Modulatory effects of dextran sulfate and fucoidan on binding and channel properties of AMPA receptors isolated from rat brain

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Abstract

Previous work showed that the glycosaminoglycan (GAG) dextran sulfate (500 kDa) altered the binding and channel properties of α-amino-3-hydroxy-5- methyl-4-isoxazolepropionic acid (AMPA)-type glutamate receptors. The current study compared the effects of dextran sulfate with another GAG, fucoidan (100-180 kDa), to determine whether GAG-mediated changes in high-affinity binding of AMPA receptors have a concomitant influence on specific channel properties. Dextran sulfate was more potent in inhibiting high-affinity AMPA binding to solubilized receptors (EC_{50} of 7 nM) compared to fucoidan (EC_{50} of 124 nM). Similarly, dextran sulfate was more potent in modulating the channel properties of purified and reconstituted AMPA receptors. Dextran sulfate, at 1 μg/ml (2 nM), produced a three to fourfold increase in open channel probability and a threefold increase in mean burst duration of channel activity elicited by 283 nM AMPA. The mean open time was increased by two to threefold and closed times were decreased by two to eightfold. Fucoidan produced similar effects at a concentration many times higher than that of dextran sulfate. Dextran sulfate and fucoidan had no effect on the single channel conductance or the ability of a specific antagonist to block AMPA channels. The effects of GAGs on multichannel patches showed an interactive channel gating behavior resulting in macroscopic currents with long lived open channel life times. These findings suggest that GAG components of proteoglycans can interact with and alter the binding affinity of AMPA receptors and modulate their functional properties.

Author keywords

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