Supplementary Information

Methods for Behavioural Testing

*Rotarod*
To test for general agility and balance, rats were individually placed onto a rotating rod which gradually increased in rotation velocity. The trial ended when offspring were no longer able to maintain balance. The time measured from the velocity increase to the end of trial was recorded.

*Social Interaction Test*
Social behaviours were evaluated using adaptations of previously reported methodology using three-chambered social testing apparatus (Poirier, et al. 2014; Zhang-James, et al. 2014). Briefly, social cue rats (unfamiliar rats to the experimental rat) were habituated to the testing environment in a large grid rod animal holder (Med Associates Inc., ENV-264A) for 10 min/day in one of the side chambers. On the test day the experimental rat was placed within the central chamber with the doors closed. Following 5 min habituation, social and inanimate cue cages were placed in the side chambers, the doors were retracted and the experimental animal explored all three chambers for 10 min. Exploration time of each chamber was recorded. Greater exploration of the chamber containing the social cue compared to the inanimate cue is a measure of social interaction.

*Elevated Plus Maze*
Anxiety-like behaviour was explored by assessing exploration in the elevated plus maze. On the test day, individual rats were placed in the centre of the maze which comprised of two open arms (50 cm x 10 cm) and two closed arms (50 cm x 10 cm x 40 cm) and was elevated 50 cm off the ground. Activity was recorded for five min. The total distance travelled, grooming behaviour and time spent in the open or closed arms were scored
Open Field

Locomotor and exploratory behaviour was assessed by using an open field experiment taking place over five days. On each day, individual rats were placed in the centre of an open field box (90 cm x 90 cm x 50 cm) and activity was recorded by video for 10 min. For the first three days, rats were placed in the centre of the field without treatment, and on test days four and five rats were subject to restraint stress for 10 min prior to testing using a restraint chamber. The total distance travelled and time spent in the centre or periphery were scored.

Object Recognition and Object In Place

All animals were handled for 5 min/day for at least five days in the week before testing. For both tests, the amount of time spent exploring each object was recorded. The discrimination ratio was calculated as an index of memory performance (time at novel − time at familiar)/(time at novel + time at familiar).

Object recognition: For three days, each animal was habituated for five min to the open field box with two identical objects present in two of the corners. On the test day, the test was divided into a sample and test phase. In the sample phase, each animal was allowed to explore two identical novel objects for 5 min, followed by a 1 h interval before the test phase. Here, one object was replaced by a completely novel object. The rat was then allowed to explore the objects/box for 5 min and the time spent actively exploring each object was recorded.

Object in Place: Each rat was habituated to the open field over four days for a five min period with the presence of different objects in all four corners. The sample phase of the test day involved the rat being placed in the open field and being allowed to explore freely for five min. After a five min interval, the test phase
commenced whereby two of the objects used in the sample phase exchanged position. The rat was then placed back in the box for five minutes with exploration of each object recorded.

**Sucrose Preference Test**

Rats were individually housed for one week before the test. When testing commenced two drinking water bottles were placed in the cage (one left and one right) with food and water made available *ad libitum*. On day 1, the rats were weighed to allow data normalisation. On days 1 and 2, both bottles were filled with normal drinking water to acclimatise the animals to the new water bottle locations. On days 3 and 4, both bottles contained a 2% solution of sucrose dissolved in drinking water. On days 5-8, one bottle contained 2% sucrose, and the other water and the location of the bottles was switched daily to counter a side preference for fluid consumption. Fluid consumption preference on days 5-8 was assessed daily by weighing the bottles.

**MRI scanning and analysis details**

A FLASH based scout scan was performed over a field-of-view (FOV) = 50 mm 50 mm, with repetition time (TR) = 200 ms, echo time (TE) = 3.8 ms, and five interlaced 1.5 mm slices with a 1.0 mm gap, in three orthogonal directions. Subsequently, a 2D multi-slice RARE sequence was used to obtain a series of T2-weighted images in three orthogonal planes, with in-plane pixel size = 70 μm 70 μm, from 800 μm thick interlaced slices, with TR = 3900 ms, TE = 36 ms, and echo train length = 8. The FOV = 35 mm 35 mm for the axial and coronal images, and 35 mm 30 mm for the sagittal image. Fat suppression was utilized for all scans.
Major structures of interest were identified in three orthogonal planes. Volumes of the whole brain, hippocampus, lateral ventricles and corpus callosum were quantified following manual segmentation, based on voxel counts in both axial and coronal orientations. Cerebellum volumes were determined in the axial plane. Segmentations were completed in duplicate for a subset of animals to demonstrate repeatability. MRI volume assessments were normalised to total brain volume.