P24

Modulation of intrinsic persistent firing by noradrenaline and serotonin in CA1 pyramidal neurons

A. REBOREDA1,2, M. J. VALERO-ARACAMA3,4, A. ARBOIT2, M. SAUVAGE1, M. YOSHIDA1,2

1. Functional Architecture of Memory, Leibniz Institute For Neurobiology., Magdeburg, Germany.
2. Cognitive Neurophysiol., German Center For Neurodegenerative Diseases-DZNE, Magdeburg, Germany.
3. Ruhr Univ. Bochum, Bochum, Germany.
4. Dept. of Physiololgy and Pathophysiology, Friedrich-Alexander-University of Erlangen-Nürnberg, Erlangen, Germany

The correct performance of working memory (WM) tasks requires a fine-tuning of different neuromodulatory systems. It is accepted in general that WM requires high cholinergic activation while other neuromodulators such as 5-HT and NA have mixed effects depending on the activation levels or the receptor subtypes involved. However, it remains unclear why these neuromodulators exert different effects.
In the present study, we focus on the effects of neuromodulators on the ability of individual neurons to support persistent firing (PF), which is one of the potential cellular correlates of WM. Using in vitro patch clamp recording in CA1 pyramidal neurons. We demonstrate that the cholinergic receptor subtypes, M1 and M2, support the generation of PF in the presence of a cholinergic agonist, pointing out that both Gq and Gi coupled receptors are required to trigger PF.
On the other hand, application of 5-HT or NA by themselves did not support generation of PF, while co-application of either of them, with a cholinergic agonist, suppressed PF. Receptor subtype studies pointed out that 5-HT6 serotoninergic and β1 adrenergic receptors are responsible for the suppressive effect, while 5-HT7 and β2 did not affect the PF. These results suggest that activation of Gs coupled receptors, which is detrimental for WM in vivo, suppresses PF in CA1 neurons.
We further explored the involvement of cAMP pathway using an adenylate cyclase (AC) activator and a PKA inhibitor. Our results suggest that the AC activator suppresses PF while the PKA inhibition rescues PF under the 5-HT activation, indicating the involvement of cAMP pathway downstream of the Gs receptor activation.
In summary, intrinsic PF in CA1 pyramidal neurons requires Gq activation and reduced levels of cAMP. Activation of Gs coupled receptors, on the other hand, inhibits the cholinergic PF through cAMP mediated activation of PKA. The similarity between the modulation of PF and WM by the neuromodulatory systems will be discussed.