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P.3.002 Stigmatic attitudes towards mentally ill patients in Hungary between 2001 and 2015: results of a time-trend analysis

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Background: Stigmatic attitudes towards people with the diagnosis of mental illness are widespread in the general public [1] and are the major obstacle for successful treatment, rehabilitation and reintegration of patients into the society [2]. Given the magnitude of this issue, and in the effort to develop effective anti stigma intervention programs, trend analysis studies were conducted, examining the changes in attitudes over the years [3]. The construct of social distance, which involves the desire to avoid contact with a particular group of people was commonly used to assess stigma. These studies have consistently reported that despite the improvement in mental health literacy of the public, social distance preferences concerning mentally ill patients have not changed over the last 20 years, and in some cases have even increased [3]. However, the number of studies using trend analysis is scarce and mainly limited to wealthier countries because such studies are both costly and time intensive. Consequently, most studies to date have been carried out in North Western Europe whereas data from Central and Eastern European countries, especially from former communist countries, is lacking [4,5].

Objective: In the face of underfinanced mental health system and the lack of any national anti-stigma programs or research, the aim of this study is to shed light into mental illness stigma in Hungary. More specifically, this study aimed to explore for the first time, potential changes concerning attitudes of the Hungarian population towards mentally ill patients.

Method: National representative surveys (N=7605) of adults aged 18-53 years were carried out in Hungary in 2001, 2003, 2007 and 2015. An interview was conducted, asking for socio-demographic information and participants' desire for social distance from mentally ill patients, measured by Bogardus social distance scale. In order to put into context the stigmatic attitudes towards mentally ill patients, participants were also asked to report on their

social distance preferences towards other minorities in the Hungarian society. Trend analysis was performed to examine the trends of social distance.

Results: Time-trend analysis indicated a significant (positive) trend in public preferences for social distance towards more accepting attitudes during the years of 2001-2015. However, closer examination reveals that the effect size is very small (0.05) and the 2015 rejection level is still high (57%) compared to over 60% in both 2001 and 2003. Moreover, during a period of 15 years, mentally ill patients are among the three most rejected groups in the society (with only alcoholics and drug users being more rejected).

Conclusions: As was found in other countries around the world, in Hungary as well, stigmatic attitudes towards mentally ill patients are highly prevalent, and have not changed over the last decade. While stressing a worrisome reality in Hungary, where no efforts to tackle mental illness stigma were done, this study also verifies the enormity of the stigma phenomenon. It is evident, maybe more than anything, that much effort is needed in Hungary, but also worldwide, in order to understand and defeat mental illness stigma.

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P.3.003 Pleiotropic genes in psychiatry: calcium channels and the stress-related FKBP5 gene in antidepressant resistance

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Background: Major depressive disorder is a high-prevalence disease associated with a heavy burden on both personal well-being and socio-economical welfare, partly as a result of lacking tailored treatment options [1]. Common single nucleotide polymorphisms (SNPs) were estimated to account for 0.42 of the variance in antidepressant response [2], confirming the hypothesis that genetic polymorphisms may be used as effective markers to provide tailored antidepressant treatments. Candidate gene and genome-wide analyses can provide a complementary strategy, since the former can be applied to clarify the role of SNPs with high pre-test probability of association with the trait and the latter is useful to study the joint effects of a number of SNPs in a gene or a set of genes [3].

Aim: We applied such a complementary strategy to the study of eight genes that are very strong candidates with previous evidence of pleiotropic effect across psychiatric traits. The genes of interest are involved in the regulation of neurotransmission (CACNA1C, CACNB2, ANK3), neural differentiation, synaptic plasticity, adhesion processes and structural organization (GRM7, TCF4, ITIH3, SYNE1) and glucocorticoid signaling (FKBP5).

Methods: Three samples with major depressive disorder (total n=671) were genotyped for 44 SNPs in strong candidate genes based on biological function and previous genome-wide association studies (CACNA1C, CACNB2, ANK3, GRM7, TCF4, ITIH3, SYNE1, FKBP5). Phenotypes were response/remission after 4 weeks of treatment and treatment-resistant depression (TRD: non response/non remission to at least two antidepressant treatments). Genome-wide data from STAR*D were used to replicate findings for response/remission (Level 1, n=1409) and TRD (Level 2, n=620). Pathways including the most promising candidate genes for involvement in TRD were investigated in STAR*D Level 2. Top pathway(s) were investigated using machine learning models.

Results: FKBP5 rs3800373, rs1360780 and rs9470080 showed replicated associations with response, remission or TRD. CACNA1C SNPs showed contradictory direction of association across samples. ANK3 rs1049862 AA genotype showed a replicated association with better outcome. In

STAR*D the best pathway associated with TRD included CACNA1C (GO:0006942, permuted $p=0.15$). Neural networks and gradient boosted machine showed that independent SNPs in this pathway predicted TRD with a mean sensitivity of 0.83 and specificity of 0.56 after 10-fold cross validation repeated 100 times.

Conclusions: FKBP5 polymorphisms should be considered for inclusion in antidepressant pharmacogenetic tests. CACNA1C is a good candidate and GO:0006942 includes several genes coding for ion channels expressed in the central nervous system and other genes relevant for excitatory mechanisms. CACNB2 and ANK3 showed replicated associations with phenotypes and further investigations could help in clarifying their role. This study may pave the way to the identification of sets of genetic predictors in specific pathways able to predict the risk of TRD. It is reasonable to hypothesize a certain degree of variability in the genetic variants involved in TRD across different patients, but the involved pathways are expected to be more stable. Validated genetic markers of TRD could have a pivotal role in the implementation of targeted antidepressant treatments.

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P.3.004 Neuropsychological correlates of ADRA2A (rs1800544) and COMT(rs4680) polymorphisms in Turkish ADHD patients

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