connections is the action of the protein called nerve growth factor (NGF). In the early 1950s, Levi-Montalcini, Hamburger, and their colleagues9 extracted from a mouse tumour an agent that stimulates the growth of two types of mammalian neurons (sympathetic and dorsal root ganglion cells). Long considered a curiosity rather than a molecule of fundamental significance, NGF's biological importance has now been firmly established¹⁰. In brief, neonatal animals immunologically deprived of this agent grow to maturity with dramatically stunted sympathetic ganglion cells11 while, on the other hand, neurons in ganglia surgically isolated from their target can be temporarily rescued from death by exogenous NGF12. These trophic effects are associated with NGF binding to specific receptors on the peripheral processes of sensitive neurons, and subsequent internalization and retrograde axonal transport¹⁰. The structure of the molecule is now known, and several groups have begun to unravel its mode of action¹³. Thus, for some neurons, there is con-

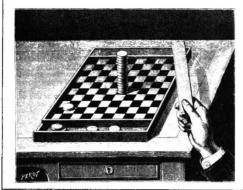


100 years ago

The monster python which is kept alive in the Antwerp museum having had inflammation of the jaw, a Belgian doctor volunteered to enter its cage in order to cure it; but the brute attempted to suffocate the poor doctor, who was glad to escape with his life.

PHYSICS WITHOUT APPARATUS

Inertia may be demonstrated by the following trick: a number of the round wooden "men" used in playing the game of draughts are piled up in a column one upon another. If the lowest one of the pile is dextrously hit with the edge of a paper-knife or other suitable article it may be knocked away from under the others without overthrowing the others. The figure shows how the experiment is arranged, the narrow slip of wood which serves as the lid of the box being here used as the weapon. Beginners in science must not mistake the meaning of the term *inertia* as applied to matter. Matter is



siderable evidence that the object of competition in the struggle for survival is NGF produced at or near the ganglionic target. The weakest link in this argument for the function of NGF has been the inability (for technical reasons) to demonstrate in an unequivocal manner production of the protein by the usual targets of NGFsensitive neurons. This part of the story has now been considerably strengthened by a report that at least one sympathetic target (the iris) does indeed produce NGF under appropriate conditions¹⁴. Since it is clear that NGF's influence is limited to a small proportion of neuronal types, a major effort is underway to discover agents presumed to operate in an analogous manner in other parts of the nervous system¹⁵.

A further aspect of the effects of NGF suggests that a common mechanism may underlie a neuron's struggle for survival and the later competition between axons during synapse formation. Campenot¹⁶ has shown that terminal processes of sympathetic neurons are influenced by local

not in itself lazy or inert. But it possesses the property of *mass*, and to set mass in motion requires the expenditure of *energy*. If we skilfully spend the energy of the rapid blow upon the one draughtsman, it is knocked away before there is time for any considerable part of the energy to be imparted to the others that are piled upon it.

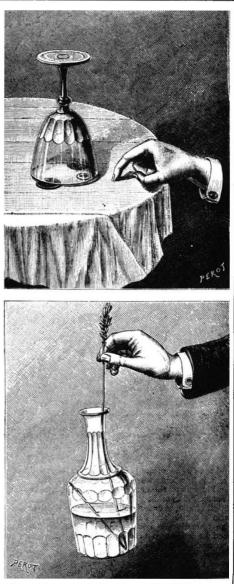
Another simple experiment, depending partly upon the inertia of matter and partly upon elasticity, is often show as an afterdinner trick. Upon a linen tablecloth is placed a threepenny-piece between two pennies or other larger and thicker coins. Over this an empty wine-glass is placed, and the puzzle is how to get out the smaller coin without touching the glass. The very simple operation of scratching with the finger-nail upon the cloth, as shown, suffices to accomplish the trick, for the little coin is seen to advance gently towards the finger until it has moved completely away from under the glass. The fibres of the linen cloth are elastic; when you scratch with your finger-nail they are drawn gently forward until the force of their elasticity becomes too great and they fly back, to be once more drawn forward, again to slip back, and so on. While the fibres are drawn forward slowly, they drag the coin with them to a minute distance. But when the slip occurs and they fly backward, they do so very rapidly, and slip back under the coin before there is time for the energy of their movement to be imparted to the coin to set it in motion. So the coin is gradually carried forward over the surface of the cloth.

We will next give a simple experiment which illustrates the principle that a substance which is very weak in one direction may be very strong in another. It is possible to lift a decanter full of water by means of a single straw. To do this the straw must be bent as shown, so that the weight comes longitudinally upon the straw. The straw is a very weak thing if it has to resist a force applied laterally. Lay a single straw horizontally, so that the two ends are supported, and then hang weights on to the middle of it: a very few ounces will break it across. But let the weights be fixed to one end of the straw, and the straw itself be hung downwards so that the pull is exerted along it, and it will support one or two pounds at least.

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concentrations of NGF in vitro in a way that seems closely related to the proliferation and regression of synaptic connections observed in vivo. In Campenot's experiment a special culture chamber was used that allowed cell bodies and their processes to be exposed to media of different composition. When the neuronal processes were bathed in medium containing NGF they remained healthy; terminal processes regressed, however, when NGF was available to cell bodies, but absent in the vicinity of the processes. An attractive inference, therefore, is that competition of nerve terminals for trophic factors is also involved in the formation and maintenance of synaptic connections.

Neuronal competition is thus emerging as the common denominator of important processes (neuron death, neonatal synapse elimination both in the periphery and centrally, synapse proliferation and regression in maturity) that previously seemed unrelated. As such, it is likely to be one of the dominant themes in neurobiology for some time to come.



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