Progress in Neuropsychopharmacology & Biological Psychiatry 77 (2017) 209–215

Contents lists available at ScienceDirect

Progress in Neuropsychopharmacology & Biological Psychiatry

journal homepage: www.elsevier.com/locate/pnp

Depressive symptoms in schizophrenia and dopamine and serotonin gene polymorphisms

Vjekoslav Peitl[a,b], Mario Štefanović[c], Dalibor Karlović[a,b,*]

[a] Department of Psychiatry, Sestre Milosrdnice University Hospital Center, Zagreb, Croatia
[b] Catholic University of Croatia, Zagreb, Croatia
[c] Clinical Department of Chemistry, Sestre Milosrdnice University Hospital Center, Zagreb, Croatia

ARTICLE INFO

Keywords:
Schizophrenia
Depression
Serotonin
Dopamine
Polymorphism
Genetic
Psychiatric status rating scales

ABSTRACT

Although depressive symptoms seem to be frequent in schizophrenia they have received significantly less attention than other symptom domains. As impaired serotonergic and dopaminergic neurotransmission is implicated in the pathogenesis of depression and schizophrenia this study sought to investigate the putative association between several functional gene polymorphisms (SERT 5-HTTLPR, MAO-A VNTR, COMT Val158Met and DAT VNTR) and schizophrenia. Other objectives of this study were to closely examine schizophrenia symptom domains by performing factor analysis of the two most used instruments in this setting (Positive and negative syndrome scale - PANSS and Calgary depression rating scale - CDSS) and to examine the influence of investigated gene polymorphisms on the schizophrenia symptom domains, focusing on depressive scores. A total of 591 participants were included in the study (300 schizophrenic patients and 291 healthy volunteers). 192 (64%) of schizophrenic patients had significant depressive symptoms. Genotype distribution revealed no significant differences regarding all investigated polymorphisms except the separate gender analysis for MAO-A gene polymorphism which revealed significantly more allele 3 carriers in schizophrenic males. Factor analysis of the PANSS scale revealed the existence of five separate factors (symptom domains), while the CDSS scale revealed two distinct factors. Several investigated gene polymorphisms (mostly SERT and MAO-A, but also COMT) significantly influenced two factors from the PANSS (aggressive/impulsive and negative symptoms) and one from the CDSS scale (suicidality), respectively. Depressive symptoms in schizophrenic patients may be influenced by functional gene polymorphisms, especially those implicated in serotonergic neurotransmission.

1. Introduction

Depressive symptoms are a part of all phases of schizophrenia and are considered to be one of its five constitutive symptom domains (Tandon et al., 2009). Prevalence rates of depression in schizophrenia range from 30% to 70% (Majadas et al., 2012; Peitl et al., 2016), while their presence has been associated with overall worse outcomes, greater comorbidity, poorer quality of life, work impairment, deterioration of psychosocial functioning, greater risk of relapse and increased risk of suicide (Tandon et al., 2009). Biological basis of depressive symptoms is still unclear, but research findings point towards the role of genetic loading and neurotransmitter systems of dopamine and serotonin (Talkowski et al., 2008; Tandon et al., 2009). Although a number of factors is interrelated in the dynamics of these two neurotransmitter systems in schizophrenia, neurotransmission itself relies mostly on the action of four distinct ones: serotonin and dopamine transporters (SERT and DAT) and enzymes monoaminooxidase A (MAO-A) and catechol-O-methyltransferase (COMT). Therefore it is no surprise that numerous polymorphisms, especially those functional, of those genes have been investigated so far. It needs to be emphasized that available findings presented an array of rather ambiguous results which we will try to briefly present.

Regarding the COMT gene and its Val1582Met polymorphism, especially Val allele, several investigations confirmed its role in the development of schizophrenia (Glatt et al., 2003; Sazci et al., 2004; Voisey et al., 2012; Wonodi et al., 2003). However, there is an abundance of research findings that failed to confirm that association (Chen et al., 2004, 2011; Fan et al., 2005; Galderisi et al., 2005; Martorell et al., 2008; Nunokawa et al., 2007; Okochi et al., 2009; Park et al., 2002; Tovilla-Zarate et al., 2013), and even a report of a mild protective effect of this polymorphism's heterozygosity (Costas et al., 2011). When looking at the possible influence of this polymorphism on schizophrenia symptom domains, Val158Met was previously reported with negative symptoms (Wang et al., 2010), especially Val/Val

* Corresponding author at: Department of Psychiatry, Sestre Milosrdnice University Hospital Centre, Vinogradska Cesta 29, 10000 Zagreb, Croatia.
E-mail address: dalibor.karlovic@unicath.hr (D. Karlović).

http://dx.doi.org/10.1016/j.pnpbp.2017.04.011
Received 21 February 2017; Received in revised form 5 April 2017; Accepted 12 April 2017
Available online 14 April 2017
0278-5846/ © 2017 Elsevier Inc. All rights reserved.

Table 1
Sociodemographic, clinical and psychometric characteristics of schizophrenic patients and healthy participants.

	Schizophrenia N = 300	Healthy N = 291	
Age in years (mean ± SD)	39.60 ± 14.07	37.62 ± 11.55	t = 1.73; p = 0.09
Gender N (%)			**χ^2 = 23.09; df = 1; p < 0.01**
Males	218 (72.7)	156 (53.6)	
Females	82 (27.3)	135 (46.4)	
Education level N (%)			**χ^2 = 80.55; df = 2; p < 0.01**
Elementary school	34 (11.3)	45 (15.5)	
High school	210 (70.0)	100 (34.4)	
Faculty	56 (18.7)	146 (50.2)	
Location N (%)			χ^2 = 1.82; df = 1; p = 0.18
Urban	230 (76.7)	209 (71.8)	
Rural	70 (23.3)	82 (28.2)	
Marital status N (%)			**χ^2 = 48.49; df = 2; p < 0.01**
Married	89 (29.7)	169 (58.1)	
Single	189 (63.0)	110 (37.8)	
Divorced	22 (7.3)	12 (4.1)	
Occupation N (%)			**χ^2 = 108.47; df = 2; p < 0.01**
Employed	97 (32.3)	218 (74.9)	
Unemployed	122 (40.7)	49 (16.8)	
Retired	81 (27.0)	24 (8.2)	
Response to treatment N (%)			
Complete	33 (11)		
Partial	187 (62.3)		
Resistant	80 (26.7)		
Suicidality N (%)			
Yes	59 (19.7)		
No	241 (80.3)		
Attempted suicide: N (%)			
Yes	42 (14)		
No	258 (86)		
Hereditary loading: N (%)			
Yes	121 (40.3)		
No	179 (59.7)		
Illness phase: N (%)			
Remission	21 (7)		
Partial remission	80 (26.7)		
Deterioration	199 (66.3)		
Number of episodes (mean ± SD)	4.90 ± 3.77		
Illness duration in years (mean ± SD)	1.86 ± 0.89		
CGI (mean ± SD)	5.52 ± 0.72		
PANSS positive (mean ± SD)	19.87 ± 6.35		
PANSS negative (mean ± SD)	27.46 ± 5.87		
PANSS general (mean ± SD)	55.29 ± 11.14		
PANSS total (mean ± SD)	102.70 ± 20.21		
CDSS total (mean ± SD)	8.27 ± 5.35		

N: number; mean: arithmetic means; SD: standard deviation; χ^2: chi-square; df: deegrees of freedom; p: statistical significance; CGI: Clinical global impression scale; PANSS: positive and negative syndrome scale; CDSS: calgary depression rating scale.
Statistical significance at the threshold of $p \leq 0.05$.

genotype (Pelayo-Terán et al., 2008), while Val allele and also Val/Val genotype were linked to more severe positive symptoms (Goghari and Sponheim, 2008). Met allele was previously associated with a deterioration of positive and aggressive symptoms of schizophrenia (Han et al., 2008). There is also some sporadic data about the Val allele being a mild risk factor for affective symptoms, especially those depressive, in psychotic patients (McClay et al., 2006). Contrary to that, there were findings of no association between this COMT polymorphism and clinical symptomatology of schizophrenia (Strous et al., 2006; Tovilla-Zarate et al., 2013).

SERT insertion/deletion (indel) promoter polymorphism has rarely been associated with schizophrenia (Bayle et al., 2003; Carlström et al., 2012; Han et al., 2004; Ikeda et al., 2006; Konneker et al., 2010; Lee et al., 2009; Peitl et al., 2015) while its association with symptom domains has mostly been negative (Bergen et al., 2009; Konneker et al., 2010; Serretti et al., 2002). However, there have been some reports of a LL genotype being associated with positive symptoms of schizophrenia (Malhotra et al., 1998). As far as the depressive symptoms are concerned, they have been associated with S allele (Han et al., 2008; McClay et al., 2006) and SS genotype (Golimbet et al., 2004). In chronic psychoses S allele has been associated with an increased risk of developing depression (Contreras et al., 2009; Goldberg et al., 2009). On the other hand, L allele has been associated with greater psychopathology and a greater depression score in patients suffering from psychosis (Sun et al., 2012).

Majority of findings argue against an association between MAO-A gene polymorphisms and schizophrenia (Li and He, 2008; Norton et al., 2002; Strous et al., 2003; Wei et al., 2011). However, several investigations suggested otherwise, mainly for less active alleles of VNTR polymorphism (Jonsson et al., 2003) and rs6323 (Qiu et al., 2009), both specifically in males. Regarding the putative association of MAO-A and symptoms of schizophrenia, most of the research focused on aggressive symptoms as this gene received a fair amount of attention on account of its suspected association with aggressive behavior (McDermott et al., 2009), but that has not been substantiated in schizophrenia research (Zammit et al., 2004). Depressive symptomatology has seldom been investigated and there is still no sufficient data for the VNTR polymorphism (Bergen et al., 2009; Camarena et al., 2012). However, in schizophrenic males three other polymorphisms (rs6323, rs1137070, rs3027407) have been associated with affective distur-

Download English Version:

https://daneshyari.com/en/article/5558062

Download Persian Version:

https://daneshyari.com/article/5558062

Daneshyari.com