Supporting Information

# Mechanism of Inhibition of the GluA2 AMPA Receptor Channel Opening by 2,3-Benzodiazepine Derivatives: Functional Consequences of Replacing 7,8-Methylenedioxy with 7,8-Ethylenedioxy Moiety

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Running title: Inhibition of AMPA Receptors by GYKI 52466 Analogues

**Figure S1:** 2,3-BDZ-11-2 did not affect the channel desensitization rate constants on GluA2Q$_{flip}$, determined at 100 $\mu$M glutamate (●) and at 3 mM glutamate (○).

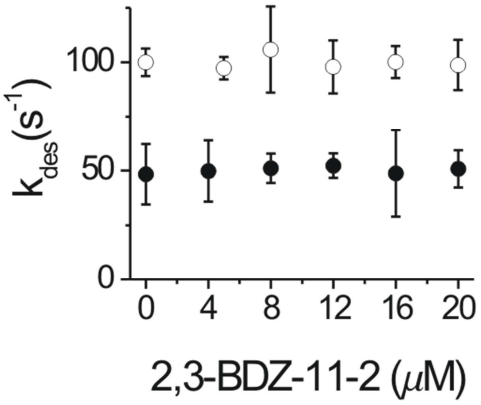

**Figure S2: (**A) Effect of 2,3-BDZ-11-2 on $k_{cl}$ obtained at 100 µM glutamate and as a function of 2,3-BDZ-11-2 concentration. From this plot, a $\overline{K_I}^*$ of 43 ± 11 µM was obtained using eq 4 (all the equations are listed in Experimental Procedures). (B) Effect of 2,3-BDZ-11-2 on $k_{op}$ obtained at 300 µM glutamate and as a function of 2,3-BDZ-11-2 concentration. From this plot, a $K_I^*$ of 39 ± 9.0 µM was determined using eq 5. Each data point shown in a plot was an average of at least three measurements collected from at least three cells.

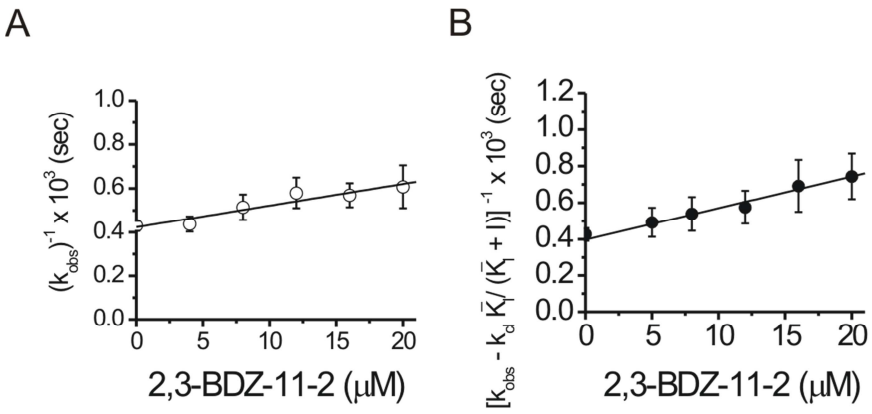

**Figure S3:** Effect of 2,3-BDZ-11-2 on the amplitude of the whole-cell current in the absence (*A*) and presence ($A_I$) of 2,3-BDZ-11-2, determined from the laser-pulse photolysis measurement. Using eqs 6a and 6b, we obtained a $K_I$ of 19 ± 1.0 μM from the $A/A_I$ value as a function of 2,3-BDZ-11-2 concentration (●) for the closed-channel state (or 100 μM glutamate). At 300 μM of photolytically released glutamate, the $K_I$ was determined to be 24 ± 4.0 μM (○). Each data point shown in this plot was an average of at least three measurements collected from at least three cells.

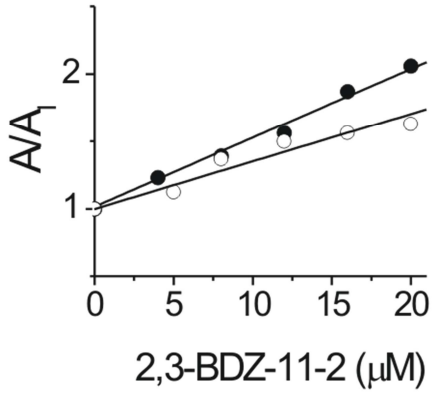

**Figure S4:** Inhibition constants of 2,3-BDZ-11-2 for the open-channel and the closed-channel states of GluA2Q$_{flip}$, estimated from the amplitude of the whole-cell current by the solution flow measurement. At 3 mM glutamate (○), a $\overline{K_I}$ of 33 ± 1.0 μM for the open-channel state was obtained by using eqs 6a and 6b. Similarly, a $K_I$ of 21 ± 0.1 μM was obtained for the closed-channel state at the glutamate concentration of 100 μM (●).

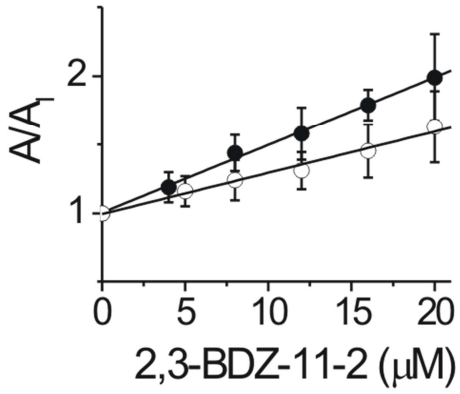

**Figure S5:** Inhibition constants of 2,3-BDZ-11-2 for the closed-channel state and open-channel states of the flop variant of GluA2 or GluA2Q$_{flop}$, obtained from the amplitude of the whole-cell current in the absence and presence of the BDZ-11-2. The amplitude was collected by using the flow measurement. At 3 mM glutamate (○), a $\overline{K_I}$ of 33 ± 1.0 µM was obtained, corresponding to the inhibition constant for the open state. At a glutamate concentration of 100 µM (●), which corresponded to the closed-channel state, a $K_I$ of 25 ± 0.3 µM was determined.