Volumetric brain changes following standardized dynamic enrichment of mice

Jan Scholz[1], Rylan Allemang-Grand[1], and Jason P Lerch[1]
[1]*Mouse Imaging Centre, Toronto, ON, Canada*

Introduction

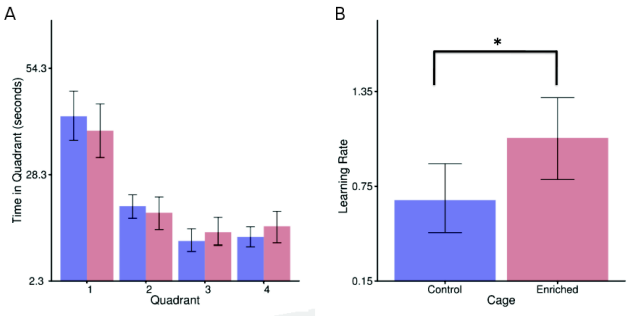
Environmental enrichment has been used for the past 50 years to study the effect of experience on the (rodent) brain. However, to date no unifying model of enrichment-related brain plasticity exists, because only small parts of the brain have been studied cross-sectionally and enrichment protocols have varied dramatically between studies. This study is set to rectify these short-comings by observing the whole brain longitudinally after enrichment with a standardized protocol.

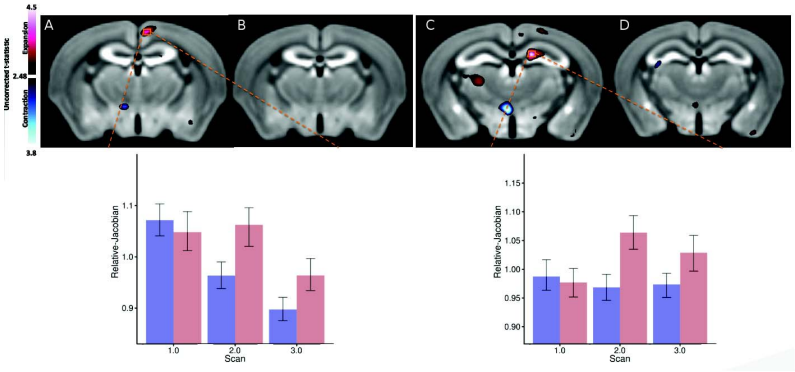
Methods

Behavioural Protocol: 28 male C57B6/J mice were evenly distributed across enrichment and control groups. Enrichment included a 3-level maze, pipes, domes, running wheels, bedding, nesting material . The maze consisted of interlocking polycarbonate walls and ceilings/floors. The walls can be easily re-arranged to change the spatial layout of the maze and create new pathways between ad lib food and water sources. *Imaging:* Enriched mice were scanned at baseline (6 weeks of age), after 3 weeks of dynamic enrichment during which the maze changed every 3 days. Controls were scanned at the same time, but experienced no enrichment. Subsequently, both groups were trained on the Barnes Maze for 3 days (3 trials/day) and probed on the 4th. Mice were scanned using Manganese-enhanced MRI (7T MRI, Gradient echo, TR/TE=100/3.6ms ,matrix= 280x168x168, 125μm^3 isotropic voxels). *Analysis:* Images were non-linearly registered. The jacobian determinants of the resulting deformation fields were used in a voxel-wise test of volumetric changes using a linear model (i.e. group x scan interaction).

Results

Both groups performed similar on the probe trial (no sig. difference in quadrant preference, Fig.1A). However, performance differed during the training phase. Enriched mice entered the target box quicker ($p<0.001$) and had an increased learning rate ($p<0.05$, Fig.1B).





Voxel-wise testing suggests that local brain morphology evolves differently for the two groups. The right retrosplenial cortex seemed to maintain its volume for the enriched mice, while it decreased for controls ($p<0.01$, uncorrected, Fig.2A). This decrease in volume was then also observed for enriched during the behavioural training period (Fig.2B). An increase in volume was observed in the right dentate gyrus for the enriched mice ($p<0.01$, uncorrected, Fig.2C). This increase was maintained during the behavioural training period. There was no change in dentate volume for controls.

Conclusion

Here we show the first application of a standardized cage design that allows the study of dynamic environmental enrichment of mice in a well-controlled fashion. Behavioural testing shows that enriched mice perform better during training on a spatial task. The comparable performance in the final probe trial could potentially be explained by ceiling effects which could be avoided by more difficulty tasks or shorter training. The retrosplenial cortex is a key area for navigation and memory. Enrichment might counteract normal age-related decline in this area. The dentate gyrus is involved in memory and has unique plasticity. Here, enrichment could be associated with aborization and neurogenesis, both potentially leading to increased volume.