Short openings in high resolution single channel recordings of mouse nicotinic receptors.

The temporal fine structure of single channel currents was studied to obtain information on how agonists open nicotinic acetylcholine receptor channels. Currents were recorded from mouse myoballs with quartz pipettes in the on-cell mode of the patch-clamp technique. With 62 kHz filter cut-off and root mean square (r.m.s.) noise levels as low as 1.45 pA at 200 mV hyperpolarization, events down to 6 microseconds duration could be resolved with negligible error rate. Three types of openings with mean durations of 750 microseconds, 89 microseconds and 4 microseconds were identified with 0.1-10 microM suberyldicholine (SubCh). The relative frequencies of the three types of openings were 84% for long, 5% for medium and 11% for short openings with 1 microM SubCh. Stability plots and single channel current amplitude comparisons suggest that the three types of openings arise from a homogenous channel population. Above 10 microM SubCh, the three types of openings could not be discerned because channel openings occurred too closely spaced and open channels were increasingly blocked. Three types of openings can be generated with a mechanistic receptor model with two unequal binding sites, short and medium openings arising from one or the other monoligated state, and long openings from the fully liganded state of the receptor. Maximum likelihood fitting of the rate constants of this model directly to the sequence of observed open and shut times.
accurately predicted the main physiological properties of the receptors with 0.1 microM SubCh. However, fitting recordings with 0.1-10 microM SubCh simultaneously revealed that this model cannot reproduce the weak influence of SubCh concentration on the proportions of the three types of openings. Therefore we conclude that short and medium openings are unlikely to arise preferentially from one or the other moniliganded state of nicotinic acetylcholine receptor channels.