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Similar Functions of Uric Acid and Ascorbate in Man?

POINTING out the structural similarity between uric acid and the stimulant purines caffeine and theophylline, Orowan[1] first proposed that the emergence of intelligence in the primate line might arise from a single evolutionary event, the loss of the enzyme uricase, with the result that uric acid became the end product of purine metabolism. The only non-primate mammalian strain whose final purine metabolite is uric acid is the Dalmatian dog.

Haldane[2], taking issue with this suggestion, proposed two hypotheses: that individuals with high serum uric acid levels should show increased intellectual abilities, and that such individuals should be unusually resistant to certain types of fatigue. Neither one of these hypotheses has received much experimental support, although serum uric acid levels have been correlated with social class, achievement, and achievement-orientated behaviour (for a review of such work, see Mueller *et al.*[3]).

I would like to propose that the loss of uricase in the primate line may be connected with another biochemical lesion which is unique to the primates, namely, the loss of the ability to synthesize ascorbic acid *de novo*. As in the case of the loss of uricase, this lesion is found in only one non-primate mammalian species (the guinea-pig[4]).

The reasoning behind this suggestion is this: a number of the physiological functions of ascorbate are generally considered to be related to the unique electron-donor properties of this compound. Uric acid (along with the rest of the purines) is also a strong electron donor[5]. In fact, on the somewhat tenuous basis of molecular orbital indices, uric acid may be a better electron donor than is ascorbate[6]. It therefore seems possible that (in the primates at least) uric acid has taken over some of the functions of ascorbate. This suggestion is not to deny any other physiological or psychological function for uric acid, but is advanced to suggest an evolutionary mechanism for the loss of the ability to metabolize this compound. For example, there might be a selective advantage in the loss of uricase in primate strains which had previously lost the ability to synthesize ascorbate *de novo* (the latter lesion might not be very important in a fruit eating animal except in times of famine or in the event of a change in diet). Any further selective advantage of high systemic levels of uric acid would tend to establish the double lesion in the population.

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Hetero-electrogenesis of the Gustatory Cell Membrane in Rat

THE receptor potential leading to the gustatory neural signal is believed to arise from stimulation by different chemicals of the microvillus membrane of the gustatory cell[1,2]. It is not yet known, however, whether receptor potentials of a cell activated by different kinds of gustatory stimulant are elicited by the same receptive process. To examine this problem, I recorded receptor potentials intracellularly from gustatory cells of fungiform papillae in rats by similar methods to those used by Kimura and Beidler[2]. While a cell was stimulated by salt or bitter substances, changes in the membrane conductance of the cell were measured with test pulses of 100 ms duration. The effects of changes in membrane potential on the receptor potentials were also studied.

Adult female Sprague-Dawley rats, anaesthetized by intravenous injection of sodium amobarbitone into the tail, were fixed on a stereotaxic table with a head holder and the trachea was cannulated. The tongue was pulled out and pinned at the tip onto cork board. Microelectrodes filled with 3 M KCl were used to penetrate the fungiform papilla with the aid of a micromanipulator under a stereomicroscope. An Ag-AgCl electrode was put onto the musculature of the throat as the indifferent lead. Both it and the microelectrode, with an inserted Ag-AgCl wire, were connected to a Wheatstone bridge to permit direct stimulation of the impaled cell. The change in potential was recorded with an ink writing oscillograph. Taste solutions were applied slowly to the tongue at the rate of about 0·2 ml. per 10 s with an injection syringe. After stimulation the tongue was washed with saline solution containing 41·4 mmole/l. NaCl, which is the mean NaCl concentration in the saliva of the rat[3].

After the microelectrode entered a fungiform papilla, a negative deflexion of about 40 mV was sometimes observed and electrotonic potentials could also be recorded. If the d.c. potential in a cell changed with various gustatory stimuli applied to the surface of the tongue near the microelectrode and returned to the original level after washing with the saline solution, then it was assumed that this cell was a taste cell and the depolarization was the receptor potential.

The amplitude of the receptor potential increased as the concentration of NaCl was increased from 0·3 to 2 mole/l. (Fig. 1*A*). The time course of the conductance change was studied by recording the electrical resistance across the cell membrane during the excitation of a cell. This was done by superimposing electrotonic potentials elicited by repetitive small square pulses of constant amplitude at a convenient frequency on the receptor potential (Fig. 1). In this cell the relationship between