The circadian molecular clock regulates adult hippocampal neurogenesis by controlling the timing of cell-cycle entry and exit.

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The subgranular zone (SGZ) of the adult hippocampus contains a pool of quiescent neural progenitor cells (QNPs) that are capable of entering the cell cycle and producing newborn neurons. The mechanisms that control the timing and extent of adult neurogenesis are not well understood. Here, we show that QNPs of the adult SGZ express molecular-clock components and proliferate in a rhythmic fashion. The clock proteins PERIOD2 and BMAL1 are critical for proper control of neurogenesis. The absence of PERIOD2 abolishes the gating of cell-cycle entrance of QNPs, whereas genetic ablation of bmal1 results in constitutively high levels of proliferation and delayed cell-cycle exit. We use mathematical model simulations to show that these observations may arise from clock-driven expression of a cell-cycle inhibitor that targets the cyclin D/Cdk4-6 complex. Our findings may have broad implications for the circadian clock in timing cell-cycle events of other stem cell populations throughout the body.