

Synaptic Accumulation of PSD-95 and Synaptic Function Regulated by Phosphorylation of Serine-295 of PSD-95

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It has been brought to our attention that the graph in Figure 2B of our paper is identical to that of Figures 1b and 1c of our recent paper in *Nature Neuroscience* (Futai et al., 2007). The graphs in question show the effect of wild-type (WT-) PSD-95 overexpression on AMPA- and NMDA-EPSC in CA1 neurons of cultured hippocampal slices.

The mistake arose as follows. During an overlapping period in 2003–2005, K.F. in Y.H.'s laboratory gathered data for Kim et al. and Futai et al. While these were separate studies, there was one data set—the effect of overexpressed WT-PSD-95 on the amplitude of AMPA-R- and NMDA-R-mediated transmission—that was used for investigating the effects of PSD-95 on paired-pulse ratio (Futai et al., 2007) and as a control for comparing the effects of serine-295 mutants (S295A and S295D) of PSD-95 (Kim et al., 2007). The data overlap is stated in the Methods section of Futai et al. (2007), but was mistakenly not mentioned in Kim et al. (2007). By error, we also included in the Kim et al. paper all the WT-PSD-95 EPSC amplitude data obtained for the Futai et al. study, including data that were not recorded in interleaved experiments with S295 mutants of PSD-95.

We here provide a new Figure 2 for the Kim et al. study, which includes only the WT-PSD-95 data that were interleaved with recordings of the cells overexpressing mutant S295A- or S295D-PSD-95 (i.e., from slices of the same hippocampi transfected with the different PSD-95 constructs in a blind manner). The same effect of WT-PSD-95 on AMPA- and NMDA-EPSC is seen with this subset of the original data set.

We noticed another error in Figure 2—two of the ten data points were missing from the NMDA-EPSC graph in Figure 2C (S295A-PSD-95) because the vertical axis was truncated at 200 pA. This has also been repaired in the corrected figure.

After correcting the figure, the conclusions of the experiment and of the paper remain the same. We apologize for the mistake and for any confusion caused.

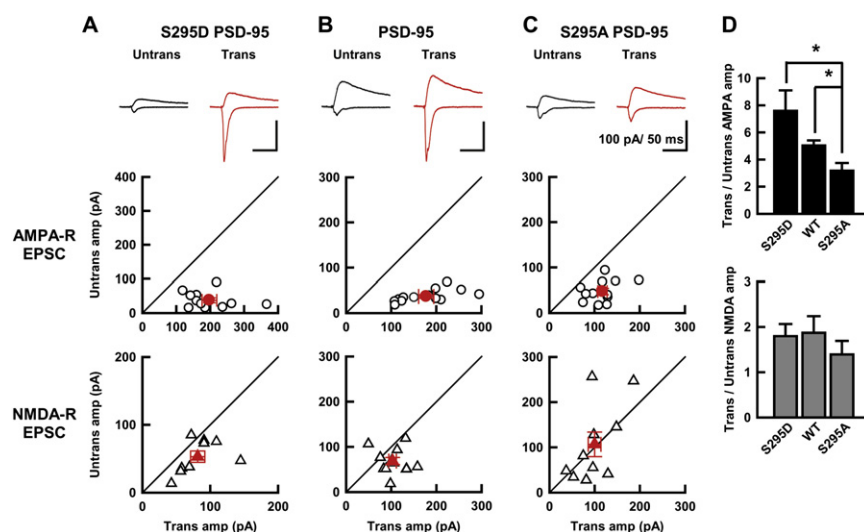


Figure 2. Effect of Ser-295 Mutants of PSD-95 on Synaptic Transmission in Cultured Hippocampal Slices

(A–C) (Top) Sample EPSC traces mediated by AMPA-R (downward) and NMDA-R (upward) from pairs of transfected (Trans) and neighboring untransfected (Untrans) cells. Stimulus artifacts were truncated. EPSC amplitudes (AMPA-R-EPSCs [middle] and NMDA-R-EPSCs [bottom]) were plotted for each pair of transfected and neighboring untransfected cells. Each open symbol represents a single pair of recordings. Mean \pm SEM are shown by filled circles. (A) S295D-PSD-95 mutant. (B) Wild-type PSD-95. (C) S295A-PSD-95 mutant. PSD-95 and its variants strongly enhanced AMPAR-EPSC amplitudes ($p < 0.00001$). In contrast, overexpression of wild-type PSD-95 and S295D-PSD-95 slightly enhanced NMDA-EPSCs ($p = 0.017$ and 0.093 , respectively), though the latter effect did not reach statistical significance. NMDA-EPSCs were not significantly changed by S295A-PSD-95 ($p = 0.623$).

(D) Summary of PSD-95 ser-295 mutant overexpression on AMPA-R-EPSCs (top) and NMDA-R-EPSCs (bottom). Each bar graph represents the average of ratios obtained from multiple pairs of transfected and untransfected neighboring neurons. Numbers of cell pairs were S295D (AMPA-R-EPSCs/NMDA-R-EPSCs: 11/9); wild-type (13/12); S295A (12/10). * $p < 0.05$, compared with neurons transfected with S295A-PSD-95.

The amplitude data for wild-type PSD-95 AMPA-R-EPSCs and NMDA-R-EPSCs form part of the data set in Figures 1b and 1c of Futai et al. (2007).

Corrected Text of Results (Replaces the Paragraph Starting on Page 489, Bottom Left Column): Ser-295 Phosphorylation of PSD-95 Influences Synaptic Potentiation

We next compared the effect of overexpression of wild-type PSD-95, S295D-PSD-95, and S295A-PSD-95 on excitatory synaptic transmission in CA1 pyramidal neurons in hippocampal slice cultures (Figure 2). Simultaneous recording of EPSCs was performed from neighboring untransfected CA1 neurons and transfected CA1 pyramidal neurons that were identified by cotransfected GFP. Wild-type PSD-95 strongly enhanced AMPA-EPSCs (5.03 ± 0.38 -fold relative to untransfected cells), as previously reported (Ehrlich and Malinow, 2004; Nakagawa et al., 2004; Schnell et al., 2002; Stein et al., 2003). Overexpression of the phosphomimicking mutant S295D-PSD-95 also caused a large increase in AMPA-EPSC (7.59 ± 1.51 -fold), but the nonphosphorylatable S295A-PSD-95 was significantly less potentiating than wild-type (3.18 ± 0.57 -fold) (Figures 2C and 2D). Overexpression of wild-type PSD-95 and S295D-PSD-95 slightly enhanced NMDA-EPSCs (1.87 ± 0.36 -fold and 1.80 ± 0.27 -fold, respectively) (Figures 2A, 2B, and 2D), though the latter effect did not reach statistical significance, and the effects were much smaller in degree than those on AMPA-EPSCs. NMDA-EPSCs were not changed by S295A-PSD-95 (Figures 2C and 2D).

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