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Exploring the relationship between body mass index and positive symptom severity in persons at clinical high risk for psychosis

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Abstract

Metabolic health and positive symptom severity has been investigated in schizophrenia (SCZ), but not in clinical high-risk (CHR) patients. We hypothesized that greater body mass index (BMI) in CHR patients would be related to less positive symptoms. We examined this relationship in CHR patients being treated with, i) no psychotropic medications (n=58), ii) an antipsychotic (n=14), or iii) an antidepressant without an antipsychotic (n=10). We found no relationship between BMI and positive symptoms in un-medicated CHR patients, the majority of whom had a narrow BMI range between 20–30. However, in the smaller sample of CHR patients taking an antidepressant or antipsychotic, BMI was negatively correlated with positive symptoms. While potentially underpowered, these preliminary findings provide initial steps in elucidating the relationships between metabolic health, neurochemistry, and symptom severity in CHR patients.

1. Introduction

It has been argued that weight gain and insulin resistance (IR) may be beneficial for treating psychosis (Sharma et al, 2014). For instance, antipsychotic medications induce weight-gain and exacerbate IR (Clark, 2004; McIntyre et al, 2001; Tschoner et al, 2007). Importantly, higher fasting serum levels of insulin are related to less psychotic symptoms in patients with SCZ (Chen et al, 2013; Fan et al, 2006). In healthy persons, acute (9-day) administration of olanzapine or aripiprazole can significantly increase IR in the absence of weight gain (Teff et al, 2013). Brain imaging studies in healthy humans suggests that obesity and IR may be associated with reduced striatal dopaminergic functioning (Caravaggio et al, 2015b). Thus, it has been hypothesized that in SCZ, states of hyperinsulinemia may promote a reduction in

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central dopamine (DA) levels and in turn a reduction in positive symptoms (Caravaggio et al, 2015c).

While several studies have examined the relationship between metabolic health and positive symptoms in persons with SCZ, to our knowledge this has not yet been examined in patients at clinical high-risk (CHR) for psychosis. In this preliminary analysis, we investigated whether body mass index (BMI) – a gross, indirect measure of metabolic health and IR – is related to the severity of positive symptoms in CHR individuals. We hypothesized that greater BMI in CHR patients would be related to less positive symptom severity, as measured by the Structured Interview for Psychosis-Risk Syndromes (SIPS) (Miller et al, 2003). We examined this relationship in CHR patients being treated with, i) no psychotropic medications, ii) an antipsychotic, and iii) an antidepressant without an antipsychotic. This was done since both antidepressants and antipsychotics have been found to alter body weight (Fava, 2000; Himmerich et al, 2015) and both are used in the treatment of psychosis in CHR. While there are several limitations to the current investigation, we hope this preliminary investigation will prompt future prospective research examining how IR might be related to symptom severity and neurochemistry in persons with attenuated psychotic symptoms.

2. Methods

2.1 Participants

Participants and clinical assessments were derived from a longitudinal cohort study of CHR patients at the Center of Prevention and Evaluation (COPE) at the New York State Psychiatric Institute/Columbia University Medical Center. COPE offers treatment to English-speaking individuals, aged 14–30, who are deemed to be at high-risk for psychosis. These CHR individuals were help-seeking and met criteria for at least one of three psychosis-risk syndromes, as assessed with the SIPS

2.2. Statistical Analyses

Statistical analyses were conducted using IBM SPSS Statistics (v.20; Armonk, NY: IBM Corp) and GraphPad (v.6.0; GraphPad Software, La Jolla California). The significance level for all tests was set at $p < .05$ (two-tailed). As our study was exploratory and preliminary in nature, we did not explicitly control for multiple comparisons.

3. Results

Fourteen CHR patients (mean age=17.75±1.67; 2 female) were receiving antipsychotics, ten were receiving antidepressants (mean age=20.33±0.97, 4 female), and fifty-eight CHR patients were not taking any psychotropic medications (mean age=22.78±3.34) (See Table 1). The BMI (mean±SD) for each group were as follows: un-medicated CHR (26±5.23), antipsychotic treatment (28±5.99), and antidepressant only treatment (27±8.17). BMI did not significantly differ between un-medicated subjects and those receiving and antidepressant ($t(66)=-.31$, $p=.76$) or an antipsychotic ($t(63)=-.90$, $p=.37$). Likewise, BMI between the two medicated groups also did not differ ($t(15)=-.36$, $p=.73$). The correlations between BMI and the positive symptom SIPS scores are presented in Table 2 and Figure 1. One subject in the antidepressant only group had a BMI of 47.60, and was thus considered

severely obese, or Obese class III. Excluding this subject from the analyses, the negative relationship with BMI remained significant for several of the SIPS scores (the following do not include covariates for demographic variables): P2 ($r(7) = -.69$, $p = .04$), P5 ($r(7) = -.73$, $p = .03$), and Total Positive Symptom scores ($r(7) = -.83$, $p = .005$); but not for P1 ($r(7) = -.46$, $p = .21$). Moreover, the relationship between BMI and P4 became significant ($r(7) = -.69$, $p = .04$).

4. Discussion

Contrary to our hypotheses, we did not observe a significant correlation between BMI and positive symptom severity in un-medicated CHR subjects. This may be due to several factors, including a reduced BMI range and inherent subject heterogeneity. However, we found that in those CHR patients receiving an antipsychotic or antidepressant, BMI was significantly negatively correlated with positive symptoms. However, these samples were small, and caution must be taken in considering these preliminary findings until replicated with larger samples. While we did not collect changes in BMI given neuroleptics, these results appear consistent with the “metabolic threshold” hypothesis of neuroleptic treatment. Namely, weight gain/IR induced by neuroleptic medications may be related to improved positive symptoms (Sharma et al, 2014), perhaps *vis-à-vis* reduced striatal dopaminergic signaling induced by this metabolic state (Caravaggio et al, 2015a). However, given that we have only collected BMI, it presently remains unclear whether glucose tolerance/IR abnormalities exist in non-medicated CHR patients at baseline. This could be addressed by future prospective studies. Of course, as is the case in persons diagnosed with SCZ, it may be that not all CHR patients in our sample have striatal DA abnormalities. The cause of their subthreshold psychotic symptoms may be the result of some other unknown pathology, and thus unrelated to DA or BMI.

There are several limitations to the present study. We are limited by the sole use of BMI. We hope our preliminary investigation will prompt research groups to prospectively collect and examine direct markers of metabolic health in CHR patients, in relation to symptom severity and neurochemistry. We did not collect metabolic data before and after treatment with psychotropics. Thus, whether changes in symptoms are related to drug-induced changes in metabolic functioning in CHR subjects is currently unknown, and should be investigated by future studies. Future studies should also employ larger sample sizes. Notably, we only observed significant negative correlations with BMI, not positive correlations, consistent with our *a priori* hypotheses.

While much remains unknown in terms of understanding how metabolic health may relate to psychotic symptoms and neurochemistry in the CHR, our preliminary findings provide rationale and groundwork for addressing these questions.

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Figure 1.
Relationship between positive symptom scores and body mass index in clinical high risk for schizophrenia subjects.

Table 1

List of CHR patients and the medications they were receiving.

Antipsychotic Group (n=14)		Antidepressant Group (n=10)		Other Medications		Other Medications	
Subject#	Antipsychotic Medications	Subject#	Antidepressant Medications	Other Medications	Other Medications	Other Medications	Other Medications
1	Aripiprazole	1				Escitalopram	
2	Quetiapine	2				Fluoxetine	Melatonin
3	Risperidone	3				Fluoxetine	
4	Risperidone	4				Fluoxetine	
5	Aripiprazole	5		Fluoxetine		Fluoxetine	
6	Aripiprazole	6		Fluoxetine		Fluoxetine	
7	Aripiprazole	7		Fluoxetine		Sertraline	
8	Risperidone	8		Bupropion		Sertraline	
9	Risperidone	9		Gabapentin		Venlafaxine	
10	Aripiprazole	10		Benzatropine Valproate		Citalopram	Bupropion Clonazepam
11	Olanzapine			Bupropion Clonazepam			
12	Aripiprazole			Bupropion Desvenlafaxine Fluvoxamine			
13	Quetiapine			Clonazepam Clonidine Escitalopram			
14	Ziprasidone			Benzatropine Fluoxetine Hydroxyzine			

Table 2

Correlations between positive SIPS scores and body mass index.

SIPS	P1	P2	P3	P4	P5	Total
Antipsychotics (n=14)						
<i>Body Mass Index</i>						
	-.07 (0.80)	.07 (0.82)	-.55* (0.04)	.37 (0.19)	-.14 (0.64)	-.17 (0.57)
Covariates						
Age, Gender, & Ethnicity	.30 (0.37)	-.02 (0.97)	-.62* (0.04)	.47 (0.15)	.008 (0.98)	-.11 (0.75)
Antidepressants (n=10)						
<i>Body Mass Index</i>						
	-.84** (0.002)	-.94*** (0.0001)	-.29 (0.42)	-.63 (0.05)	-.81** (0.004)	-.93*** (0.0001)
Covariates						
Age, Gender, & Ethnicity	-.84* (0.02)	-.94** (0.002)	-.35 (0.45)	-.69 (0.08)	-.87* (0.01)	-.95** (0.001)
Non-medicated (n=58)						
<i>Body Mass Index</i>						
	-.19 (0.16)	-.09 (0.53)	-.16 (0.22)	-.08 (0.55)	-.16 (0.24)	-.17 (0.21)
Covariates						
Age, Gender, & Ethnicity	-.24 (0.07)	-.14 (0.30)	-.12 (0.38)	-.14 (0.31)	-.16 (0.25)	-.20 (0.15)

* Denotes significance at the $p < .05$ level (two-tailed)** Denotes significance at the $p < .01$ level (two-tailed)*** Denotes significance at the $p < .001$ level (two-tailed)