Personalized health in psychiatry:
the example of obesity and metabolic syndrome

Prof Chin Eap
Unit of Pharmacogenetics and Clinical Psychopharmacology
Centre for Psychiatric Neurosciences
Psychiatry Department, University Hospital
University of Lausanne
SWITZERLAND
Cardiovascular diseases (CVD) : Greater contributors to mortality than suicide in psychiatric populations!

In psychiatric patients, metabolic disorders lead to an estimated reduced life expectancy of about 15 to 25 years.
Genes, illness and environment: Weight gain and metabolic syndrome induced by psychotropic drugs

Several psychotropic drugs can induce severe weight gain and/or metabolic disorders
Clinical and pharmacogenetic study of metabolic syndrome induced by psychotropic drugs

Ongoing study, presently about 1500 patients included
Several genes found to be strongly associated with weight gain and/or other symptoms of the metabolic syndrome (e.g. diabetes, dyslipidemia) during psychotropic drug treatment

Genes and weight gain:
One example: CRTC1

Use of clinical data (weight monitoring)
Early weight gain as a predictor for important long term weight gain during psychotropic treatment:

Combination of extensive genetic testings (POLYGENIC RISK SCORES) with clinical factors to predict weight gain BEFORE treatment
CRTC1 and weight gain

CRTC1: CREB regulated transcription co-activator 1

Wild Type Knock Out

CRTC1 knock-out mice develop obesity

Target genes: BDNF, CART, KISS1, PEPCK

CRTC1: transcriptional regulation factor involved in energy balance and obesity

CRTC1 and BMI in 3 psychiatric samples

Choong et al., JAMA Psychiatry 2013;70(10):1011-1019

CRTC1 gene polymorphism strongly associated with weight, in particular in women: Women <45-years: 3.9 kg/m² difference of BMI between different genotypes

Influence of CRTC1 on BMI confirmed by a GWAS study (Lu et al., Nature Communications 2016)
>5% of weight increase at one month best predictor of long term weight change (>15% at 3 months and >20% at 1 year)

Worsening of metabolic parameters (in particular dyslipidemia) at one year is more important in patients gaining >5% weight in the first month.

F Vandenberghe et al., J Clinical Psychiatry 2015 (76):11:e1417-e1423
Prediction of weight increase based on GENETIC and CLINICAL factors

- Polygenic risk scores (> 20 genes)
- Plus clinical factors (age, baseline BMI etc) to identify patients at risk for rapid weight gain BEFORE starting the treatment

F Vandenberghe et al., Pharmacogenetics & Genomics (in press)
Evolution of weight over the first 3 months of treatment in patients predicted to have >5% WG or ≤5% WG at one month using CLINICAL and GENETIC data

F Vandenberghe et al., Pharmacogenetics & Genomics (in press)
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