RESEARCH ARTICLE

G protein-coupled receptor 37-like 1 modulates astrocyte glutamate transporters and neuronal NMDA receptors and is neuroprotective in ischemia

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. Gpr37l1

2.8 | Intracellular solutions

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2.17 | Novel-object recognition

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To confirm these results, we used Gpr37l1-LacZ heterozygous mice in which a LacZ cassette was inserted into the first exon of the Gpr37l1 gene (inactivating the protein product). Immunolabelling for b-galactosidase confirmed that Gpr37l1-LacZ was expressed in PDGFRA-positive OPs in the cortex (Supporting Information Figure 2a) but not in CC1^{1} mature OLs, NEUN^{1} neurons or IBA1^{1} microglia (Supporting Information Figure 2b–d). In addition, Gpr37l1-LacZ was expressed in the cerebellum in Bergman glia and in OL-lineage cells identified by SOX10 immunolabelling (Supporting Information Figure 2e,f).

Expression of Gpr37l1 was developmentally regulated. At postnatal day 1 (P1), Gpr37l1 mRNA was not detectable in any brain area examined (Figure 2a–c) but at P8 Gpr37l1 was strongly expressed in both astrocytes (Figure 2d–f) and OPs (not shown). At P15 (not shown) and during adulthood, Gpr37l1 expression in astrocytes (Figure 2g–i) and OPs (not shown) remained at high levels. Thus, GPR37L1 might have a functional role from the period of synaptogenesis and the onset of myelination through to adulthood (Figure 2j).

3.2 | Gpr37l1 and Gpr37 are expressed in different cells

GPR37L1 and its close relative GPR37 share 48% amino acid identity in human (Valdenaire et al., 1998). ISH for Gpr37 mRNA showed that Gpr37 was expressed in many cells in subcortical structures such as the hypothalamus and thalamus as well as in the corpus callosum, and in smaller numbers of cells in the cortex and hippocampus (Figure 3). Gpr37 was mostly in OLIG2^{1} oligodendrocyte (OL)-lineage cells (Figure 3a–c) but not in PDGFRA^{1} cells (Figure 3d–f), suggesting that mature OLs but not OPs express Gpr37. We observed no expression of Gpr37 in GFAP^{1} astrocytes (not shown). Occasionally, Gpr37 expression was seen in some NEUN^{1} neurons but not in IBA1^{1} microglia (not shown).

In contrast to Gpr37, Gpr37l1 is not expressed in CC1^{1} mature OLs, judging by immunolabelling of Gpr37l1-LacZ heterozygous mice for b-galactosidase (Figure 3g–i; Supporting Information Figure 2b). Thus, Gpr37l1 and Gpr37 are expressed in complementary cell types, Gpr37l1 being highly expressed in astrocytes and OPs whereas Gpr37 is ee7Tc51647 Tc.979 d8i261p6 7.9b)1

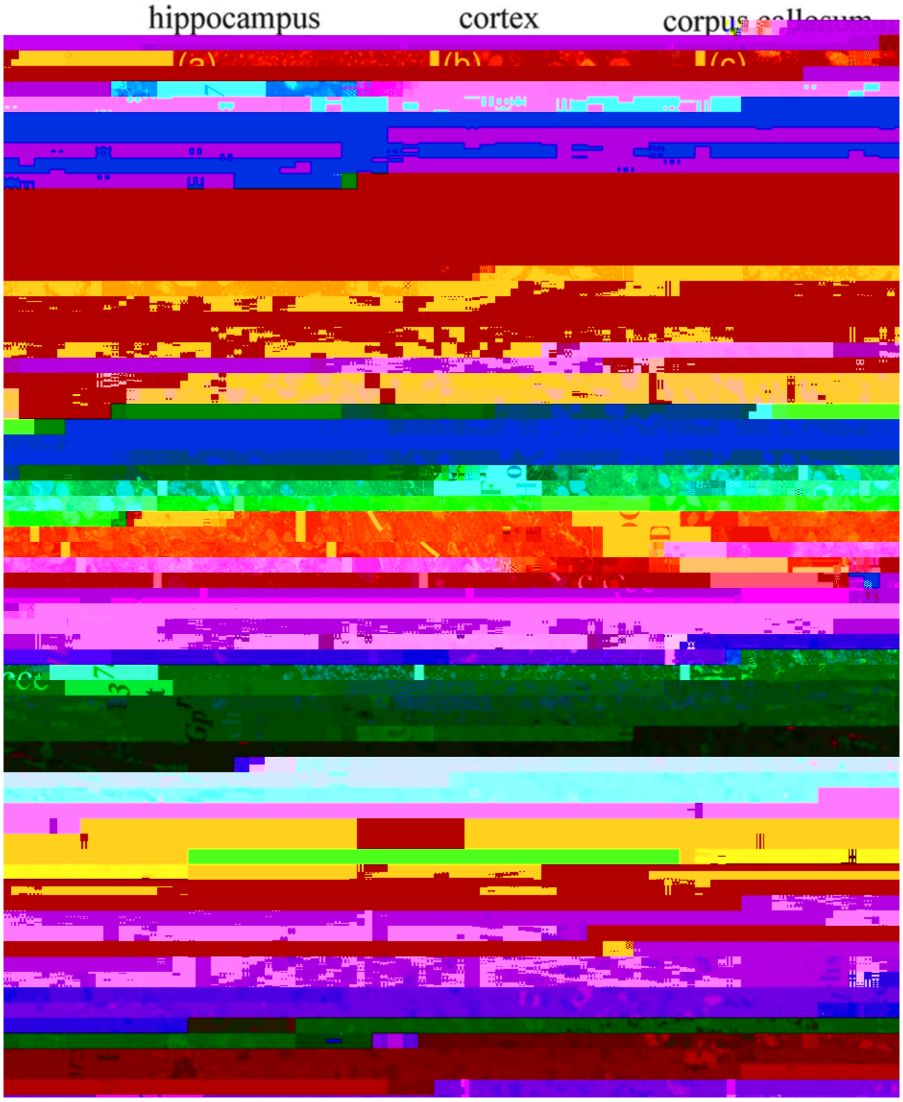

FIGURE 3 Gpr37l1 Gpr37 - . - . (- (– . .)- . ( ) . (( )- (. - . ( ) . ( )- . (- . - . (- .) . () ( ) ( )-.- -

Gpr37l1$^{- -}$ Gpr37l1$^{+ +}$ (t , $p =$. , –), (t , $p =$. , ,). - ( ), - ($p =$.), ($p =$.), ($p =$.) (–).

3.4 | Gpr37l1 KO does not alter the input resistance of astrocytes or neurons or neuronal excitability

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. Gpr37l1 , Gpr37l1-GFP , (, $p =$.) (, $p =$.). , Gpr37l1$^{+ +}$ Gpr37l1$^{- -}$ (, $p =$.) (, $p =$.). Gpr37l1$^{+ +}$ Gpr37l1$^{- -}$ (, , $p =$. $p =$. ,)

Gpr37l1 - (, $p =$.) (- +-), (, $p =$.).

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Gpr37l1$^{+ +}$ Gpr37l1$^{− −}$.

Glast Glt1D-.0142Tc[an2(n2e)25.4(l)255.)23.M1.1020TD0h70.7(1(/)13.9(el)1l)19.1(0s53.7(s)15.6(e)29ivgs

Gpr37l11

3.6 | GPR37L1 signalling decreases neuronal responses to prolonged NMDA application

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Gpr37l1

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