

nonresponsiveness. The decision to discontinue medication during the early phase of psychosis should be considered carefully.

151. BROMOCRIPTINE CHALLENGE AFFECTS WORKING MEMORY PROCESSING IN HUMANS DEPENDING ON DRD2-RELATED GENES

Giulio Pergola^{*1}, Pierluigi Selvaggi², Barbara Gelao¹, Pasquale Di Carlo¹, Maria Antonietta Nettis², Graziella Amico¹, Valentina Felici¹, Leonardo Fazio¹, Antonio Rampino¹, Fabio Sambataro³, Giuseppe Blasi⁴, and Alessandro Bertolino¹
¹Università degli Studi di Bari Aldo Moro; ²King's College London; ³University of Udine; ⁴Azienda Ospedaliero-Universitaria Consorziale Policlinico

Background: Dopamine D2 receptors (D2R) contribute to the inverted-U shaped relationship between dopamine dorsolateral prefrontal cortex (DLPFC) and working memory (WM). Genetic variation in DRD2 coding for D2Rs modulates D2 signaling, but other genes in its pathway may be involved. In a previous work, using gene co-expression networks we identified 84 partner genes coregulated with DRD2 and eight single nucleotide polymorphisms (SNPs) predicting coexpression of the whole gene set in the human DLPFC [1]. These SNPs combined into a polygenic coexpression index (PCI) predicted WM performance and DLPFC activity in two independent samples of living healthy humans [1]. Here, we asked whether response to D2R targeting drugs is associated with this PCI. Thus, we investigated the interaction between WM behavioral/brain response to the D2R agonist Bromocriptine (BRO) and the PCI.

[1] Pergola G, Di Carlo P, et al. (In press). Translational Psychiatry.

Methods: Fifty healthy volunteers entered a double-blind, crossover, randomized, placebo-controlled fMRI study with BRO 1.25 mg and performed the N-Back WM task during the fMRI scanning session. We computed the PCI for all participants and investigated its association with WM-related behavior and brain activity using general linear models.

Results: A PCI by drug interaction was significant on both DLPFC signal (right BA46, 242 voxels, $F(1, 48) = 24$; right BA9, 177 voxels, $F(1, 48) = 19$; $P < .05$ cluster-level FWE corrected) and behavioral scores, $F(1, 46) = 4.6$, $P = .045$, using a U-shaped quadratic model. The U-shaped relationship between the PCI and WM processing found on placebo was reversed on BRO. Furthermore, the increase in behavioral performance on BRO correlated with a decrease in BA46 activity, $t(48) = -2.0$, $P = .049$.

Conclusion: The combined effect of multiple alleles on DRD2 coexpression covaried with drug response such that different allelic patterns were associated with similar responses, as in the inverted U-shaped model of WM. Thus, multiple genes and multiple allelic patterns are implicated in the inverted U-shaped dopamine/WM relationship. This relationship is reversed when individuals are administered BRO, suggesting that brain and behavioral response to this pharmacological challenge depends on a pleiotropic individual genetic background. Hence, pharmacogenomics in schizophrenia should take into account allelic patterns associated with molecular phenomena such as gene expression to predict drug response.

152. CANCER CARE AND MORTALITY IN PATIENTS WITH SCHIZOPHRENIA, SUBSTANCE USE, AND MOOD DISORDERS IN FINLAND

Jaana Suvisaari^{*1}, Kristiina Manderbacka¹, Ilmo Keskimäki¹, Martti Arffman¹, Aulikki Ahlgren-Rimpiläinen¹, and Eero Pukkala²

¹National Institute for Health and Welfare; ²Finnish Cancer Registry

Background: Previous research suggests that people with schizophrenia may not have an increased risk of cancer, but the cancer mortality is

higher among them than in other cancer patients. In this study, we compared cancer mortality in patients with a history of schizophrenia, substance use disorders (SUD), or mood disorders diagnosed with any cancer in patients with cancer who did not have a history of SMI. We examined whether differences in survival rates could be explained by detection at a later stage, having more comorbid physical illnesses, or by differences in cancer treatment.

Methods: The population with their first cancer diagnosis in 1990–2013 was obtained from the National Cancer Register including all cancer patients in Finland. Information concerning hospital admissions due to severe mental illness (SMI), grouped as schizophrenia spectrum psychosis (hereafter schizophrenia), SUD and mood disorders, before cancer diagnosis was individually linked to them from the Hospital Discharge Register (HRD) for years 1969–2013. Comorbidities were also obtained from the HRD and individually linked to the study population and Charlson index was calculated from them. Cancer stage at presentation was categorized as localized, other and unknown. Information on cancer treatment was obtained from the National Cancer Register. Information concerning mortality was obtained from the Finnish Causes of Death Statistics.

Results: Cancer-specific mortality was higher among men with history of schizophrenia and SUD, whereas there were few differences between those with mood disorder and those without history of SMI. Among women a stepwise gradient was found from those without SMI through mood disorders and SUDs to those with psychosis.

The difference between patients with schizophrenia, and SUD among men and those without SMI remained significant after adjusting for age, year of cancer diagnosis, type of cancer, stage at presentation, cancer treatment, and Charlson comorbidity index. While all the examined factors were important predictors of mortality, the only factor that had an effect on differences between patient groups was cancer treatment.

When examining the average annual decrease in cancer specific mortality, we found that the decrease was 3.1% (95% CI 3.0–3.2) among men and 3.2% (3.1–3.3) among women without history of SMI. Among patients with history of schizophrenia ($P = .0015$) or substance use disorder ($P < .0001$) the decrease was significantly slower.

Conclusion: Patients with a history of schizophrenia and substance use disorder have increased cancer mortality compared to patients with cancer with no SMI, which is partly explained by poorer quality of cancer treatment. Moreover, the mortality gap between patients with schizophrenia and substance use disorders and other cancer patients is increasing. Treatment of cancer in patients with SMI should be improved.

153. FACIAL EMOTION RECOGNITION IN INDIVIDUALS WITH SCHIZOPHRENIA WITH OR WITHOUT SOCIAL ANXIETY

Tania Lecomte^{*}, and Laurence Thérioux
 University of Montreal

Background: Social anxiety is highly prevalent in individuals with schizophrenia with studies suggesting rates from 15% to 30%. This study aimed at determining if social anxiety was linked to specific emotion perception deficits and to specific social functioning deficits. We hypothesized that individuals with schizophrenia and more social anxiety would have worse social functioning and would be better at recognizing facial emotions of fear or anger than individuals without social anxiety, because they are more likely to have an attentional bias towards those emotions.

Methods: 47 participants with a diagnosis of schizophrenia, average age of 38 (SD 9.7) were recruited in the Psychotic program (outpatient service) of a large psychiatric hospital in Montreal (IUSMM). The assessments included measures of facial recognition (Eckman; FEIT), facial discrimination (FEDT), ToM (Cartoon Stories), social anxiety (SIAS, BSPS), psychiatric symptoms (BPRS), and social functioning (SFS and role-plays).

Results: 22 (47%) of participants rated as significantly socially anxious according to the SIAS.