Molecular interaction of α-conotoxin RgIA with the rat α9α10 nAChR

Layla Azam, Athanasios Papakyriakou, Marios Zouridakis, Petros Giastas, Socrates J. Tzartos and J. Michael McIntosh

Figure S1. Sequence alignment of human and rat α9 and α10 nAChR subunits color-coded by similarity and topological domain (red for signal peptide residues).

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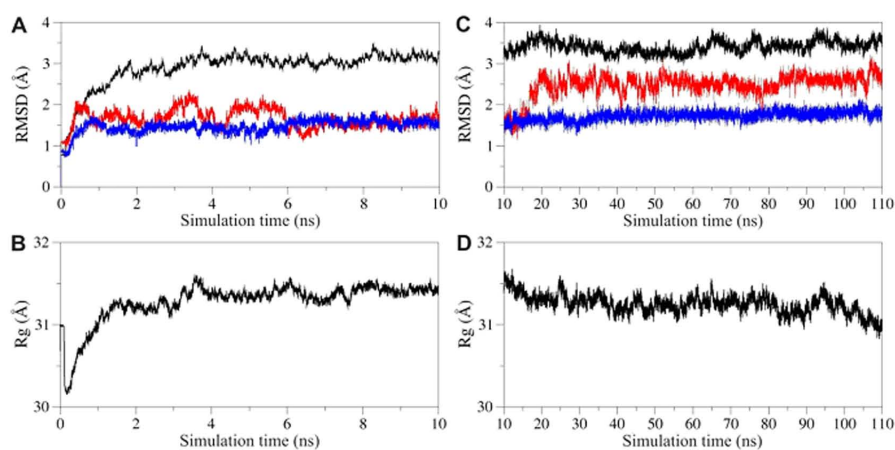
Figure S2. (A) Positional root-mean-square deviation (RMSD) from the initial model of rat $(\alpha9)_2(\alpha10)_3$ ECD complex with RgIA during the equilibration phase, calculated for the backbone atoms of the receptor (black line) and the two bound α-conotoxin ligands (red and blue lines). (B) Radius of gyration (Rg) of the receptor during the course of the equilibration phase of the MD simulations. (C) and (D) are the same as (A) and (B), respectively, during the course of the100-ns production MD runs.

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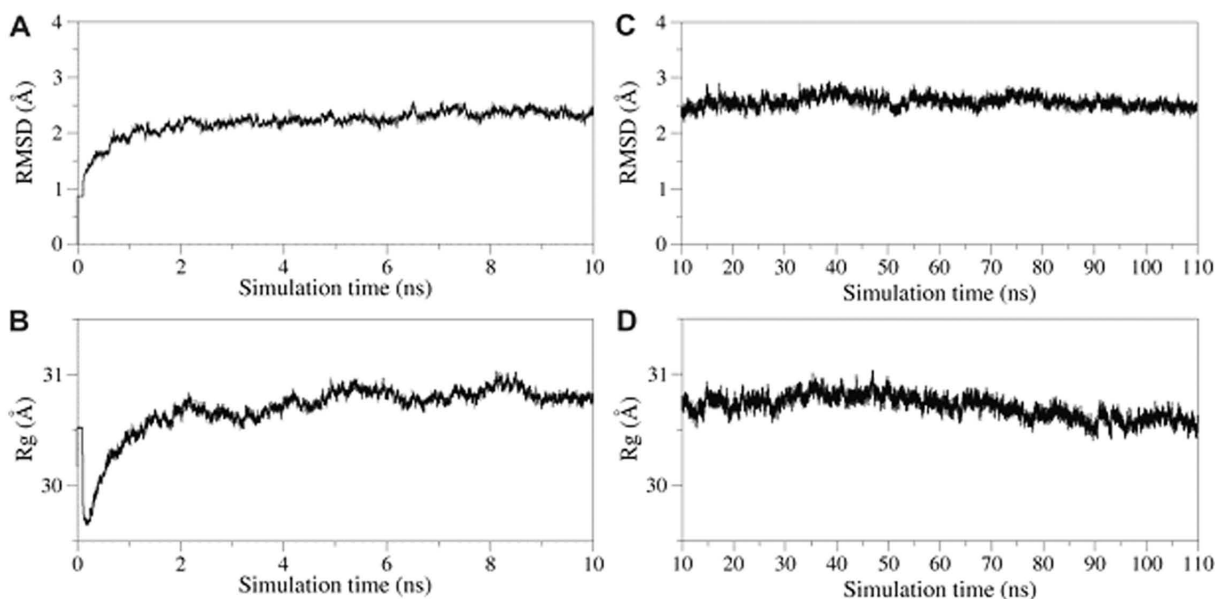
Figure S3. (A) Postitional root-mean-square deviation (RMSD) of the backbone atoms of the receptor from the initial model of rat $(\alpha 9)_2(\alpha 10)_3$ ECD complex with ACh during the equlibration phase. (B) Radius of gyration (Rg) of the receptor during the course of the MD simulations. (C) and (D) are the same as (A) and (B), respectively, during the course of the 100-ns production MD runs.

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Figure S4. Distance between D201-C$^{\gamma}$ of α10(+) subunit and R7-C$^{\zeta}$ of RgIA as a function of simulation time taken from : (A) the MDs of the native receptor, and (B) the MDs of the α9α10P200Q mutant.

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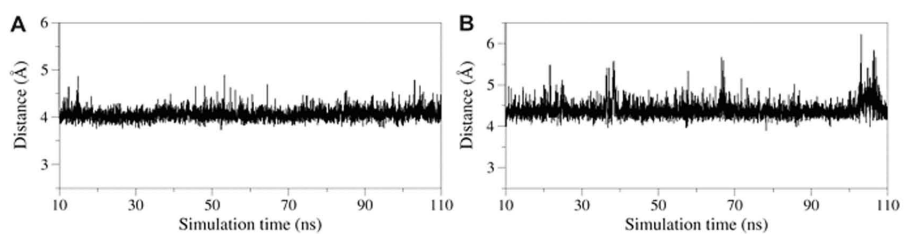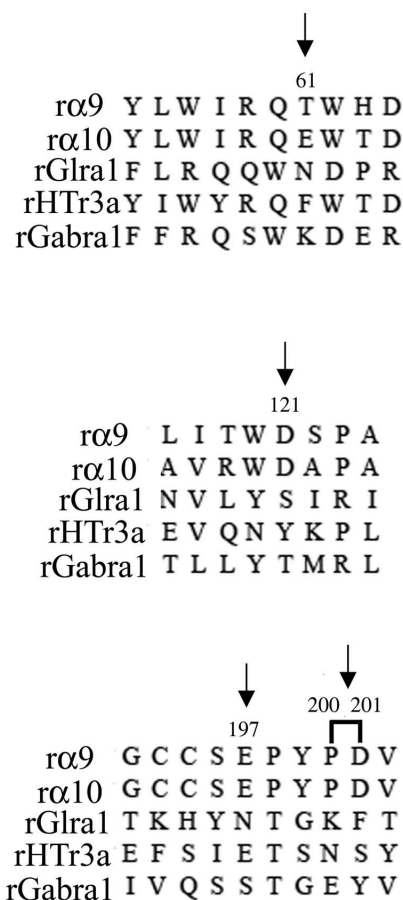
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                              ↓
                              61
               rα9    Y L W I R Q T W H D
               rα10   Y L W I R Q E W T D
               rGlra1 F L R Q Q W N D P R
               rHTr3a Y I W Y R Q F W T D
               rGabra1 F F R Q S W K D E R


                              ↓
                             121
               rα9     L I T W D S P A
               rα10    A V R W D A P A
               rGlra1  N V L Y S I R I
               rHTr3a  E V Q N Y K P L
               rGabra1 T L L Y T M R L


                          ↓       ↓
                         197   200 201
                                 ⌐¬
               rα9    G C C S E P Y P D V
               rα10   G C C S E P Y P D V
               rGlra1 T K H Y N T G K F T
               rHTr3a E F S I E T S N S Y
               rGabra1 I V Q S S T G E Y V
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Figure S5. Alignment of critical α-CTx RgIA binding residues in ECDs of the rat α9 and α10 nAChR subunits with other rat Cys-loop ligand-gated ion channels. These other pentameric channels include glycine (Glra1), 5-HT$_3$ (HTr3a) and GABA$_A$ (Gabra1). The sequence alignment among the rat ECDs was performed with MacVector 10.5.1 ClustalW alignment, using the UNIPROT accession codes P43144 for rat α9, Q9JLB5 for rat α10, P35563 for 5HT3A, P62813 for GABA$_A$ alpha1 subunit and P07727 for Glycine receptor alpha1 subunit. Note that few of the residues are conserved in the non-nicotinic receptors. Numbering is for the α9 and α10 nAChR subunits.