Supplementary

**1. Methods**

**1.1 Doublecortin (DCX) Immunohistochemistry**

Doublecortin (DCX) immunohistochemistry was conducted as previously described ([David et al., 2009](#_ENREF_1)) and ([Mendez-David et al., 2014](#_ENREF_2)) and conducted to assess the number of newborn neurons in the hippocampus following chronic treatment with vortioxetine (Vh, n=8; Vortioxetine, n=8). Briefly, sections were rinsed in 0.1 M TBS (3x15 min) and treated with 0.3% H2O2 in 1X PBS/methanol (1:1) for 15 min in order to quench endogenous peroxidase activity and enhance dendritic stain. Sections were incubated in 10% normal donkey serum (NDS) in 0.1 M TBS with 0.5% Triton X-100 for 2 hours, followed by incubation with the goat anti-DCX primary antibody (1: 500; Santa Cruz, #SC 8066) in TBS/Triton X/NDS overnight at 4°C. The secondary antibody used was biotinylated donkey anti-goat (1:500) (Jackson ImmunoResearch, #705-065-003, PA, USA) in TBS for 2 hours at room temperature. DCX immunostaining was revealed by avidin-biotin complex (Vector, CA, USA) and DAB kit.

**2. Results:**

**2.2 The effects of treatment with vortioxetine on DCX positive cells in the adult mouse hippocampus**

The effects of vortioxetine treatment in cell maturation (DCX immunohistochemistry) are shown in Suplementary Figure 1 and statistical. Vortioxetine treatment induced a trend in increasing the number of DCX positive cells when compared to the vehicle group in the dentate gyrus of the hippocampus (unpaired one-tailed student's t-tests analysis: vehicle vs vortioxetine: t=1,663 df=11; p= 0,0622).

**REFERENCES**

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Mendez-David I, David DJ, Darcet F, Wu MV, Kerdine-Romer S, Gardier AM, Hen R (2014) Rapid anxiolytic effects of a 5-HT(4) receptor agonist are mediated by a neurogenesis-independent mechanism. Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology 39:1366-1378.