Exercise-induced activated platelets increase adult hippocampal neurogenesis

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Physical exercise is associated with systemic changes and represents a strong positive physiological stimulus of neural precursor cell proliferation. However, the mechanisms underlying these effects are largely unknown. We show that dentate gyrus primary cultures form significantly more neurospheres when treated with serum from running mice. Using proteomic screening of mouse plasma following exercise, we identified platelets and their released factors as potential mediators of this effect. We found that platelets are activated after short periods of exercise and that activated platelets promote neurogenesis. Similarly, treatment with platelet factor 4, a protein released after platelet activation and elevated in the plasma of running mice, increased neurogenesis. *Ex vivo*, the neurogenesis-promoting effects of activated platelets and platelet factor 4 were exclusively observed in dentate gyrus primary cultures but not in cultures derived from the subventricular zone. Moreover, in mice depleted of circulating platelets, the dentate gyrus-specific running-induced increase in precursor cell proliferation was absent. Our data demonstrate that platelets and their released factors can modulate adult neural precursor cells under physiological conditions and provide an intriguing link between running-induced platelet activation and the regulation of neural precursor cells following exercise.