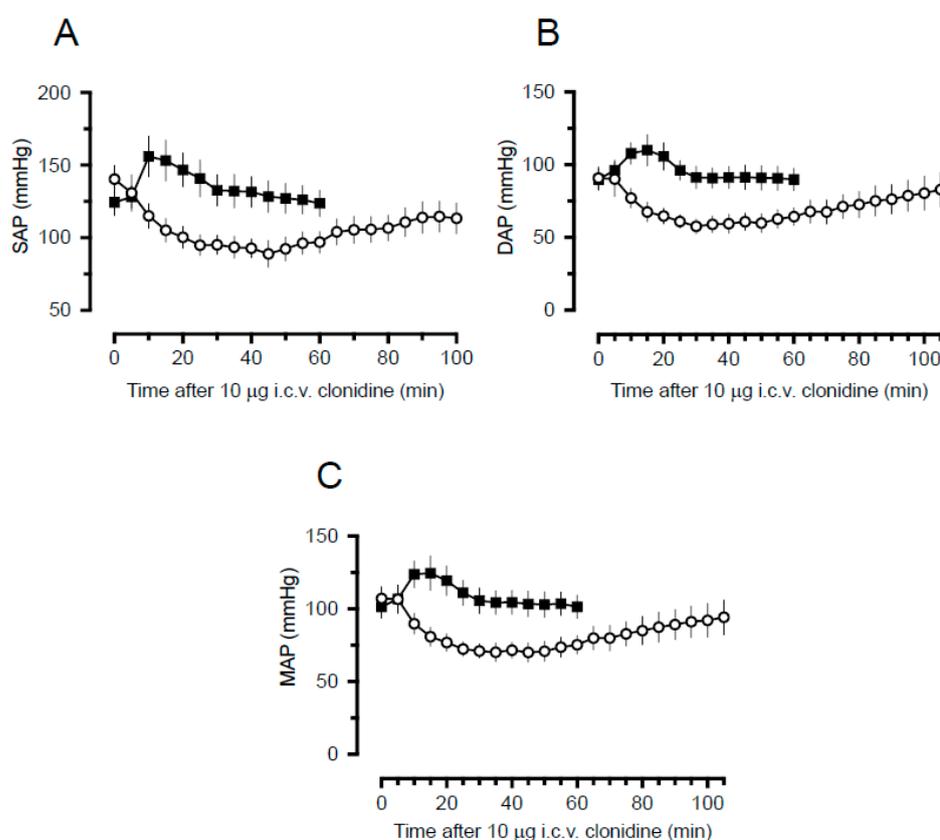


# Supplementary Materials: The Dual Cardiovascular Effect of Centrally Administered Clonidine: A Comparative Study between Pentobarbital- and Ketamine/Xylazine-Anesthetized Rats

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**Figure S1.** Differential influence of pentobarbital- and ketamine/xylazine-induced anesthesia in the vascular effects of centrally administered clonidine in rats. The results show the mean  $\pm$  standard error of the mean of the values of systolic (SAP, A), diastolic (DAP, B) and mean (MAP, C) arterial pressures recorded in animals subjected to pentobarbital- or ketamine/xylazine-induced general anesthesia, before (time “0”) and after the intracerebroventricular (i.c.v.) injection of 10  $\mu$ g clonidine. The values presented in this figure were used to calculate the changes in the SAP, DAP and MAP presented in Figures 2C, E and G of this study.

**Table S1.** Basal cardiovascular parameters in pentobarbital- and ketamine/xylazine-anesthetized rats.

|            | Pentobarbital ( <i>n</i> = 5) | Ketamine/xylazine ( <i>n</i> = 6) | <i>P</i> value |
|------------|-------------------------------|-----------------------------------|----------------|
| SAP (mmHg) | 140.3 ± 9.6                   | 124.3 ± 9.2                       | 0.2623         |
| DAP (mmHg) | 90.9 ± 7.7                    | 89.9 ± 7.5                        | 0.9252         |
| MAP (mmHg) | 107.2 ± 8.2                   | 101.4 ± 7.9                       | 0.625          |
| HR (bpm)   | 344.1 ± 10.8                  | 259.9 ± 5.5                       | < 0.0001       |

The values show the mean ± standard error of the mean of the arterial pressure and heart rate obtained in animals anesthetized with pentobarbital (50 mg/kg, i.p.) or ketamine/xylazine combination (100/20 mg/kg, i.m.). SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; HR, heart rate.

**Table S2.** Effects of the centrally administered clonidine in cardiovascular parameters of pentobarbital and ketamine/xylazine anesthetized rats.

|            | Pentobarbital ( <i>n</i> = 5) | Ketamine/xylazine ( <i>n</i> = 6) | <i>P</i> value |
|------------|-------------------------------|-----------------------------------|----------------|
| SAP (mmHg) | -54.0 ± 9.0                   | 35.1 ± 7.0*                       | <0.0001        |
| DAP (mmHg) | -35.5 ± 5.5                   | 26.5 ± 4.2*                       | <0.0001        |
| MAP (mmHg) | -40.7 ± 6.3                   | 29.4 ± 5.1*                       | <0.0001        |
| HR (bpm)   | -133.7 ± 15                   | -33.6 ± 5*                        | <0.0001        |

The values show the mean ± standard error of the mean of the maximal effect of i.c.v. clonidine (10 µg/5 µL) in animals anesthetized with pentobarbital (50 mg/kg, i.p.) or ketamine/xylazine combination (100/20 mg/kg, i.m.). SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; HR, heart rate. \* indicates a value of *P* < 0.05, compared with the effect recorded in the pentobarbital group.

**Table S3.** Influence of yohimbine in the cardiovascular effect of intracerebroventricular clonidine and dexmedetomidine in ketamine/xylazine anesthetized rats.

|                        | Before yohimbine<br>(n = 6) | After yohimbine<br>(n = 6) | P value |
|------------------------|-----------------------------|----------------------------|---------|
| <i>Clonidine</i>       |                             |                            |         |
| SAP (mmHg)             | 30.5 ± 5.6                  | 12.8 ± 2*                  | 0.0098  |
| DAP (mmHg)             | 23.7 ± 5.2                  | 10 ± 2.3*                  | 0.0359  |
| MAP (mmHg)             | 23.5 ± 3.4                  | 9.9 ± 2.3*                 | 0.0033  |
| HR (bpm)               | -16.8 ± 6.6                 | 17.7 ± 12.7                | 0.0544  |
| <i>Dexmedetomidine</i> |                             |                            |         |
| SAP (mmHg)             | 26.5 ± 3.5                  | 7.4 ± 1.8*                 | 0.0053  |
| DAP (mmHg)             | 19.3 ± 3.8                  | 6.4 ± 0.9*                 | 0.0296  |
| MAP (mmHg)             | 21 ± 3.7                    | 6.7 ± 1.1*                 | 0.0209  |
| HR (bpm)               | -50.8 ± 15.5                | -23.7 ± 8.1                | 0.1449  |

The values show the mean ± standard error of the mean of the maximal effects of i.c.v. clonidine (10 µg/5 µL) and dexmedetomidine (0.6 µg/5 µL) in animals anesthetized with ketamine/xylazine combination (100/20 mg/kg, i.m.). In these experiments, the effects of clonidine and dexmedetomidine were recorded twice, before and 15 min after the i.c.v. administration of the  $\alpha_2$ -adrenoceptor antagonist yohimbine (5 µg/5 µL). SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure; HR, heart rate. \* indicates a value of  $P < 0.05$ , compared with the effect recorded before yohimbine.