P6.23.

Investigation of the role of preprotachykinin A and C (TAC1 and TAC4) gene-derived peptides in anxiety, stress and depression-like behaviour in mice

Borbély, É.[1*]; Hajna, Z.[1]; Simon, G.[1]; Berger, A.[2]; Paige, C.[2]; Quinn, J.[3]; Pintér, E.[1]; Szolcsányi, J.[1]; Helyes, Z.[1]

1: Department of Pharmacology and Pharmacotherapy, Faculty of Medicine, University of Pécs, Hungary
2: Ontario Cancer Institute, University Health Network, Toronto, Canada
3: School of Biomedical Sciences, Liverpool University, Liverpool, UK

Substance P (SP) and neurokinin A (NKA) encoded by the preprotachykinin A (TAC1) gene have been evidenced to play an important role in psychiatric disorders including anxiety and depression via neurokinin 1 and 2 (NK1, NK2) receptor activation, respectively. The recently discovered TAC4 gene-derived NK1 receptor agonist hemokinins (HK) are also expressed in several brain regions, they might have different binding sites, receptor activation mechanisms and signal transduction pathways. Therefore, we investigated the role of TAC1 and TAC4 gene-derived peptides in anxiety, stress and depression-like behaviour with gene-deleted (TAC1-/-, TAC4-/- and TAC1-/-/TAC4-/-) mice. TAC4-/-, but not the other knockouts spent significantly less time in the light phase of the light-dark box during 20 minutes compared to C57Bl/6 wildtypes. Similarly, only TAC4-/- mice showed significantly reduced motility, less field-crossing and rearing activities in the open field test within 5 minutes, as well as increased immobility in the 4-minute period of the forced swim test. We conclude that TAC4-derived tachykinins exert anti-anxiety and stress-coping actions, which is counteracted by an opposite effect of TAC1-coded peptides. Expression pattern of SP and HK1 in the brain and/or signal transduction activation in response to their NK1 receptor binding might be different, but NK2 receptor activation by NKA can also modify the neuronal responses. Elucidating these mechanisms needs further investigations.