

Supplemental Figure 1

Title: GluN2D NMDAR subunit contribution to the stimulation of brain activity and gamma oscillations by ketamine; implications for schizophrenia

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Prepulse inhibition in WT and GluN2D-KO mice. (A) The startle response amplitude to a 120 dB tone without a prepulse tone in GluN2D-KO mice and WT mice. (B) Prior presentation of a prepulse tone elicited a larger inhibition of the startle response at each of the three prepulse intensities than in the WT mice. Data represent mean number ± SEM, **p < 0.01.

Prepulse inhibition (PPI), wherein a weak preceding auditory tone reduces the startle response to a loud tone, has been associated with SZ symptoms in humans and in animal models of SZ (Javitt and Freedman, 2015). A defect in PPI is also seen following
NMDAR antagonists, including ketamine. Given the apparent contribution of GluN2D subunits to ketamine's actions on brain activation and gamma oscillations, it is noteworthy that PPI has been reported to be intact in GluN2D-KO mice (Takeuchi et al., 2001). For comparison, we evaluated PPI in WT and GluN2D-KO mice, and confirmed that in GluN2D-KO mice, a prepulse tone produces a robust inhibition to the startle response (Figure 6E). GluN2D-KO mice had a larger PPI than WT mice at each prepulse intensity (74 dB, $p = 0.0020$; 78 dB, $p = 0.0055$; 84 dB, $p = 0.0028$). The startle response itself to the 120 dB tone without a preceding prepulse was not different between WT and GluN2D-KO mice (Figure 6D, $p = 0.08$).

Methods: Prepulse-inhibition (PPI) was performed using the acoustic startle system from Coulbourn Instruments (Whitehall, PA). Mice were placed in a small box, which was placed on an accelerometer platform in a larger sound-proof box with speakers inside. A 120 dB tone generates a startle response that is measured by the pre-calibrated accelerometer. Computer-generated tones of lower intensity (74 dB, 78 dB, and 84 dB) were presented with a random sequence/interval given 300 msec before the 120 dB tone on background of 70 dB. For each mouse, there were 25 trials without a prepulse tone (100% startle response) and 10 prepulse presentations for each of the 3 intensity levels of prepulse tones. The percent inhibition of the prepulse presentations to the startle response to the 120 dB tones was then measured.

References: