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Interleukin-6 and interleukin-1B polymorphisms show different interaction patterns with stressors on trait anxiety

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Neuroinflammatory mechanisms received more and more attention recently in neuroscience examining depression and anxiety. Disturbances in the genetic expression profile of proinflammatory cytokines such as Interleukin-1B (IL-1B) and Interleukin-6 (IL-6) has been reported to influence these mood disorder pheontypes profoundly, however it has been also shown that different stressors are needed to exert such effect. That means that significant main effects of these genes on depression and anxiety are lacking, but highly significant interaction effects could be observed even after correcting for multiple testing [1,2]. The interactions carried by the large array of different environmental effects are far from clear at this moment.

The aim of this study was to represent how the different stress clusters can interact with two IL-1B, and an IL-6 polymorphisms, influencing anxiety phenotype in a normal population sample from Hungary. For the analysis 1093 people were recruited, provided genetic samples and phenotypic information. Linear regression analyses were carried out with PLINK

program to assess the main effect of the polymorphisms (IL-1B: rs16944, rs1143643, IL-6: rs1800795) and the interactions with Recent Life Events (RLE), Childhood Adversity (CHA), and Pain Background information (PBGR). False discovery rate (FDR) correction for multiple testing was applied. Anxiety phenotype was measured by the trait subscale of State-Trait Anxiety Inventory (STAI) questionnaire.

As expected significant gene-environment interaction effects were found. The interaction effects for the different polymorphisms was affected differently by the various stressors. Robust interaction was found between CHA and IL-1B polymorphism rs16944 (FDR corrected p values: padd = 0.001, pdom = 0.012, prec = 0.005), while the other polymorphism rs1143643 also showed significant interaction with this stressor (FDR corrected p values: padd = 0.053, pdom = 0.012). In contrast PBGR showed interaction only with the IL-6 functional polymorphism rs1800795 (FDR corrected p values: padd = 0.027, pdom = 0.070, prec = 0.070). RLE, however modulated both IL-1B (rs16944 FDR corrected p values: padd = 0.097, pdom = 0.027) and IL-6 (rs 1800795 FDR corrected p values: padd = 0.059, prec = 0.005) functional polymorphism's effect on STAI trait phenotype. No significant main effects were found that means that the polymorphisms were not able to affect the phenotype without interacting stressors.

This study provides an example for the interplay among interaction patterns in the pathomechanism of anxiety symptoms. Among the examined stress types we found that IL-1B polymorphisms are more sensitive to early life stress than any other interaction we found. Also somatic stress type represented by painful states had unique connection with the IL-6 polymorphism. Recent life stress, however did not show exact preference among the polymorphisms of the two genes, furthermore, it influenced the effect of both on STAI trait phenotype. The represented examples, and also the lack of genetic main effect strongly suggest to take stress factors into account when the role of genetic polymorphisms of proinflammatory cytokines on anxiety phenotypes are studied. In conclusion, in the development of anxiety, similar to those described in depression, gene environment interactions could be identified.

References

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