GS03-1 **Involvement of serotonergic neuron on doxorubicin and cyclophosphamide combination treatment-induced anxiety-like behavior in rats**

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We examined the influence of combination treatment with doxorubicin and cyclophosphamide, a traditional chemotherapy for breast cancer, on anxiety-like behavior in rats. Furthermore, we evaluated the serotonin (5-HT) receptor subtypes functions on the chemotherapy-induced anxiety-like behavior. Doxorubicin and cyclophosphamide were injected intraperitoneally once per week for 2 weeks. This treatment produced anxiety-like behavior using the light-dark test of rats. In addition, we measured 5-HT_{2A} receptor in the frontal cortex and 5-HT_{1A} receptor in the hippocampus, and 5-HT_{1A} receptor and 5-HT_{2A} receptor-mediated behavioral response in rats. Doxorubicin and cyclophosphamide produced anxiety-like behavior in light-dark test of rats. The combination treatment with doxorubicin and cyclophosphamide significantly increased (±)-DOI, 5-HT_{2A} receptor agonist-induced wet-dog shakes, and 5-HT_{2A} receptor protein in the frontal cortex. The anxiety-like behavior significantly inhibited by mirtazapine, 5-HT_{2A} receptor antagonist/5-HT_{1A} receptor agonist properties, and tandospirone, partial 5-HT1A receptor agonist, but not fluoxetine, selective serotonin reuptake inhibitor. Chemotherapy for the combination treatment with doxorubicin and cyclophosphamide-induced anxiety-like behavior is mediated by the hyperfunction of 5-HT_{2A} receptor subtypes. It is possible that the effect of 5-HT_{2A} receptor antagonistic or 5-HT_{1A} receptor agonistic activity can be useful in chemotherapy-induced anxiety disorder.