## PPARgamma activation prevents impairments in spatial memory and neurogenesis following transient illness.

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**Public Summary:**
This study shows how common illnesses can influence stem cell activity in the brain and impair the production of new neurons that are important for normal learning and memory. Stem cells in the hippocampal formation of the brain continually produce new neurons throughout adult life. We have previously shown that inflammation caused by brain injury or degenerative disease can impair stem cell activity in the hippocampus and here we show that even mild activation of immune signaling following a peripheral immune stimulus in mice impairs neurogenesis and causes defects in learning and memory. We also show that certain non-steroidal anti-inflammatory drugs can prevent the defects in neurogenesis that accompany illness. One such drug, rosiglitazone, is commonly used to treat diabetes but also has anti-inflammatory effects. This drug was surprisingly effective at protecting neurogenesis in mice and may prove useful in clinical applications aimed at protecting stem cells and neurogenesis from the detrimental effects of inflammation.

**Scientific Abstract:**
The detrimental effects of illness on cognition are familiar to virtually everyone. Some effects resolve quickly while others may linger after the illness resolves. We found that a transient immune response stimulated by lipopolysaccharide (LPS) compromised hippocampal neurogenesis and impaired hippocampus-dependent spatial memory. The immune event caused a 50% reduction in the number of neurons generated during the illness and the onset of the memory impairment was delayed and coincided with the time when neurons generated during the illness would have become functional within the hippocampus. Broad spectrum non-steroidal anti-inflammatory drugs attenuated these effects but selective Cox-2 inhibition was ineffective while PPARgamma activation was surprisingly effective at protecting both neurogenesis and memory from the effects of LPS-produced transient illness. These data may highlight novel mechanisms behind chronic inflammatory and neuroinflammatory episodes that are known to compromise hippocampus-dependent forms of learning and memory.