persed between the A and B consensus sequences is a second type of consensus sequence which seems to be associated with DNA binding and with metal binding. This sequence, CXXC-$(X)_n$-CXXC (where C is cysteine and X is any residue), occurs twice and, in addition, a vestigial trace of -CXXC- only occurs once. The two complete units occur in different environments relative to the ATP-binding A and B sequences. The ability to bind to DNA is of course an essential part of its function, so the A-sequence results are gratifying. They will no doubt also lead to direct biochemical experiments that should help to clarify the mechanism of action of the excision nuclease. Doolittle *et al.* have already found that bound zinc is present in the Uvr proteins. The role of the different sites can now be probed, for example, by replacing key amino-acid residues using site-directed mutagenesis. □

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Neurobiology

Routes for development

from R.W. Guillery

A RECENT conference* that focused on the long-term changes in the nervous system demonstrated the extent to which some basic ideas may be applied to quite different levels of neuronal organization, from the cellular to the behavioural and from the earliest embryonic changes to the adult. It also showed that what we know about long-term changes is critically dependent on the techniques available, techniques that are currently being advanced, both by recombinant DNA methods and by improvements in imaging and staining methods; surgical procedures; and care in following definable neural relationships for weeks or months.

The broader relevance of the conference, which concerned the environmental influence on cerebral development, was addressed most particularly by a comparison of the development of cognitive and motor skills in normal infants with those seen in apparently normal but prematurely born infants (F. Duffy, Harvard University). Even though the premature group was barely distinguishable from the normal, full-term group when tested initially at comparable post-conception ages, new evidence suggests that over a five-year period the pre-term group score lower in tests of complex behaviour patterns, although standard neurological examinations show no deficits. The extent to which premature, inappropriate sensory stimuli set the developing brain along abnormal developmental routes was briefly and tantalizingly raised.

The possibility that finer details of neuronal organization can be observed in a single experimental subject over extended periods of time was raised for single cells and synapses (D. Purves, Washington University, St Louis) and for complex cortical maps (M.M. Merzenich, University of California, San Francisco). Such observations of single cells in adult rats have now been extended from earlier studies of the superior cervical ganglion, where long-term changes of dendritic arbors were shown, to surprisingly stable neuromuscular junctions, which show no continuous sprouting activity. Synaptic junctions in parasympathetic ganglia have only axosomatic junctions, so that axonal changes can in future be evaluated without confusion by dendritic changes. The vital staining methods being used for these studies are likely to be widely exploited.

In the cortical maps it appears that details can be altered by changes of the peripheral input. Peripheral nerve cuts or digital amputations can produce shifts of the evoked responses elicited from adjacent normal regions. These changes occur over distances of 500–1,200 μm but are thought not to be based on new anatomical connections. Either increased use or cross-innervations of two skin areas can also produce changes when evoked responses are studied by closely spaced microelectrode punctures at widely separated time intervals.

Studies of the neuromuscular junction and the climbing-fibre innervation of Purkinje cells illustrate general principles that may apply at all levels of development. At each site an early multiple innervation is reduced during normal development to a one-to-one relationship. In each situation this reduction is activity-dependent, the activity reduces the synthesis of a 'factor' for stabilizing synaptic relationships and competition between presynaptic fibres for a limited supply of the factor leads to the elimination of all but one of the fibres by a 'selectionist' process (J.P. Changeux, Institute Pasteur, Paris). Other speakers reported the role of chemical factors, of activity or of competitive interactions for the control of transmitter production in single sympathetic cells *in vitro* (E.J. Furshpan, Harvard; I.B. Black, Cornell); for the *in vivo* development of sexually dimorphic neural centres (A.P. Arnold, University of California, Los Angeles); and for the development of the visual pathways (see below).

Sympathetic ganglion cells can be induced to synthesize one or more of four distinct transmitters (noradrenaline, acetylcholine, serotonin and substance P) in varying proportions; either specific chemical factors or membrane depolarization can influence the choice of transmitter production. The critical role of activity in neural development was demonstrated for the production of maps in the retinotectal pathways of fish (J.T. Schmidt, State University of New York at Albany) where both the normal sharpening of the map and the normal reduction of axonal arbor size are abolished by manipulations preventing normally correlated discharge patterns in the axons.

Brain Beyond Genes New York, 2 – 4 June 1986.

100 years ago

There is no question that the voice, whether the note be high or low, whether a chest or head note, whether bass or falsetto, is produced by vibration of the free edges of the vocal cords, which are two movable ligamentous bands about half and inch long stretched from back to front of the larynx. In other words, the only place where all notes, whatever their character may be, can be produced, is in the larynx.

The new and important observation which Dr. Mackenzie has made is, that in the head note of women and in falsetto singing only the anterior third of the vocal cords, as shown in Figs. 3 and 4, vibrate, and the remainder of the cords are in firm contact with one another.

The long-reed or chest voice is generally used by sopranos, Figs. 1 and 2 showing the position of the cords in the case of Mesdames Nilsson, Albani, and Valleria; on the other hand, the high notes of mezzo-sopranos and contraltos are short-reed, *e.g.* Madame Patey, as shown in Fig. 3. Tenors use both reeds, while the long only is used by the basses, and commonly by the barytones. Alto singers among men use the short-reed, whilst boys always use the long. In falsetto the false vocal cords, which are movable bands of tissue superior to the true vocal cords, also approximate considerably.

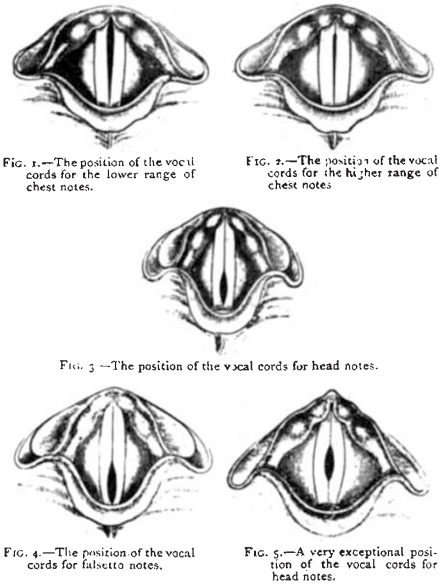

Fig. 1.—The position of the vocal cords for the lower range of chest notes.

Fig. 2.—The position of the vocal cords for the higher range of chest notes.

Fig. 3.—The position of the vocal cords for head notes.

Fig. 4.—The position of the vocal cords for falsetto notes.

Fig. 5.—A very exceptional position of the vocal cords for head notes.

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