

Synapses established by the median raphe contain glutamate receptors in the mouse forebrain

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The typically serotonergic median raphe nucleus (MR) takes part in the subcortical modulation of cortical information processing and our workgroup showed recently that MR establishes fast and precise, partly glutamatergic excitatory synaptic contacts with a specific subpopulation of GABAergic interneurons in the hippocampus (HC). This feature of the synapses of the MR was not known so far in other brain areas. In these raphe-hippocampal synapses the terminals contain vesicular glutamate transporter type 3 (vGluT3) and we have shown the presence of postsynaptic AMPA-type glutamate receptors before. Because NMDA receptors (NMDARs) play an important role in excitatory transmission and synaptic plasticity mechanisms, we tested, whether MR synapses can act via NMDARs in its different target areas. Using double immunohistochemistry in the HC, we labeled the vGluT3-positive boutons originating in the MR and we found that at least about 88% of these synapses are NMDAR-positive. Using anterograde tracing and NMDAR immunohistochemical staining, we showed that at least one-third of the synapses established by the MR in the HC, medial septum (MS) and prefrontal cortex (PFC) contain NMDARs, which changes our view about this pathway. Finally, using double retrograde tracing, we found that there are cells in the MR that innervate the HC and PFC or MS and PFC simultaneously. These observations suggest that MR can act via glutamatergic NMDA receptors not only in the HC, but also in the MS and the PFC and these areas may be synchronously stimulated by the same MR neurons.