Supporting Information

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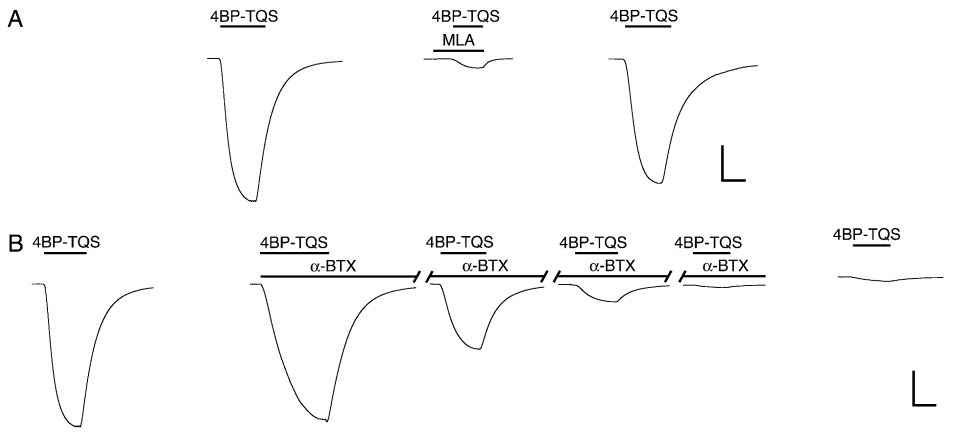

Fig. S1. Antagonism of 4BP-TQS responses by metyllycaconitine (MLA) and α-bungarotoxin (α-BTX) on α7 nicotinic acetylcholine receptors (nAChRs) expressed in *Xenopus* oocytes. (*A*) Responses to 4BP-TQS (10 μM) (*Left*) were blocked by MLA (5 nM, MLA was preapplied for 15 s and also coapplied with 4BP-TQS) (*Center*). Responses to 4BP-TQS showed complete recovery after a 2-min wash (the shortest time point examined) (*Right*). (*B*) Responses to 4BP-TQS (10 μM) (*Left*) were blocked by α-BTX (10 nM) but the block was slow to develop (*Center*: traces were recorded 0, 2, 6, and 12 min after exposure to α-BTX). Complete block was not observed until receptors had been exposed to α-BTX for several minutes. Only minimal recovery from block by α-BTX was observed, even after washing for 15 min (*Right*). (Scale bars: vertical, 0.5 μA; horizontal, 20 s.)

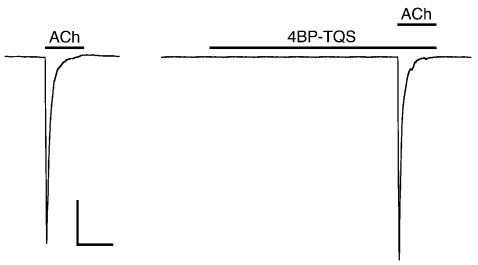

Fig. S2. Mutation M253L, located in the α7 nAChR M2 transmembrane domain, blocks both the allosteric agonist and the potentiating (PAM) activity of 4BP-TQS. A protocol similar to that described in Fig. 6 was used to examine α7 nAChRs containing the M253L mutation. Application of acetylcholine (3 mM) resulted in rapidly desensitizing responses typical of α7 nAChRs (*Left*). In contrast to the situation observed in wild-type α7 nAChRs (Fig. 6), no agonist activation was observed when 4BP-TQS (10 μM) was applied to receptors containing the M253L mutation (*Right*). In addition, subsequent coapplication of acetylcholine (3 mM) with 4BP-TQS (10 μM) gave no evidence of potentiation of the acetylcholine response. Similar data were obtained with lower (e.g., EC_{10}) concentrations of acetylcholine. (Scale bars: vertical, 100 nA; horizontal, 5 s.)