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BRAIN RESEARCH

Research Report

Changes in glycine receptor subunit expression in forebrain regions of the Wistar rat over development

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ABSTRACT

Glycine receptors (GlyRs) are pentameric membrane proteins in the form of either α-homomers or α–β heteromers. Four out of five subunits; α1–3 and β, have been found in the mammalian brain. Early studies investigating subunit composition and expression patterns of this receptor have proposed a developmental switch from α2 homomers to α1β heteromers as the CNS matures, a conclusion primarily based on results from the spinal cord. However, our previous results indicate that this might not apply to e.g. the forebrain regions. Here we examined alterations in GlyR expression caused by developmental changes in selected brain areas, focusing on reward-related regions. Animals of several ages (P2, P21 and P60) were included to examine potential changes over time. In accordance with previous reports, a switch in expression was observed in the spinal cord. However, the present results indicate that a decrease in α2 subunit expression is not replaced by α1 subunit expression since the generally low levels, and modest increases, of α1 could hardly replace the reduction in α2-mRNA. Instead mRNA measurements indicate that α2 continues to be the dominating α-subunit also in adult animals, usually in combination with high and stable levels of β-subunit expression. This indicates that alterations in GlyR subunit expression are not simply a maturation effect common for the entire CNS, but rather a unique pattern of transition depending on the region at hand.

1. Introduction

The implications of the neurotransmitter glycine and its receptor in bodily functions, and dysfunctions, are diverse. This diversity has created an increasing interest in the glycine receptors (GlyRs), which are pentameric membrane proteins existing either as α-homomers or α–β heteromers with a subunit stoichiometry of 2α3β (Grudzinska et al., 2005). Until now

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Abbreviations: ACTB, beta-actin; DA, dopamine; FC, frontal cortex; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; GlyR, glycine receptor; IHC, immunohistochemistry; nAc, nucleus accumbens; nAChR, nicotinic acetylcholine receptor; PFC, prefrontal cortex; qPCR, quantitative polymerase chain reaction; RPL 19, ribosomal protein L19; SC, spinal cord; Sdha, succinate dehydrogenase complex, subunit A, flavoprotein; Str, striatum; Ywhaz, tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide

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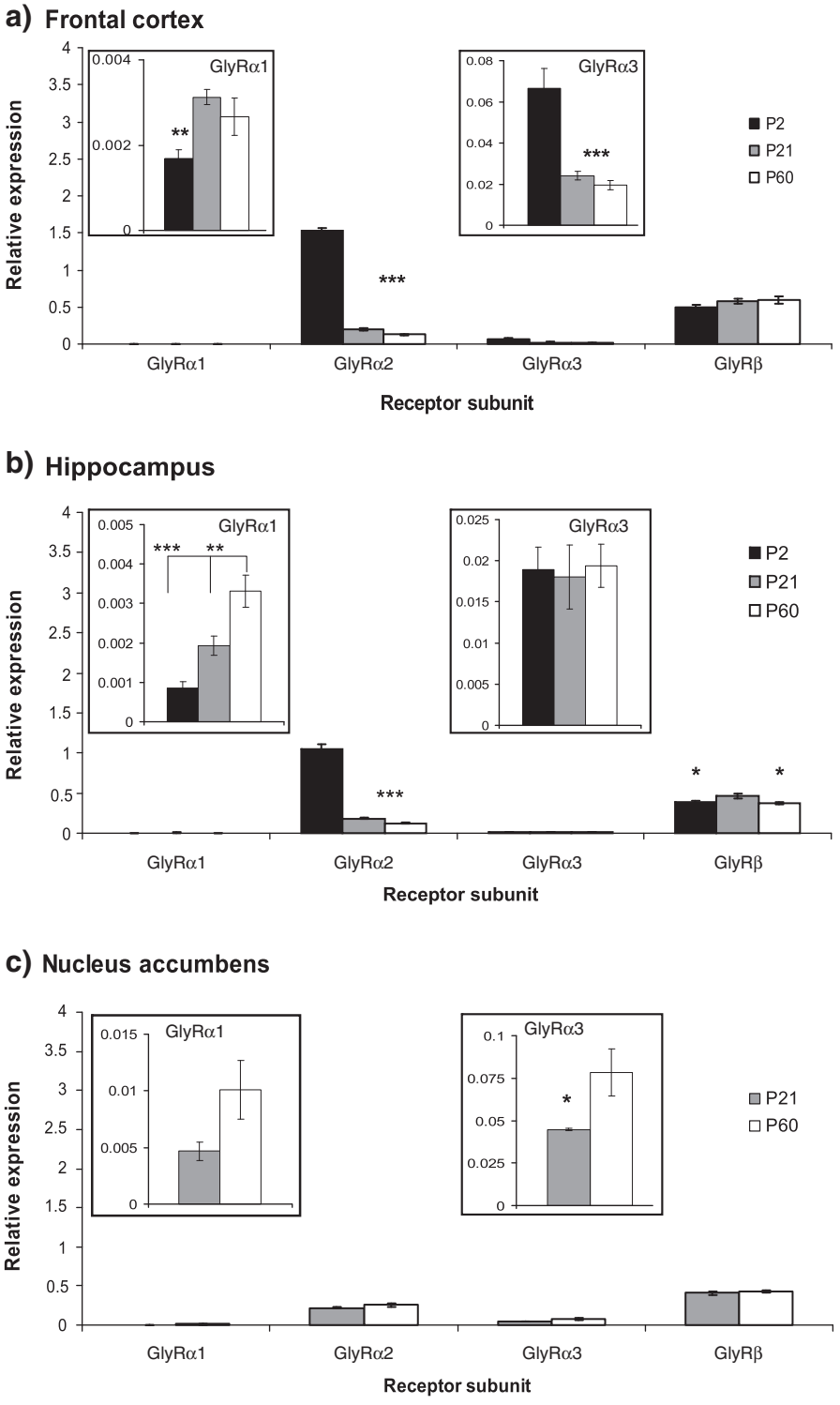

Fig. 1 – The relative expression of glycine receptor subunits in P2, P21 and P60 animals in a) frontal cortex n = 6–9, b) hippocampus n = 8–10, c) nucleus accumbens n = 10, d) spinal cord n = 10 and e) striatum n = 10. The most prominent changes in all areas and for all subunits occurred between P2 and P21. In general the highest levels of expression were observed at P2, except for the α1 subunit which more often increased with time. The most explicit expression patterns were those of α2 and β. However, the usually high expression at P2 followed by a significant decrease for α2 was often in sharp contrast to the regularly stable β levels. Error bars show SEM. Significant differences are indicated by * for $p < 0.05$, ** for $p < 0.01$, and * for $p < 0.001$. # bar truncated at 4.0 for GlyRα2 in striatum, actual relative expression value was 6.8.**