Oxidative Stress Mediates the Stimulation of Sympathetic Nerve Activity in the Phenol Renal Injury Model of Hypertension

Shaohua Ye, Huiquin Zhong, Vito M. Campese

Abstract—Renal injury caused by the injection of phenol in the lower pole of one kidney increases blood pressure (BP), norepinephrine secretion from the posterior hypothalamic nuclei (PH), and renal sympathetic nerve activity in the rat. Renal denervation prevents these effects of phenol. We have also demonstrated that noradrenergic traffic in the brain is modulated by NO and interleukin-1β. In this study, we tested the hypothesis that the increase in sympathetic nervous system (SNS) activity in the phenol renal injury model is because of activation of reactive oxygen species. To this end, we first examined the abundance of several components of reduced nicotinamide-adenine dinucleotide phosphate oxidase (identified as the major source of reactive oxygen species), including gp91phox/Nox2, p22phox, p47phox, and Nox3 using real-time PCR. Second, we evaluated the effects of 2 superoxide dismutase mimetic, tempol (4-hydroxy-2,2,6,6-tetramethyl piperidinol), and superoxide dismutase-polyethylene glycol on central and peripheral SNS activation caused by intrarenal phenol injection. Intrarenal injection of phenol raised BP, NE secretion from the PH, renal sympathetic nerve activity, and the abundance of reduced nicotinamide-adenine dinucleotide phosphate and reduced the abundance of interleukin-1β and neural-NO synthase mRNA in the PH, paraventricular nuclei, and locus coeruleus compared with control rats. When tempol or superoxide dismutase-polyethylene glycol were infused in the lateral ventricle before phenol, the effects of phenol on BP and SNS activity were abolished. The studies suggest that central activation of the SNS in the phenol-renal injury model is mediated by increased reactive oxygen species in brain nuclei involved in the noradrenergic control of BP. (Hypertension. 2006;48:309-315.)

Key Words: hypertension, renal • sympathetic nervous system • nitric oxide • interleukins • oxidative stress

The kidney is a sensory organ richly innervated with both mechanosensitive and chemosensitive afferent nerve fibers,1–6 and renal afferent nerves project directly to a number of areas in the central nervous system contributing to arterial pressure regulation.7,8 Renal injury caused by the injection of phenol in the lower pole of one kidney caused an immediate and persistent elevation of blood pressure (BP), norepinephrine (NE) secretion from the posterior hypothalamic nuclei (PH), and renal sympathetic nerve activity (RSNA) in the rat.9,10 Renal denervation prevented the effects of renal injury on BP, NE secretion from the PH, and RSNA.

Considerable attention has been given to the effects of short-lived reactive oxygen species (ROS) and reactive nitrogen species on BP and cardiovascular toxicity. ROS or oxygen free radicals are O2 molecules with an unpaired electron and include superoxide anion (O2•−), hydrogen peroxide, and hydroxyl ion. These molecules are chemically unstable and highly reactive, and NADPH oxidase, xanthine oxidase, and NO synthase (NOS) enzymes regulate their concentration. NADPH oxidase is a multimeric enzyme and is responsible for the reduction of oxygen, electron transport, and superoxide production at the cell surface.11 The phagocyte NADPH oxidase is composed of 2 essential membrane-bound components, gp91phox/Nox2 and p22phox, and 4 cytosolic components, p47phox, p67phox, p40phox, and Rac1/2.12 On stimulation, the 4 cytosolic components translocate to the membrane and increase the activity of NADPH oxidase. In nonphagocytic cells, 4 homologues of gp91phox/Nox2 have been identified, called Nox1 and Nox3 to 5.13

ROS production is increased in several experimental models of hypertension14–16 and in human hypertension.17 A causative role of ROS is supported by evidence that scavengers of ROS, such as dimercaptosuccinic acid, lazaroids, cicietanine, tempol (as superoxide dismutase mimetic), and vitamin C and E ameliorate or abrogate hypertension in animal models.18,19 Conversely, depletion of glutathione, an endogenous scavenger of ROS, by means of the glutathione synthase inhibitor, butathione sulfoximine, caused a marked elevation of nitrotyrosine, the footprint of peroxynitrite, and marked elevation of BP in rats.20 The exact mechanisms through which oxidative stress may raise BP have not been fully elucidated, but reduced availability of NO is the prevailing hypothesis. Evidence sug-
gests that ROS may raise BP through activation of the sympathetic nervous system (SNS). Because NO exerts a tonic inhibition on central SNS activity, increased production of ROS may activate the SNS through oxidation/inactivation of NO. NO actively reacts with $O_2$ and other ROS to produce peroxynitrate, a highly cytotoxic reactive nitrogen species. In this study, we have tested the hypothesis that the increase in SNS activity in the phenol renal injury model is because of activation of ROS. To test this hypothesis, first we examined the abundance of several components of NADPH oxidase, including gp91phox/Nox2, p22phox, p47phox, and Nox3 in the PH, paraventricular nuclei (PVN), and locus coeruleus (LC) using real-time PCR. Second, we evaluated the effects of 2 superoxide dismutase mimetic, tempol (4-hydroxy-2,2,6,6-tetramethyl piperidinoxyl), and superoxide dismutase (SOD)-polyethylene glycol (SOD) on central and peripheral SNS activation caused by intrarenal phenol injection.

**Methods**

**Animals and Surgical Methods**

For these studies, we used male Sprague–Dawley rats weighing 200 to 250 g fed with normal rat chow (ICN Nutritional Biochemical) and tap water. For measurements of arterial pressure and administration of drugs, we anesthetized animals with sodium pentobarbital (35 mg/kg IP followed by an infusion of 5 mg/kg per hour) and implanted catheters (PE-10) in a femoral artery and vein.

The Phenol–Renal–Injury Model

After a dorsal incision, we exposed the left kidney and injected 50 $\mu$L of 10% phenol in the lower pole. Control rats received 50 $\mu$L of normal saline in the lower pole of the kidney. Arterial pressure (BP) was continuously recorded (Physiograph, Grass Instrument). As a marker of central noradrenergic trafficking, we measured NE secretion from the PH before the intrarenal injection of phenol and every 5 minutes for 60 minutes thereafter. As a measure of peripheral SNS activity, we continuously measured RSNA before the intrarenal injection of phenol and for 60 minutes thereafter.

NE Secretion From the PH Using the Microdialysis Technique

To measure NE secretion from the PH, we placed rats in a stereotoxic apparatus, implanted a 2-mm long Teflon 22-gauge guide cannula (IV Catheter Placement Unit; Critikon, Inc) using coordinates anterior-posterior (A-P) at $-4.2$ mm, lateral at 0.4 mm, and vertical (V) at 8 mm and secured the guide in place with dental cement. A 28-gauge stainless steel stylus was lowered through the guide cannula to a depth 1.5 mm dorsal to the dorsoventral coordinate for PH, namely $-8.5$ mm from the skull surface. The stylus was removed from the guide cannula and replaced with a microdialysis probe (CMA Microdialysis AB), which was secured to the guide with sticky wax. The inlet tubing of the dialysis probe was connected by PE-20 tubing to a 1-mL disposable syringe driven by a microinfusion pump (Model A-99; Raziel Scientific Instruments, Inc) and an infusion of artificial cerebrospinal fluid (aCSF; in mM: Na$^+$ 150, 3.0 K$^+$, 1.4 Ca$^{2+}$, 0.8 Mg$^{2+}$, 1.0 phosphorus, and 155 Cl$^- ;$ pH 7.2) was initiated at a rate of 1.7 $\mu$L per minute. PE-10 tubing was attached to the outlet side of the probe, and the free end led to a 0.5-ML vial set in a small box of ice. The vial contained 2 $\mu$L of 0.1 N HCl for preservation of NE. All of the samples were immediately frozen and stored at $-70^\circ$C until the time of assay. After 90 minutes of dialysis equilibration, dialysate samples were collected every 5 minutes for the entire duration of the experiments.

Renal Nerve Recording

For renal nerve recording, we prepared rats according to the method of Lundin and Thoren as modified by DiBona et al. To avoid the possibility that intact renal nerve activity produced by phenol injection might reflect an increase in both afferent and efferent renal nerve activity, we injected phenol in the lower pole of the left kidney and measured RSNA in the contralateral kidney.

We exposed retroperitoneal both the left and right kidney via flank incisions. The left kidney was only used for intrarenal injection of phenol. We exposed the right kidney, the renal artery, and abdominal aorta, and we dissected a renal nerve branch, usually from fat and connective tissue for the length of $\sim 10$ mm. We left the renal branch intact and placed it on thin (0.005 inch) bipolar platinum electrodes (Cooner Wire Company) and connected to a high impedance probe Grass HIP 511 (Grass Instrument Co). RSNA was amplified ($\times 10,000$ to 50,000) and filtered (low, 30; high, 3000) with a Grass 511 bandpass amplifier. The amplified and filtered signal was channeled to a Tektronix 5113 oscilloscope (Tektronix, Inc) for visual evaluation, to an audio amplifier/loud speaker (Grass Model AM 8 audio monitor) for auditory evaluation, and to a rectifying voltage integrator (Grass Model 7P10). The output signal of the Grass 7P10 was then displayed on a Grass Polygraph. The quality of the renal nerve activity was assessed during operation by examining the magnitude of changes in recorded RSNA during sinoaortic baroreceptor unloading with injection of acetylcholine ($1 \mu$g IV) and during sinoaortic baroreceptor loading with the injection of NE ($5 \mu$g IV). When an optimal recording was achieved, the nerve on the electrode was isolated with silicone rubber (Wacker Sil-Gel 604; Wacker Inc). Throughout the experiments, animals were kept warm under heated lamps and received an infusion of 30 $\mu$L/min of 5% dextrose in normal saline. Arterial pressure, heart rate, and RSNA were continuously monitored. A postmortem background signal was determined and the experimental data corrected for this.

**Preparation for Intracerebroventricular Infusion**

For intracerebroventricular infusion of tempol and PEG-SOD, we placed a cannula (23-gauge) in the right lateral ventricle (coordinates: 1.4 mm lateral, 0.8 mm posterior, and 3.8 mm deep from the bregma).

**Effects of Tempol and PEG-SOD on BP, NE Secretion From the PH, and RSNA**

To test the hypothesis that ROS may modulate SNS activation caused by intrarenal phenol injection, we infused tempol ICV (50 $\mu$L/g per kilogram of body weight per minute) starting 15 minutes before the intrarenal injection of phenol or saline and continuously for 60 minutes thereafter. We evaluated the effects on BP, NE secretion from the PH, and RSNA. Because we have shown previously that Tempol in the dose used in this study itself lowers BP and to test the specificity of tempol effects, in separate groups of rats we evaluated the effects of a different SOD mimetic, PEG-SOD (in dose of 80 U/kg dissolved in 10 $\mu$L of aCSF, infused over 10 minutes) on BP, NE secretion from the PH, and RSNA when given 15 minutes before the intrarenal injection of phenol. We have shown previously that this dose of PEG-SOD by itself does not alter BP, NE secretion from the brain, or RSNA. In a subset of 5 rats, we infused PEG-SOD (in dose of 80 U/kg dissolved in 10 $\mu$L of aCSF) 30 minutes before the intrarenal injection of phenol and we evaluated the effects on BP, NE secretion from the PH, and RSNA.

**Determination of nNOS and Interleukin-1$\beta$ mRNA Abundance in the Brain**

At the end of the experiments, rats were euthanized by decapitation and brains immediately removed, frozen in dry ice, and stored at $-70^\circ$C until assay but for no longer than 3 weeks. Brains were cut into consecutive 200-$\mu$m sections in a cryostat at $-20^\circ$C and bilateral micropunches 0.5 mm in diameter from several brain nuclei obtained as described previously. In the experiments where microdialysis was performed, we isolated the nuclei from the contra lateral side to that of the implantation of the microdialysis probe. The coordinates for the PH were: A-$P$, $-3.5$ to $-4.1$ mm; lateral, 0.3 mm; and V, 8 mm; coordinates for the PVN were: A-$P$, from $-1.4$ to 2.0 mm; lateral, $\pm 0.3$ mm; and V, 7.9 mm; and for the LC were: A-$P$, from $-9.8$ to 10.2 mm; lateral, $\pm 1.4$ mm; and V, 7.2 mm.
The nuclei so isolated were used to measure IL-1β and neural-NOS (nNOS) mRNA gene expression. We selected those 3 nuclei because they are all involved in the noradrenergic control of BP.

Total RNA extraction and real-time reverse transcription (RT) were performed by methods described previously by us.24 PCR was performed on the RT product using specific oligonucleotide primers for either nNOS or interleukin (IL)-1β derived from cDNAs cloned from rat brain25 (Genbank, accession X59949) or rat liver.26 A master mix of PCR reagents was made for duplex reactions containing primers for the housekeeping gene β-actin (Genbank accession Joo691) and primers for either neuronal NOS (Genbank, accession X59949) or IL-1β (Accession M98820).

The RT-PCR products were quantified by the method of Higuchi and Dollinger.27 Fluorescence was measured in a fluorescence spectrofluorometer (F-2000, Hitachi Ltd). Excitation was at 280 nm, and emitted light was selected at 590 nm. Results were expressed as a ratio of the resultant optical densities for the specific gene to β-actin.

Random hexamers, DTT, Super Scrip Super RT with reaction buffer (×5; 20 mmol/L Tris-HCl, 10 mmol/L NaCl, 0.1 mmol/L EDTA, 1 mmol/L DTT, 0.01% NP-40, and 50% glycerol), TaqDNA polymerase with reaction buffer (×10; 50 mmol/L Tris-HCl, 10 mmol/L NaCl, 0.1 mmol/L EDTA, 5 mmol/L DTT, 50% glycerol, and 1.0% Triton X-100), 2′-deoxynucleoside 5′-triphosphate, and MgCl2, were purchased from Gibco/BRL.

### Determination of Catalytic Components of NADPH Oxidase in Brain Nuclei

Total RNA was prepared as described above. RT-PCR was performed with gene-specific primers as shown in the Table, using the same methods described for nNOS. We measured several components of the NADPH oxidase, including rat p22-phox, p47 phox, gp91phox/Nox2, and Nox3.

### NE Microassay

We used a highly sensitive microradioenzymatic assay.28 A total of 10 μL of dialysate was added to 5 μL of reaction mixture containing 1 μL of 3.7 mol/L Tris base (with 0.37 mol/L EGTA and 1.8 mol/L MgCl2; pH 8.2), 0.06 μL of 36 mmol/L benzoxylamine, 1.5 μL of S-[methyl-3H]adenosyl-l-methionine, and 2.4 μL of partially purified catechol-O-methyltransferase and incubated for 60 minutes at 37°C. The sensitivity of this method is 0.5 pg.

### Statistical Analyses

Data were analyzed by 1-way ANOVA and by Fisher’s exact test when indicated. A 2-way ANOVA was used to examine interactions among the effects of phenol injection, tempol, and PEG-SOD. The computer program Prism (GraphPad Software) was used for the analyses. Results are expressed as mean±SEM.

### Results

#### Interaction of Tempol and PEG-SOD With the Phenol-Renal Injury–Induced Effects on BP NE Secretion From the PH and RSNA

Intrarenal injection of phenol significantly (P<0.01) raised mean BP, RSNA, and NE secretion from the PH (Figures 1–3). By contrast, the administration of saline in the kidney caused no change in BP or NE secretion from the PH.

When tempol (50 μg/μL per kilogram per minute dissolved in aCSF) was given intracerebroventricularly 15 minutes before the phenol injection, the effects of phenol on BP and NE secretion from the PH and RSNA, after an initial surge, were completely abolished (Figures 1–3).

Because we showed previously that at the dose of 50 μg/μL per kilogram per minute, tempol by itself reduced BP,
NE secretion from the PH, and RSNA,\textsuperscript{31} this might suggest that the ability of tempol to block the effects of phenol-renal injury on BP, NE secretion, and RSNA may not necessarily depend on interference with renal injury–mediated ROS activation. Instead, renal injury and tempol could have independent and opposite effects on BP.

To partially deal with this possibility, we used a different SOD agonist: PEG-SOD. PEG-SOD given alone in a dose of 80 U/kg of body weight has no direct effects on BP, NE secretion from the PH, and RSNA. However, this dose of PEG-SOD, after an initial surge, significantly attenuated the effects of phenol-induced renal injury on BP, NE secretion from the PH, and RSNA (Figures 1–3).

Because injecting PEG-SOD 15 minutes before the injection of phenol might not give the drug the necessary time to fully activate enzyme activity, in a subset of rats, we repeated the same experiments, but we infused the same dose of PEG-SOD 30 minutes before the intrarenal injection of phenol. In this case, the initial surge in BP, NE secretion from the PH, and RSNA were completely abolished (Figures 1–3). There was a statistically significant interaction ($P<0.001 \times 2$-way ANOVA) among PEG-SOD, renal injury, and BP, NE secretion from the PH, and RSNA.

**Effects of Tempol, PEG-SOD, and Renal Injury on nNOS and IL-1$\beta$ Abundance in the PH, PVN, and LC**

The intrarenal injection of phenol significantly ($P<0.01$) reduced the abundance of IL-1$\beta$ in the PH (from 75.0±2.3 to 37.0±1.6), PVN (from 76±2.4 to 45.2±1.8), and LC (from 56.1±2.3 to 42.5±1.8) compared with control rats (Figure 4B). Intrarenal phenol also significantly ($P<0.01$) reduced the abun-

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**Figure 2.** The line graph with ● shows levels of norepinephrine secretion from the PH of rats before and after the intrarenal injection of phenol. The line with ▲ shows levels of norepinephrine secretion of rats pretreated with tempol (50 $\mu$g/µL per kilogram of body weight per minute ×60 minutes) infused in the lateral ventricle starting 15 minutes before the intrarenal injection of phenol. The line with ■ shows levels of mean arterial pressure of rats pretreated with PEG-SOD (80 U/kg body weight) infused in the lateral ventricle 15 minutes before the intrarenal injection of phenol. The line with △ shows levels of mean arterial pressure of rats pretreated with PEG-SOD (80 U/kg body weight) infused in the lateral ventricle 30 minutes before the intrarenal injection of phenol. The line with ○ shows levels of norepinephrine secretion of control rats. Values are mean±SEM. *$P<0.01$. Each group includes 5 rats.

**Figure 3.** The line graph with ● shows levels of RSNA of rats before and after the intrarenal injection of phenol. The line with ▲ shows levels of RSNA of rats pretreated with tempol (50 $\mu$g/µL per kilogram of body weight per minute ×60 minutes) infused in the lateral ventricle starting 15 minutes before the intrarenal injection of phenol. The line with ■ shows levels of mean arterial pressure of rats pretreated with PEG-SOD (80 U/kg body weight) infused in the lateral ventricle 15 minutes before the intrarenal injection of phenol. The line with △ shows levels of mean arterial pressure of rats pretreated with PEG-SOD (80 U/kg body weight) infused in the lateral ventricle 30 minutes before the intrarenal injection of phenol. The line with ○ shows levels of RSNA of control rats. Values are mean±SEM. *$P<0.01$. Each group includes 5 rats.
dance of nNOS mRNA in the PH (from 77.3 ± 2.4 to 52.5 ± 1.8), PVN (from 75.4 ± 3.4 to 50 ± 1.7), and LC (from 73.3 ± 2.7 to 56.0 ± 2.1; Figure 4A). Pretreatment with tempol or PEG-SOD abrogated the effects of intrarenal injection of phenol on the abundance of nNOS and IL-1β (Figure 4A and 4B).

Effects of Intrarenal Phenol on the Abundance of NADPH Subunits in Brain Nuclei

The intrarenal injection of phenol caused a significant increase in the abundance of several components of NADPH, including gp91phox/Nox2, p22phox, nox3, and p47phox (Figure 5).

Discussion

These studies have confirmed that an intrarenal injection of phenol raises BP, NE secretion from the PH, and RSNA and reduces the abundance of nNOS and IL-1β in several brain nuclei. Tempol and PEG-SOD, 2 SOD mimetics, abolished the effects of intrarenal phenol injection on BP, NE secretion from the PH, and RSNA and on nNOS and IL-1β. In addition, the intrarenal injection of phenol caused a significant increase in the abundance of several components of NADPH in a variety of brain nuclei involved in the noradrenergic control of BP. The data support the hypothesis that ROS may modulate central and peripheral SNS activation that follows intrarenal phenol injection. Tempol is a membrane-permeable and metal-independent SOD mimetic that has been widely used for the removal of intracellular and extracellular O2_, and has proven antioxidative activity in various tissues. In coronary arteries, O2_ has been shown to inactivate NO, and O2_ is important in the decomposition of NO to peroxynitrite.

The effects of tempol on BP have been controversial. Large doses of tempol given intravenously have been shown to acutely lower BP in normotensive and hypertensive rats and result in reflex activation of the SNS. By contrast, Xu et al. observed that tempol (300 μmol/kg IV) lowered BP and RSNA in urethane-anesthetized DOCA–salt-hypertensive rats. In a previous study, we observed that tempol infused intracerebroventricularly reduced BP, NE secretion from the PH, and RSNA. By contrast, Shokoji et al. observed no effects of tempol on BP and RSNA when bolus doses of this agent were infused ICV in SHR and WKY rats. Differences in dosing, type of administration, and animal model could explain the difference in results among these studies.

To further substantiate a role for O2_ in renal injury–mediated activation of SNS, we evaluated the effects of a different SOD agonist, PEG-SOD. PEG-SOD in a dose of 80 U/kg of body weight infused intracerebroventricularly caused no direct ef-
effects on BP and SNS activity. However, when administered 15 minutes before the intrarenal injection of phenol, PEG-SOD reduced the effects of renal injury on BP, NE secretion from the PH, and RSNA. When we infused PEG-SOD 30 minutes before the intrarenal injection of phenol, the effects of renal injury on BP, NE secretion from the PH, and RSNA were completely abolished.

NOS is present in a specific area of the brain involved in the noradrenergic control of BP, and it is an important component of transduction pathways that tonically inhibit sympathetic nerve activity.27 NO actively reacts with O2 and other ROS to produce peroxynitrite, a highly cytotoxic reactive nitrogen species. Increased production of ROS could enhance oxidation/inactivation of NO and result in activation of the SNS. The current studies support this possibility. Intrarenal phenol reduced the abundance of nNOS in brain nuclei involved in the noradrenergic control of BP resulting in increased SNS activity and BP. By contrast, intracerebroventricular infusion of tempol and PEG-SOD abrogated these effects of phenol. This lends further support to our hypothesis that oxygen radicals may modulate central and peripheral SNS activation caused by intrarenal phenol injection.

We did not measure directly ROS production in the brain but, as an indirect marker, we measured several components of the NADPH oxidase, including rat p22-phox, p47 phox, gp91phox/Nox2, and Nox3. The abundance of all of these components was significantly raised in rats injected with phenol compared with control animals. This lends further support to our hypothesis that activation of SNS activity in the phenol-renal injury model is mediated by increased local production of ROS. We have shown previously that IL-1β plays a modulatory role on the SNS. Administration of IL-1β in the lateral ventricle of 5 of 6 nephrectomized and control rats caused a dose-dependent decrease in BP and NE secretion from the PH, and an increase in nNOS-mRNA abundance in several brain nuclei.39 By contrast, intracerebroventricular infusion of a specific antirat IL-1β antibody decreased NOS-mRNA expression in the PH, PVN, and LC and raised BP and NE secretion from the PH in these rats. In the present studies, phenol injection in the kidney reduced the abundance of IL-1β and nNOS mRNA in the PH, PVN, and LC. By contrast, tempol and PEG-SOD abolished the effects of phenol injection on IL-1β. This suggests that ROS may inhibit IL-1β and nNOS production at a transcriptional level and participate in the central activation of the SNS in the phenol-renal injury model.

We have hypothesized previously that locally produced angiotensin II (Ang II) in the brain may mediate central activation of the SNS in the phenol-renal injury model. Losartan, an Ang II type 1 (AT-1) receptor antagonist, completely reversed the effects of phenol-renal injury on BP and SNS activity.40 This hypothesis is supported by evidence that locally produced Ang II may activate SNS activity in the central nervous system via increased superoxide generation.41–43

In summary, these studies support the hypothesis that a renal injury caused by intrarenal injection of phenol activates the production of ROS in specific brain regions leading to activation of the SNS and hypertension. The data also support the hypothesis that downregulation of nNOS and IL-1β may mediate the central effects of ROS.

Perspectives
Hypertension associated with kidney disease is very prevalent and difficult to control with currently available antihypertensive agents. The phenol-renal injury model offers a unique opportunity to study the mechanisms of hypertension associated with renal injury. The current studies extend previous observations that renal injury may activate afferent pathways connecting with brain regions involved in the noradrenergic control of BP. We have shown previously that locally activated Ang II in the brain may mediate central sympathetic activation caused by renal injury through increased oxidative stress. The current studies have shown that tempol and PEG-SOD attenuate the effects of renal injury on central SNS activation and BP, lending further support to our hypothesis that increased oxidative stress in brain regions involved in the noradrenergic regulation of BP mediates the effects of renal injury on SNS activity and BP.

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Disclosures
None.

References


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In a Hypertension article by Ye et al (Ye S, Zhong H, Campese VM. Oxidative stress mediates the stimulation of sympathetic nerve activity in the phenol renal injury model of hypertension. Hypertension. 2006;48:309–315), an author was omitted. The correct author list is Shaohua Ye, Huiquin Zhong, Swati Yanamadala, and Vito M. Campese. The authors regret the error.