psychosocial factors that worsen or buffer the adverse effects of antipsychotic medication on weight.

Keywords

atypical antipsychotics; stress; weight; prodrome

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1. INTRODUCTION

Individuals at clinical high risk (CHR) for psychosis experience attenuated psychotic symptoms such as perceptual abnormalities, suspiciousness, grandiose ideas, disorganized communication, and unusual thought content. In addition, CHR individuals have been found to experience greater life-events stress and rate the events they endorse as being more subjectively stressful (Trotman et al., 2014). Research also indicates that these individuals have higher cortisol levels (Walker et al., 2013), and are also typically in a developmental period, adolescence, that involves significant transitions (Jankord et al., 2011; Lenz, 2001). The age range for initial onset of attenuated symptoms is usually in adolescence/young adulthood, with the mean age of first attenuated psychotic symptoms appearing around sixteen years old (Addington et al., 2015).

Compared to the general population, CHR individuals are more likely to be prescribed atypical antipsychotic (AT) medications (Cadenhead et al., 2010; Walker et al., 2009), and these medications have been associated with elevated weight gain, a side effect that is especially distressing for youth (Allison et al., 2009; De Hert et al., 2009). Similarly, heightened stress exposure can lead to the maladaptive eating behaviors to manage stress (Adam & Epel, 2007). Stress-induced eating can influence underlying neurobiology and lead to increased weight (Yau & Potenza, 2013). To date, however, the joint or potential interactive effects of ATs and stress on weight gain in CHR youth have not been examined.

1.1 Mechanisms underlying weight gain from ATs

There are multiple mechanisms that may subserve the increase in weight among those taking ATs, including the role of serotonergic 5-HT_{2c} receptors, D₂ antagonists, and muscarinic M₃ antagonists (Nasrallah, 2003; Starrenburg & Boggers, 2009). The hypothesis with the strongest research support pertains to analog interactions with histamine binding sites on neurons in the hypothalamus (Kraus et al., 1999; Kroeze et al, 2003; Masaki et al., 2004; Matsui-Sakata, Ohtani, Sawada, 2005; Melkersson, Hulting, & Brismar, 2000; Starrenburg & Boggers, 2009). Notably, the average amount of weight gained while taking ATs varies by type, with clozapine and olanzapine shown to be associated with the most weight gain (Bak et al., 2014; Allison et al., 1999; Maayan et al., 2011; Nasrallah, 2003; Starrenburg & Boggers, 2009). Ziprasidone, aripiprazole, and quetiapine have been associated with relatively less weight gain (Bak et al., 2014; Nasrallah, 2003). Despite this, switching type of medication has not been found to be helpful in reducing weight (Bak et al., 2014).

AT associated weight gain and its consequences are well-documented in patients with psychosis (Allison et al., 1999; Bak et al., 2014; Maayan et al., 2011; Newcomer, 2005). Weight gain from AT use can contribute to decreased medication compliance (Cooper & Moison, 2007; Valenstein et al, 2004; Weiden, Mackell, & McDonnell, 2004), and in turn higher rates of relapse and hospitalization in these patients (Sun, Liu, Christiansen, & Fu, 2007).

1.2 The role of stress in weight gain

It is well-established that stress negatively impacts physical (Boardman, 2004) and mental (Aneshensel & Sucoff, 2006; Turner, Finkelhor, & Ormrod, 2006) health. Biological and behavioral factors are involved in the relation of stress with weight (Wilson & Sato, 2014; van Jaarsveld et al., 2009). For example, stress hormone (i.e., cortisol) secretion can alter neurobiological processes, thereby contributing to increased vulnerability to maladaptive eating behaviors. As noted, individuals at CHR for psychosis experience a greater number of life events stressors, as well as has greater sensitivity to such stressors (Trotman et al., 2014). Therefore, it is particularly important to examine the role of stress and increased weight in this population.

Sympathetic nervous system reactions and cortisol release are assumed to mediate the link between stress and weight gain. Cortisol, a glucocorticoid, in the presence of insulin, promotes an increase in the amount of fat deposits in the abdomen, as there are increased glucocorticoid receptors in this area (Yau & Potenza, 2013). Notably, intra-abdominal fat is most related to stress and metabolic problems (Björntorp, 2001). Glucocorticoids also interact with other hormones—inhibiting the action of insulin and leptin that regulate hunger and satiety. Glucocorticoid release also increases neuropeptide Y (NPY), a hormone that counteracts the stress response as well as increases appetite, making it a potential facilitator in “stress eating,” or “emotional eating” (Adam & Epel, 2007). When these homeostatic mechanisms that control weight are out of balance, eating behavior is altered.

These biological processes also contribute to increased eating through interactions with the brain’s reward system. Specifically, increased glucocorticoids augment cravings for highly palatable foods that engage the reward system via opioid and dopaminergic processes. It has been hypothesized that, over time, persistent stimulation of dopaminergic systems promotes desensitization, making one feel as if they need more highly palatable foods to feel satisfied (Adam & Epel, 2007; Yau & Potenza, 2013; Berridge, 2009).

In addition to triggering the above biological processes, it is well established that increased stress leads to eating as a method for coping with negative affect (Adam & Epel, 2007). This has been demonstrated in adult (van Strien, Konttinen, Homberg, Engels, & Winkens, 2016), child (Jenkins, Rew, & Sternglanz, 2005), clinical (Goossens, Braet, Van Vlierberghe, & Mels, 2009), and non-clinical samples (Webber, Hill, Saxton, Van Jaarsveld, & Wardle, 2009). Further, individuals with mental illness are more likely to engage in other behaviors that impact weight, (e.g., smoking), and are less likely to have access to resources that afford physical activity or the consumption of healthy foods (De Hert et al., 2009).

1.3 Present Study

In sum, individuals at CHR for psychosis are more likely to be exposed to two factors that contribute to weight gain; the use of AT medications and heightened stress. Excessive weight gain has a variety of adverse health consequences for youth and, as noted above, AT-induced weight gain is a primary cause of treatment noncompliance. To date, there has been no published research that simultaneously examines the relations of ATs and stress exposure with weight in clinical samples, including CHR youth. Such research is important, because

CHR individuals may be at even greater risk for adverse effects of weight gain, as they are in a period of heightened developmental transition and experience a higher rate of stressful life events. Further, noncompliance resulting from weight gain may jeopardize subsequent medication compliance and worsen prognosis in those at greatest risk for psychosis. Thus, research on factors that moderate AT-related weight gain is especially important in CHR youth.

The current cross-sectional study examines AT use and weight in a large sample of youth at CHR for psychosis. Both the direct and potential moderating effects of life-event stress on the relationship between ATs and weight are tested. It is predicted that: 1) both AT use and self-reported stress will be positively related to weight in CHR subjects, and 2) stress will moderate the positive relationship between AT use and weight, such that the strength of the relation between ATs and weight will be amplified by higher levels of stress exposure.

2. METHOD

2.1 Sample

All participants were part of Phase 2 of the North American Prodrome Longitudinal Study (NAPLS-2), a multi-site, longitudinal study that aims to enhance the prediction of psychosis in CHR subjects and shed light on the neural mechanisms of conversion. Individuals were excluded from the study if they had an Axis I psychotic disorder, an IQ below 70, history of a central nervous system disorder, or a substance use disorder (Addington et al., 2012). For more detailed information about the study procedures and sample characteristics, see Addington, et al., (2012). The present study included 534 CHR participants in NAPLS-2 for whom baseline data were available on current psychotropic medication, body weight, and life event stress.

2.2 Assessment Procedures

As part of the NAPLS-2 protocol, each participant received an extensive diagnostic assessment, and information on past and current medical history, including psychotropic medication, was obtained (Addington et al., 2012).

2.3 Measures

Diagnostic Assessment—The Structured Interview for Psychosis-Risk (originally titled Prodromal) Syndromes (SIPS) was used to determine CHR status and includes the Scale of Psychosis-Risk (originally titled Prodromal) Symptoms (SOPS). Symptoms are rated on a scale of 0 (absent) to 6 (very severe and psychotic). A detailed description of how CHR is determined can be found in previous reports (Miller et al., 1999; Miller et al., 2002).

Psychotropic Medication—Current psychotropic medication data were coded by specific medication type, and then aggregated by class. The primary classes of psychotropic medication in the sample were ATs and antidepressants (ADs), as described in Cadenhead et al. (2010). Some participants were also receiving psychological treatment while enrolled in the study (Woodberry et al., 2016). Medication dosage data were also collected. In previously published papers, detailed descriptions of the procedures for calculating

chlorpromazine (CPZ) equivalents (Leucht et al., 2014), and the mean values for the NAPLS CHR subsamples are provided (Woods et al., 2013). Because medication dosage information could not be established for all participants receiving one or more psychotropic, the present study examined the presence/absence (i.e., “on/off”) of medication rather than dosage. Weight (in pounds) was obtained via participant report.

Life-event Stress—A modified version of the Life Events Scale (LES) (Dohrenwend et al., 1978), a standard self-report measure of stress, was administered. The modified scale contained 59 items about events that could potentially occur in the adolescent/young adult age-range included in the sample. Participants reported the frequency with which each event occurred and rated how stressful the event was on a scale from 1 (not stressful) to 7 (highly stressful). For the present study, the summed severity scores were used. The LES scale allows for the derivation of four subscale scores for life events. The *dependent* life events subscale contains items that tap issues that are potentially secondary to the participant’s symptoms (e.g., interpersonal conflicts). The *independent* life events subscale contains items that tap issues not likely to be due to participant illness (e.g., death/illness of a friend). The *desirable* life events subscale contains items that are considered to tap life events that are generally positive or desirable (e.g., initiation of a new relationship). This is in contrast to the *undesirable* life events subscale that contains items that are thought to tap life events that are considered to be negative or undesirable (e.g., was victim of a crime) (Dohrenwend et al., 1978). The subscales include overlapping items. For example, an item can be both undesirable and independent (i.e. family member dies). In the analyses presented below, the four scores described above were used to examine the main and interactive effects of stress. Subscales were assessed separately in order to better assess subtypes of the participants’ reported stress experience.

2.4 Statistical Analyses

Statistical analyses were conducted with IBM SPSS Statistics 21 (SPSS Inc., Chicago, Illinois). Frequency analyses were used to determine the demographic composition of the sample. Chi square analyses were used to test for group differences in demographic variables and medication status. Bivariate correlations were used to assess the relation between stress subscales and weight. Because those at CHR for psychosis are often prescribed AD and AT medications (Walker et al., 2009), and AD medications have also been linked to weight changes (Serretti & Mandelli, 2010), all analyses were performed for both ATs and ADs, the majority of which were selective serotonin reuptake inhibitors (SSRIs) (Woods et al., 2013). Analyses of covariance, all controlling for age, were used to analyze weight differences for those on and off ATs, and for those on and off ADs. A preliminary regression analysis showed that sex did not moderate the relationship between AT use and weight, $F(1, 4) = 35.83$, $MSE = 1.63$, $p = .20$; nor did it for AD use and weight $F(1, 4) = 1.6034.80$, $MSE = 1.60$, $p = .43$. Therefore, all subsequent analyses were conducted on the total sample with males and females combined.

Regression analyses were conducted to test the main effects of stress, psychotropic medication (AT and AD), and their interaction, in predicting weight. Stress predictor variables were log-transformed. All regression analyses results are presented as one-tailed

given the directional nature of the hypotheses. The covariates age, sex, race, and AD use were entered in block one. The main effects were entered in block two (variable coded for “on/off” AT medication) and block three (respective stress variable). The interaction term [(Stress Variable X Medication (AT))] was entered in block 4. The same regression analyses were also conducted to test the effects of AD medication and stress on weight, when controlling for AT use. Age continued to be entered as a covariate.

3. RESULTS

3.1 Demographics

Demographic information for those on and off (on/off) atypical ATs and ADs are presented in Table 1. There were significant differences between those on/off ATs in weight, $F(1, 531) = 4.55, p = .033$, and age, $t(532) = 2.27, p = .023$, in that those on ATs weighed more and were younger. There was also a significant sex difference between those on/off ATs, $X^2(1) = 3.94, p = .047$, and between racial group categories, $X^2(9) = 18.78, p = .027$, such that males were more likely to be on ATs compared to females, and Caucasians were more likely to be on ATs compared to other racial groups.

As might be expected for CHR individuals, there were significant differences in the use of other psychotropic medication between those on/off ATs, such that those on ATs were also more likely to be on ADs, $X^2(1) = 60.92, p < .001$, mood stabilizers, $X^2(1) = 12.23, p < .001$, stimulants, $X^2(1) = 4.10, p = .043$, and benzodiazepines, $X^2(1) = 8.16, p = .004$. However, as previously reported, the rates of use of mood stabilizers, stimulants and benzodiazepines were too low to permit reliable tests of their relation with weight (Woods et al., 2013).

3.2 Correlation Analyses

The results of correlational analyses (one-tailed significance) are presented in Table 2. For those taking ATs, there were significant positive correlations between weight and dependent life events, $r = .257, p = .019$, desirable life events, $r = .247, p = .020$, and undesirable life events, $r = .230, p = .034$. For CHR participants not taking antipsychotics, there were no significant correlations between weight and the stress variables.

For those taking ADs, there were no significant correlations between weight and stress variables. For those not taking ADs, there was a modest, but significant correlation between dependent life event stress and weight, $r = .113, p = .029$.

3.3 Analysis of Covariance

When controlling for age, there was a significant weight difference as a function of AT medications $F(1, 1) = 4.55, p = .03, partial \eta^2 = .009, power = .56$. However, when controlling for both age and sex, there was not a significant weight difference for males and females, nor across the age spectrum as a function of AT medications $F(3, 1) = 2.43, p = .11, partial \eta^2 = .005, power = .34$. There was no significant weight difference between those on/off AD medications when controlling for age and sex $F(3, 1) = 1.43, p = .23, partial \eta^2 = .003, power = .22$.

3.4 Regression Analyses to Test for Main and Interaction Effects

Results of the multiple regression analyses, with weight as the dependent variable, are presented in Table 3. In testing the relation of dependent life events and AT use with weight, the overall variance explained by Block 1 (controlling for age, sex, race, and AD use) was significant, with age and sex being significant independent predictors $F(4, 501) = 32.39, p < .001$. The R^2 change with the addition of Blocks 2 (AT use; $F(1, 500) = 2.35, p = .063, R^2 = .004$) and 3 (dependent life events; $F(1, 499) = .00, p = .982, R^2 = .000$) did not result in a significant increase in the variance explained in predicting weight. The addition of the interaction term (AT use X dependent life events) in the fourth block, however, did result in a significant increase in the variance explained $F(1, 498) = 2.74, p = .049, R^2 = .004$. As reflected in the results of the correlational analyses presented above, and as shown in Figure 1a, this was due to a stronger relation between dependent life event stress and weight among those on atypical antipsychotics.

Similarly, in the regression using desirable life events, ATs, and their interactions as the predictors, the interaction term in the fourth block did result in a significant increase in the variance explained, $F(1, 508) = 3.68, p = .02, R^2 = .006$ (Figure 1b).

In contrast to the above findings, after controlling for age, sex, race, and AD use, there was no significant main or interactive effect of either independent life events or undesirable life events with ATs in the prediction of weight.

When the same regression analyses were conducted to test for the effect of ADs and stress in the prediction of weight, there were no significant main effects of ADs or interactions between stress and AD use with dependent life events, $F(1, 498) = .024, p = .43$, independent life events, $F(1, 488) = .002, p = .48$, desirable life events, $F(1, 508) = .313, p = .28$, or undesirable life events, $F(1, 500) = .040, p = .421$.

Lastly, in order to determine whether the duration of AT exposure was relevant to weight, bivariate correlations and regression analyses were conducted with months of exposure as a covariate. In this sample, duration of AT use was not correlated with weight ($r = .065, p = .13$), nor did controlling for AT duration substantively change the study findings (Dependent: $t = 1.62, p = .05$; Independent: $t = .132, p = .44$; Desirable: $t = 1.85, p = .03$; Undesirable: $t = 1.13, p = .12$).

4. DISCUSSION

The present investigation examined the relationships among stress, AT use, and weight for those at clinical high-risk (CHR) for psychosis. Contrary to prediction, after controlling for demographic variables and AD use, there was no significant main effects of ATs or the stress indices on weight. However, consistent with prediction, three of the four life-event stress indices, desirable life events, dependent life events, and undesirable life events, were significantly and positively correlated with weight among those CHR subjects on an AT. Of the three subscales, desirable life events and dependent life events significantly moderated the relationship between atypical antipsychotic use and weight. Undesirable life events did not significantly moderate the relationship between atypical antipsychotic use and weight.

Thus, the study results suggest that stress interacts with AT use, such that certain indices of stress are more strongly associated with body weight among those on antipsychotic medication.

Although the relation of AT use with weight was not statistically significant, it trended in the expected direction when controlling for demographic variables. In interpreting these results, it is important to keep in mind that the present study is cross-sectional and naturalistic, in that participants were not randomly assigned to medication conditions. Concerns about weight gain, including the individual's pre-prescription weight, may have influenced the likelihood that they received an antipsychotic prescription, and thus attenuated the relationship between antipsychotic use and weight. Similarly, post-prescription weight gain may influence AT continuation; several CHR individuals in the present study who previously experienced weight gain on an AT reported discontinuing the medication before they were enrolled in the study.

Similarly, the bivariate relations between the stress indices and weight were not significant in the absence of AT use. This may reflect the constricted range of stress scores in the CHR sample. As mentioned above, previous studies comparing the CHR sample with a matched healthy comparison group showed that the CHR sample reported significantly greater life event stress (Trotman et al., 2014). Thus, there were relatively fewer CHR individuals who reported low stress levels, skewing their distribution of stress scores to the higher end of the distribution.

It is of interest that the relationship between stress and weight varied as a function of the type of stress reported. For both desirable and dependent life events stress there was an interaction between antipsychotic use and the prediction of weight; this relationship did not hold for undesirable and independent life events stress. It is not clear why only two stress measures interacted with antipsychotic use. Particularly, why those on antipsychotic medication with higher desirable life events had higher weight, while those off antipsychotic medication did not show fluctuations in weight relative to increasing desirable life events. The results may have simply occurred by chance, given that the life events stress subscales are highly inter-correlated, and the bivariate correlations show that all but the measure of independent life-events were significantly correlated with weight in the CHR sample on an AT. This is plausible given that the contextual nature of actual stressors vary (Park & Folkman, 1997), and that individual differences influence how one experiences stressors (Watson, 1988).

Given that individuals at CHR for psychosis experience more life events stressors and rate them as more stressful compared to control populations (Trotman et al., 2014), one may expect heightened stress in response to various contextual factors. First, CHR individuals are most likely to be in adolescence and young adulthood, a time period that is known for being one of great transition and change (Jankord et al., 2011; Lenz, 2001). Even, for individuals *not* at CHR, change and transition is often experienced as stressful (Almeida & Wong, 2009). Therefore, one could surmise that any type of event, positive or negative could bring about stress that is experienced more strongly in individuals at CHR.

Second, an individual's level of self-efficacy, or one's belief that they have the ability to manage stressors or transitions, may impact their ability to manage such stressors (Jerusalem & Mittag, 1995). Levels of self-efficacy vary greatly in individuals with severe mental illness (Corrigan & Watson, 2002). Similarly, according to the cognitive-relational stress theory, inter-individual differences in stress perception can greatly impact how one is able to manage positive and negative life transitions (Lazarus & Folkman, 1987). This highlights the possibility of contextual variation in the frequency and intensity of endorsed stressors in this group, as well as explains why the pattern of heightened stress due to common stressors may not be as predictable.

Finally, it is also important to consider the impact that increased weight may have on life stress, particularly in adolescents with prodromal symptoms that may already have impaired tolerance to common stressors. Being, or believing that, one is of increased weight may exacerbate subjective distress in response to interpersonal stressors.

4.1 Clinical Utility

Findings from this study suggest that more attention should be given to current psychosocial stressors that patients prescribed ATs may experience. The acquisition of behavioral strategies to cope with stress in adaptive ways, such as with exercise, meditation, and perhaps stimulus control around food management, may help mitigate the amount of weight gained while taking atypical antipsychotic medications (Duncan, Davison, Remington, & Faulkner, 2017). Notably previous research suggesting that changing the type of AT medication does not result in less weight gained (Bak et al., 2014) highlights the potential role that behavior also plays in the acquisition of excess weight, suggesting that behavioral interventions may be particularly useful.

Further, the use of cognitive strategies by CHR individuals may also be helpful as a way to manage stressors (Morrison et al., 2004). Indeed, studies suggest that cognitive and behavioral interventions can aid in reducing weight in individuals with psychosis taking atypical antipsychotics. For example, Weber and Wyne (2006) found that weight loss was attained after a 16-week cognitive/behavioral intervention for weight loss in individuals with schizophrenia currently taking an AT. Stress management was a module in the program (Weber & Wyne, 2006). Further, Centorrino and colleagues (2006) found a significant reduction in weight in a sample of individuals diagnosed with schizophrenia or schizoaffective disorder, and currently being treated with an atypical antipsychotic medication, who were enrolled in a 24-week diet and exercise program (Centorrino et al., 2006). Additionally, treatment modalities such as acceptance and commitment therapy may also be useful for this clinical group, as it promotes mindfulness in the experience of negative emotions (i.e. stress) and focusing attention on achieving valued goals (Gaudiano & Herbert, 2006).

4.1 Strengths and Limitations

The NAPLS project is one of the largest investigations of CHR for psychosis in the world, making this an ideal sample in which to examine the interaction between the use of ATs and the experience of stress in affecting weight. Further, the analysis of these processes in

individuals identified early in potential illness progression strengthens the argument for the potential utility of early intervention to decrease stress as well as weight gain.

However, this study does have limitations. Height was not assessed or reported for this sample, so BMI could not be calculated. BMI is considered a more standardized metric of weight, especially in this age range. Adjusting for effects of age and sex, both of which typically correlate with height and weight, mitigated this limitation to some degree. Further, weight was self-reported and self-report indices of stress were used. Although reliance on self-reported weight is a limitation, it is noteworthy that in the present study weight was related to demographic variables (i.e., sex and age) in the way that would be expected (age: $r = .211$, $p = .01$; sex: $t = 8.52$, $p = <.001$). Further, most measures of life-event stress are based on self-report because access to archival records of life events is typically not feasible. Nonetheless, previous research indicates that self-reports of stressful events potentially linked to illness onset do not provide as much information as more in depth clinical interviews, as they obtain information on the individual's subjective experience (Turner & Wheaton, 1995). Finally, although research shows that the amount of weight gained varies by type of AT prescribed (Bak et al., 2014; Allison et al., 1999; Maayan et al., 2011; Starrenburg & Boggers, 2009), the number of NAPLS subjects on any specific AT is not large enough to perform analyses by AT subtype.

4.2 Directions for Future Research

With these limitations in mind, future studies are needed to attempt to replicate findings using measured BMI. Longitudinal studies that utilize growth curve analyses would also provide a more reliable measure of weight gain over time as a results of AT use and stress. Further, more work is needed to understand the degree to which the experience of stress might be related to a poor response to the various weight control interventions that already exist for those who are taking ATs and are gaining weight.

Also of note, nonwhite race has been associated with greater weight gain with some AT medications (Basson et al., 2001). Research suggests that being a member of a minority group is related to heightened stress (Williams, Jackson, & Anderson, 1997), and that many minority groups are at heightened risk for obesity and metabolic issues (Clarke, O'Malley, Johnston, & Schulenberg, 2009; Smith et al., 2005), it is important to examine the interaction of stress and AT use in different racial/ethnic groups to determine whether certain groups are at amplified risk for weight gain.

A potential moderator not assessed in this study is the impact of treatment utilization including therapy (i.e. individual, family, group). The use of such services could mitigate the direct impact of stress and perhaps even the use of maladaptive coping strategies. Therefore, future research should explore the role of treatment as a potential moderator in the relationship between AT use and stress.

Finally, further research on the relationships among stress, weight, and AT use could include bioindicators of stress, such as cortisol. Given the relationship between cortisol release and weight gain in individuals without severe mental illness (Adam & Epel, 2007), as well as the

increased cortisol release in CHR individuals (Walker et al., 2013), one might expect cortisol to mediate the relationship between AT use and increased weight in this group.

4.3 Conclusion

In conclusion, the present study provided support for the hypothesis that increased stress and AT use interact to promote greater weight among those at CHR for psychosis. The effect may be based, in part, on heightened change and transition occurring in CHR adolescents. Longitudinal research is needed to elucidate the specific nature and biological mechanisms in the relationship between stress and weight gain over time.

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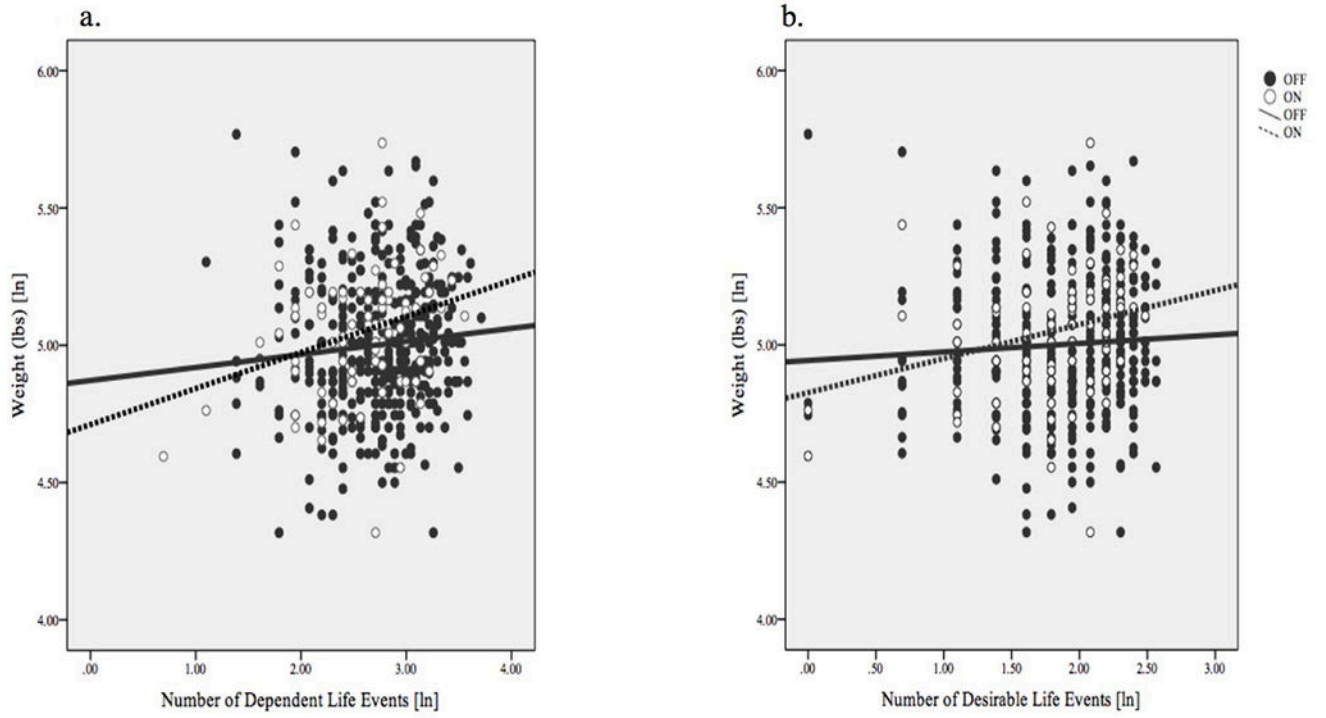


Figure 1. Moderation Analyses for Number of (a) Dependent Life Events, and (b) Number of Desirable Life Events.

Table 1

Demographic information for individuals at CHR on/off atypical antipsychotics (ATs), and on/off antidepressants (ADs), that have weight data

Variable	ON ATs (n = 90)	OFF ATs (n = 444)	F/t/ χ^2	p-value
Weight (lbs) (Mean)*	159.84 (SD = 36.28)	153.61 (SD = 38.69)	F = 4.55	.033
Age (Mean)*	17.82 (SD = 3.83)	18.92 (SD = 4.25)	t = 2.27	.023
Sex (% Male)*	54.60 (n = 63)	58.80 (n = 261)	$\chi^2 = 3.94$.047
Race/Ethnicity (% White)*	73.30 (n = 66)	55.60 (n = 247)	$\chi^2 = 18.78$.027
Other Medications				
% Antidepressants*	58.90 (n = 53)	61.90 (n = 86)	$\chi^2 = 60.92$	<.001
% Mood Stabilizers*	11.10 (n = 10)	2.20 (n = 10)	$\chi^2 = 12.23$	<.001
% Stimulants*	13.30 (n = 12)	7.00 (n = 31)	$\chi^2 = 4.10$.043
% Benzodiazepines*	13.30 (n = 12)	5.20 (n = 23)	$\chi^2 = 8.16$.004
% Conventional ATs	(n = 0)	.40 (n = 2)	$\chi^2 = .738$.390
Variable	<u>ON ADs (n = 139)</u>	<u>OFF ADs (n = 395)</u>		
Weight (lbs) (Mean)	157.70 (SD = 41.22)	153.60 (SD = 37.30)	F = 1.27	.260
Age (Mean)	18.27 (SD = 3.77)	18.90 (SD = 4.34)	t = 1.50	.134
Sex (% Male)	60.40 (n = 84)	60.80 (n = 240)	$\chi^2 = .005$.946
Race/Ethnicity (% White)	67.60 (n = 94)	55.40 (n = 219)	$\chi^2 = 13.93$.125
Other Medications				
% ATs*	58.90 (n = 53)	41.10 (n = 37)	$\chi^2 = 60.92$	<.001
% Mood Stabilizers	5.80 (n = 8)	3.00 (n = 12)	$\chi^2 = 2.12$.145
% Stimulants*	14.40 (n = 20)	5.80 (n = 23)	$\chi^2 = 10.24$.001
% Benzodiazepines*	15.10 (n = 21)	3.50 (n = 14)	$\chi^2 = 22.53$	<.001
% Conventional ATs*	1.40 (n = 2)	(n = 0)	$\chi^2 = 5.41$.020

Note.

* indicates significant difference between those "on" and "off" atypical antipsychotics/antidepressants for that particular variable.

Table 2

Correlations between weight and stress for those on/off atypical antipsychotics, and on/off antidepressants.

	Atypical Antipsychotics		Antidepressants	
	Weight (ON)	Weight (OFF)	Weight (ON)	Weight (OFF)
1. Dependent Life Events	.257 ** (n = 84)	.079 (n = 423)	.067 (n = 131)	.113 * (n = 376)
2. Independent Life Events	.133 (n = 86)	.063 (n = 429)	.041 (n = 133)	.075 (n = 384)
3. Desirable Life Events	.247 * (n = 88)	.053 (n = 429)	.078 (n = 133)	.076 (n = 384)
4. Undesirable Life Events	.230 * (n = 85)	.065 (n = 424)	.082 (n = 132)	.085 (n = 377)

**
 $p < .01$

*
 $p < .05$

Note. Tests are one-tailed.

Table 3
Regression analyses: Relation of atypical antipsychotic use and stress with weight

	Unstandardized Coefficients	Standardized Coefficients	t	P value	R ² Change
	b	β (Beta)			
Block 1:					
Age	.017	.293	6.372	<.001	.205
Sex	-.165	-.334	-8.30	<.001	
Race	-.002	-.016	-.408	.683	
Antidepressant Use	.005	.023	.197	.844	
Block 2:					
ATs	.043	.028	1.53	.063	.004
Block 3:					
Dependent Life Events	.001	.001	.023	.491	.000
Block 4:					
AT X Dependent Life Events	.087	.350	1.65	.049	.004
Block 1:					
Age	.016	.279	6.62	<.001	.206
Sex	-.171	-.346	-8.49	<.001	
Race	-.002	-.014	-.344	.731	
Antidepressant Use	.003	.024	.139	.889	
Block 2:					
ATs	.041	.028	1.46	.070	.003
Block 3:					
Independent Life Events	.007	.018	.383	.351	.000
Block 4:					
AT X Independent Life Events	.009	.016	.175	.430	.000
Block 1:					
Age	.018	.308	6.83	<.001	.204
Sex	-.162	-.330	-8.28	<.001	
Race	-.002	-.013	-.328	.743	

	Unstandardized Coefficients	Standardized Coefficients	t	p value	R ² Change
	b	SE	β (Beta)		
Antidepressant Use	.006	.023	.11	.265	.791
Block 2:					.004
ATs	.041	.027	.65	1.52	.060
Block 3:					.001
Desirable Life Events	-.015	.024	-.28	-.626	.266
Block 4:					.006
AT X Desirable Life Events	.105	.055	.301	1.91	.026
Block 1:					<.001
Age	.016	.003	.279	6.41	<.001
Sex	-.168	.020	-.339	-8.45	<.001
Race	-.002	.005	-.020	-.495	.621
Antidepressant Use	.005	.023	.10	.230	.818
Block 2:					.004
ATs	.044	.028	.68	1.604	.061
Block 3:					.001
Undesirable Life Events	.017	.018	.42	.956	.169
Block 4:					.002
AT X Undesirable Life Events	.047	.043	.154	1.07	.140

Note. All significance values associated with directional hypotheses are one-tailed. Stress variables normalized. Values significant at the p<0.05 level.