Supporting Information

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SI Methods

Histology. Nissl staining was performed on 50-μm-thick floating brain sections prepared on a vibratome. For luxol fast blue staining of myelin, 5-μm-thick paraffin sections were stained with 0.1% luxol fast blue solution at 56 °C overnight, differentiated in 0.05% lithium carbonate, and counterstained in cresyl violet solution.

Immunohistochemistry. Immunohistochemistry analyses were performed using 50-μm-thick vibratome sections or 5-μm-thick paraffin sections. Primary antibodies were against β-gal (ICN Biomedical), DARPP32 (BD Biosciences), dopamine transporter (Chemicon), enkephalin (Chemicon), GFAP (BD Biosciences), NeuN (Chemicon), tyrosine hydroxylase (Chemicon), and TrkB (Dr. Louis Reichardt, University of California San Francisco). A microwave antigen-retrieval method was used for all immunostainings on paraffin sections. Primary antibodies were visualized by Cy2-, Cy3-, or Cy5-conjugated secondary antibodies (Jackson Immunoresearch), and counterstained with DAPI (Vector Laboratories). Alternatively, the ABC Kit and DAB substrate (Vector Laboratories) were used to detect primary antibodies, followed by counterstaining with nuclear fast red or cresyl violet solution. Fluorescent images of immunostaining were captured on a Zeiss LSM-510 confocal microscope, with a Nikon DXM1200 camera used for bright-field images.

Histological Quantification. To calculate the volume of the striatum, dentate gyrus (DG), and cortex, one of every six 50-μm-thick sections throughout the forebrain was stained with cresyl violet solution. Images of the stained sections were captured, and the areas of the striatum (bregma: 1.78 mm to −2.18 mm), DG granular layer, and neocortex were outlined and measured (1). To quantify spine density and length on Golgi-stained neurons, images of individual secondary dendrites along the *z*-axis were captured with a Nikon CCD camera and compiled using MetaMorph software (Molecular Devices). Image analyses and quantification were performed as described previously (2). To measure striatal neuron size and density, images of NeuN immunostaining in the striatum were captured. The areas of NeuN immunopositive nuclei and the numbers of NeuN-immunopositive cells per mm^2 were measured using ImageJ.

Statistical Analysis. Student *t* tests were applied to determine statistical differences between two groups of samples. ANOVA was used for comparisons of more than two groups, followed by Bonferroni post hoc analysis. Generalized linear models were used for unbalanced data. A P value < 0.05 was deemed statistically significant.

1. Li Y, et al. (2008) TrkB regulates hippocampal neurogenesis and governs sensitivity to antidepressive treatment. *Neuron* 59:399–412.

2. Luikart BW, et al. (2005) TrkB has a cell-autonomous role in the establishment of hippocampal Schaffer collateral synapses. *J Neurosci* 25:3774–3786.

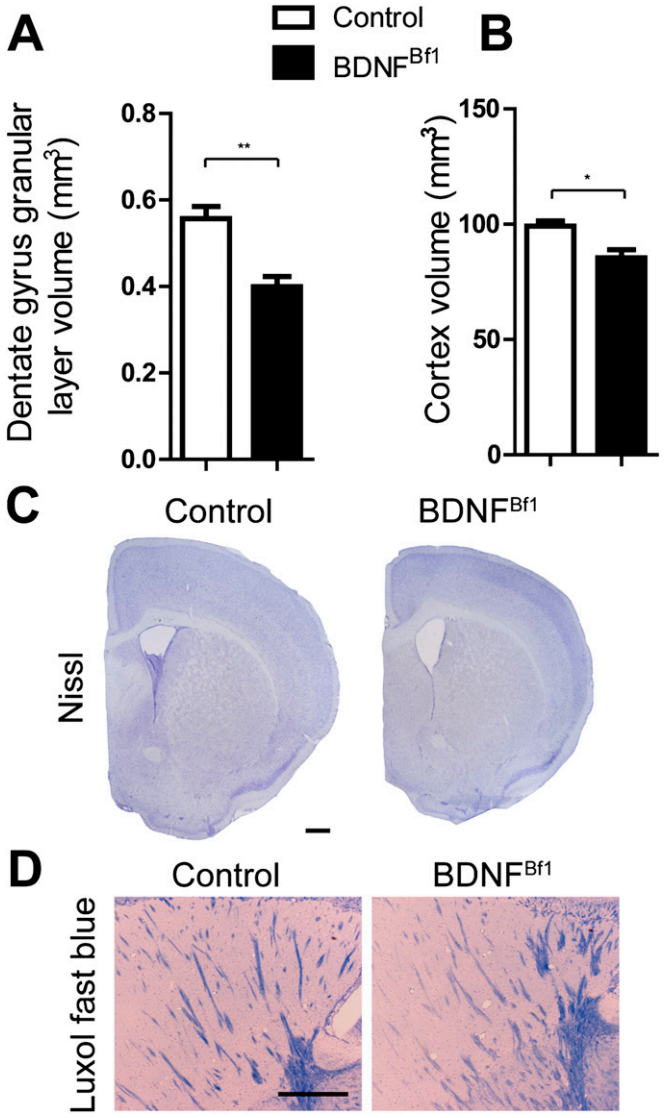

Fig. S1. Reduced brain size but normal striatal structural formation in the BDNF^{Bf1} mice. (*A* and *B*) BDNF^{BF1} mice had reduced DG volume (*A*) and cortex volume (*B*) at postnatal age 3 wk. $n = 5$ for each. (*C* and *D*) Nissl (*C*) and luxol fast blue (*D*) staining showed normal structural formation of the striatum in 3-wk-old BDNF^{Bf1} mice. (Scale bars: 500 μm.) Results are mean ± SEM. $^{**}P < 0.01$; $^{*}P < 0.05$.

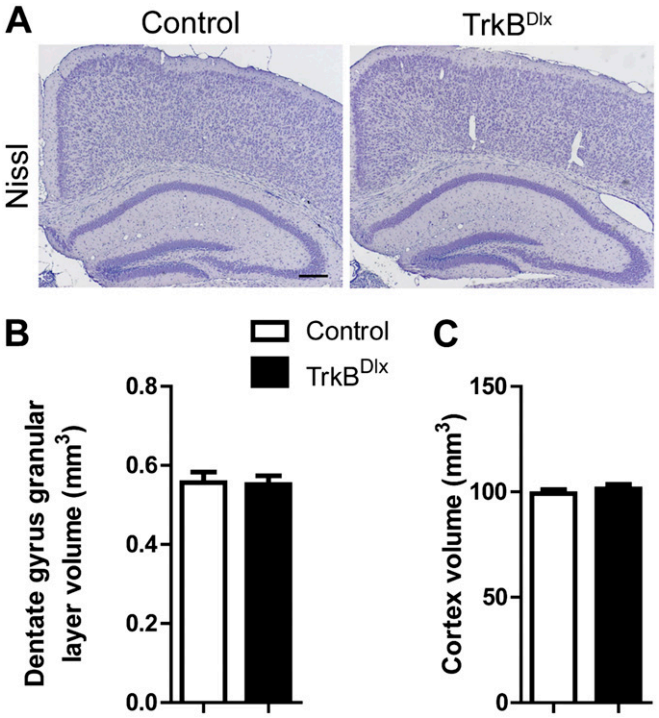

Fig. S2. Normal cortical and hippocampal morphology in the TrkB^{Dlx} mice. (*A*) Nissl staining showed normal-sized cortex and hippocampus in the TrkB^{Dlx} mice. (Scale bars: 200 μm.) (*B* and *C*) TrkB^{Dlx} mice had normal DG volume (*B*) and cortex volume (*C*) at postnatal 3 wk. n = 5–6 for each. Results are mean ± SEM.