

Heparan sulphate proteoglycans in glia and in the normal and injured CNS: expression of sulphotransferases and changes in sulphation.

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Abstract

Heparan sulphate proteoglycans (HSPGs) have multiple functions relevant to the control of the CNS injury response, particularly in modulating the effects of growth factors and localizing molecules that affect axon growth. We examined the pattern of expression and glycanation of HSPGs in the normal and damaged CNS, and in astrocytes and oligodendrocyte precursors because of their participation in the injury reaction. The composition of HS glycosaminoglycan (GAG) chains was analysed by biochemical analysis and by the binding of antibodies that recognize sulphated epitopes. We also measured levels of HS sulphotransferases and syndecans. Compared with oligodendrocytes, oligodendrocyte precursors have more 2-O-sulphation in their HS GAG. This is accompanied by higher expression of the enzyme responsible for 2-O-sulphation, HS 2-O-sulphotransferase (HS2ST) and a fall in syndecan-1. Astrocytes treated with tumour growth factor (TGF) α or TGF β to mimic the injury response showed upregulation of syndecan-1 and HS2ST correlating with an increase in 2-O-sulphate residues in their HS GAGs. This also correlated with increased staining with AO4B08 anti-GAG antibody that recognizes high sulphation, and reduced staining with RB4EA12 recognizing low sulphation. After injury to the adult rat brain there was an overall increase in the quantity of HSPG around the injury site, mRNA for HS2ST was increased, and the changes in staining with sulphation-specific antibodies were consistent with an increase in 2-O-sulphated HS. Syndecan-1 was upregulated in astrocytes. The major injury-related change, seen in injured brain and cultured glia, was an increase in 2-O-sulphated HS and increased syndecan-1, suggesting novel approaches to modulating scar formation.

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