Response to Glutamate Receptors and Presympathetic Neuronal Hyperactivity of the Central Nervous System in Hypertension

We thank Dr Tsuda for his interest in our work and his comments about the important role of N-methyl-d-aspartate (NMDA) receptors in the central nervous system in the control of sympathetic vasomotor tone in hypertension. In our recent publication, we reported that group II metabotropic glutamate receptors can be targeted to reduce sympathetic discharges by reducing synaptic glutamate release in the paraventricular nucleus (PVN) of spontaneously hypertensive rats. Previously, we used brain slice recordings to show that the postsynaptic NMDA receptor activity of spinally projecting PVN neurons is increased in spontaneously hypertensive rats. Similarly, increased NMDA receptor activity of spinally projecting PVN neurons has been demonstrated recently in angiotensin II–induced hypertension in rats. These studies provide strong evidence that in addition to group II metabotropic glutamate receptors, the NMDA receptor activity is potentiated in the PVN in hypertension.

We have shown that microinjection of the NMDA receptor antagonist into the PVN significantly decreases the sympathetic nerve discharge and blood pressure in spontaneously hypertensive rats. Other investigators have reported that blocking ionotropic glutamate (including NMDA) receptors in the PVN reduces the blood pressure in Dahl salt-sensitive hypertensive rats. Thus, these findings indicate that increased NMDA receptor activity in the PVN plays a critical role in elevated sympathetic vasomotor tone in hypertension.

We agree with Dr Tsuda’s comments that further studies are needed to define the precise relationship between various glutamate receptors in the central nervous system and increased sympathetic tone in hypertension. It is not yet clear how NMDA receptors and group II metabotropic glutamate receptors are upregulated in sympathetic-related neurons in the brain in hypertension. The importance of various glutamate receptors in the regulation of sympathetic outflow in hypertension should ultimately be investigated in clinical settings.

Disclosures

None.

Zeng-You Ye
De-Pei Li
Hui-Lin Pan
Division of Anesthesiology and Critical Care
The University of Texas MD Anderson Cancer Center
Houston