



Fig. 3. Postnatal changes in relative levels of GABA_A receptor mRNAs across rat brain regions. Relative levels of a1, a2, b1, b2, g2L, and g2S subunit mRNAs in rat cerebral cortex A, hippocampus B, and cerebellum C, at 0, 6, 14, 21, 29, and 90 postnatal days were assessed by RNase protection assay using ³²P-labeled riboprobes. For each region and age *n* = 4, values expressed indicate the mean value of GABA_A receptor subunit mRNA: 18S mRNA ± S.E.M., based on Phosimage densities corrected for relative probe sizes and specific activities. A riboprobe for ribosomal 18S mRNA was included as an internal standard in each sample. See text and legend to Fig. 1 regarding calculation of relative mRNA levels. * Identifies a statistically significant effect of age indicated by ANOVA. Results of post-hoc analyses are discussed in Section 3.2 of the text.

limited to a modest decrease between P14 and P21. In addition, ANOVA revealed a significant effect of age on b1 mRNA levels that was identified by post-hoc analysis as a small, but significant increase from P14 to P21 ($p < 0.01$), coincident with the observed decrease in a2 mRNA. As in the cortex, no change in b2 mRNA level was observed in hippocampus over the ages examined. A significant effect of age on both g2S ($p < 0.0001$) and g2L ($p < 0.0001$) mRNA was revealed by ANOVA, with a developmental pattern that resembled that of cortex, except that the greatest increase in hippocampal g2L mRNA ($\sim 2 \times$) occurred in the second, rather than the third, postnatal week, coincident with the rise in a1 mRNA. As in cortex, g2L mRNA increased significantly between the ages of P6 and P29, whereas g2S mRNA dropped significantly from P6 to P21. Thus, a remarkable similarity was observed between cerebral cortex and hippocampus in terms of postnatal changes in the levels of a1, g2L, thegG293hatu.618 0 4(In)ppe04(o)-38pd

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may be that Nadler et al. (1991) were primarily detecting the
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4.4. Conclusion

We have used highly quantitative methods to assess the temporal relationship between postnatal development of three distinct zolpidem binding sites and changing levels of mRNAs encoding predominant GABA_A receptor subunits across several brain regions in a single species, the Long–Evans strain of rat. As discussed above, the results of these experiments demonstrate regional heterogeneity of zolpidem binding sites, and $\alpha 1$, $\alpha 2$, $\beta 1$, $\beta 2$, $\gamma 2S$ and $\gamma 2L$ mRNAs, within the cerebral cortex, the hippocampal formation, and the cerebellum over the entire period of juvenile development. Indeed, the high degree of regional heterogeneity in zolpidem binding sites and GABA_A receptor subunit expression is consistent with the hypothesis that zolpidem binds to a distinct population of GABA_A receptors in the brain.

The levels of zolpidem binding sites and GABA_A receptor subunit mRNAs in the brain are highly correlated, suggesting that the levels of zolpidem binding sites and GABA_A receptor subunit mRNAs are regulated in a similar manner.

acid benzodiazepine receptor subunit mRNAs in the murine inferior olivary complex, *J. Comp. Neurol.* 356 1995 615–628., C.K. Kellogg, G. Chen, P.Q. Trombley, A.N. van den Pol, Excitatory actions of GABA in developing hypothalamic neurons, *J. Physiol.* 494 1996 .

