portion is necessary for entrainment to a 24-h light-dark cycle[2].

On the other hand, the light pulse applied from the late subjective day to the early subjective night had very small effects on the phases of the two circadian rhythms. Previously, Wever et al.[8] determined the range of entrainment of body temperature rhythm to artificial bright light cycles; the upper limit for it was 29.0 h. From these figures, a delay shift of about 4 h is expected. The absence of prominent delay shifts in the present study is contradictory to the finding of Czeisler et al.[5], in which a bright light of 4 h duration, applied for one week to an elderly woman before going to bed, produced a 6-h delay shift of temperature and serum cortisol rhythms. One possible explanation for this discrepancy is a difference in the intensity of bright light used. In Czeisler's experiment, the subject was exposed to bright light of 7,000–12,000 lx continuously for 4 h, while in the present study, the intensity was 5000 lx and the subject was allowed to sleep during the light pulse. In fact, subject C slept in bright light, which might reduce the phase-shifting effect of the bright light pulse. This explanation, however, is not possible for subject D, who did not sleep during bright light pulses. Another explanation for the disagreement is a difference in the intrinsic period of the circadian rhythm, which was shorter than 24 h in Czeisler's subject and was longer than 24 h in ours. The phase-delay portion in a PRC is important for the circadian rhythm to entrain to a 24-h light cycle, whose intrinsic period is shorter than 24 h.

Another interesting finding of the present study is a demonstration of internal dissociation between the sleep and temperature rhythms after a bright light pulse. The temperature rhythm phase-advanced always soon after the light pulse, while the sleep rhythm phase-advanced sometimes with transients. Different mechanisms have been suggested to be involved in the circadian sleep and temperature rhythms[9], and are still a matter of debate[10]. A large phase-angle difference between the sleep and temperature rhythms on the first day of internal dissociation may suggest that the oscillatory mechanism for the temperature rhythm reacts to light directly, while that for the sleep rhythm responds to it indirectly. The phase shift of the sleep rhythm can be interpreted as a result of secondary interaction with the temperature rhythm which phase-shifted primarily. However, a possibility remains that both mechanisms react to light, but differently.

Splitting of the sleep rhythm after a light pulse was an unexpected result, and raises a possibility of a two-oscillatory pacemaking system, as has been suggested for activity rhythms in rodents[11].

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Age-related disappearance of Mayer-like heart rate waves

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Summary. Healthy elderly subjects (≥ 65 years) did not show the prominent low frequency (0.07–0.09 Hz) heart rate oscillations (Mayer waves) recorded in young adults immediately following passive upright tilt. This difference may be related to altered autonomic function with physiologic aging.

Key words. Aging; autonomic nervous system; heart rate variability; Mayer waves.

Acute intravascular volume shifts due to postural change or blood loss may induce relatively low frequency (~ 0.02–0.10 Hz) oscillations in systemic arterial blood pressure[1–5]. Periodic fluctuations of this kind, termed Mayer waves[6,7], are coherent with oscillations in heart rate which have been observed in healthy human subjects following passive upright tilt[5]. Although their precise mechanism is unknown, these heart rate variations apparently require functionally intact parasympathetic and sympathetic nervous systems[5,8]. We postulated that autonomic changes associated with physiologic aging[9–12] would alter this oscillatory behavior. Spectral analysis of post-tilt heart rate data demonstrated a loss of the Mayer-like waves in healthy elderly subjects.

The study groups consisted of 6 normal male volunteers (ages 22–26 years) and 8 healthy, older subjects (5 males, 3 females; ages 65–84 years) on no medication. As previously described[13], subjects underwent a 60° upright tilt over 9 s using the Stryker Circu-electric bed. A lead II electrocardiogram was recorded continuously beginning just prior to tilt and for 3 min post-tilt.

All young subjects showed prominent heart rate oscillations beginning shortly after tilt and persisting to the end of the observation period with a spectral peak at about 0.07–0.09 Hz. Oscillations at this frequency were absent or markedly attentuated in all elderly subjects (fig. 1). Principal component analysis[14] of the heart rate spectra showed a clear separation of the two groups related to the absence of the relatively low frequency oscillations in the elderly subjects (fig. 2). Cuff systolic blood pressure levels (Dinamap Automatic Sphygmomanometer) at 1, 2 and 3 min post-tilt were not significantly different from pre-tilt levels in either group[13].

Dynamic changes associated with physiologic aging are incompletely understood. Attenuation of both sympathetic and parasympathetic function has been described in older individuals[9,11,12]. Heart rate variability under resting condi-

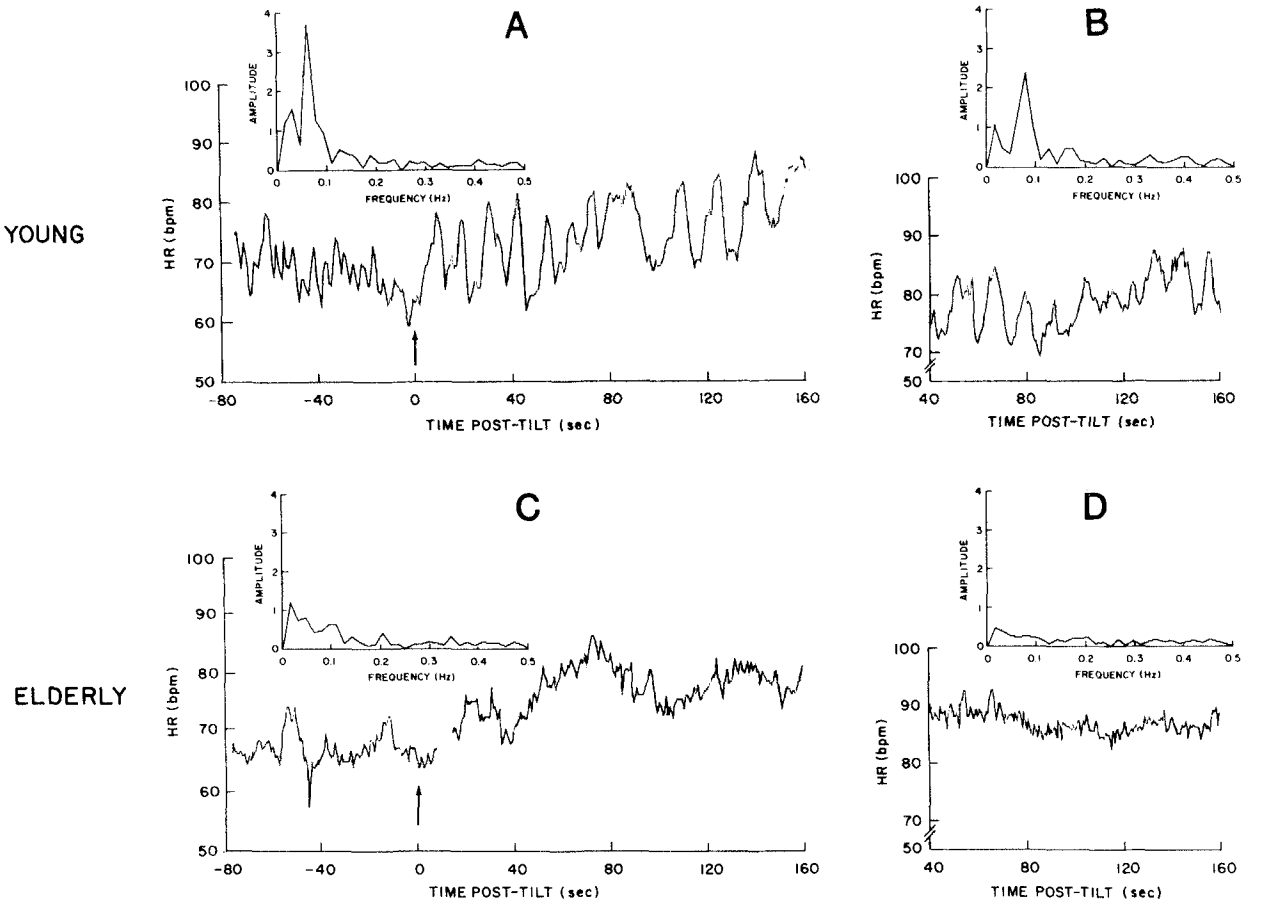

Figure 1. Representative heart rate time series and frequency spectra for young adults and elderly subjects. *A* 22-year-old male; *B* 33-year-old male; *C* 84-year-old male; *D* 79-year-old male. Vertical arrows indicate time of tilt. Note prominent, relatively low frequency (0.07–0.09 Hz) oscillations in heart rate following passive upright tilt in young subjects that are absent or markedly attenuated in the elderly. A possible very low (~ .015 Hz) frequency oscillation in subject C beginning about 40 s post-tilt was not a consistent finding. Heart rate was computed from manually digitized R-R intervals from the electrocardiogram. Non-sinus R-R intervals (< 2% of total) associated with extrasystoles were replaced by linearly interpolated values from neighboring beats. Heart rate spectra were computed using the fast Fourier transform algorithm for a time window 40–104 s post-tilt after removal of linear trends. Ordinate gives relative spectral amplitude in arbitrary units.

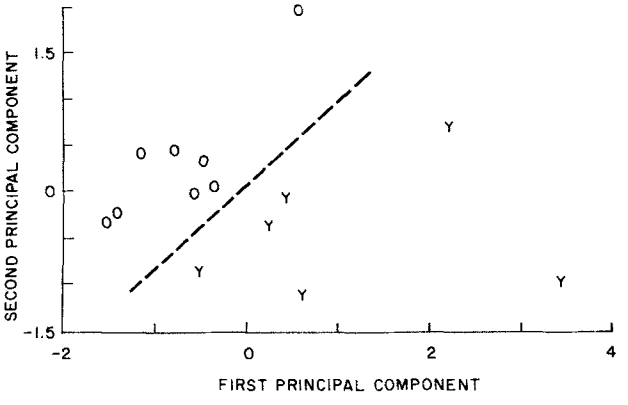

Figure 2. Principal component analysis of heart rate spectra post-tilt shows clear separation of young (Y) and old (O) subjects with reference to a linear discriminant (broken line). The first principal component, predominant in younger subjects, reflects the relatively low (0.07–0.09 Hz) spectral peak. Second principal component, predominant in older subjects, reflects the very low frequency (< 0.05 Hz) band.

tions declines with age in normal subjects, independent of changes in mean heart rate[10]. Decreased heart rate variability has also been reported in a number of pathologic conditions associated with dysautonomia, including diabetes mellitus and multiple sclerosis[15]. Relatively high frequency (~ 0.2 Hz) fluctuations in heart rate, mediated primarily by changes in vagal tone during breathing (respiratory sinus arrhythmia), also diminish with advancing age[16]. Sinus node responsiveness may also decline in older individuals[17].

The present study demonstrates clearly the loss or marked attenuation of a physiologic control mechanism associated with relatively low frequency fluctuations in heart rate. These oscillations, in contrast to those associated with respiratory sinus arrhythmia, appear to depend on sympathetic as well as parasympathetic function[5,8]. Whether these prominent Mayer-like fluctuations represent an amplification of the physiologic, low amplitude (~ 0.1 Hz) heart rate oscillations associated with baroreflex control in normal, supine subjects[8,18,19] has not been established. Large amplitude oscillations in heart rate comparable to those post-tilt have also been reported in young adults immediately after standing[8] and in the supine position after cessation of brief bicycle exercise[20]. Our data differ from Pagani and co-workers[5] who failed to observe any age-related decrease in the post-tilt heart rate oscillations. However, the oldest of their subjects was only 60 years old. It remains to be determined if Mayer-like oscillations decline gradually in amplitude with age, analogous to respiratory sinus arrhythmia[16], decrease gradually in frequency, or if more abrupt changes occur. In any case,

our findings are consistent with the concept of a 'dysautonomia of aging'. Postural stress testing with spectral analysis of heart rate fluctuations affords a simple, quantitative means of studying cardiovascular dynamics and may provide a useful way of assessing physiologic vs chronologic age.

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Arylsulfatase B synthesis and clearance in inbred mouse strains

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Summary. Arylsulfatase B activity levels were approximately 2–3-fold higher in adult C57BL/6J liver and kidney compared to corresponding tissues from A/J inbred mice. In vivo incorporation of tritiated leucine into C57BL/6J hepatic arylsulfatase B reached a maximum approximately 15 h after injection. The label was cleared from C57BL/6J arylsulfatase B with an apparent half-life of 36 h. The relative rates of synthesis of C57BL/6J and A/J arylsulfatase B were similar; however, the A/J enzyme was cleared more rapidly from liver tissue. C57BL/6J kidney arylsulfatase B appeared to be synthesized at a 2-3-fold higher rate than the corresponding A/J enzyme. These trends suggest genetic regulation of arylsulfatase B is effected through different means in liver and kidney from adult mice of these two inbred strains.
Key words. Arylsulfatase B; lysosomal enzymes; mouse; sulfatase.

Arylsulfatase B (arylsulfate sulfohydrolase EC 3.1.6.1) is a lysosomal hydrolase which catalyzes the hydrolysis of the sulfur to oxygen bond of a variety of synthetic substrates including p-nitrocatechol sulfate (pNCS) and 4-methylumbelliferyl sulfate (4MUS)[1]. The enzyme also hydrolyzes N-acetylgalactosamine 4-sulfate residues from glycosaminoglycans including chondroitin 4-sulfate and dermatan sulfate, and deficiency of arylsulfatase B has been described in patients with Maroteaux-Lamy syndrome and combined sulfatase deficiency disease[2,3].

Relatively little is known regarding regulation of arylsulfatase B expression in human tissues; however, several genes have been described which influence arylsulfatase B activity in murine tissues[4–7]. The structural gene for murine arylsulfatase B *(As-ls)* has been mapped to chromosome 13 near *pe*[8]. A cis-acting regulatory element *(As-lr)* and a trans-acting temporal element *(As-lt)* also map to this region[5,6]. Processing of murine arylsulfatase B, as well as several other acid hydrolases, is affected by *Neu-ls*, the putative structural gene for a liver-specific neuraminidase[7]. Finally, several coat color mutations impair secretion of arylsulfatase B and other lysosomal hydrolases by the kidney proximal tubule[9].

This report describes studies of the in vivo synthesis and clearance of arylsulfatase B from liver and kidney tissues of C57BL/6J (high arylsulfatase B activity) and A/J (low arylsulfatase B activity) inbred mice.

Methods. 5-week-old female C57BL/6J and A/J mice were obtained from the Jackson Laboratory, Bar Harbor, Maine, and maintained on commercial feed and water ad libitum for 1–4 weeks prior to use. Mice were grouped in blocks of 4–5 according to strain and injected i.p. with 200 µCi of tritiated L-leucine (140 Ci/mmol, New England Nuclear) and sacri-

Table 1. Relative rate of synthesis of C57BL/6J and A/J arylsulfatase B in liver and kidney

Tissue	Haplotype *As-ls*	*As-lr*	*As-lt*	Activity (units/g)	Protein* (dpm × 10^{-7})	RRI** (×10^5)
Kidney						
C57BL/6J	b	b	b	268 ± 17	5.7 ± 0.2	4.0 ± 0.4
A/J	b	a	a	132 ± 7	6.1 ± 0.3	1.7 ± 0.2
Liver						
C57BL/6J	b	b	b	238 ± 14	7.2 ± 0.3	1.4 ± 0.3
A/J	b	a	a	99 ± 9	6.4 ± 0.4	1.7 ± 0.4

* Estimated from incorporation of tritiated leucine into TCA-precipitable protein from the homogenate (per g wet wt). ** Ratio of incorporation into immunoprecipitable enzyme to incorporation into TCA-precipitable protein. Incorporation into enzyme was corrected for enzyme loss during isolation as described in 'Methods'. Entries represent the mean and SE of 3 experiments.

Table 2. Clearance of arylsulfatase B from C57BL/6J and A/J liver

Time	C57BL/6J RRI / A/J RRI	C57BL/6J activity* / A/J activity
90 min	1.03	2.70
24 h	1.24	3.27
48 h	1.42	2.55
5 days	2.68	2.47

* Expressed as units/g.