(0.1Hz) and parasympathetic (0.25Hz) efferents that increased and decreased the open probability of ion channels respectively. Average heart-rate (beats per minute) and variability (standard deviation as a percentage of mean heart rate) at varying levels of input from the sympathetic and parasympathetic systems are shown in Table 1. Maximal variability was seen when depolarization occured under both sympathetic and parasympathetic control (SD=34%). Variability was considerably lower when only one of the autonomic components was active (17%) and lowest when the heart was completely isolated from the autonomic inputs (0.1%).

We provide the first comprehensive model of HRV based on interactions between SAN ion channels and autonomic nerves. This model acknowledges two well recognized but, hitherto unexplained, features of HRV: namely (1) Low levels of HRV can be demonstrated in the absence of autonomic inputs (e.g isolated heart preparations); and (2) HRV is reduced during both sympathetic blockade (2) and sympathetic stimulation (3).

Sympathetic input	Parasympathetic input	Mean heart rate (bpm)	Variability SD as % of mean
0.0	0.0	60.0	0.13
0.0	1.0	43.4	16.7
1.0	0.0	89.0	17.4
1.0	1.0	61.0	33.9

Average heart rate and variability (SD of heart rate as a % of mean heart rate), under varying conditions of autonomic control

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Where applicable, the authors confirm that the experiments described here conform with The Physiological Society ethical requirements.

PC16

Comparative physiology of the sinoatrial pacemaker of cold-blooded vertebrates

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It is known that the proximal and distal ends of the tubular heart of tunicates have two centres of automatism that work alternately. As a result, the blood advances by peristaltic contracting waves. Active animal living has led to the appearance of a bent tube with various chambers and valves between them. The pacemaker's cytoarchitecture also has changed. The aim of our study was to analyse the main parameters of the action potential (AP) in true pacemaker cells in the hearts of different poikilotherm species, including inhabitants of water (ammocoete, Lampetra fluviatilis, dace, Leuciscus rutilus) and land (frog, Rana temporaria, tortoise, Testudo horsfieldi). Experiments were carried out on spontaneously beating strips of sinoatrial (SA) tissue (control conditions: 20°C, 0.9 mM Ca^{2+}), using the standard microelectrode technique. In cold-blooded animals, in the evolutionary scale from Cyclostomata to Reptiles, true pacemaker cells are located along the full border between the sinus venosus and atrium. Two SA valves originated at this site and formed a roller called 'the sinoatrial ring'. These modifications changed the working regime of the vertebrate's electromechanical pump from a peristaltic one to an impulse one. When the isolated SA ring of the dace's heart was divided into two, the frequency of AP generation in the left and right segments was 69±11 min^{-1}, (n=11 strips) and 72±9 min^{-1} (n=11, $p>0.05$), respectively. However, the frequency of AP generation was higher (91±12 min^{-1}, $p<0.05$) in the non-divided isolated dace's SA ring. The action potential duration at 90% repolarization (APD_{90}) increased from the ammocoete (0.11±0.02 s, n=39 cells) to the tortoise (1.1±0.15 s, n=72). The rate of change of membrane potential (dV/dt) during phase 3 was highest in the ammocoete (1.2 V s^{-1}) and lowest in the tortoise (0.2 V s^{-1}). Interestingly, the SA pacemaker of different animal species appeared to be heterogeneous in its resistance to Ca^{2+}-free solution. In particular, the ammocoete's heart continued generating APs for longer than 10 hours in Ca^{2+}-free solution, while complete blockade of AP generation was observed in strips of the tortoise heart after 5 min of perfusion with 0.45 mM Ca^{2+} solution. We propose that many of the Ca^{2+}-dependent mechanisms of pacemaker function can be found even in more genetically primitive creatures such as Metazoa.

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Gi2 plays a critical role in the short-term modulation of heart rate dynamics

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Acetylcholine released from the vagus nerve acts on cardiac M2 receptors to cause negative chronotropic responses and this is due, in part to an increase in K^+ conductance mediated by G-protein inwardly rectifying potassium (GIRK)channels (Sakmann et al. 1983. This process is pertussis toxin sensitive implicating Gi/o in GIRK channel activation. Ablation of cardiac GIRK channels at a molecular level leads to impaired parasympathetic responses in vivo (Wickman et al. 1994). Giα2 is considered the most abundant cardiac isoform. We screened mice on an Sv129 background with global genetic deletions of Gαi2 and Gαi 1 and 3 as a double knockout with littermate controls (adjusted for age, weight and sex) and assessed negative chronotropic responses to intraperitoneal carbachol administration (500ng/g) under inhalation isoflurane anaethesia. Maximal relative inhibitory response was attenuated in Gαi2-deficient mice (mean inhibition 0.1152 ± 0.024, n=6) compared to control (0.3261 ± 0.054, n=6) or Gαi1/3 (0.3280 ± 0.080, n=6). Additionally, using heart rate variability analysis (HRV) of ECG data collected from implantable telemetry devices we were able to measure heart rate dynamics in conscious freely moving mice (Gehrmann et al. 2000). Our results suggest differential heart rate responses with respect to particular Giα isoform. Mean heart rate (HR) over 48hrs demonstrated that Gαi2 (-/-) deficient mice had significantly higher nocturnal HR (Gαi2, 617.6 ± 11.89 (n=5) vs control, 568.5 ± 14.64 (n=6) vs Gαi1/3, 579 ± 8.2 (n=6) (1-way