Disclaimer

- Talks
- Facilitator of the CTF Exam Prep Course
Aims

- Should psychiatrists be bothered about the metabolic syndrome?
- Why should we care?
- What action do we take?
IDF Consensus world wide definition of metabolic syndrome 2006

- Raised Serum Triglyceride
- Reduced Serum HDL
- Central Obesity
- Hypertension
- Raised Fasting plasma glucose
Prevalence of Metabolic Syndrome

<table>
<thead>
<tr>
<th></th>
<th>Metabolic syndrome prevalence</th>
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<tbody>
<tr>
<td>general population</td>
<td>10</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>45</td>
</tr>
<tr>
<td>Bipolar disorder</td>
<td>25</td>
</tr>
<tr>
<td>Major Depression</td>
<td>12</td>
</tr>
<tr>
<td>Anxiety</td>
<td>8</td>
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</tbody>
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- Bipolar disorder
- Major Depression
- Anxiety

- General population: 10
- Schizophrenia: 45
- Bipolar disorder: 25
- Major Depression: 12
- Anxiety: 8
Monitoring Practices

- **UNITE Global survey** - (McIntyre R, J clin Psych 2009)
  - Metabolic consequences of psychotropic medication are the most concerning aspect of medication treatment for patients, contributing to perceived morbidity, quality-of-life reduction, and reduced satisfaction with care.

- **Survey of 500 Psychiatrists (U.S)** (Suppes T, Psychopharmacol Bull 2007)
  - Nearly all respondents have metabolic concerns with medical therapies used to treat bipolar disorder.
  - Many now routinely monitor weight and other metabolic parameters.
  - Most have referred patients for medical management and adjusted bipolar therapies due to metabolic abnormalities.

- **Survey of 718 European Psychiatrists** (Bauer M, Eur Psych 2008)
  - European psychiatrists view metabolic syndrome as highly prevalent in the general population and in bipolar patients.
  - 2/3rds have changed their management of bipolar patients because of metabolic health concerns.

- **Prospective study of 106 patients in North East England** (Mackin P et al, BMC Psychiatry 2007)
  - Poor monitoring Practices with worsening Physical health
Childhood obesity. Don’t take it lightly.

Food Stamps can help. Call 1-888-328-3483 to see if you qualify.

my kinda shoppin’ spree

Dollar McDonald Menu
Does Fat make us Fat??

CRAP
Now Low Fat!
Insulin-dependent lipases in fat cells are normally inhibited by insulin.

As insulin resistance worsens, inappropriately high levels of lipolysis lead to the release of excess amounts of free fatty acids that are hepatically transformed into TG.

The TG: HDL ratio is a sensitive marker of insulin resistance.

*Meyer JM, Act Psych Scand, 2009*
The Insulin Resistance Syndrome

Clinical Manifestations

- Central Obesity
- Glucose Intolerance
- Atherosclerosis
- Hypertension
- First degree relative with type 2 diabetes
- History of gestational diabetes
- Polycystic ovary syndrome
- Acanthosis nigricans

Biomechanical Abnormalities

<table>
<thead>
<tr>
<th>Carbohydrate</th>
<th>Lipid</th>
<th>Fibrinolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose intolerance</td>
<td>High TG</td>
<td>Increased PAI-1</td>
</tr>
<tr>
<td>Hyperinsulinemia</td>
<td>Low HDL-C</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>Small, dense LDL particles</td>
<td></td>
</tr>
</tbody>
</table>
But, what’s it got to do with mental illness??

- Tyrosine Hydroxylase/IGF Growth Factor
- Chromosome 11
Insulin and cognitive function

Normal Insulin Metabolism:
- Glucose enters the cell via insulin.
- Functioning insulin receptor site.
- Normal Intracellular Glucose.

Insulin Resistance:
- Glucose not effectively entering the cell due to malfunctioning insulin receptor site.
- Low Intracellular Glucose.
Prevalence of CV risk factors in Schizophrenia and bipolar disorder

Newcomer J, J Clin Psych 2006
Largest family study

9 million individuals from more than 2 million families over a 30-year period, showed that first-degree relatives of individuals with either schizophrenia (35,985 individuals) or bipolar disorder (40,487) had a significantly increased risk for these disorders.

Full siblings were 9 times more likely than the general population to have schizophrenia and 8 times more likely to have bipolar disorder

Implications for the newer diagnostic classifications

Craddock N et al, BJPych 2005
Liechtenstein P et al, Lancet 2009
The Metabolic highway
Schizophrenia and Metabolic syndrome

- Individuals with schizophrenia have 3× intra-abdominal fat compared to controls matched for age, gender and lifestyle (*Ryan M et al. Life Sciences 2004*).

- Individuals with schizophrenia make poor dietary choices characterised by diet high in saturated fat and lower intake of fibre (*McCreadie R et al BMJ 1998*).


- Mean insulin sensitivity was 42% lower in a Canadian cohort of drug naïve schizophrenia patients.

- Neuroleptic naïve patients with schizophrenia showed pre treatment hepatic insulin resistance (*Van Nimwegen LJM et.al, J Clin Endocrinol Metab 2008*).
Mood Disorders and Metabolic Syndrome

- Proposal that the pathophysiology of depressive disorders to include metabolic networks as explanatory variables

- Individuals with bipolar disorder are more centrally obese than control group, which is exacerbated by antipsychotic drugs (Elmslie J et al., J Clin Psychiatry 2000)

- Depression is associated with Type II Diabetes (Musselman D et al., Biol Psychiatry 2003)

- Bipolar disorder may be an independent risk factor for type II diabetes (Regenold W et al., J Affect disorder 2002)
Increased Mortality Rates for Medical Disorders in Mental Illness

- 50% increased risk of death from medical causes in schizophrenia and 20% shorter lifespan

- Bipolar and unipolar affective disorders also associated with higher SMRs from medical causes
  - 1.9 males/2.1 females in bipolar disorder
  - 1.5 males/1.6 females in unipolar disorder

- Cardiovascular mortality in schizophrenia increased from 1976-1995, with greatest increase in SMRs (8.3 males/5.0 females) from 1991-1995.

SMR = standardized mortality ratio (observed/expected deaths)

*Harris et al. Br J Psychiatry, 1998*
*Osby et al. Arch Gen Psychiatry. 2001*
*Osby et al. BMJ. 2000.*
Causes of Death in patients with SMI’s

Leading causes of death (n= 608) among 20,018 persons admitted to an Ohio public mental health hospital between 1998 and 2002

- Heart disease: 21
- Suicide: 18
- Accidents: 14
- Malignant neoplasms: 7
- Not classified: 5
- Chronic LRD: 5
- Diabetes Mellitus: 3
- Pneumonia: 3
- Cerebrovascular disease: 2
- Assault: 2

Miller BJ et al. Psychiatr Serv.2006
Role of Antipsychotics

Allison DB et al, Am J Psych 1999
Weight gain in CATIE trial

Lieberman JA et al NEJM 2005
Schizophrenia is an independent risk factor for type 2 diabetes and type 2 diabetes has been associated with typical and atypical antipsychotics. (Bushe C & Leonard B. Br J Psych 2004)

Antipsychotics increase lipids and blood glucose independent of adiposity (De Leon J et al. Schizophr Res 2007, Haupt DW & Newcomer JW Arch Gen Psychiatry 2002)
Causes of Weight gain with Antipsychotics

- Effect on energy expenditure
  - Leptin
  - Ghrelin
  - Orexins
  - H1 receptor
  - Serotonin antagonism
Antipsychotics, Glucose and Lipids

- Mechanism of Hyperinsulinaemia, Insulin Resistance and Triglyceride elevation has not been clearly identified
- Rapid reversal in parameters following discontinuation of antipsychotics
- Role of Hypothetical Receptor X
- M3 Antagonism

Adapted from Stahl S et al, Acta Psychiatr Scandinavica 2009
**Drug Naive patient**

- **Baseline Monitoring**
  - Personal and Family history of obesity, DM, Dyslipedemia, HT or CVD
  -Weight and Height (Calculate BMI)
  -Waist circumference at the level of umbilicus
  -Blood Pressure, Fasting Blood Glucose, Fasting Lipids (HDL, LDL, Cholesterol and TGL's)

- **Nutritional and Physical activity counselling**
  - Health care professional with expertise in weight management if obese or overweight or using SGA with significant weight gain potential
  - Educate patient, patient’s family or care giver of signs and symptoms of diabetes and encourage them to monitor these.

**Follow up**

- Monitor BMI and waist-hip ratio every visit or every 3 months (AUDG)
- Monitor weight at 4, 8 and 12 weeks after initiating and changing SGA therapy and 3 monthly thereafter (ADA)
- Blood glucose, blood pressure and lipid profile 3 months after initiation of AP’s, annually thereafter (ADA)
- Blood glucose immediately after starting or changing antipsychotic medication 3 and 6 monthly thereafter (AUDG)
- Blood pressure and lipid profile every 6 months

- **Weight gain > 5%**
  - Symtomatic hyperglycaemia or raised blood glucose
  - Switch antipsychotic gradual cross-titration (ADA)

*Rege S, ANZJP 2008*
Dualism
Increased appetite
Weight gain
↑TGs
Insulin resistance
Hyperinsulinemia
Beta cell failure
Prediabetes
Diabetes
Cardiovascular events
Premature death and loss of 20-30 years of life span

Antipsychotic action

Weight gain and antipsychotics: Major cause of cardiometabolic risk or just the first step down the slippery slope?
Treatment of the Metabolic Syndrome

- Treat the obesity
  - Healthy eating and physical activity
- Treat the glucose intolerance and diabetes
- Treat the dyslipidemia
- Treat the hypertension
- Treat the prothrombotic state
- Stop smoking
Diabetes
Obesity and increased BMI
Hyperinsulinemia
Insulin resistance
Beta cell failure
Prediabetes
Cardiovascular events
Triglycerides
Increased appetite
Weight gain
Premature death and loss of 20-30 years of normal life span

Where on the METABOLIC HIGHWAY should psychopharmacologists monitor antipsychotics?

Monitor antipsychotic action

Beware: Cardiovascular risk ahead

Adapted from Stahl S, 2009
CVD risk calculator

http://www.cvdcheck.org.au/
Drug therapy indicated for those with >10-15% risk of a CVD event in the next 5 years

If Metabolic syndrome present / family history of premature CHD

Statin is recommended first line treatment
  Monitor CK at 3 and 6 months
  Monitor LFT’s
  Fibrates + statins
Management of Type 2 diabetes (NDSS)

Symptoms of diabetes and random glucose >11mmol/L
Fasting plasma glucose ≥ 7mmol/L

Nutrition, Physical activity

Insufficient control

Start metformin

No contraindication for metformin

Contraindication

sulfonylurea
Management of Weight Gain

Pharmacological Management
- Orlistat
- Sibutramine
- Rimonabant
- H2 Antagonists
- Metformin
- Others (topiramate, antidepressants)
- Switching

Psychological management
- Cognitive behavioural therapy
- Behavioural therapy
- Nutritional interventions
- Combination therapy

Rege S, ANZJP, 2009
Summary of Management strategies

- Bridging the Gap between Psychiatry and Medicine

- Psychiatrist to initiate and familiarise oneself with treatment of Hyperlipidemia and Type 2 diabetes

- Psychological treatments like lifestyle modifications, nutritional interventions and behavioural treatments are beneficial in promoting weight loss but need long term input.

- Behavioural strategies and lifestyle modification programs are resource intensive.

- Confusion amongst health professionals about responsibility in monitoring and treatment.

Rege S, ANZJP 2008
What do we aim for?

- BGL – 4-6 mmol/L
- HbA1C - ≤ 7%
- LDL-C - <2.5mmol/L
- Total cholesterol < 4.0 mmol/L
- HDL-C >1.0 mmol/L
- Triglycerides <1.5 mmol/L
- BP - ≤ 130/80 mm/hg
Impact of interventions

- Lowering blood cholesterol by 10% decreases risk of CHD by 30%.
- Lowering BP by 6mm/hg (>90 mm/hg in diastolic) can reduce risk of CHD by 16% and stroke by 42%.
- Cigarette smoking cessation reduces risk of CHD by 50% even in the elderly.
- Maintaining a BMI of < 25 results in a 35-55% reduction in CHD.
- Active lifestyle that includes one 20 minute walk per day results in a 35-55% reduction in CHD.
Psychiatrist to take on primary care role with regards to monitoring and initial prescribing

Shared decision making model between patient, carers and clinicians

Commitment to monitoring of metabolic parameters with explicit identification of responsible individual/team

Adoption of clear structured protocols that involves greater collaboration between health professionals from psychiatric and medical specialist services.
Thank You !!

Presentation can be found on
www.ctfcourse.com