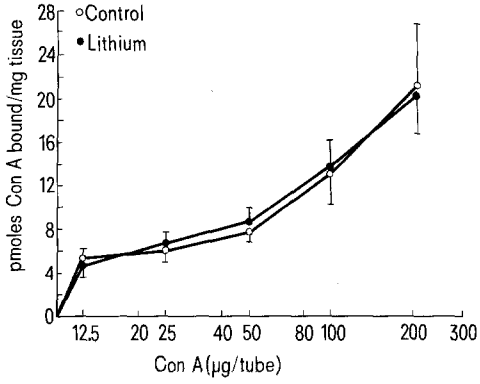
specific lectin binding was reversed by the addition of 50 mM α-methyl-d-mannoside. All assays were run in duplicate. Glass fibre filters were each suspended in 10.0 ml of Aquasol scintillation fluid (New England Nuclear) for determination of incorporated $^3$H.

*Results and discussion.* The displacement of $^3$H-labeled Con A bound to rat striatal membranes by various quantities of unlabeled Con A occurs in a dose-dependent manner from 25 to 200 µg Con A per assay (figure). Saturation of binding sites was not observed at the highest concentration of Con A studied (200 µg/assay). Cuatrecasas et al.[7] have reported similar results for fat cells where levels of 1 mg/ml were required to approach saturation. In addition, the Con A binding profile shown in the figure is similar to that described by Carter et al.[8] for the binding of Con A to rat liver plasma membranes. The figure shows that Con A binding to striatal cell-surface components does not differ for the sodium or lithium treated groups for all animals tested at the end of the 4-week period. We conclude that chronic lithium treatment does not appear to alter mannose-containing cell-surface glycoproteins or glycolipids in this brain region under the conditions studied. However, it is not possible to conclude that there are no effects on membrane components which do not contain mannose, or components which contain mannose but where the carbohydrate residue is not susceptible to Con A binding because of steric hindrance.

Although previous reports[6] indicate that possible alterations in cell-surface glycoproteins may occur in rat choroid plexus during chronic lithium administration, our present results do not indicate any significant alterations in cell-surface components susceptible to Con A binding in rat corpus striatum. Further studies of this nature should be carried out in other brain regions along with additional lectins which have different carbohydrate specificities, i.e., wheat germ agglutinin.




Binding of concanavalin A to cell-surface components in rat corpus striatum. Data reported as mean±SE, n=8 for each group of lithium and sodium (control) treated rats for a 1 month period. ○, control; ●, lithium.

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## β-Adrenoceptor blocking drugs, heart rate and genetic hypertension development in rats[1]

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*Summary.* In spontaneously hypertensive rats (SHRs) chronically treated during their growth with β-adrenoceptor blocking drugs, no correlation was found between the reduction in heart rate and the prevention of genetic hypertension development.

Chronic administration of some β-adrenoceptor blocking drugs, e.g. propranolol, metoprolol and atenolol[3,4] to young spontaneously hypertensive rats (SHRs) has been shown to prevent to a large extent genetic hypertension development (GHD). This effect suggests that the high level of sympathetic activity[5] and the subsequent elevated heart rate (HR) observed in young SHRs might play an important role in GHD. We now report the effects of chronic administration of 7 different β-adrenoceptor blocking agents on GHD and HR in SHRs.

8 groups of 5-week-old male SHRs (Charles River) were used. (ystolic blood pressure (SBP) was determined in the conscious animals by the indirect tail-cuff method (DMP Narcobiosystems Inc.) on their 40th day of life and then at 8, 12, 16 and 20 weeks of age at least 20 h after the last drug administration. HR was obtained from the pressure tracings. Starting from the 40th day of life, the different groups of rats (untreated controls n=36, treated n=12) were given orally by gavage (1 ml/100 g b.wt) every day at the same time for 14 weeks, either distilled water (controls) or atenolol (200 mg/kg), propranolol (100 mg/kg), nadolol (100 mg/kg), penbutolol (100 mg/kg), pindolol (20 mg/kg), acebutolol (100 mg/kg) and the acetyl metabolite of acebutolol (Ac-acebutolol) (100 mg/kg). All doses refer to the base. Treated/control animals ratios (±SEM) for SBP and HR values were then calculated for each drug at each time of measurement and the difference between these ratios and unity was analyzed statistically.

In the control group, SBP values were 129.4±2.6, 161.0±2.7, 183.9±3.8, 198.4±2.9 and 204.4±4.1 mm Hg at the ages of 40 days, 8, 12, 16 and 20 weeks. The corresponding HR values were: 475.2±13.5, 472.1±12.0, 473.4±18.9,

Treated/control SBP and HR ratios during aging in SHRs

| Treatment | | Age (weeks) 8 | 12 | 16 | 20 |
|---|---|---|---|---|---|
| Atenolol | SBP | $0.91^{c} \pm 0.02$ | $0.81^{c} \pm 0.01$ | $0.81^{c} \pm 0.01$ | $0.79^{c} \pm 0.03$ |
| | HR | $0.86^{c} \pm 0.01$ | $0.89^{c} \pm 0.01$ | $0.83^{c} \pm 0.02$ | $0.83^{c} \pm 0.03$ |
| Propranolol | SBP | $0.93^{c} \pm 0.01$ | $0.95^{c} \pm 0.02$ | $0.88^{c} \pm 0.01$ | $0.93^{c} \pm 0.02$ |
| | HR | $0.83^{c} \pm 0.01$ | $0.76^{c} \pm 0.01$ | $0.76^{c} \pm 0.02$ | $0.75^{c} \pm 0.01$ |
| Nadolol | SBP | $0.92^{b} \pm 0.02$ | $0.92^{b} \pm 0.02$ | $0.94^{b} \pm 0.02$ | $0.95^{a} \pm 0.02$ |
| | HR | $0.88^{c} \pm 0.02$ | $0.88^{c} \pm 0.01$ | $0.87^{c} \pm 0.03$ | $0.85^{c} \pm 0.02$ |
| Pindolol | SBP | $0.87^{b} \pm 0.03$ | $0.91^{a} \pm 0.04$ | $0.94^{a} \pm 0.02$ | $0.95 \pm 0.02$ |
| | HR | $0.95 \pm 0.03$ | $0.90^{b} \pm 0.02$ | $0.90^{b} \pm 0.03$ | $0.93^{a} \pm 0.03$ |
| Penbutolol | SBP | $0.94^{a} \pm 0.02$ | $0.96 \pm 0.02$ | $1.02 \pm 0.02$ | $0.96 \pm 0.03$ |
| | HR | $0.88^{c} \pm 0.02$ | $0.81^{c} \pm 0.03$ | $0.90^{b} \pm 0.02$ | $0.94^{a} \pm 0.02$ |
| Acebutolol | SBP | $0.97 \pm 0.03$ | $0.98 \pm 0.02$ | $1.05 \pm 0.05$ | $0.94 \pm 0.05$ |
| | HR | $0.96 \pm 0.02$ | $0.93^{b} \pm 0.02$ | $1.00 \pm 0.02$ | $0.96 \pm 0.02$ |
| Ac-acebutolol | SBP | $1.08^{b} \pm 0.02$ | $1.02 \pm 0.02$ | $1.07^{b} \pm 0.02$ | $1.14^{c} \pm 0.03$ |
| | HR | $0.91^{b} \pm 0.03$ | $0.94^{a} \pm 0.02$ | $0.95 \pm 0.03$ | $0.87^{b} \pm 0.03$ |

Values significantly different from unity. [a] $p < 0.05$, [b] $p < 0.01$, [c] $p < 0.001$.

467.9±11.0 and 468.8±8.5 beats/min. The table illustrates the changes in treated/control ratios for SBP and HR during aging as determined in the treated groups. In the doses used, only propranolol, atenolol, nadolol and pindolol were able to prevent GHD to a large extent while simultaneously inducing an important decrease in HR. Penbutolol reduced HR but did not oppose GHD, while Ac-acebutolol, an active metabolite of acebutolol in man that is formed only in small quantities by the rat[6], reinforced GHD despite reducing HR. Finally, acebutolol which in the dose used produced hardly detectable blood levels, had no effect either on HR or on GHD.

Thus, these results demonstrate that there is no correlation between reduction in HR and GHD prevention. If, with some drugs, e.g. atenolol[7], the induced bradycardia plays a major role in their antihypertensive effect, this factor is not the only one involved, since propranolol, which is more effective in reducing HR than atenolol, is less antihypertensive than the latter, and since Ac-acebutolol and penbutolol do not oppose GHD despite their lowering effect on HR.

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## Isolation of a neurosecretory substance which stimulates RNA synthesis in regenerating planarians[1]

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*Summary.* An approach to the isolation of neurosecretory material from planarians is described. This material stimulated RNA synthesis, in a dose-dependent response, in regenerating *Dugesia tigrina*. The data support the concept that neurosecretion plays a key role in the process of regeneration in planarians.

The presence of neurosecretory cells has been established for a variety of species of planarians where they are believed to play a central role in regeneration[2-4]. Following transection of *Polycelis nigra*, the numbers of paraldehyde fuchsinophilic neurosecretory cells in the brain and the anterior nerve cords, as well as the amount of material within these cells, increases to a maximum within 3 days[5]. The number of cells then decreases precipitously and control levels are restored by the 4th day. Gabriel[6] found that following transection of *Dugesia lugubris* the quantity of RNA in the tissues of the animal increased during the first 3 days of regeneration. Similarly, in an investigation of the regenerative scissiparity cycle of *D. gonocephala*, Lender[7] found a close correlation between the numbers of stainable neurosecretory cells and RNA synthesis: when the numbers of neurosecretory cells rose so did the rate of uridine incorporation.

Classical ablation and replacement experiments in planaria are technically difficult. On the other hand, it is now well established that certain vertebrate neurosecretions are rich in cystine[8] and it is the presence of sulphur groups which forms the basis of their affinity for paraldehyde fuchsin. With this rationale in mind we expected a preferential incorporation of cystine into neurosecretory material of *Dugesia tigrina* during the initial stages of regeneration.

Asexual specimens of *D. tigrina* were transected just an-