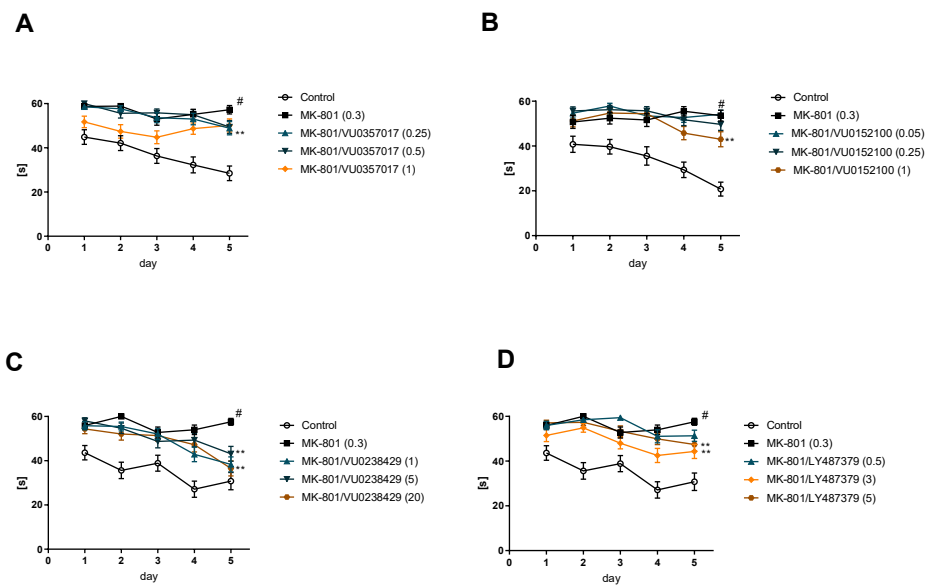
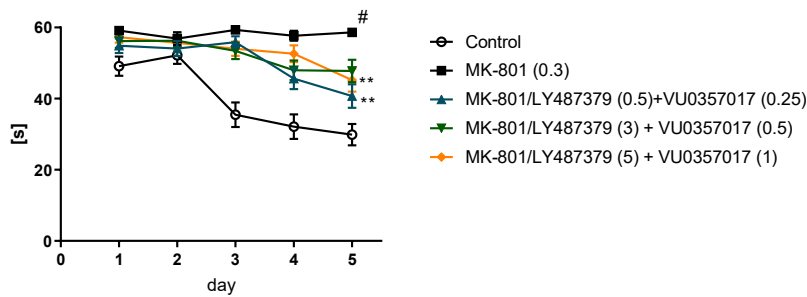
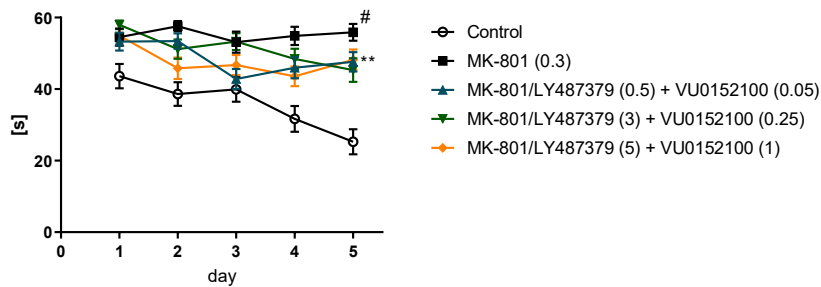
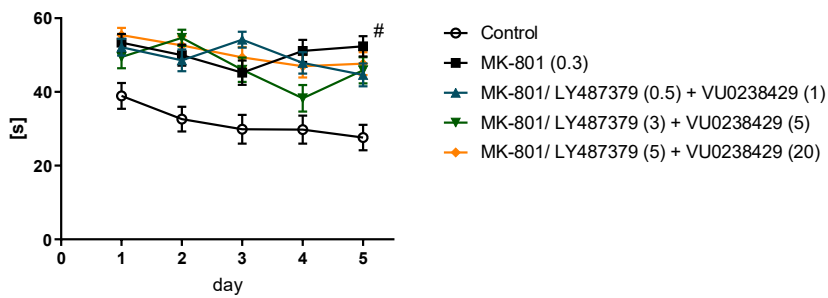


# Figures.

## Acquisition Trial



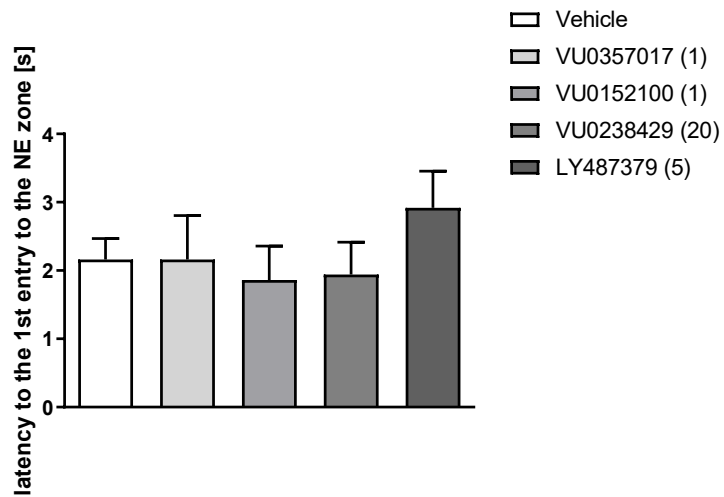
**Figure S1.** The effects of VU0357017 (A), VU0152100 (B), VU0238429 (C) and LY487379 (D) on MK-801-induced amnesic effect on the acquisition of spatial memory in the MWM in CD1 mice. The values are expressed as the means $\pm$ SEM. #P<0.001 indicates the difference MK-801-treated mice vs. the respective vehicle (at least N=10) and \*\* P<0.05 indicates the difference between MK-801 group and the treatment groups.

**A****B****C**

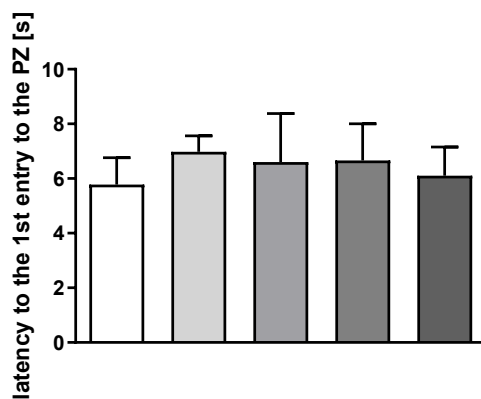
**Figure S2.** The effects of concomitant administration of LY487379 with VU0357017 (A), LY487379 with VU0152100 (B), and LY487379 with VU0238429 (C) on MK-801-induced amnesic effect on the acquisition of spatial memory in the MWM in CD1 mice. The values are expressed as the means $\pm$ SEM. # $P<0.001$  indicates the difference MK-801-treated mice vs. the respective vehicle (at east  $N=10$ ) and \*\* $P<0.05$  indicates the difference between MK-801 group and the treatment groups.

## Retention trial

**A**

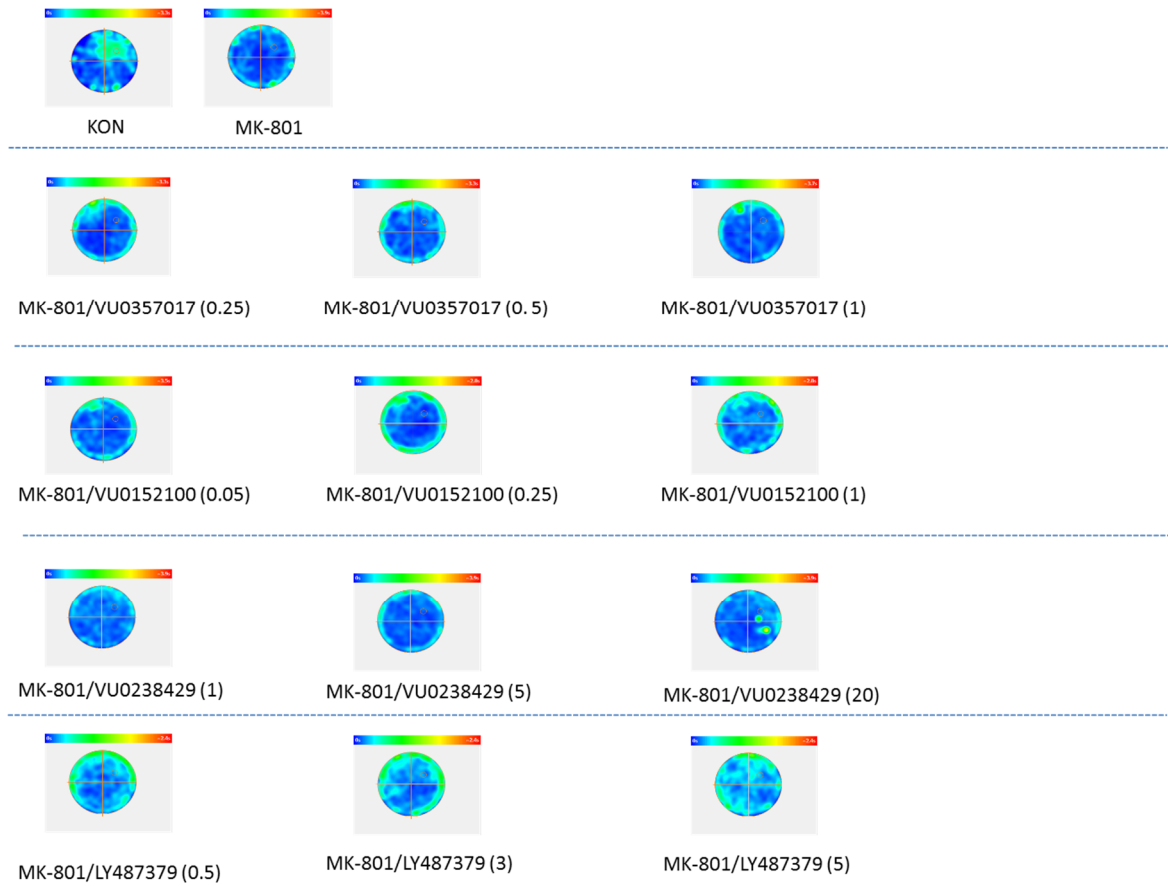


**B**

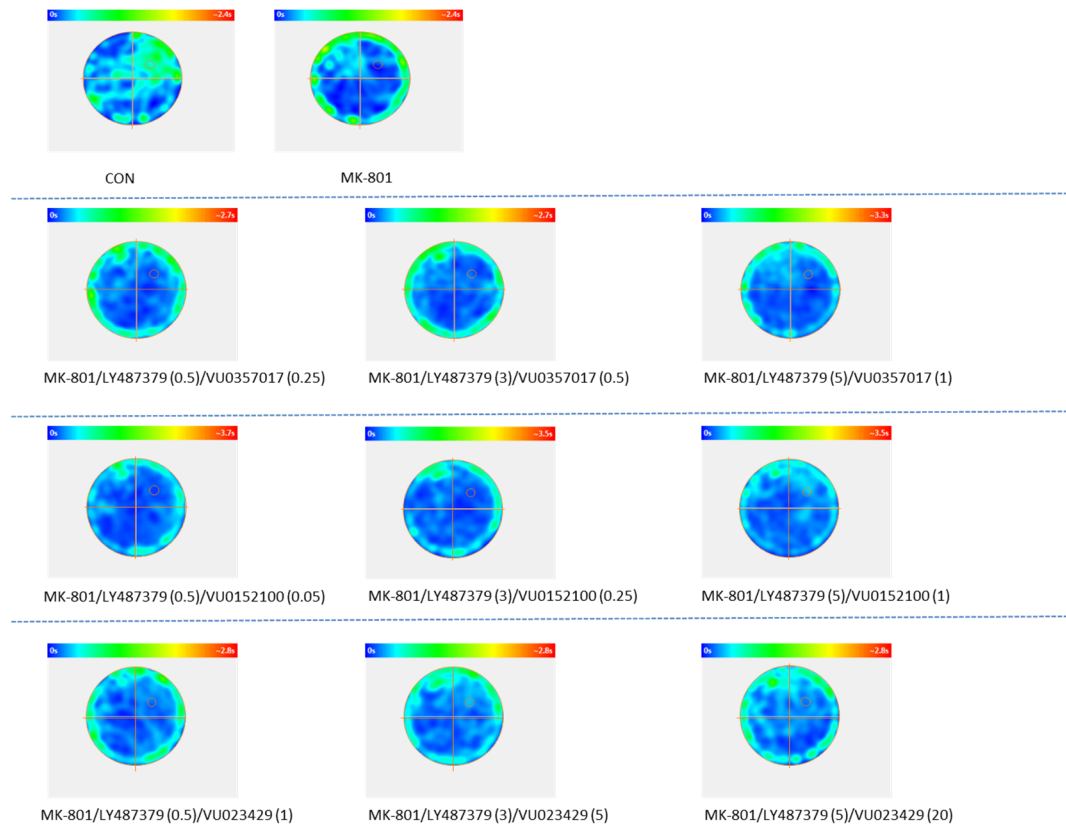


**Figure S3.** The effects of VU0357017, VU0152100, VU0238429 and LY487379 alone in the retention of spatial memory in the MWM in CD1 mice. The values are expressed as the means $\pm$ SEM. Doses (mg/kg) are indicated in parentheses. Results are given as the latency to the 1<sup>st</sup> entry to NE zone (A) and latency to the 1<sup>st</sup> entry to PZ (B).

## Heat maps.



**Figure S4.** Heat maps reflecting the time spent swimming in particular areas of the maze. The maps show mean data for different treatment groups. Dark blue – no time spent in the area, red – the most time spent in the area. The circle represents platform zone.



**Figure S5.** Heat maps reflecting the time spent swimming in particular areas of the maze. The maps show mean data for different treatment groups. Dark blue – no time spent in the area, red – the most time spent in the area. The circle represents platform zone.

# Tables

|                           | Average speed [m/s] |             |
|---------------------------|---------------------|-------------|
| control                   | 0                   | 0,219±0,02  |
| MK-801                    | 0.3 mg/kg           | 0,213±0,028 |
| MK-801+VU0357017          | 0.25 mg/kg          | 0,250±0,029 |
|                           | 0.5 mg/kg           | 0,231±0,042 |
|                           | 1 mg/kg             | 0,240±0,039 |
| MK-801+VU0152100          | 0.05 mg/kg          | 0,210±0,034 |
|                           | 0.25 mg/kg          | 0,239±0,041 |
|                           | 1 mg/kg             | 0,233±0,029 |
| MK-801+VU0238429          | 1 mg/kg             | 0,231±0,02  |
|                           | 5 mg/kg             | 0,245±0,047 |
|                           | 20 mg/kg            | 0,246±0,071 |
| MK-801+LY487379           | 0.5 mg/kg           | 0,226±0,032 |
|                           | 3 mg/kg             | 0,228±0,024 |
|                           | 5 mg/kg             | 0,241±0,030 |
| MK-801/LY487379/VU0357017 | 0.5+0.25 mg/kg      | 0,258±0,041 |
|                           | 3+0.5 mg/kg         | 0,269±0,038 |
|                           | 5+1 mg/kg           | 0,245±0,031 |
| MK-801/LY487379/VU0152100 | 0.5+0.05 mg/kg      | 0,248±0,02  |
|                           | 3+0.25 mg/kg        | 0,245±0,016 |
|                           | 5+1 mg/kg           | 0,237±0,037 |
| MK-801/LY487379/VU0238429 | 0.5+1 mg/kg         | 0,228±0,040 |
|                           | 3+5 mg/kg           | 0,259±0,029 |
|                           | 5+20 mg/kg          | 0,229±0,042 |

**Table S1.** Average speed of animals measured during one minute trial during the retention phase. Results are indicated as means ± SEM and indicated as [m/s].

## Statistical analysis

|  | NE-zone related parameters | PZ parameters          |
|--|----------------------------|------------------------|
| Latency to the 1 <sup>st</sup> entry to the zone           | t=2.310, df=18, P<0.05     | t=2.565, df=12, p<0.05 |
| Number of entries  | t=2.172, df=17, p<0.05     | t=2.732, df=16, p<0.05 |
| Distance travelled until 1 <sup>st</sup> entry to the zone | t=3.894, df=16, p<0.01     | t=3.197, df=8, p<0.05  |
| Path efficiency to the 1 <sup>st</sup> entry to the zone   | t=2.55, df=17, p<0.05      | t=2.55, df=17, p<0.05  |
| Time in the zone   | t=2.35, df=17, p<0.03      | <i>Not measured</i>    |
| Distance travelled in the zone                             | <i>Not measured</i>        | t=2.825, df=18 p<0.05  |

**Table S2.** Specification of parameters measured in MWM both in the NE zone and in the PZ (platform zone), that were impaired by MK-801 administration in the retention phase. Statistical analysis were performed with the Student's t-test.

|  | VU0357017<br>(0.25, 0.5, 1 mg/kg)                       | VU0152100<br>(0.05, 0.25, 1 mg/kg)         | VU0238429<br>(1, 5, 20 mg/kg)                           | LY487379<br>(0.5, 3, 5 mg/kg)                           |
|--|---|--|---|---|
| <b>NE zone parameters</b>                                    |   |  |   |   |
| number of entries into the zone                              | <b>F<sub>(3,35)</sub> = 2.968</b><br><b>p &lt; 0.05</b> | F <sub>(3,36)</sub> = 1.489<br>p = 0.2339  | <b>F<sub>(3,33)</sub> = 2.956</b><br><b>p &lt; 0.05</b> | F <sub>(3,35)</sub> = 1.077<br>p = 0.3717               |
|  | <b>1 mg/kg</b>  |  | <b>20 mg/kg</b>   |   |
| time in the zone   | F <sub>(3,36)</sub> = 0.9181<br>p = 0.4419              | F <sub>(3,35)</sub> = 0.6410<br>p = 0.5938 | H(3) = 2.457<br>p = 0.4832                              | F <sub>(3,35)</sub> = 0.3405<br>p = 0.7961              |
| distance travelled in the zone                               | n/a   | F <sub>(3,36)</sub> = 0.9426<br>p = 0.4302 | n/a   | n/a   |
| distance travelled until 1 <sup>st</sup> entry into the zone | n/a   | <b>H(3) = 8.393</b><br><b>p &lt; 0.05</b>  | <b>H(3) = 8.273</b><br><b>p &lt; 0.05</b>               | <b>F<sub>(3,35)</sub> = 3.554</b><br><b>p &lt; 0.05</b> |
|  |   | <b>0.5, 1 mg/kg</b>                        | <b>20 mg/kg</b>   | <b>5 mg/kg</b>  |
| latency to 1 <sup>st</sup> entry into the zone               | n/a   | <b>H(3) = 12.11</b><br><b>p &lt; 0.01</b>  | <b>H(3) = 7.905</b><br><b>p &lt; 0.05</b>               | <b>H(3) = 9.159</b><br><b>p &lt; 0.05</b>               |
|  |   | <b>0.05, 0.5, 1 mg/kg</b>                  | <b>5, 20 mg/kg</b>                                      | <b>5 mg/kg</b>  |
| path efficiency to 1 <sup>st</sup> entry into the zone       | n/a   | H(3) = 5.400<br>p = 0.1448                 | H(3) = 2.665<br>p = 0.4462                              | <b>F<sub>(3,33)</sub> = 3.282</b><br><b>p &lt; 0.05</b> |
|  |   |  |   | <b>5 mg/kg</b>  |
| <b>PZ parameters</b>   |   |  |   |   |
| number of entries into the zone                              | H(3) = 1.327<br>p = 0.7226                              | H(3) = 2.029<br>p = 0.5665                 | H(3) = 2.307<br>p = 0.5112                              | H(3) = 3.597<br>p = 0.3083                              |
| time in the zone   | H(3) = 1.019<br>p = 0.6007                              | H(3) = 3.125<br>p = 0.3727                 | H(3) = 2.166<br>p = 0.5387                              | <b>H(3) = 8.282</b><br><b>p &lt; 0.05</b>               |
|  |   |  |   | <b>0.5, 5 mg/kg</b>                                     |
| distance travelled until 1 <sup>st</sup> entry into the zone | <b>H(3) = 9.653</b><br><b>p &lt; 0.05</b>               | n/a  | n/a   | n/a   |
|  | <b>0.5, 1 mg/kg</b>                                     |  |   |   |
| latency to 1 <sup>st</sup> entry into the zone               | <b>H(3) = 0.0217</b><br><b>p &lt; 0.05</b>              | H(3) = 3.603<br>p = 0.3077                 | H(3) = 6.900<br>p = 0.0751                              | <b>F<sub>(3,23)</sub> = 3.575</b><br><b>p &lt; 0.05</b> |
|  | <b>0.5, 1 mg/kg</b>                                     |  |   | <b>3, 5 mg/kg</b>                                       |
| path efficiency to 1 <sup>st</sup> entry into the zone       | <b>H(3) = 12.13</b><br><b>p &lt; 0.01</b>               | n/a  | n/a   | n/a   |
|  | <b>0.5, 1 mg/kg</b>                                     |  |   |   |

**Table S3.** Statistical analysis of the results obtained in the retention phase of MWM for individual compounds. Investigated doses are indicated in parentheses. n/a— not applicable.



| Treatment | Structure | ANOVA results                    | Tukey's post hoc comparison |                              |
|-----------|-----------|----------------------------------|-----------------------------|------------------------------|
|           |           |                                  | MK-801 vs. MK-801/treatment | Control vs. MK-801/treatment |
| VU0357017 | FC        | $F_{(2,20)} = 29.29, p < 0.0001$ | $p < 0.0001$                | $p < 0.007$                  |
|           | Hipp      | $F_{(2,21)} = 25.19, p < 0.0001$ | $p < 0.0001$                | $p < 0.002$                  |
| VU0152100 | FC        | $F_{(2,20)} = 30.39, p < 0.0001$ | $p < 0.0001$                | $p < 0.004$                  |
|           | Hipp      | $F_{(2,21)} = 49.40, p < 0.0001$ | $p < 0.0001$                | $p < 0.0001$                 |
| VU0238429 | FC        | $F_{(2,20)} = 25.82, p < 0.0001$ | $p < 0.0001$                | $p < 0.04$                   |
|           | Hipp      | $F_{(2,21)} = 24.97, p < 0.0001$ | $p < 0.0001$                | $p < 0.0003$                 |
| LY487379  | FC        | $F_{(2,20)} = 38.76, p < 0.0001$ | $p < 0.0001$                | $p < 0.0006$                 |
|           | Hipp      | $F_{(2,20)} = 25.84, p < 0.0001$ | $p < 0.0001$                | $p < 0.0003$                 |

**Table S4.** Statistical analysis of the cGMP levels after administration of individual compounds at highest doses. FC—frontal cortex, Hipp—hippocampus.