

ROLE OF AUTO-ANTIBODIES AGAINST THE NICOTINIC ACETYLCHOLINE RECEPTORS IN NEUROLOGICAL AND PSYCHIATRIC DISEASES

FARKAS Ferenc Balázs, CONTE Giorgia

Department of Neuroscience (IP); Department of Medical Microbiology (SE)

Semmelweis University, Budapest, Hungary

Uwe Maskos, PhD; Béla Kocsis, associate professor, MD, PhD

Autoimmune diseases affect 6-7% of the world population. In many cases autoantibodies (AA) are involved in these processes. Additionally, in a significant proportion of the general population brain reactive AAs are present in the serum. The potential relation between these AA-s and neurological disorders was confirmed in connection with anti-NMDA-receptor encephalitis syndrome, which is an acute form of brain inflammation, potentially lethal, occurring when antibodies produced by the body's own system attack the NMDA receptors in the brain.

According to our hypothesis AA-s against nicotinic acetylcholine receptors (nAChRs) have a central role in the development of neuroinflammation and in pathologies affecting brain structures. One example is a major psychiatric disorder, schizophrenia where 30% of patients do not respond to conventional antipsychotic therapy. In our present research we conducted a comprehensive study of these circulating AAs.

In the first phase of our experiments we tested 165 monoclonal AA samples produced by B-lymphocytes isolated from the liquor of patients with an acute episode of NMDA-R encephalitis syndrome using indirect ELISA method. The antigens used in these experiments were the extracellular domains of the $\alpha 2$, $\alpha 7$ and $\alpha 4\beta 2$ subunits of the nAChR. Of these, 29 were positive in the following distribution: 9 for [$\alpha 7$], 8 for [$\alpha 4\beta 2$], 1 for [$\alpha 2$], 6 for [$\alpha 4\beta 2 + \alpha 2$], 1 for [$\alpha 4\beta 2 + \alpha 7$], 2 for [$\alpha 2 + \alpha 7$], 2 for [$\alpha 2 + \alpha 7 + \alpha 4\beta 2$].

In the next phase we tested the functional activity of the samples found positive for $\alpha 7$ in *Xenopus laevis* oocytes expressing $\alpha 7$ -nAChR using voltage clamp technique. In 5 cases the current generated by the activation of these receptors was reduced by more than 50% in the presence of the AAs, suggesting an inhibition of intracellular Ca^{2+} levels.

Based on our results we can conclude that a large number of patients with an acute episode of anti-NMDA-receptor encephalitis syndrome had nAChR-specific and functionally active AA producing cell in their central nervous system. In the next step of our research, we aim to test in vivo the effect of AAs by performing intracerebroventricular osmotic mini-pump infusions in a C57BL/6J animal (mouse) model. This observation opens new perspective in understanding diseases affecting the central nervous system and suggest new therapeutic strategies against autoimmune diseases.