Peripheral activity



Total activity

**Supplementary Figure 1, Total, peripheral, central and rearing locomotor activity.** No major differences were observed between WT and KO mice over the 2 h period. n=8 per group.



### Supplementary Figure 2, Latency to immobility in the forced swim test.

There was no significant difference in the latency to first immobility between WT and KO (p=0.12). n=8 per group.



### Supplementary Figure 3, Measurement of acoustic startle response.

A significant increase in the acoustic startle response was observed in *Pick1* KO mice, \*p<0.05 n=7 (WT), n=11 (KO).



### Supplementary Figure 4, Molecular characterization of the frontal cortex.

Quantitative RT-PCR with the homogenates of the frontal cortex. *Pick1* knockout mice were significantly different from wild-type mice for *Stargazin* and *Parvalbumin*, p\*<0.05, but not for *Gad67*. n=14 WT, n=6 KO.



### Supplementary Figure 5, Spontaneous alternations in the Y-maze after neonatal D-serine

#### treatment.

Neonatal saline injections masked the deficit shown by naïve *Pick1* knockout mice.

D-serine showed a trend of beneficial influences on KO, but due to the baseline changes, it did not reach significance. n=11 WT (saline), n=12 WT (D-serine), n=8 KO (Saline), and n=7 KO (D-serine).



#### Supplementary Figure 6, Effect of adult D-serine treatment on prepulse inhibition and Y-maze.

a) Prepulse inhibition after adult D-serine treatment. Repeated injections in adulthood significantly altered the baseline response in both wild-type and knockout mice, so we could not make any conclusive statement. n=7 WT (saline), n=6 WT (D-serine), n=5 KO (Saline), and n=5 KO (D-serine).
b) Spontaneous alternations in the Y-maze after adult D-serine treatment. D-serine had no effect on the performance. n=10 WT (saline), n=8 WT (D-serine), n=7 KO (Saline), and n=7 KO (D-serine). p\*<0.01.</li>

# Supplementary Table 1

	Baseline	NMDA (4µM)	NMDA (4µM) + SKF (2µM)
Wild-type (WT)	$6.6 \pm 0.5$	11.4 ± 2.8	13.1 ± 4.8
Pick1 KO (KO)	5.8 ± 1.7	7.8 ± 2.3	$8.5 \pm 3.4$
Neonatal D-serine treated KO	3.9 ± 1.2	7.4 ± 3.2	8.9 ± 3.6
Adult D-serine treated KO	5.7 ± 1.7	8.2 ± 3.2	9.7 ± 3.6

**Supplementary Table 1.** The number of action potentials evoked with intracellular current injections at baseline, after NMDA perfusion, and after the combined perfusion of NMDA and the D1 agonist SKF38393 (SKF) in prefrontal cortical slices from wild-type, *Pick1* KO, neonatal D-serine treated *Pick1* KO and adult D-serine treated *Pick1* KO.