Supplemental Material

Kurnik D et al. Genetic variations in the α_{2A}-adrenoreceptor are associated with blood pressure response to the agonist dexmedetomidine.

SNP position in haplotype	Chromosome position	rs number	Nucleotide change	MAF (%)	
				White subjects	Black subjects
1	112835159	rs11195418	A>G	10.0	0.0
2	112836503	rs1800544	C>G	31.1	62.5
3	112837073	rs2484516	C>G	0.0	8.3
4	112837538	rs1800545	G>A	14.9	31.9
5	112838552	rs1800035	C>G	0.0	8.3
6	112838892	rs1800038	C>A	0.0	4.2
7	112839282	rs34303217	T>A	0.0	5.6
8	112839579	rs553668	A>G	14.9	19.4
9	112839601	rs3750625	C>A	7.4	19.4

Table S1: Minor allele frequencies of 9 *ADRA2A* tagSNPs in white and black subjects. Chromosome positions refer to Genome build GRCh 37.1., August 2009. SNP=single nucleotide polymorphism; MAF=minor allele frequency.

Haplotype family	SNP positions in haplotype	Haplotype frequency (%)	
	1-2-3-4-5-6-7-8-9	White subjects	Black subjects
1	A-C-C-G-C-C-T-G-C	71.4	29.2
2	A-C-C-G-G-C-T-G-C	0.0	8.3
3	A-G-C-G-C-C-T-G-C	1.4	11.1
4	A-G-C-G-C-C-T-A-C A-G-G-G-C-C-T-A-C A-G-C-G-C-C-A-A-C A-G-C-G-C-A-T-A-C A-G-G-G-C-C-A-A-C A-G-G-G-C-C-A-A-C A-G-C-G-G-A-T-A-C	14.9	19.4
5	A-G-C-A-C-C-T-G-C A-G-C-A-C-C-T-G-A G-G-C-A-C-C-T-G-C A-G-C-A-G-C-T-G-C G-G-C-A-C-C-T-G-A	15.7	31.9

Table S2. Definition and distribution of haplotype families. Minor alleles are shadowed in grey. Haplotypes were grouped in haplotypes families as previously defined.[1]

	ΔAUC_{SBP} mmHg*hr	ΔAUC_{DBP} mmHg*hr	ΔAUC_{HR} bpm*hr
HT 2	3.7 (-1.6 to 8.9) P=0.16	1.0 (-3.4 to 5.4) P=0.65	-0.9 (-5.9 to 4.2) P=0.73
HT 3 carrier	-6.1 (-10.8 to -1.3) P=0.013	-3.8 (-7.7 to 0.0) P=0.052	-3.7 (-8.2 to 0.9) P=0.11
HT4	2.9 (0.0-5.8) P=0.047 P_{rec}=0.007	0.9 (-1.5 to 3.2) P=0.47 P_{rec}=0.10	-0.5 (-3.3 to 2.4) P=0.75 , P_{rec} =0.069
HT 5	-1.1 (-3.7 to 1.6) P=0.43	-0.3 (-2.5 to 1.9) P=0.80	-0.1 (-2.7 to 2.5) P=0.93

Table S3. Effect of all haplotypes combined on decrease in blood pressure and heart rate. The table shows means and 95% CI of the β-coefficients. P-values are adjusted for all other haplotypes, age, sex, race, BMI, AUC_{Plac} of the respective outcome, and dexmedetomidine plasma concentrations. P_{rec} denotes P-values derived from analyses in which HT4 was treated as a recessive (rather than additive) trait.

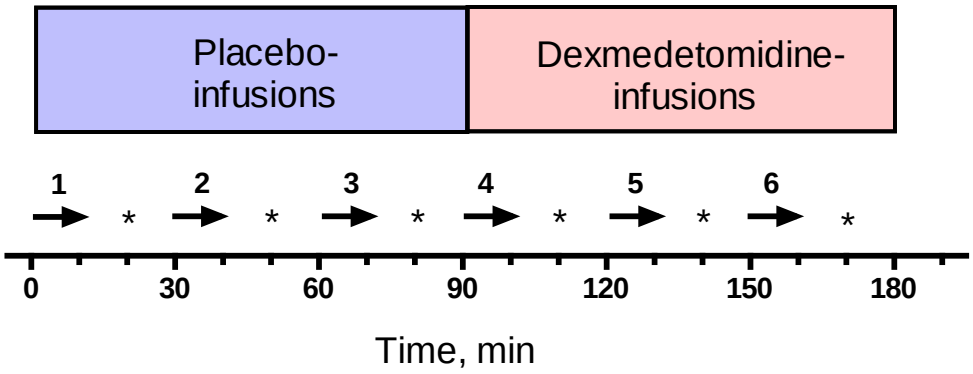

Figure S1. Diagram of study protocol. After baseline measurements, subjects received 6 infusions (10 minutes each, indicated by horizontal arrows). Ten minutes after completion of the infusions, blood pressure was determined and a blood sample taken (indicated by asterix). The first three infusions were placebo, the last three were dexmedetomidine infusions at doses of 0.1, 0.15, and 0.15 mcg/kg body weight, respectively.

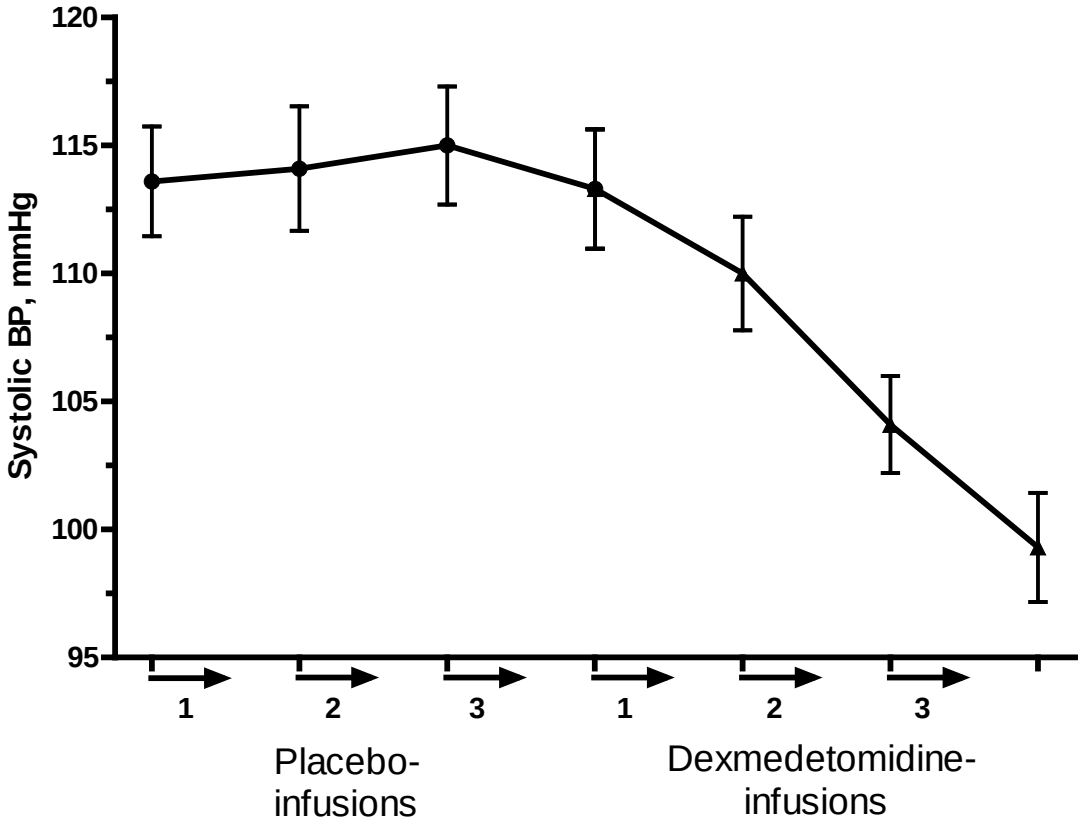

Figure S2. Systolic blood pressure during placebo and dexmedetomidine infusion in 73 subjects. Data points represent the mean, error bars the 95% confidence intervals of systolic blood pressure measured 10 minutes after completion of each infusion (represented by horizontal arrows). The blue and red areas represent the AUC_{SBP} during placebo and dexmedetomidine, respectively.

Supplement reference

1. Kurnik D, Muszkat M, Li C, Sofowora GG, Solus J, Xie HG, Harris PA, Jiang L, McMunn C, Ihrie P, Dawson EP, Williams SM, Wood AJ, Stein CM. Variations in the alpha2A-adrenergic receptor gene and their functional effects. *Clin Pharmacol Ther* 2006; 79:173-85.