Morphology and anatomy

Increase of visual cortical thickness[1] dentritic branches[2], higher order branches[3] with changes in dentritic spines[4], hippocampal thickness[5], brain weight and number of granule cells in the dorsal hippocampus[6], and increase of dentritic length, nodes and spines of pyramidal neurons in the hippocampus and layer III of the cortex[7,8]

Neurogenesis

Increase of proliferation, survival of BrdU positive cells[9] and neurogenesis when enrichment protocols started at 6[10],10 weeks[11], 2[12-15], 3[16,17], 6[18,9], 10[19] and 18 months of age[20], or no change in 25 months old[13]

Neurotrophic and growth factors

Increase of BDNF mRNA in the dorsal hippocampus[21,22] or no change[23-25]

Increase of BDNF protein level in the hippocampus[26-29] or no change[7,30-32]

Increase of BDNF mRNA in the striatum[33], decrease in the substantia nigra pars compacta[34] or no change in the striatum and the cortex[34]

Increase of protein level of BDNF in the cortex, basal forebrain and the hindbrain[28], the cerebellum, prefrontal cortex and the striatum[35], occipital cortex[36], superior colliculus and the visual cortex[37] and retina[37,38]

No effect on protein level of BDNF in the amygdala and the prefrontal cortex[31], the anteromedial cortex[30], the frontal cortex[39] and the striatum[30,32]

Increase of NGF gene expression in the hippocampus[21,40]

Increase of NGF protein level in the hippocampus[28,41,42], the basal forebrain and the hindbrain[28], the visual cortex[40,42] and the entorhinal cortex[42] or no change in the cortex[28]

Increase of GDNF mRNA in the substantia nigra pars compacta[34] and protein level in the hippocampus[29] or no change of GDNF mRNA in the striatum[34]

Increase of NT-3 protein level in the cortex and no change in the hippocampus[28]

Increase of VEGF mRNA in the hippocampus[43,44]

Neurotransmitters

Increase of the glutamate decarboxylase (GAD) activity in the hippocampus but not in the neocortex[45]

No effect on extracellular concentration of GABA in CA3 area of the hippocampus[13]

Increase of the extracellular concentration of glutamate in the CA3 area of the hippocampus[13]

Increase of the extracellular concentration of glutamate in the CA3 area of the hippocampus[13]

No effect on extracellular concentration of glutamate in the nucleus accumbens[46] and the prefrontal cortex[47]

No effect on acetylcholine concentration in the prefrontal cortex[31,48,49] and on choline acetyltransferase (ChAT) protein level in the hippocampus[50]

Decrease of mRNA level of dopamine transporter (DAT) in the striatum[33] and the substantia nigra pars compacta[34]

No effect on tissue dopamine content in the prefrontal cortex[31,48,51,52], the frontal cortex[39,53], the frontoparietal cortex[54], the parieto-temporal-occipital cortex, the pons/medulla oblongata[53], the hippocampus[54], the striatum[52,55] and the nucleus accumbens[56]

Increase of noradrenaline (NA) concentration in the dorsal hippocampus[54], the parieto-temporal-occipital cortex, the cerebellum and in the pons/medulla oblongata[53]

Decrease in the basal concentration of serotonin (5-HT) in the ventral hippocampus[54]

No effect on 5-HT concentration in the frontoparietal cortex[54], the pons/medulla oblongata, the cerebellum and the parieto-temporal-occipital cortex[53]

Neurotransmitters receptors

Increase of NMDA subunit NR2A mRNA level in the right hemisphere[57] and the hippocampus[58]

Increase of NMDA subunits NR2A and NR2B protein level in the forebrain[59] but not in the anterior cingulate cortex[60]

No effect on NMDA subunit NR1 gene expression in the whole brain[23,61], protein level in the forebrain[59] and the nucleus accumbens[61,62]

Increase of metabotropic glutamate receptors mGluR1/R5 and mGluR2/3 protein levels in the dorsal prefrontal cortex, but no effect on the ventral prefrontal cortex and the striatum[47]

Increase of AMPA subunits GluR2 and GluR4 mRNA in the hippocampus[63]

No effect on transcript and protein levels of GluR1, GluR2 and GluR3 subunits in the hippocampus[58,64,65] and on GluR1 protein level in the nucleus accumbens[62], in the forebrain[59], in the visual cortex[66] in the striatum and the frontal cortex[64]

No effect on GABA A receptor transcript level in the striatum[67]

Decrease of dopamine 1 (D1) receptor protein level in the prefrontal cortex[49]

No effect on D1 and D2 receptors in the striatum[67] and the nucleus accumbens[68]

Increase of 5-HT1A receptor gene expression in the hippocampus[69]

No effect of 5-HT2A gene expression and protein level in the hippocampus and the striatum[69,70]

Immediate early genes

Increase of Zif268 mRNA in the CA2[71], CA3-CA4[61] and CA1 areas of the hippocampus[72] and in the visual cortex[73]

Increase of Krox-20 gene expression in the cortex[72,74], the hippocampus[75] and in CA3 area of the hippocampus[72]

Increase of NGFI-B transcript level in CA1-CA2 area of the hippocampus[71]

Increase of Arc gene expression in the hippocampus[71,74], in the striatum and the cortex[74]

Transcpritomic and proteomic large scale analysis

Changes in expression of genes whose products are involved in DNA/RNA synthesis, neuronal growth/structure, protease/cell death, protein processing and neuronal signaling in the cortex[76]

Increase in 34 genes and decrease in 14 genes involved in signal transduction, cell proliferation/differentiation, transcription and translation, structural rearrangements and metabolism[77]

Proteins implicated in the cytoplasmic organization and energy metabolism in the hippocampus are the most altered[78]

Long term potentiation (LTP)

No effect on LTP recorded from dentate gyrus of hippocampal slices[79-81]

Increase of LTP measured on slices in CA1 area[82-85] and in the layer II-III of neurons in the anterior cingulate cortex[60]

Increase[86] or no change[87] of LTP in the dentate gurys of freely moving rats

Cognition and behavior

Enhanced performance in the Morris water maze test[88-91] or no change[27,92-94]

Decreased anxiety-like behavior in the Elevated plus maze (EPM) test[95-99] or no change[100-103]

Brain protection

Prevents memory deficit in Alzheimer's disease[18,104], reduces cell death in Parkinson's disease[33,34], improves motor symptoms in Huntington's disease[30], attenuates learning deficits in brain trauma[24], improves motor coordination in Rett's syndrom model[32], ameliorates functional recovery in cranial irradiation[21], protects against behavioral alterations in lead toxicity model[105], reverse cocaine addiction[106] and prevents cognitive impairment in epilepsy [10,75,93,107,108]