# Impaired glucose tolerance in first-episode drug-naïve patients with schizophrenia.

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# Impaired Glucose Tolerance in first-episode drug-naïve patients with schizophrenia.

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**Structured Summary**

Aims

To determine whether there is an association between Type 2 diabetes mellitus and schizophrenia independent of medication.

Methods

In this cross-sectional study we performed an oral glucose tolerance test on 38 non-obese white Caucasians who fulfilled criteria for first episode drug naïve schizophrenia, an equal number of controls (matched for age, sex, smoking status, alcohol intake and ethnicity) and 44 first-degree relatives of the patients.

Results

The frequency of impaired glucose tolerance (IGT) was 10.5% (n=4) in patients with schizophrenia, 18.2% (n=8) in unaffected relatives and were no different between theses two groups ($\chi^2$=1.92, df=1, p=0.1) as defined by WHO criteria.

Conclusions

The high point prevalence of IGT in never treated patients and relatives indicates a shared propensity to Type 2 diabetes mellitus, which may be an inherent part of the illness itself or pre-treatment lifestyle choices. Both patients and their relatives present an ideal cost-effective opportunity to screen for Type 2 diabetes mellitus, as they are both easily identifiable.

Key words – impaired glucose tolerance, schizophrenia.

## Introduction

Type 2 DM is more common in patients with schizophrenia compared to that in an age-dependent general population (1,2). At present it is unclear whether second generation antipsychotic medications or the illness of schizophrenia is primarily responsible for the increased rates of Type 2 DM observed (3). The Clinical Antipsychotic Trials of Intervention Effectiveness, a US National Institute of Mental Health, a multi-site double blind study reported that metabolic disturbances occurred more commonly with certain atypical antipsychotics yet the incidence of Type 2 DM was no different between the agents compared (4). Cohen et al (5) performed oral glucose tolerance tests (OGTTs) in patients with schizophrenia and did not find a difference in the rates of Type 2 DM between the various agents used. Studies conducted in the pre-neuroleptic era support the hypothesis that Type 2 DM may occur more commonly in schizophrenia than expected though these observations are limited by the fact that the definitions for both of these conditions differ from those used today (6). A recently published study has shown that up to 16% of patients with first episode drug naïve schizophrenia have impaired fasting glucose (IFG) (7). Cohn et al (8) have shown using the frequently sampled intravenous glucose tolerance test and minimal model analysis that young drug-free patients with schizophrenia have insulin resistance and are susceptible to Type 2 DM independent of medication usage. Additional evidence comes from the finding that unaffected first-degree relatives of those with schizophrenia have rates of Type 2 DM that are much higher than expected, varying from 17-30% (9,10). Yet, there are two problems with the last two pieces of evidence. Firstly, IFG may miss up to 60% of patients screened for Type 2 DM (11). Secondly, the studies by Mukherjee et al (9) and Lamberti et al (10) relied

on recall alone in order to determine if there was a family history of Type 2 DM. We, therefore, performed a standard oral glucose tolerance test (OGTT) in a group of first episode drug naïve patients with schizophrenia and their unaffected relatives who were free of a diagnosis of Type 2 DM prior to testing.

**Patients & Methods**

Thirty eight (28 males and 10 females) white Caucasians who fulfilled DSM-IV (12) criteria for schizophrenia, an equal number of controls (matched for age, sex, smoking status, alcohol intake and ethnicity) and 44 first degree relatives of the patients (28 males and 16 females) were recruited for this study. The study had Ethics Committee approval and after complete description of the study to the subjects, written informed consent was obtained. All patients were hospitalized at the time of testing. All patients were first episode and drug naive as confirmed by obtaining a collateral history from their family members and primary care physicians. None of the patients had co-morbid DSM-IV (12) diagnoses and all were physically healthy. A family history of Type 2 DM was not an exclusion factor although none of the patients had such a history.

The normal control group, recruited from within the local community, were physically healthy and had no personal or family history of psychiatric or physical illness. A family history of Type 2 DM was not an exclusion factor although none of the controls had such a history. None of the subjects was taking any form of prescribed or over the counter medication. Patients and normal controls were matched in terms of age, sex, smoking habits, social class and alcohol intake. Each

participating relative was not aware of a diagnosis of diabetes, was physically healthy and did not have a psychiatric diagnosis.

All subjects had a full physical examination performed to outrule co-morbid medical illness along with a urinary drug-screen and routine blood tests, which were within normal limits. BMI ($kg/m^2$) and waist circumference (cm) were calculated. Diet and exercise were rated using the DINE questionnaire (13) and the Leisure Time Questionnaire (14), respectively. A Structured Clinical Interview was performed with resultant DSM-IV diagnosis (SCID) (12). The severity of illness was rated in all of the recruited patients by one researcher (LS), using the Brief Psychiatric Rating Scale (BPRS) (15), the Schedule for Assessment of Negative Symptoms (SANS) (16), and the Abnormal Involuntary Movement Scale (AIMS) (17).

All subjects had an antecubital vein cannulated at 0800h after a 12-hour overnight fast. At 0830h an OGTT was performed on all subjects using WHO guidelines (18). Plasma levels of glucose, insulin, and cortisol were taken in the fasting state, 1 hr and 2 hr after the glucose load (75 gm). Samples for fasting lipids, glycosylated haemoglobin (HbA1C), and serum leptin were also obtained. After centrifugation of blood at 2500 rpm for 10 minutes at 4 degrees centigrade, two aliquots of 2mls serum or plasma were placed in cryogenic tubes and flash frozen at –20 degrees centigrade until batch analysis. Insulin resistance was calculated using homeostasis model assessment (HOMA = fasting insulin (μU/ml) x fasting glucose (mmol/L)/22.5) (19). We used the diagnostic values for diabetes and impaired glucose tolerance as recommended by the WHO (17). One-way and two way ANOVAs with appropriate co-variates and post-hoc tests (Tukey's), student's t tests (two tailed) and Pearson's product-moment correlational analyses were used when appropriate. All results are expressed as

mean ± standard deviation (SD) and the data was analyzed by means of Statgraphics version 7.0 (19).

**Results**

Demographic and anthropometric data is given in Table 1. Patients and healthy controls were matched for age and sex, however, relatives were older compared to patients and controls. Patients had lower BMIs than first degree relatives and controls though there were no significant differences in waist circumference or leptin between the 3 groups. Patients and relatives had unhealthy diets as compared to controls. Patients engaged in significantly less mild, moderate and strenous exercise than both the healthy control group and relatives.

The frequency of impaired glucose tolerance (IGT) was 10.5% (n=4) in patients with schizophrenia, 18.2% (n=8) in unaffected relatives and 0.0% in healthy controls ($\chi^2$=4.22, df=2, p<0.05) as defined by WHO criteria (18). The rates of IGT were not significantly different patients and relatives ($\chi^2$=1.92, df=1, p=0.1). One of the relatives had undiagnosed Type 2 DM as compared to no cases in the patient and control groups although this will need to be confirmed as only one value in an asymptomatic individual although this will need to be confirmed as it is a single value in an asymptomatic individual (18). Biochemical and clinical data is given in Table 2. Baseline levels of plasma glucose were the same between the 3 groups, however, a one-way ANOVA indicated that baseline plasma levels of insulin in patients with schizophrenia and relatives, though similar to eachother, were significantly higher than in controls. A repeated measures two-way ANOVA to compare glucose and insulin responses over time between the 3 groups yielded a significant group by time

interaction. Post hoc tests (Tukeys) indicated that plasma levels of glucose and insulin in patients and relatives, though similar to eachother, were significantly higher than in healthy controls 2 hours following the administration of the oral glucose ($p<0.01$). Patients and relatives had similar levels of insulin resistance as measured by HOMA-IR though these were significantly higher than those found in healthy controls. The relatives had higher total cholesterol than the other 2 groups. Serum cortisol was significantly higher in patients as compared to relatives and controls. Introducing age, BMI, saturated fat intake, unsaturated fat intake, fibre intake, exercise taken or cortisol levels as co-variates did not alter the levels of significance of 2 hr plasma levels of glucose, baseline levels of insulin or indeed 2 hr levels of plasma insulin in patients ($p<0.01$). Similarly, in relatives introducing sex, age, BMI, saturated fat intake, unsaturated fat intake, fibre intake, exercise taken, total cholesterol or cortisol levels as co-variates did not alter the levels of significance of 2 hr plasma levels of glucose, baseline levels of insulin or indeed 2 hr levels of plasma insulin ($p<0.01$).

**Discussion**

To the best of our knowledge this is the first study to conduct standard OGTTs in non-obese first episode drug naïve patients with schizophrenia and unaffected family members and demonstrate that the rates of IGT were higher in relatives (18.5%) and patients (10.2%) as compared to patient-matched controls. Both patients and relatives had higher levels of insulin at baseline and at 2 hr and were insulin resistant as compared to controls. None of the 3 cohorts was obese and patients were lighter than either relatives or controls.

This paper differs from our earlier work (7), though agrees with two other studies that recruited first episode patients with schizophrenia (21,22) in that we found no evidence of fasting hyperglycaemia a fact which may be accounted for by the older age of our earlier patient cohort. In terms of point prevalence, studies conducted in the UK indicate that the rates of IGT range from 4.1 to 16.7%, however those studied, were over 40 years of age and there was a clear relationship between being older, obese and an increasingly sedentary lifestyle (23). Studying an Australian population from a mostly Europid background, Dunstan et al (24) report an IGT rate of 5.7% in an age group, 25-34 years, which is comparable to our three cohorts. An Irish study has reported rates of IGT in a community sample aged 40 years and over to be 2.7% (25). Our findings of IGT rates of 10.2% (patients) (mean age ± SD = 25.2 ± 5.6 yrs) and 18.5% (relatives) (mean age ± SD = 33.7 ± 10.8 yrs) are clearly higher than what has been documented thus far in either the same country of origin (2.7%) (25) or comparable age group (5.7%) (24). This study shows that patients with schizophrenia at the time of diagnosis and their psychiatrically-well first degree relatives have IGT and are at higher risk for developing Type 2 DM. From a clinical perspective, screening for diabetes is an expensive procedure whose yield is not always optimal (26). This study would indicate that both groups are ideal screening populations as patients with schizophrenia and their relatives are relatively easy to identify and appear to be at high risk of developing Type 2 DM.

From a mechanistic perspective, IGT is associated with high triglyceride levels, ethnicity, a positive family history of type 2 diabetes, increasing age, obesity (central and total) and physical inactivity (27). The first two associations are unlikely to explain our findings as none of the subjects had high levels triglycerides and all

subjects were white Caucasians. Probandwise concordance rates for IGT are 0.63 in monozygotic and 0.43 dizygotic twin pairs giving a heritability estimate of 61% (28) which concurs with our observations of IGT in unaffected first degree relatives. Obesity is another major determinant of IGT (29). Yet none of the three groups was obese; in fact, patients had a lower BMI than did controls and relatives. Furthermore, the three groups did not differ in terms of their leptin levels indicating that they had similar amounts of total fat mass. However, the location of the fat may explain our findings, as there is a clear and well-documented relationship between IGT and visceral obesity (29,30). Two previous studies have documented that first episode drug naïve patients with schizophrenia have between 3 to 3.4 times more visceral fat than appropriately matched age-, sex- (31) and BMI matched controls (32) providing some evidence to support this hypothesis. Finally, both patients and family members were insulin resistant indicating that though insulin resistance is a heterogenous condition which may have a hereditary component that is linked to visceral obesity (33).

Studies have demonstrated that schizophrenia is associated with poor lifestyle choices (34) and our study confirms this observation in that both patients and relatives had a diet rich in saturated fats and poor in fibre though only patients took less exercise than did relatives and controls. Low levels of physical activity appear to be associated with the development of IGT (35). However, the same may not be true of a high saturated fat intake and IGT or indeed, insulin sensitivity or secretion (36). Therefore, the lack of exercise but not the low fibre-high saturated fat diet, may in part explain the higher rates of IGT observed in patients in our study. The same does not appear to hold true

for relatives as they took similar amounts of exercise to controls though their diet was worse in terms of saturated fat intake but similar in terms of fibre intake to controls.

Whether the 'stress' of acute psychosis may be associated with reduced β-cell function and insulin sensitivity leading to higher than expected levels of IGT has been a point of dispute (37). Though cortisol levels were high in patients with schizophrenia there was no positive correlation between this endocrine parameter or BPRS (an indicator of acute psychosis) and either glucose or insulin levels. Furthermore, the prevalence of IGT was numerically higher in the first degree relatives with schizophrenia (though this did not reach statistical significance) however, their cortisol levels were no different to controls. All of these findings would indicate that acute elevations of cortisol and therefore, acute stress may not be directly responsible for our findings. Finally, medication may induce hyperglycaemia and hyperinsulinaemia, though this cannot explain our findings, as our patients were drug naïve and first episode (3). Furthermore, their first-degree relatives were also drug naïve and had never suffered from any psychiatric illness.

**References**

1. Adams PF, Marano MA. Current estimates for the national health interview survey 1994. National Centre for Health Statistics, *Vital Health Stat* 1995; **10**: 193.

2. Subramaniam M, Chong SA, Pek E. Diabetes mellitus and impaired glucose tolerance in patients with schizophrenia. *Can J Psychiatry* 2003; **48**: 345-7.

3. American Diabetic Association. Consensus Development Conference on Antipsychotic Drugs and Obesity and Diabetes. *Diabet Care* 2004; **27**: 596-601.

4. Cohen D, Stolk RP, Grobbee DE, Gispen-de Wied CC. Hyperglycemia and diabetes in patients with schizophrenia or schizoaffective disorders. *Diabet Care* 2006; **29**: 786-91.

5. Lieberman JA, Stroup TS, McEvoy JP, Swartz MS, Rosenheck RA, Perkins DO, Keefe RS, Davis SM, Davis CE, Lebowitz BD, Severe J, Hsiao JK; Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. *N Engl J Med* 2005; **353**: 1209-23.

6. Ryan MCM, Thakore JH. Physical consequences of schizophrenia. *Life Sci* 2002; **71**: 239-257.

7. Ryan MCM. Collins P, Thakore JH. Impaired Fasting Glucose and Elevation of Cortisol in Drug-Naïve First-Episode Schizophrenia. *Am J Psychiatry* 2003; **160**: 284-289.

8. Cohn TA, Remmington G, Zipursky RB, Azad A, Connolly P, Wolever MS. Insulin resistance and Adiponectin levels in drug-free patients with schizophrenia: A preliminary report. *Can J Psychiatry* 2006; **51**: 382-386.

9. Mukherjee S, Schnur DB, Reddy R. Family history of type 2 diabetes in schizophrenic patients. *Lancet* 1989; **1(8636)**: 495.

10. Lamberti JS, Crilly JF, Maharaj K, Olson D, Wiener K, Dvorin S, Costea GO, Bushey MP, Dietz MB. Prevalence of diabetes mellitus among outpatients with severe mental disorders receiving atypical antipsychotic drugs. *J Clin Psychiatry* 2004; **65**: 702-6.

11. Tai ES, Lim SC, Tan BY, Chew SK, Heng D, Tan CE. Screening for diabetes mellitus--a two-step approach in individuals with impaired fasting glucose improves detection of those at risk of complications. *Diabet Med* 2000; **17**: 771-5.

12. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders 4th edn. Washington, DC: *American Psychiatric Association* 1994.

13. Roe L, Strong C, Whiteside C, Neil A, Mant D. Dietary intervention in primary care: validity of the DINE method of diet assessment. *Fam Pract* 1994; **11**: 375-381.

14. Godin G, Shephard RJ. A simple method to assess behavior in the community. *Can J Appl Sports Sci* 1985; **10**: 141-146.

15. Overall JE, Gorham DR. The Brief Psychiatric Rating Scale. *Psychol Rep* 1962; **10**: 799-812.

16. Andreasen NC. The Scale for the Assessment of Negative Symptoms (SANS). Iowa City: The University of Iowa, 1983.

17. Guy W (Ed). ECDEU Assessment Manual for Psychopharmacology: Publication ADM 76-338. Washington, DC, *US Department of Health, Education and Welfare*, 1976: 534-537.

18. Alberti KG, Zimmet PZ. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of Diabetes Mellitus, provisional report of a WHO commission. *Diabet Med* 1998; **15**: 539-553.

19. Mathews DR, Hosker, JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC. Homeostasis model assessment: insulin resistance and beta cell function from fasting plasma glucose and insulin concentrations in man. *Diabetologia* 1985; **28**: 412-419.

20. Statistical Graphics Corporation. New York: *Statgraphics* v.7.0; New York: 1993.

21. Zhang ZJ, Yao ZJ, Liu W, Fang Q, Reynolds GP. Effects of antipsychotics on fat deposition and changes in leptin and insulin levels: Magnetic resonance imaging study of previously untreated people with schizophrenia. *Br J Psychiatry* 2004; **184**: 58-62.

22. Arranz B, Rosel P, Ramirez N, Duenas R, Fernandez P, Sanchez JM, Navarro MA, San L. Insulin resistance and increased leptin concentrations in noncompliant schizophrenia patients but not in antipsychotic-naive first-episode schizophrenia patients. *J Clin Psychiatry* 2004; **65**: 1335-42.

23. Williams DR, Wareham NJ, Brown DC, Byrne CD, Clark PM, Cox BD, Cox LJ, Day NE, Hales CN, Palmer CR, et al. Undiagnosed glucose intolerance in the community: the Isle of Ely Diabetes Project. *Diabet Med* 1995; **12**: 30-5.

24. Dunstan DW, Zimmet PZ, Welborn TA, De Courten MP, Cameron AJ, Sicree RA, Dwyer T, Colagiuri S, Jolley D, Knuiman M, Atkins R, Shaw JE. The rising prevalence of diabetes and impaired glucose tolerance: the Australian Diabetes, Obesity and Lifestyle Study. *Diabet Care* 2002; **25**: 829-834.

25. Smith SM, Holohan J, McAuliffe A, Firth RG. Irish diabetes detection programme in general practice. *Diabet Med* 2003; **20**: 717–722.

26. Hoerger TJ, Harris R, Hicks KA, Donahue K, Sorensen S, Engelgau M. Screening for type 2 diabetes mellitus: a cost-effectiveness analysis. *Ann Intern Med* 2004; **140**: 689-99.

27. Harris MI, Flegal KM, Cowie CC, Eberhardt MS, Goldstein DE, Little RR, Wiedmeyer HM, Byrd-Holt DD. Prevalence of diabetes, impaired fasting glucose, and impaired glucose tolerance in U.S. adults. The Third National Health and Nutrition Examination Survey, 1988-1994. *Diabet Care* 1998; **21**: 518-24.

28. Poulsen P, Kyvik KO, Vaag A, Beck-Nielsen H. Heritability of type II (non-insulin-dependent) diabetes mellitus and abnormal glucose tolerance - a population-based twin study. *Diabetologia* 1999; **42**: 139-45.

29. Ohlson LO, Larsson B, Svardsudd K, Welin L, Wilhemsen L, Bjorntorp P, Tibblin G. The influence of body fat distribution on the incidence of diabetes mellitus – 13.5 years of follow up. *Diabetes* 1985; **34**: 1055-1058.

30. Pascot A, Despres JP, Lemieux I, Bergeron J, Nadeau A, Prud'homme D, Tremblay A, Lemieux S. Contribution of visceral obesity to the deterioration of the metabolic risk profile in men with impaired glucose tolerance. *Diabetologia* 2000; **43**: 1126-35.

31. Thakore JH, Mann JN, Vlahoos J, Martin A, Reznek R. Increased visceral fat distribution in drug-naïve and drug-free patients with schizophrenia. *Int J Obes Relat Metab Disord* 2002; **26**: 137-41.

32. Ryan MCM, Flanagan S, Kinsella U, Keeling F, Thakore JH. Atypical antipsychotics and visceral fat distribution in first episode, drug-naive patients with schizophrenia. *Life Sci* 2004; **74**: 1999-2008.

33. Despres JP. Lipoprotein metabolism in visceral obesity. *Int J Obes* 1991; **15** (Suppl 2): 45-52.

34. McCreadie RG; Scottish Schizophrenia Lifestyle Group. Diet, smoking and cardiovascular risk in people with schizophrenia: descriptive study. *Br J Psychiatry* 2003; **183**: 534-9.

35. Mohan V, Shanthirani CS, Deepa R. Glucose intolerance (diabetes and IGT) in a selected South Indian population with special reference to family history, obesity and lifestyle factors--the Chennai Urban Population Study (CUPS 14). *J Assoc Physicians India* 2003; **51**: 771-7.

36. Larsson H, Elmstahl S, Berglund G, Ahren B. Habitual dietary intake versus glucose tolerance, insulin sensitivity and insulin secretion in postmenopausal women. *J Intern Med* 1999; **245**: 581-91.

37. Thakore JH. Acute Stress Is Not Responsible for Glucose Dysregulation in Chronic Schizophrenia: Response to Shiloah et al. *Diabet Care* 2003; **26**: 2967-2968

**Table 1: Demographic and anthropometric data**

| Characteristic | **Patients** | **Controls** | **Relatives** | |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| **Number (male / female)** | 38 (28/10) | 38 (28/10) | 44 (26/18) | |
| **Age** | 25.2 ± 5.64 | 25.2 ± 5.69 | 33.7 ± 10.8 | (F=6.76, df=2, 117, p<0.001) |
| **BMI** | 22.8 ± 3.1 | 24.2 ± 2.9 | 23.9 ± 2.6 | (F=4.43, df=2, 117, p< 0.05) |
| **Waist (cm)** | 84.9 ± 10.2 | 86.2 ± 7.9 | 82.0 ± 7.9 | p NS |
| **Saturated fat u/w** | 39.5 ± 11.3 | 26.8 ± 7.8 | 51.1 ± 9.8 | (F=8.24, df=2, 117, p<0.001) |
| **Unsaturated fat u/w** | 7.89 ± 3.76 | 9.6 ± 2.24 | 15.0 ± 5.78 | (F=3.9, df=2, 117, p<0.05) |
| **Fibre** | 21.9 ± 7.2 | 31.7 ± 7.06 | 24.8 ± 6.9 | (F=-6.9, df=2. 117, p<0.001) |
| **Exercise Mild e/w** | 3.9 ± 2.1 | 7.7 ± 3.2 | 7.4 ± 3.8 | F=6.7, df =2, 117, p < 0.01) |
| **Exercise Mod. e/w** | 0.08 ± 0.3 | 1.55 ± 1.78 | 1.25 ± 1.5 | F=5.4, df =2, 117, p < 0.01) |
| **Exercise Vig. e/w** | 0.0 | 0.18 ± 0.56 | 0.18 ± 0.54 | F=7.1, df = 2, 117, P < 0.01) |

**u/w** denotes units per week.

**e/w** denotes episodes per week

**Table 2: Biochemical & Clinical data**

| Clinical variable | Patients | Controls | Relatives | |
|---|---|---|---|---|
| **Fasting glucose** | 4.65 ± 0.54 | 4.54 ± 0.48 | 4.44 ± 0.57 | p NS |

| | | | | |
|---|---|---|---|---|
| **mmol/L** | | | | |
| **2 hr glucose mmol/L** | 6.01 ± 1.69 | 4.51 ± 0.81 | 5.68 ± 1.77 | (F=6.1, df=2, 111, p<0.001) |
| **HbA1C%** | 5.3 ± 0.4 | 5.2 ± 0.3 | 5.3 ± 0.3 | p NS |
| **Fasting insulin mmol/L** | 38.75 ± 20.1 | 27.27 ± 12.2 | 40.18 ± 23.9 | (F=3.7, df=2, 117 , p<0.01) |
| **2 hr insulin pmol/L** | 205.2 ± 124.8 | 77.5 ± 36.6 | 160.0 ± 116.2 | (F=8.5, df=2, 111, p<0.001) |
| **HOMA IR** | 1.15 ± 0.7 | 0.78 ± 0.3 | 1.15 ± 0.8 | (F=3.2, df=2, 117, p<0.05) |
| **Cortisol µg/dl** | 12.3 ± 4.3 | 8.5 ± 2.4 | 7.9 ± 1.2 | (F=5.87, df=2, 117, p<0.001) |
| **Total cholesterol mmol/L** | 4.32 ± 0.9 | 4.40 ± 0.6 | 4.71 ± 0.7 | (F = 3.22, df = 2,117, p<0.05) |
| **HDL mmol/L** | 1.15 ± 0.3 | 1.21 ± 0.2 | 1.31 ± 0.3 | p NS |
| **LDL mmol/L** | 2.86 ± 0.9 | 2.81 ± 0.6 | 2.54 ± 1.2 | p NS |
| **Triglycerides nmol/L** | 1.26 ± 0.7 | 1.07 ± 0.45 | 1.41 ± 0.5 | p NS |
| **Leptin nmol/L** | 3.71 ± 2.3 | 3.56 ± 3.2 | 3.45 ± 1.6 | p NS |
| **BPRS** | 44.4 ± 9.0 | Not applicable | Not applicable | |
| **AIMS** | 0.39 ± 1.02 | Not applicable | Not applicable | |
| **SANS** | 0.15 ± 0.49 | Not applicable | Not applicable | |