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Reduction of autophagy markers mediated protective effects of JNK inhibitor and bucladesine on memory deficit induced by Aβ in rats.

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Introduction and Background: Autophagy, the process of self-degradation of cellular components, has an important role in neurodegenerative diseases, such as Alzheimer's disease(1). In this study, we investigated the effects of SP600125 as c-Jun N-terminal kinase (JNK) inhibitor and bucladesine as a cyclic adenosine 3',5'-monophosphate (cAMP) analog on spatial memory and expression of autophagic factors in Aβ-injected rats(2).

Methods: Male Wistar rats were used. Rats were randomly allocated into five groups as following: amyloid beta (Aβ)-only group, Aβ + SP600125 (30 μg/1 μ/side, n = 7) and/or bucladesine (100 μM/1 μl/side, n = 7), and the normal control (vehicle only) group. The treatments were administered bilaterally to the CA1 sub-region of the hippocampus stereotaxically. Spatial reference memory was performed using Morris Water Maze 21 days later. The expression of authophagy markers (beclin1, Atg7, Atg12, and LC3 II/LC3 I) in the hippocampus was evaluated using western blotting.

Results: Compared to the vehicle group, Aβ administration reduced spatial reference learning ($P < 0.001$) and memory ($P < 0.01$) and up regulated the expression of beclin1, Atg7, Atg12, and LC3 II/I ($P < 0.0001$). Compare to Aβ-only group, the administration of SP600125 and/or bucladesine improved spatial reference learning ($P < 0.001$) and memory ($P < 0.01$). Compared to the Aβ-only group, the treatment with SP600125 and/or bucladesine also reduced beclin1, Atg7, Atg12, and LC3 II/I ($P < 0.0001$) which was similar to amount of normal rats.

Discussion and Conclusion: In summary, it seems that the improvement of spatial memory by SP600125 and/or bucladesine in Aβ-injected rats is in relation with normalizing of autophagy to the physiologic level, possibly through neuroprotection and/or neuroplasticity.

Keywords: Alzheimer disease; Amyloid beta (Aβ); Autophagy; Bucladesine; SP600125

References:

1. Najafi S, Payandemehr B, Tabrizian K, Shariatpanahi M, Nassireslami E, Azami K, et al. The role of nitric oxide in the PKA inhibitor induced spatial memory deficits in rat: involvement of choline acetyltransferase. Eur J Pharmacol. 2013 Aug 15;714(1-3):478-85.
2. Pickford F, Masliah E, Britschgi M, Lucin K, Narasimhan R, Jaeger PA, et al. The autophagy-related protein beclin 1 shows reduced expression in early Alzheimer disease and regulates amyloid beta accumulation in mice. J Clin Invest. 2008 Jun;118(6):2190-9.

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