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Magnesium-Induced Stress Resilience Mediated by Dopamine D1 Receptor Signaling

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Summary

Because of the high prevalence of depression, improvement of prevention methods is the most important issue. The greatest risk for depression is stress, but most people do not develop depression even if they are stressed, because they have an adaptive mechanism for stress called resilience. Elucidating the mechanism of resilience would to be an effective approach to overcome depression. Since magnesium deficiency has been reported to be associated with depression, magnesium may have stress resilience effects. Magnesium contributes to the regulation of various enzymes and is known to enhance the activity of adenylate cyclase, a cAMP-producing enzyme. Since cAMP pathway is thought to be important for antidepressant effects, magnesium may contribute to prevention of depression by enhancing this pathway. Previous studies, including our own, have shown that hippocampal dopamine D1 receptors contribute to antidepressant effects. Since D1 receptors activate adenylate cyclase, magnesium is expected to enhance this signaling pathway.

In our recent study, we found that hippocampal dopamine D1 receptors are strongly activated by noradrenaline. Furthermore, we showed that this D1 receptor activation is enhanced by exercise and stress and promotes the effects of antidepressants. In the present study, we investigated the possibility that magnesium enhances hippocampal dopamine D1 receptor signaling in mice, resulting in stress resilience. In naïve mice, magnesium-deficient diets or magnesium supplementation had no effect on D1 receptor activation induced by noradrenaline. No effects of low or high magnesium were observed in mice under stress or subjected to wheel running. There was also no apparent effect on hypoactivity seen in stressed mice. However, under the combined stress and exercise condition, there was an apparent decrease in D1 receptor signaling in the low magnesium group, although the difference was not statistically significant. We have shown that stress and exercise cooperatively enhance the D1 receptor signaling. The present results suggest that the magnesium deficiency may affect this interaction between exercise and stress rather than D1 receptor signaling itself.