Supplementary Material

to

Cardiovascular "patterns " of H₂S and SSNO⁻-mix evaluated from 35 rat hemodynamic parameters

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Description and abbreviation of 35 hemodynamic parameters (for details see Kurakova et al. [1] and Misak et al. [2]).



Figure S1. The left common carotid artery pulse waveform (APW) in the anesthetized rat. **A:** Control APW (red) with marked ten points **a** - **j** (black circles) before Na₂S administration. APW recorded 15 s after Na₂S (10 μ mol kg⁻¹) i.v. administration (blue). **B:** Fluctuation of minimum diastolic BP, point **a** (**a1** or **a2**).

Ten points **a** - **j** (in bold letters) are from Figure S1A and they mark the values of BP and time that are used to define (calculate) specific hemodynamic parameters (HP).

- (a) Systolic blood pressure in mmHg; point **c** or **f**.
- (b) Heart rate in min⁻¹; 60 / (j a); (j a) represents time interval between **a** and **j**, **a** and **j** are two reference points to diastolic BP value.
- (c) Systolic area in mmHg s; integral BP of **a** to **h**; **h** refers to BP at the dicrotic notch (dicrotic BP).
- (d) dP/dt_{max} in mmHg ms⁻¹; maximum derivative at the point **b**; P is BP in mmHg.
- (e) dP/dt_{max} relative level; relative level (shortly RL) of point **b**; $(\mathbf{b} \mathbf{a}) / (\mathbf{c} \text{ (or } \mathbf{f}) \mathbf{a})$ in mmHg/mmHg (dimensionless).
- (f) dP/dt_d in mmHg ms⁻¹; negative maximum derivative at the point **i**; the point **i** is the BP at the middle of the time interval between **h** and **j**.
- (g) dP/dt_d relative level, relative level of point **i**; $(\mathbf{i} \mathbf{a}) / (\mathbf{c} \text{ (or } \mathbf{f}) \mathbf{a})$ in mmHg/mmHg (dimensionless).
- (h) $dP/dt_d dP/dt_{max}$ in s; time interval between **b** and **i**, $dP/dt_d dP/dt_{max} = (\mathbf{i} \mathbf{b})$.
- (i) $dP/dt_d dP/dt_{min}$ in s; time interval between **g** and **i**, $dP/dt_d dP/dt_{min} = (\mathbf{i} \mathbf{g})$; dP/dt_{min} is negative maximum derivative at the point **g**.
- (j) Diastolic blood pressure in mmHg; the point **a** or **j**.
- (k) Pulse BP in mmHg; $(\mathbf{c} \mathbf{a})$ or $(\mathbf{f} \mathbf{a})$.
- (l) Diastolic area in mmHg s; integral BP of **h** to **j**.
- (m) dP/dt_{min} in mmHg ms⁻¹; dP/dt_{min} is maximum negative derivative at the point **g**.
- (n) dP/dt_{min} relative level, relative level of point **g**; $(\mathbf{g} \mathbf{a}) / (\mathbf{c} \text{ (or } \mathbf{f}) \mathbf{a})$ in mmHg/mmHg (dimensionless).
- (o) dP/dt_{min} delay in s; delay in s of point g; (g a) time interval between a and g.
- (p) dP/dt_d delay in s; delay in s of point i; (i a) time interval between a and i.
- (q) $dP/dt_d dP/dt_{max}$ in mmHg; (i b) BP difference between b and i.
- (r) $dP/dt_d dP/dt_{min}$ in mmHg; (i g) BP difference between g and i.
- (aa) Systolic blood pressure in mmHg; point **c** or **f**. Plot (aa) is the same as (a).
- (bb) Anacrotic notch in mmHg; BP at the point **d**.
- (cc) Anacrotic notch relative level; relative level of point \mathbf{d} ; $(\mathbf{d} \mathbf{a}) / (\mathbf{c} \text{ (or } \mathbf{f}) \mathbf{a})$ in mmHg/mmHg (dimensionless).
- (dd) Anacrotic notch delay in ms; delay in ms of point d; (d a) time interval between a and d.
- (ee) Anacrotic notch relative delay; relative delay (shortly RD) of point d; (d a) / (j a) in ms/ms (dimensionless)
- (ff) [Dicrotic notch (DiN) in s] [Anacrotic notch (AnN) in s] in s; (**h d**) time interval between **d** and **h**.
- (gg) $[(DiN AnN) in s] / [dP/dt_{min} in mmHg \mu s^{-1}] in s/mmHg \mu s^{-1}; (h d) / g.$
- (hh) $[(DiN AnN) in s] / [dP/dt_{max} in mmHg \mu s^{-1}] in s/mmHg \mu s^{-1}; (h d) / b.$
- (ii) [AnN in ms] [1Max (point c or the 1th. maximum) in ms] in ms; (d c) time interval between c and d.
- (jj) Augmentation index relative; $(\mathbf{f} \mathbf{c}) / (\mathbf{f} \mathbf{a})$ in mmHg/mmHg (dimensionless).
- (kk) Dicrotic notch in mmHg; BP at the point **h**.
- (ll) Dicrotic notch relative level; relative level of point \mathbf{h} ; $(\mathbf{h} \mathbf{a}) / (\mathbf{c} (\text{or } \mathbf{f}) \mathbf{a})$ in mmHg/mmHg (dimensionless).
- (mm) Dicrotic notch delay in ms, delay in ms of point \mathbf{h} ; ($\mathbf{h} \mathbf{a}$).time interval between \mathbf{a} and \mathbf{h} .
- (nn) Dicrotic notch relative delay; relative delay of point \mathbf{h} ; $(\mathbf{h} \mathbf{a}) / (\mathbf{j} \mathbf{a})$; in ms/ms (dimensionless)
- (oo) [DiN in mmHg] [AnN in mmHg] in mmHg; (h d) BP difference between d and h;
- (pp) $[(DiN AnN) in mmHg] / [dP/dt_{min} in mmHg ms^{-1}] in mmHg/mmHg ms^{-1}; (h d) / g;$
- $(qq) \quad [(DiN AnN) in mmHg] / [dP/dt_{max} in mmHg ms^{-1}] in mmHg/mmHg ms^{-1}; (h d) / b.$
- (rr) [AnN in mmHg] [1Max (point **c** or the 1th. maximum) in mmHg] in mmHg; $(\mathbf{d} \mathbf{c})$ BP difference between **c** and **d**.





Figure S2. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 µmol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration. For the definition of HPs, see the text below Figure S1.





Figure S3. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 μ mol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration.





Figure S4. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 μ mol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration.





Figure S5. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 μ mol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration.





Figure S6. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 μ mol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration.





Figure S7. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 μ mol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration.





Figure S8. Time-dependent changes of HPs of anesthetized rat after I.V. bolus administration of 10 μ mol kg⁻¹ Na₂S (marked by dash lines). Colors: time period corresponds to the decrease of systolic BP (red), increase of systolic BP to the control value (blue), further increase of systolic BP to maximum (green) and decrease of systolic BP to the control value (black). The red line starts 3 s before Na₂S administration.





Figure S9. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S2. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.





Figure S10. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S3. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.





Figure S11. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S4. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.





Figure S12. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S5. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.





Figure S13. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S6. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.





Figure S14. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S7. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.





Figure S15. Relationships of HPs to the systolic BP after administration of 10 μ mol kg⁻¹ Na₂S. The colors and (time-dependent) data correspond to Figure S8. The hysteresis was arbitrary defined as HP – Systolic BP (in mmHg) loop > 5 mmHg of Systolic BP.



Figure S16. Number of rats representing the non-hysteresis/hysteresis patterns of the relationships of HPs to systolic BP after administrations of 10 μ mol kg⁻¹ Na₂S during increase (green line in Figures 2 and S9-S15) and decrease (black line in Figures 2 and S9-S15) of BP. Data were taken from Figures 2 and S9-S15. The total number of rats in which non-hysteresis (blue) or hysteresis (red) patterns were evaluated is n = 8. The hysteresis was arbitrary defined as HP – systolic BP loop > 5 mmHg of systolic BP.



Figure S17. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (12-20 min). (**B**): The fluctuation of AnN delay (**dd**); (13-14 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of AnN delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure S2.



Figure S18. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (15-24 min). (**B**): The fluctuation of AnN delay (**dd**); (16-17 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of AnN delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure S3.



Figure S19. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (21-27 min). (**B**): The fluctuation of AnN delay (**dd**); (22-23 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of AnN delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure S4.



Figure S20. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (11-18 min). (**B**): The fluctuation of AnN delay (**dd**); (12-13 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of AnN delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure S5.



Figure S21. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (11-16 min). (**B**): The fluctuation of AnN delay (**dd**); (12-13 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of AnN delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure S6.



Figure S22. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (40-44 min). (**B**): The fluctuation of AnN delay (**dd**); (40-41 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of anacrotic notch delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure S7.



Figure S23. Time-dependent effect of 10 µmol kg⁻¹ Na₂S on three HPs: (**A**): systolic BP (Syst. BP, mmHg) (**aa**), AnN (Anacr. N., mmHg) (**bb**) and AnN delay (Anacr. N. delay, ms) (**dd**); (10-17 min). (**B**): The fluctuation of AnN delay (**dd**); (11-12 min) reflects the time interval fluctuation between **a1** and **a2** points (Figure S1). The higher value of anacrotic notch delay in ms indicates that diastolic BP at the point **a1** was lower than at the point **a2**. (**C**): The example of the fluctuation between **a1** and **a2** points in pulses (circles) showed at high resolution after the 10 µmol kg⁻¹ Na₂S administration (**dd**). Data were taken from Figure 1.

References

- Kurakova, L.; Misak, A.; Tomasova, L.; Cacanyiova, S.; Berenyiova, A.; Ondriasova, E.; Balis, P.; Grman, M.; Ondrias, K. Mathematical relationships of patterns of 35 rat haemodynamic parameters for conditions of hypertension resulting from decreased nitric oxide bioavailability. *Exp. Physiol.* 2020, 105, 312–334, doi:10.1113/ep088148.
- Misak, A.; Kurakova, L.; Berenyiova, A.; Tomasova, L.; Grman, M.; Cacanyiova, S.; Ondrias, K. Patterns and Direct/Indirect Signaling Pathways in Cardiovascular System in the Condition of Transient Increase of NO. *Biomed. Res. Int.* 2020, 2020, 6578213, doi:10.1155/2020/6578213.