Role of NMDAR in Homocysteine-induced Glomerular Injury

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The N-methyl D-aspartate (NMDA) receptors are a glutamate receptor which has been found extensively expressed in the central nervous system.

It has been reported that Hcys-induced damage is related with NMDA receptors.

Our previous studies have shown that Hcys can induce glomerular injury.
NMDA receptor

http://homepage.psy.utexas.edu/homepage/class/Psy301/Salinas/sec2/L&M/23.GIF
Hyperhomocysteinemia-Induced Glomerular Damage

1. Cell proliferation
2. Mesangial expansion
3. Capillary collapse

B

Score of Glom. Damage

Control  Methionine

*
Hypothesis

- hHcys may induce glomerular sclerosis through the activation of NMDA Receptors and blocking the action of NMDAR will alleviate glomerular sclerosis.
Confirmation of NMDAR in Glomeruli

A

NMDA R1  NMDA R2A  NMDA R2B  NMDA R2C  NMDA R2D  β-actin

B

Relative mRNA level of NMDA-1 R (Normalized to RMC)

glomeruli

RMC

0  5  10

*
Effect of MK-801 on Hcy-induced Proteinuria

![Graph showing the effect of MK-801 on proteinuria in different diets. The graph compares UProtein (mg/24h) between Normal Diet and FF Diet for Vehicle and MK-801 treatments. The graph indicates a significant decrease in proteinuria with MK-801 compared to Vehicle in the FF Diet.]
Morphological Change of Hcy-induced Glomerular Injury

A

B

Vehicle
MK-801

Glomerular Damage Index (GDI)

ND
ND+MK-801

FF
FF+MK-801

* #
**Effect of MK-801 on NMDARs Expression**

<table>
<thead>
<tr>
<th></th>
<th>ND</th>
<th>ND+MK</th>
<th>FF</th>
<th>FF+MK</th>
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<tbody>
<tr>
<td><strong>NMDAR 1</strong></td>
<td><img src="image1.jpg" alt="Image" /></td>
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<td><strong>NMDAR 2A</strong></td>
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Effect of MK-801 on Hcy-induced Superoxide Production

Fold changes of $O_2^-$ production (Normalized to ND)

- Vehicle
- MK-801

Bars represent mean ± SEM.

- ND: **p < 0.01
- FF: #p < 0.05
Conclusion

Hcy -NMDAR

NOX activation

MK801

O2^- production

Glomerulosclerosis
Acknowledgment

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