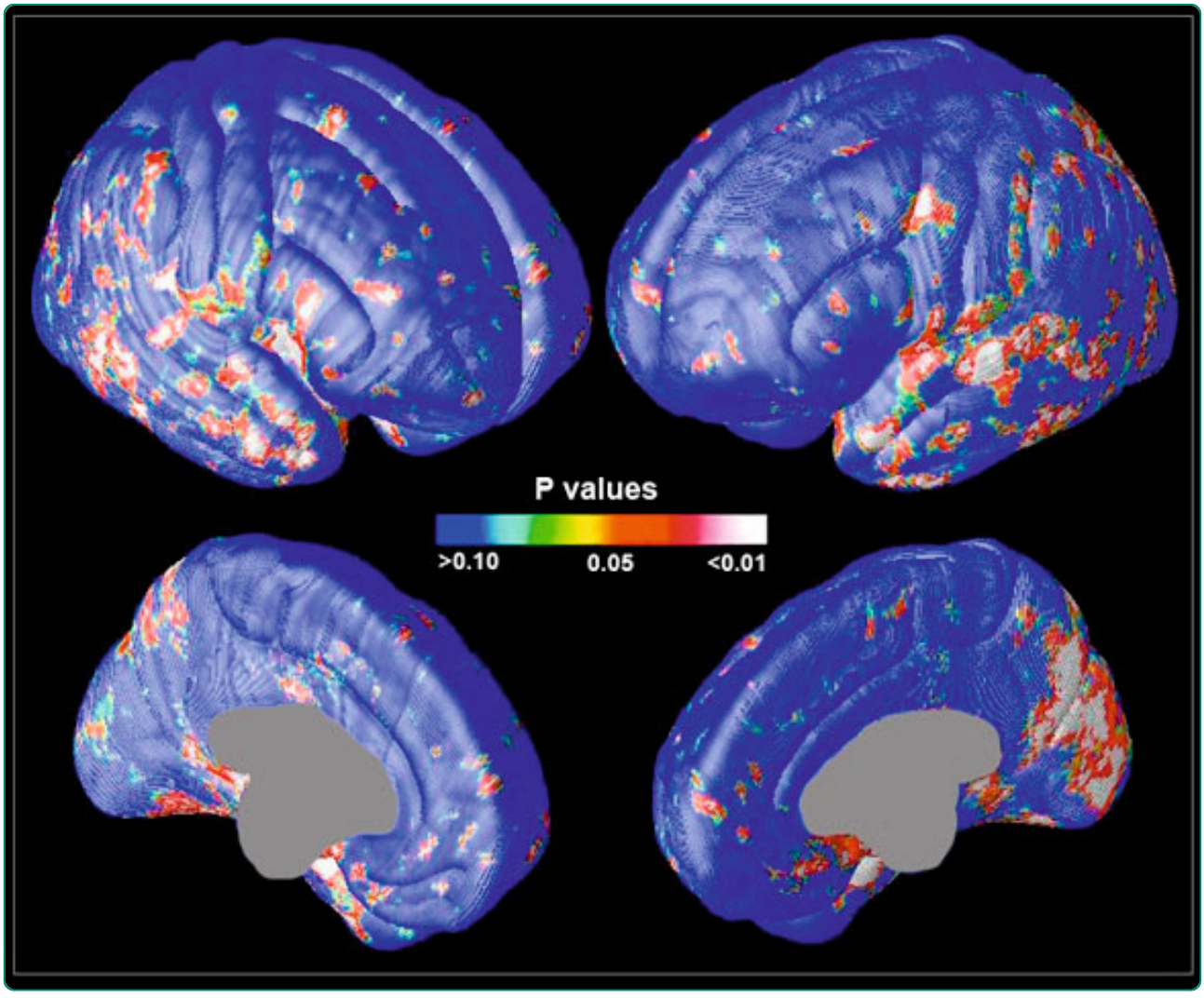
Genome Medicine



Phospholipids and insulin resistance in psychosis: a lipidomics study of twin pairs discordant for schizophrenia

Orešič *et al.*

BioMed Central

Orešič *et al. Genome Medicine* 2012, **4**:1
http://genomemedicine.com/content/4/1/1 (18 January 2012)

Genome Medicine

RESEARCH Open Access

Phospholipids and insulin resistance in psychosis: a lipidomics study of twin pairs discordant for schizophrenia

Matej Orešič[1*], Tuulikki Seppänen-Laakso[1], Daqiang Sun[2], Jing Tang[1], Sebastian Therman[3], Rachael Viehman[2], Ulla Mustonen[3], Theo G van Erp[4], Tuulia Hyötyläinen[1], Paul Thompson[5], Arthur W Toga[5], Matti O Huttunen[3], Jaana Suvisaari[3], Jaakko Kaprio[3,6], Jouko Lönnqvist[3,7] and Tyrone D Cannon[2,8]

Abstract

Background: Several theories have been proposed to conceptualize the pathological processes inherent to schizophrenia. The 'prostaglandin deficiency' hypothesis postulates that defective enzyme systems converting essential fatty acids to prostaglandins lead to diminished levels of prostaglandins, which in turn affect synaptic transmission.

Methods: Here we sought to determine the lipidomic profiles associated with schizophrenia in twin pairs discordant for schizophrenia as well as unaffected twin pairs. The study included serum samples from 19 twin pairs discordant for schizophrenia (mean age 51 ± 10 years; 7 monozygotic pairs; 13 female pairs) and 34 age and gender matched healthy twins as controls. Neurocognitive assessment data and gray matter density measurements taken from high-resolution magnetic resonance images were also obtained. A lipidomics platform using ultra performance liquid chromatography coupled to time-of-flight mass spectrometry was applied for the analysis of serum samples.

Results: In comparison to their healthy co-twins, the patients had elevated triglycerides and were more insulin resistant. They had diminished lysophosphatidylcholine levels, which associated with decreased cognitive speed.

Conclusions: Our findings may be of pathophysiological relevance since lysophosphatidylcholines, byproducts of phospholipase A2-catalyzed phospholipid hydrolysis, are preferred carriers of polyunsaturated fatty acids across the blood-brain barrier. Furthermore, diminishment of lysophosphatidylcholines suggests that subjects at risk of schizophrenia may be more susceptible to infections. Their association with cognitive speed supports the view that altered neurotransmission in schizophrenia may be in part mediated by reactive lipids such as prostaglandins.

Background

Several theories have been proposed to conceptualize the pathological processes inherent to schizophrenia, among others altered neurotransmission, autoimmune dysfunction and dysregulation of inflammation [1,2]. The phospholipid hypothesis suggests that deficient uptake or excessive breakdown of membrane phospholipids or changes in membrane phospholipid composition may be associated with schizophrenia [3]. The hypothesis is supported by studies finding lipid abnormalities both in postmortem gray and white matter samples and from peripheral red blood cells of patients with schizophrenia [4]. Moreover, phospholipase A2 activity is increased particularly in the first-onset patients with schizophrenia and associates with structural brain changes, particularly in the prefrontal cortex and thalamus [5]. Nevertheless, the evidence for the phospholipid hypothesis is not conclusive [6]. Prior to the phospholipid hypothesis, a prostaglandin deficiency hypothesis was proposed [7]. Phospholipid abnormalities and prostaglandin deficiency may be related since prostaglandins are synthesized via hydrolysis of phosphatidylcholine (PC) by action of phospholipase A2,

* Correspondence: matej.oresic@vtt.fi
[1]VTT Technical Research Centre of Finland, Tietotie 2, Espoo, FI-02044 VTT, Finland
Full list of author information is available at the end of the article