A017 Enhanced complexity of hippocampal dentate gyrus newly-generated neurons in mice following Coriolus versicolor biomass administration

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CENTROSS

Introduction

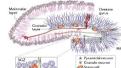
Brain cognitive reserve refers to the ability of the brain to manage different challenges that arise throughout life, making it resilient to neuropathology. Hippocampal adult neurogenesis has been considered as a relevant contributor for brain cognitive reserve and brain plasticity. The production of adult hippocampal neurons requires the continuous division of neural stem/progenitor cells, differentiation of newly-generated granule cells and their integration into the preexisting circuits under specified extracellular conditions. This integration into the hippocampal circuitry relies on newly-formed dendritic branches of pre-matured neurons that reach the dentate gyrus (DG) molecular layer (ML).

The Wnt/β-catenin signaling pathway and epigenetic mechanim are amenable to modulation by diet and play a major role in neurogenesis. Discovering dietary tools that promote neurogenesis is seemingly an useful strategy for providing the brain with means to cope with several insults including aging.

Coriolus versicolor (CV), a common healthful mushroom, was previously described to have antitumoral, anti-inflammatory, antioxidant, antibacterial, and immunomodulatory properties, including in the hippocampus.

Herein, we analyzed the influence of CV biomass oral administration for 2.5 months on hippocampal neurogenic reserve under normal/physiological conditions.





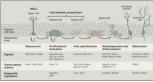
Methods

Two and a half-month-old wild-type mice (C57BL/6 x 129 background. male) were randomly divided in two experimental groups (n=10 per group): i) Saline-administered and ii) CV-administered (200 mg/kg bw, suspended in saline). The administration of CV or saline was performed every day for 2.5 months by oral gavage. CV biomass was supplied by Mycology Research Laboratories Ltd, Luton, U.K.

Hippocampal dentate gyrus (DG) granular cell layer (GCL) and subgranular zone (SGZ) volumes and number and dendritic complexity of hippocampal newly-generated neurons were quantified by immunohistochemistry, as well as β-catenin levels in DG newly-generated immature neurons. Levels of mRNA expression of epigenetic choreographers of neurogenesis (HDAC1, DNMT1 and Mecp2) were measured by quantitative real time PCR in total

Statistical significance was determined using One-way ANOVA with repeated measures followed by Bonferroni post hoc test, unpaired Student's t-test or non-parametric Mann-Whitney test. p<0.05 was considered statistically significant.



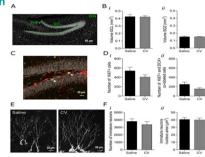


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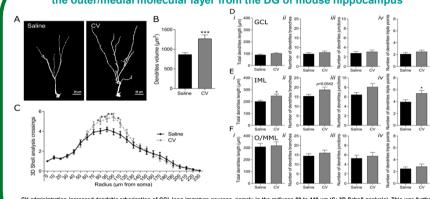
Results

GCL and SGZ volumes, proliferation and the number of immature neurons in mouse hippocampus are kept unchanged following CV administration ,



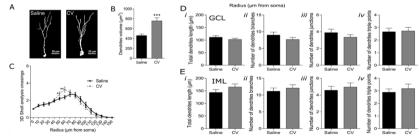
O Julinimisation in unit significant process of the continues of executions in the GCL of mouse hippocampus. (A) Conficial microscope image showing files SGZ and GCL (B) processing the separation between th roscope images showing immature neurons in the hippocampal DG. Immature neurons were stained with doublecortin antibody. (F) Quantification of the num irons in the GCL (i) and immature neurons nucleus area (ii). Data are expressed as mean ± SEM.

CV promotes dendritic branching and volume of immature neurons reaching the outer/medial molecular layer from the DG of mouse hippocampus



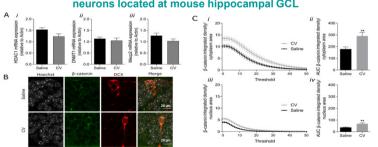
confirmed by an increase in their dendritic volume (B) and in the total dendrites length and number of dendrites triple points (junctions with three branches) located at the DG IML (E/i/V). (A) Three dimensional reconstructions of long immature neurons (EF DCX-positive cells that reach the QMML, (B) penditive solume. (C) 30 Sholl a Dendities length (I), number of neuronal branches (ii), number of neuronal junctions (iii) and number of triple points (iv) in the GCL (D), IML (E) and O/MML (F) of the hippocampal DG. Deversesded as mean ± SEM.

CV promotes dendritic branching and volume of immature neurons not reaching the outer/medial molecular layer from the DG of mouse hippocampus



CV blomass significantly increased the number of dendritic intersections, in the radius 50 and 60 um, of GCL short immature neurons (C: 3D Scholl analysis) length, the number of dendrites branches, dendrites junctions or the number of dendrites triple points (junctions with three branches) in both the granular cell per (GCL) and inner molecular layer (ML) of short cells (Di-IV) and Ei-IV). (A) The demandance of the control o

CV increases cytoplasmatic and nuclear β-catenin density in immature neurons located at mouse hippocampal GCL



CV administration increased β-catenin levels both in the nucleus (C) and cytoplasm (D) of GCL immature neuron. No alterations were observed in mRNA expression of epigenetic choreographers of neurogenesis (A-iii), A) mRNA expression levels of HDAC1 (i), DNMT1 (ii) and Mecp2 (iii) in the mouse hippocampus. (B) Confocal microscope images showing β-catenin staining in immature neurons in the hippocampal DG (nuclei in grey, DCX in red and β-catenin in green). Merge images show the presence of β-catenin in the nucleus and cytoplasm of immature neuron. (C) β-catenin integrated

Conclusions

- > CV biomass oral administration promotes a significant increase in dendritic length and branching, and total dendritic volume of immature neurons, suggesting a positive effect in the hippocampal neurogenic reserve.
- > Increased β-catenin levels in cytoplasm and nucleus of DG immature neurons suggests that Wnt/β-catenin signaling plays an important role in CV positive effect on dendritic complexity of hippocampal newly-generated neurons.
- This so far unexplored neurogenic potential of CV supplementation emerges as a possible preventive strategy for different neurological conditions.