Introduction: The pressor response to voluntary isometric forearm contraction is often used in studies of neurogenic influences on blood pressure. It has been assumed to be under autonomic control. Direct experimental evidence for this hypothesis is lacking in systemic studies in human subjects. We used adrenergic receptor agonists and antagonists to quantify the sympathetic influence on the haemodynamic response to isometric contraction.

Methods: 12 healthy volunteers (6 female), matched for age and body mass index, performed a (baseline) isometric forearm contraction at <5% of their maximum grip and an isometric forearm contraction at 40% of their maximum grip. Plasma catacholamines were measured at baseline and after effort. Tasks were repeated in the presence of intravenous 0.9% saline, esmolol (β1-antagonist, 0.2 mg/kg) and phentolamine (α-antagonist, 5 mg), with a 60-minute washout period between drugs. Peripheral alpha and beta adrenoreceptor sensitivity and baroreeptor sensitivity were calculated by measuring the haemodynamnic response to infused isophrenaline (β-agonist, 0–2 mg) and phenylephirine (α-agonist, 0–200 mg).

Results: Voluntary isometric forearm grip induced a rise in heart rate, $p < 0.05$ and in blood pressure, $p < 0.05$. Plasma noradrenaline was increased by isometric contraction, $p < 0.05$. Plasma adrenaline was not altered. Esmolol abolished the positive chronotropic response pressor response, $p < 0.05$ but not the pressor response. Phentolamine abolished the pressor response, $p < 0.05$, and induced a positive chronotrophic response, $p < 0.05$. There was no correlation between alpha and beta adrenoreceptor sensitivity or baroreceptor sensitivity.

	Saline	Esmolol	Phentolamine
Mean % Change in SBP	10.7 ± 2.6*	7.9 ± 3.8*	3.7 ± 3.0*
Mean % Change in DBP	17.2 ± 4.5*	12.5 ± 4.4*	-1.3 ± 2.5
Mean % Change in MAP	13.9 ± 3.2*	10.1 ± 3.4*	0.8 ± 2.6
Mean % Change in HR	9.5 ± 4.75*	2.7 ± 3.6	10.2 ± 5.1*

Figure 1: SBP = systolic blood pressure. DBP = diastolic blood pressure. MAP = mean arterial pressure. HR = heart rate. Date are means ± $CI_{95\%}$. (*) $p < 0.05$.

Discussion: The pressor response to voluntary isometric grip is under α-adrenoreceptor mediated, autonomic, control. This is the first time that this has been demonstrated systemically in human subjects using a pharmacological approach.

PP.32.264 NICOTINIC RECEPTORS SUPPRESS BETA-ADRENOCEPTOR CONTRIBUTION AND VAGAL INTERACTION IN TACHYCARDIA FOLLOWING 4-AMINOPYIDINE-INDUCED NORADRENALINE RELEASE IN HYPERTENSIVE RATS (SHR)

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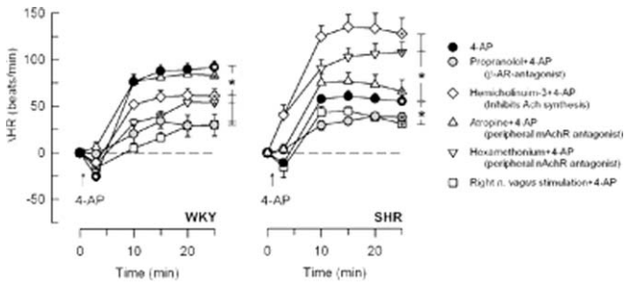
Objective: The parasympathetic and sympathetic nervous control of heart rate (HR) is dysfunctional in essential hypertension in man and spontaneous hypertension in rats (SHR). We aimed to study the nature of this autonomic dysfunction and the mechanisms involved, using SHR as a model.

Design and Methods: The experiments were carried out on 12–14 weeks old, male SHR and their normotensive controls (WKY). The rats were anaesthetized with Nembutal, which abolished baroreceptor reflexes. We studied the HR-response to a bolus injection of 4-aminopyridine (4-AP). 4-AP inhibits voltage-sensitive K+ channels, thus causing depolarization and opening of voltage-sensitive Ca2+ channels. The entry of Ca2+ elicits transmitter release from cholinergic and sympathetic nerve endings, and, through that, 4-AP activates a cardiovascular response.

Results: 4-AP induced an immediate atropine-sensitive bradycardia, followed by a sustained reserpine-sensitive tachycardia. Thus, the HR-response comprised an initial parasympathetic activation, followed by tachycardia due to sympathetic nerve transmitter release.

In WKY, the 4-AP-induced tachycardia was eliminated by β-adrenoceptor (AR) antagonist, and was opposed by electrical vagal nerve stimulation. Furthermore, inhibition of acetylcholine (Ach) synthesis and nicotinic receptor (nAchR) antagonist reduced the tachycardia, indicating a role of presynaptic noradrenaline release-stimulating nAchR in WKY. In SHR, propranolol and vagal nerve stimulation had little effect on the tachycardia, whereas Ach synthesis inhibitor and nAchR but not muscarinic (mAchR) antagonist enhanced the response.



Conclusion: In SHR, activation of peripheral nAchR suppressed 4-AP-induced β-AR-mediated tachycardia and prevented β-AR / vagal nerve interaction.

PP.32.265 COMPARATIVE EFFECTS OF AMLODIPINE AND CILNIDIPINE ON SYMPATHETIC NERVOUS MODULATION IN PATIENTS WITH HYPERTENSION

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Objective: Sympathetic nervous activity may be augmented with the calcium channel blocker (CCB) treatment as a result of decreased blood pressure despite the advent of long-acting CCBs. A dihydropyridine CCB, cilnidipine blocks not only L type but also N type of calcium channels. Accordingly, we compared the effects of amlodipine and cilnidipine on autonomic nervous activity in hypertensive patients.

Design and Methods: Eighteen hypertensive patients under the treatment of amlodipine monotherapy for at least 6 months were randomized to the 2 treatment arms. In 8 patients (70±9 (SD) years, 1 man and 7 women), amlodipine monotherapy was further continued for 6 months. In 10 patients (70±4 years, 3 men and 7 women), amlodipine treatment was switched to cilnidipine treatment. Before and after 6-month treatment with amlodipine or cilnidipine, each patient underwent 30 min resting electrocardiographic recording in the morning after an overnight fasting. By using spectral analysis of heart rate variability, frequency-domain measures were calculated. The low frequency (LF: 0.04 to 0.15 Hz)/high frequency (HF: 0.15 to 0.40 Hz) power ratio was used as an index of sympathovagal balance, and HF/total power (TP) ratio was used as an index of vagal activity. Plasma norepinephrine levels were measured by radioimmunoassay.

Results: In patients with continuous amlodipine treatment, systolic and diastolic blood pressures (SBP, DBP) and heart rate (HR) remained unchanged. LF/HF and HF/TP ratios also remained unchanged (LF/HF 1.77±1.05 vs. 1.83±1.22, HF/TP 0.419±0.122 vs. 0.402±0.116). Plasma norepinephrine levels were comparable (370±88 pg/ml vs. 491±137 pg/ml). In patients switched to cilnidipine, SBP, DBP and HR were similar before and after switching. Interestingly, LF/HF ratio decreased significantly ($p = 0.012$) from 2.37±1.56 to 1.89±1.42, and HF/TP ratio increased significantly ($p = 0.049$) from 0.366±0.132 to 0.417±0.156, despite the comparable HR. Plasma norepinephrine concentrations decreased significantly ($p = 0.009$) from 359±65 pg/ml to 282±72 pg/ml.

Conclusions: These findings suggest that cilnidipine may provide beneficial prognosis for hypertensive patients because it suppresses sympathetic nervous activity.

PP.32.266 AUTONOMIC BALANCE AND HEMODYNAMIC PATTERNS IN PRE-HYPERTENSION

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Introduction: Autonomic imbalance and hemodynamic disturbances has been described in pre-hypertensive patients (PHT-JNC-VII), with increments in sympathetic drive, cardiac index (CI) and vascular resistances[1]. However, these autonomic alterations arenŕ present in all of PHTs, and different status of autonomic balance (AB) could be coexisting with different hemodynamic patterns (HP), as distinct stages in the evolution to sustained HT.