The relationship between intrinsic heart rate and thyroid status in man

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Increased responsiveness of hyperthyroid patients to adrenergic stimulation has been demonstrated (Prange, French, McCurdy, Van Wyk & Lipton, 1968), but evidence obtained from experimental animals and the effects of some β-adrenoceptor blocking agents is controversial (Wilson, Thielen & Fletcher, 1964). The response of hyperthyroid patients to propranolol is, however, indistinguishable from that of patients with anxiety states (Turner, Granville-Grossman & Smart, 1965).

The intrinsic heart rate (i.h.r.) was measured in twenty-two female and three male hyperthyroid and five female and one male hypothyroid patients, and in sixteen normal subjects. The effect of propranolol (0.15 mg/kg intravenously, Chamberlain & Shinebourne, unpublished observations) on the resting heart rate was recorded on an electrocardiograph at minute intervals until maximum sympathetic blockade occurred. Atropine (0.04 mg/kg intravenously, Chamberlain, Turner & Sneddon, 1967) was slowly administered and the rate recorded every minute for 5 min. The final rate was accepted as the i.h.r. Four female patients whose i.h.r. had been recorded when they were hyperthyroid were studied in an identical manner when they had become euthyroid.

The i.h.r.s showed a significant negative correlation with age ($r = -0.476$ with 95% limits -0.753 to -0.199). When the rates were adjusted for age and submitted to covariate analysis, the mean rate of hyperthyroid patients was significantly higher ($P<0.01$) than normal subjects while that of hypothyroid patients was lower ($P<0.1$). These results confirm those of Jose (1966), Frick, Heikkilä & Kahanpää (1967), and McDevitt, Shanks, Hadden, Montgomery & Weaver (1968). The wide scatter of the i.h.r. of hyperthyroid subjects, however, suggests that this alone is not responsible for their tachycardia, and in keeping with this is the variable fall in i.h.r. ranging from 0–16 beats/min that was found after treatment. As with euthyroid subjects, the fall in heart rate in hyperthyroid patients after propranolol was negatively correlated with the rise after atropine ($r = -0.426$, $P<0.01$). This implies that patients with high resting rates have less vagal and more sympathetic tone.

In the investigation and treatment of hyperthyroid tachycardia it is important to use β-adrenoceptor blocking agents that possess no significant sympathmimetic effects (Hill & Turner, 1968). It may be that such effects account for the differing results previously obtained (Wilson *et al.*, 1964). The increased i.h.r. and exaggerated response to sympathetic stimulation in hyperthyroidism can both be explained by an increase in tissue 3′, 5′-AMP (Robison, Butcher & Sutherland, 1966). It has been shown that this agent produces, in normal subjects, cardiovascular changes identical to those found in hyperthyroidism and after β-adrenoceptor stimulation (Levine, Dixon & Franklin, 1968).

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Discrepancies in results obtained with activity cages and by observation

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The development of psychoactive drugs is heavily dependent on the initial screening tests. Usually these involve assessing the "spontaneous" activity of animals (Kinnard & Watzman, 1966), either by standardized observation or by automatic recording. Photocell activity cages yield counts of the number of times beams of light are broken by animals' movements, but little information is available about the kinds of behaviour actually picked up, or on how far observation and automation tally when directly compared.

Our results demonstrate that, predictably, typical photocell counts do not measure simple or homogeneous behaviour even in undrugged animals; with drugs, complex changes of behaviour may be masked by the relatively crude photocell counts. Refined observation may not only be more informative, but also quicker and cheaper (Krsiak & Janku, 1966), the objectivity and convenience of activity cages notwithstanding.

Rats were observed in cube-shaped activity cages equipped with two beams. The numbers of "walks" across the cage and of "rears" were correlated with photocell counts ($r=0.77$ and 0.80 respectively), but time spent "washing and grooming" was not. Multiple linear regression analysis showed that walks and rears combined accounted for 85% of the variance of the photocell counts, and thus apparently were the two components which mainly determined photocell counts from undrugged rats.

Dexamphetamine (0.25–2.0 mg/kg, subcutaneously, 35 min earlier) increased photocell counts as expected, with a maximum about twice the control count—by 0.5 mg/kg ($P<0.001$). The observed number of walks and rears also increased, but rather less ($P<0.05$ and <0.1, respectively). Washing and grooming, however, dropped sharply—to about one sixth of control levels ($P<0.001$); this could not have been detected by the photocell counts. At each dose photocell counts remained highly correlated with the number of walks, but not with the number of rears where correlations fell to zero at the higher doses. Perhaps such discrepancies