A role of adult neurogenesis in the reaction to novelty

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The extent to which adult born neurons in the dentate gyrus are involved and necessary for cognitive and affective behaviour remains controversial. This is largely due to the difficulty in distinguishing if observed behavioural differences are mediated by neurogenesis, or, if behavioural and neurogenesis alterations are regulated in concert. To obtain a better understanding of the adult neurogenesis-behaviour relationship more refined experimental and statistical designs are necessary.

Here we present a high power unbiased assessment of the relationship between a range of behavioural variables and adult neurogenesis measured in untreated, common laboratory mice. The two strains of mice used, C57BL/6 and DBA, are characterized by a high and low levels of basal adult hippocampal neurogenesis (AHN) respectively. We also made use of age as a second natural factor regulating neurogenesis. Both strains were tested at the age of 9 and 17 weeks. The strong negative correlation between age and the extent of neurogenesis predicts a decrease of 60% in AHN between the two age groups. Behavioural variables were collected using the IntelliCage system in which animals were subjected to several behavioural paradigms testing motor impulsivity, anxiety and exploration without interference of the experimenter. Stereologically assessed numbers of proliferating cells (Ki67) and young cells of the neuronal lineage (doublecortin, DCX) were used to determine the level of adult hippocampal neurogenesis.

1993 behavioural variables were collected and have been tested in a linear model (ANCOVA) for possible relationships with adult neurogenesis. Due to the number of variables tested, several steps have been taken to eliminate false positive results. After correction, the majority of behavioural variables show no significant association with neurogenesis, including variables assessing motor impulsivity and anxiety. The notable exception being variables measuring exploration, where a range of variables measuring specifically novel exploration show a significant association with neurogenesis. These variables include the latency to start exploring different regions of the cage, the frequency of actions and the general activity of the animals exclusively in the first week after introduction into the novel environment. Neurogenesis does not have a uniform effect on these behavioural variables, higher neurogenesis exaggerates differences between strains while dampening others. The net effect of these modulatory actions of neurogenesis is one of animals with higher neurogenesis being slower to explore novel environments.

The notion that this particular behavioural trait is associated with neurogenesis could partly explain the conflicting results in behavioural studies investigating the effect of neurogenesis. Depending on the experimental design, the difference in reaction to novelty may have a major impact on behavioural outcomes, which in turn would correlate with the level of neurogenesis.