

SUPPLEMENTAL MATERIAL

Online Supplemental Table 1. Haemodynamics at Baseline and During Complete Autonomic Blockade for Subjects Grouped According to Homozygous Arg16 vs. Gly16

Measure	Condition	Position 16 group		<i>P</i> _{ANOVA}
		Arg16 (n=13)	Gly16 (n=27)	
HR (bpm)	Baseline	66 ± 2	60 ± 2	0.04
	Trimeth.*	87 ± 3	82 ± 2	ns
CO (L/min)	Baseline	5.6 ± 0.5	6.4 ± 0.4	ns
	Trimeth.	5.6 ± 0.4	6.1 ± 0.4	ns
MAP (mmHg)	Baseline	89 ± 2	87 ± 1	ns
	Trimeth.*	74 ± 3	72 ± 1	ns
SVR (units)	Baseline	19.0 ± 3.0	14.8 ± 0.8	0.09
	Trimeth.*	13.6 ± 0.8	12.4 ± 0.7	ns
SV (mL)	Baseline	86 ± 10	107 ± 7	0.08
	Trimeth.*	66 ± 6	77 ± 5	ns

Values are mean ± SEM. HR, heart rate; CO, cardiac output; MAP, mean arterial pressure; SVR, systemic vascular resistance with units = MAP/CO; SV, stroke volume. Trimeth.* indicates a significant effect of trimethaphan on all values for all groups (*P* < 0.01). *P*_{ANOVA} indicates comparisons across groups in the time-specific condition.

Online Supplemental Table 2. Haemodynamics Immediately Before and During Terbutaline Infusions by Position 16

		Position 16 Group		P_{ANOVA}
		Arg16 (n=13)	Gly16 (n=27)	
Heart Rate (bpm)	BL _{Trimeth + PE}	86 ± 2	78 ± 2	0.005
	Terb 33	101 ± 2	91 ± 2	0.007
	Terb 67	117 ± 3	106 ± 2	0.01
	$P_{genotype} / P_{dose} / P_{interaction}$	< 0.01, < 0.01, 0.28		
	$\Delta P_{genotype} / P_{dose} / P_{interaction}$	0.15, < 0.01, 0.18		
Cardiac Output (L/min)	BL _{Trimeth + PE}	6.7 ± 0.6	6.8 ± 0.4	ns
	Terb 33	7.4 ± 0.6	8.0 ± 0.5	ns
	Terb 67	8.0 ± 0.6	9.3 ± 0.6	ns
	$P_{genotype} / P_{dose} / P_{interaction}$	0.41, < 0.01, 0.11		
	$\Delta P_{genotype} / P_{dose} / P_{interaction}$	0.1, < 0.01, 0.06		
MAP (mmHg)	BL _{Trimeth + PE}	95 ± 3	94 ± 2	ns
	Terb 33	82 ± 4	77 ± 2	ns
	Terb 67	68 ± 3	66 ± 2	ns
	$P_{genotype} / P_{dose} / P_{interaction}$	0.38, < 0.01, 0.33		
	$\Delta P_{genotype} / P_{dose} / P_{interaction}$	0.36, < 0.01, 0.36		
SVR (units)	BL _{Trimeth + PE}	15.1 ± 0.9	14.8 ± 0.7	ns
	Terb 33	11.8 ± 0.8	10.6 ± 0.8	ns
	Terb 67	8.9 ± 0.7	7.5 ± 0.3	0.03
	$P_{genotype} / P_{dose} / P_{interaction}$	0.34, < 0.01, 0.56		
	$\Delta P_{genotype} / P_{dose} / P_{interaction}$	0.15, < 0.01, 0.40		

Stroke	BL _{Trimeth + PE}	78 ± 7	88 ± 5	ns
Volume	Terb 33	75 ± 7	90 ± 7	ns
(mL)	Terb 67	70 ± 7	92 ± 7	0.07
<i>P</i> _{genotype} / <i>P</i> _{dose} / <i>P</i> _{interaction}		0.13, 0.54, 0.24		
Δ <i>P</i> _{genotype} / <i>P</i> _{dose} / <i>P</i> _{interaction}		0.09, 0.56, 0.10		

Values are mean ± SEM. HR, heart rate; CO, cardiac output; MAP, mean arterial pressure; SVR, systemic vascular resistance with units = MAP/CO; SV, stroke volume. Analyses were performed using raw values with measures obtained at baseline and each terbutaline dose and also using change from baseline at each terbutaline dose (Δ). *P*_{genotype} indicates main effect of genotype, *P*_{dose} indicates main effect of terbutaline dose, *P*_{interaction} indicates haplotype-by-dose interaction. *P*_{ANOVA} indicates comparisons across groups at the given dose of terbutaline.

Online Supplemental Table 3. Forearm Haemodynamics at Baseline, After Trimethaphan, and Immediately Before and During Terbutaline Infusions

Condition		Haplotype Group			P_{ANOVA}
		Arg16 + Gln27 (n = 13)	Gly16 + Gln27 (n = 6)	Gly16 + Glu 27 (n = 21)	
Forearm Blood Flow (ml/dl/min)	Baseline	1.5 ± 0.1	1.5 ± 0.3	1.7 ± 0.1	ns
	Trimeth.*	2.8 ± 0.3	3.2 ± 0.7	2.8 ± 0.3	ns
	BL _{Trimeth + PE}	5.1 ± 0.9	5.5 ± 2.2	4.3 ± 0.6	ns
	Terb 33	7.0 ± 1.0	7.6 ± 2.5	6.2 ± 0.6	ns
	Terb 67	10.2 ± 0.9	11.8 ± 2.3	9.4 ± 0.7	ns
$P_{genotype} / P_{dose} / P_{interaction}$		0.69, < 0.01, 0.63			
$\Delta P_{genotype} / P_{dose} / P_{interaction}$		0.97, < 0.01, 0.45			
Forearm Vascular Conductance (units)	Baseline	1.7 ± 0.2	1.7 ± 0.4	1.9 ± 0.1	ns
	Trimeth.*	3.7 ± 0.5	4.2 ± 1.1	3.7 ± 0.3	ns
	BL _{Trimeth + PE}	5.2 ± 0.8	5.3 ± 2.0	4.4 ± 0.5	ns
	Terb 33	8.1 ± 1.1	8.1 ± 2.2	7.3 ± 0.7	ns
	Terb 67	15.1 ± 1.6	16.0 ± 2.2	14.3 ± 1.1	ns
$P_{genotype} / P_{dose} / P_{interaction}$		0.84, < 0.01, 0.92			
$\Delta P_{genotype} / P_{dose} / P_{interaction}$		0.92, < 0.01, 0.86			
Forearm Vascular Resistance (units)	Baseline	68.8 ± 8.1	70.4 ± 13.2	58.9 ± 5.3	ns
	Trimeth.*	32.9 ± 4.3	36.1 ± 10.4	31.9 ± 3.1	ns
	BL _{Trimeth + PE}	25.3 ± 3.4	36.0 ± 11.6	27.6 ± 2.6	ns
	Terb 33	15.7 ± 2.1	16.8 ± 4.0	15.7 ± 1.5	ns

Terb 67	7.7 ± 0.9	6.9 ± 1.0	8.0 ± 0.7	ns
$P_{\text{genotype}} / P_{\text{dose}} / P_{\text{interaction}}$		0.26, < 0.01, 0.72		
$\Delta P_{\text{genotype}} / P_{\text{dose}} / P_{\text{interaction}}$		0.75, < 0.01, 0.78		

Values are mean ± SEM. FBF, forearm blood flow; FVC, forearm vascular conductance with units = FBF/MAP x 100; FVR, forearm vascular resistance with units = MAP/FBF. Trimeth.* indicates a significant effect of trimethaphan on all values for all groups (P < 0.01). Analyses were performed using raw values with measures obtained at baseline and each terbutaline dose and also using change from baseline at each terbutaline dose (Δ). P_{genotype} indicates main effect of genotype, P_{dose} indicates main effect of terbutaline dose, $P_{\text{interaction}}$ indicates haplotype-by-dose interaction. P_{ANOVA} indicates comparisons across groups at the given dose of terbutaline.