FROM THE ARCHIVES

A human experiment in nerve division by W. H. R. Rivers MD FRS, Fellow of St John’s College, Cambridge and Henry Head MD FRS, Physician to the London Hospital, Brain 1908: 31; 323–450

Despite having studied in detail the symptoms and signs of recovery from peripheral nerve injury in patients at the London Hospital with Mr James Sherren, Dr Head knows that much of importance is missing from these accounts. Moreover, Dr Rivers—who has advised Sherren and Head on psychophysical aspects of their work throughout—is frustrated by the relative paucity of his own observations. The solution is simple. Dr Rivers will cut and suture all cutaneous branches of Dr Head’s radial nerve at the left elbow sparing any muscular innervations and, together, they will study the patterns of recovery. Surgery takes place on 25 April 1903 in the house of Mr Dean, with Mr Sherren assisting.

Continuing with his practice at the London Hospital but traveling to Cambridge for examination in Dr Rivers’s College room at weekends—in order to avoid ‘the ordinary distractions of a busy life…fatal to the detachment required by the sensory tests we wished to apply’—Dr Head summarizes his responses to the examination of the affected and his normal parts over the next 4 years. Overall, Dr Head is examined over several hours on each of 167 days at intervals between 26 April 1903 and 13 December 1907, during which he is not aware of the precise nature or order of the tests being applied (Fig. 1). Sensation is mapped systematically in a grid of 1 cm squares. A variety of instruments are used: reliance is placed on the use of cotton wool; graduated tactile and pain hairs provided by Professor Maximilian von Frey that stimulate at between 8 and 266 g/mm$^2$; Cattell’s pressure algometer; temperature applied by a flat-bottomed 1.25 cm diameter silver tube; heat and cold spots detected using the 1 mm$^2$ tip of a soldering iron; discrimination of the two points of a carpenter’s compass; and the use of Graham Brown’s aesthesiometer for detecting roughness. The experiment is made difficult by Dr Head’s propensity to formulate and report all forms of stimulus—sensory, olfactory and auditory—as visual images, such that Dr Rivers often has to repeat tests in order to elicit a reliable and stable response, especially for impressions of sensory discrimination. Knowing the nature of the test procedures in principle but masked from the details, Dr Head has to be protected from clues as to the nature of the stimulus being applied—’the clinking of ice against the glass, the removal of the kettle from the hob’. His sensory attention is often blunted by repeated testing so that he cannot give a response until recalibrated by the application of an extreme stimulus. With repeated testing, he is easily distracted such that his responses lose accuracy in the context of extraneous noise or attention to other matters.

There is immediate insensitivity to pain and temperature and loss of sensory discrimination within the radial nerve territory of the left forearm but localization of pressure is preserved. Over the next 125 pages, Dr Rivers and Dr Head show that, with deep sensation preserved, recovery goes through stages of intense protopathic sensibility followed by the re-emergence of normal cutaneous awareness as the epicritic component is restored. Sensation returns differentially on the stimulus applied and unevenly in affected parts of the hand and forearm. There is some awareness of pain from Day 43; of temperature (cold before hot) from Day 112; of hair stimulation from Day 161; and of touch from Day 365. Trophic changes develop on Dr Head’s forearm in the weeks after surgery—redness, scaling, dry and inelastic skin, and lack of sweating and the pilomotor response. These start to improve at variable rates after 107 days and all have disappeared by Day 190. A trophic ulcer induced by the test procedure lasts until Day 185. At Day 567 ‘the greater part of the affected area on the back of the hand [and forearm] had become sensitive to cutaneous tactile stimuli, and temperature below 37°C evoked sensations of warmth’ but sensibility to cotton wool has yet to return on the dorsum of the hand.

Taken as a whole, the experiment is a great success. The result of preserving the nerve supply to muscles and assessing the effect on superficial sensation in denervated skin ‘far exceeded our expectation…we found that deep sensibility is an important

![Figure 1](https://academic.oup.com/brain/article-abstract/132/11/2903/330994)
factor in the sum of afferent impulses which pass into the central nervous system…for the impulses conducted by the afferent fibres of these deep nerves underlie our sensations of tactile and painful pressure, of the locality of deep touch and of the position of the parts in space’. Collectively, these properties are designated as ‘deep sensibility’. The critical component on which they depend is pressure that Dr Head is able to detect immediately on recovering from his anaesthetic. Deformation of the skin, but not pinch, is felt as aching pain if muscular innervation is intact. Awareness of pressure also explains Dr Head’s appreciation of roughness applied by the Graham Brown aesthesiometer. This sense is even enhanced by the lack of sensory distraction from normally competing but now impaired cutaneous sensibilities. Muscular movement itself and the localization of tactile pressure are intact but spatial discrimination and appreciation of size and shape are lost.

Against this background, the efforts of Dr Rivers and Dr Head to dissociate the different components of cutaneous sensibility are not so easily explored. Only in a small zone over the back of the hand and another in the first inter-osseus space can touch, temperature and pain be separated. This allows Dr Head to appreciate that although the threshold for a response is raised, pain is exquisitely unpleasant once detected such that he cries out when tested and involuntarily withdraws his hand. Localization is impaired and the sensation often diffuses to a stereotyped set of referred spots, placed at the boundary of the anaesthetic zone. Rivers and Head designate these features as protopathic pain. Loss of localization and reference to stereotyped spots are only detected during the protopathic phase of recovery outside the range 26–37°C, respectively. These spots are mapped to a grid on Dr Head’s hand—16 hot and 51 cold zones being consistently present of 25 cm² areas on the dorsum of his hand. Within each, there is an increased threshold for stimulation but the experience is diffuse and unpleasant, especially with a large stimulus, irrespective of its temperature compared with a large stimulus, irrespective of its temperature compared with a more extreme but spatially confined thermal probe (Fig. 2). It seems ‘that, of the sum of afferent impulses starting from the periphery, a large number arise from the activity of organs situated other than in the skin…deep innervations [play] a greater part in the sum of sensory experience from the periphery…and much of what is called “touch” is due to the activity of this afferent mechanism, and not to stimulation of the cutaneous “pressure spots” only’. During this protopathic period, the return of cutaneous sensibility is anticipated by the re-awakened awareness of mechanical hair displacement. This stimulation elicits generalized and diffuse tingling—together, a complex sensation that cannot be reproduced by any stimulus to hairless zones within the affected areas.

By way of control, the authors turn to the work of Professor von Frey and Dr Rivers studies the characteristics of sensation on Dr Head’s glans penis. Unlike the skin of the penis itself or the foreskin, the glans is normally insensitive to cotton wool and tactile von Frey hairs but faithfully registers all the features of protopathic and deep sensation experienced in his denervated left forearm and hand when subjected to pressure—intense diffuse, boring or stinging sensations referred to the urethra and with pain spots showing variable thresholds for sensory perception. Dipping the glans penis with the foreskin withdrawn in hot or cold water produces no awareness for Dr Head of wetness but provokes protopathic pain at temperatures <26°C or >38°C. Above 45°C, heat is paradoxically felt as cold, as it is in the protopathic skin on his left hand.

The awareness of light touch with cotton wool, independent of hair stimulation or pressure, does not start to return for almost 2 years. As this epicritic sensation is restored, the characteristic features of protopathic sensibility begin to fade. Precision improves in localizing a stimulus which is now felt as sharp but not painful and pointed rather than diffuse. Awareness of temperatures within the 26–37°C range returns. Radiation and referred sensation diminish, and the number of heat and cold spots reduce. But these improvements are fragile and not only does cooling the limb artificially restore protopathic pain but Dr Head also notices that he is worse each winter and better during the summer on his visits to Cambridge where sessions are interspersed with a walk or ride and time spent on the river Cam. Adaptation to heat and cold is explored in more detail. The shift in neutral point of thermal sensibility seen normally with an alteration in ambient temperature within the range 26–37°C is lost in the context of protopathic pain, when lack of adaptation renders the part more sensitive to a cold stimulus. Now, spatial discrimination improves and the ability to detect compass points is restored (although still with errors after 4 years), indicating that protopathic sensibility distorts these properties through the intrusion of diffused sensitivity and referral to remote sites. Reflecting on localization and spatial discrimination, Dr Head and Dr Rivers emphasize: that deep sensibility enables localization of a part exposed to pressure but not two point cutaneous discrimination or the appreciation of size and shape; that the patterns of reference to other sites during the period of protopathic sensibility are constant (Fig. 3); and that precision and two point discrimination improve only with the return of epicritic sensation. It follows that ‘sense of position in space depends on deep sensibility alone; spacial [sic] discrimination on the activity of the epicritic system only’.

Only one part disobeys the principle of re-emerging epicritic sensation signalling the retreat of protopathic discomfort.

**Figure 2** Lateral view of the hand taken on 3 October 1904. The dotted line encloses the area of diminished sensibility. The unbroken line encloses the parts in a condition of protopathic sensibility.
This is a small triangle on the wrist where cutaneous touch and all modalities of deep sensibility are intact but appreciation of pain and temperature outside the 26–37°C range distorted or completely absent (Fig. 4). Within this patch, Dr Head detects cotton wool and is aware of hair displacement by gentle blowing; but his impression is nonetheless that sensation is reduced and, objectively, there is an increased threshold for sensory awareness. Recovery of pain sensation in this triangle begins at Day 76 and thermal sense at Day 173 with heat spots detected from Day 198. But unlike the rest of his denervated forearm, the pain does not diffuse or refer to adjacent areas.

Dr Rivers and Dr Head conclude that the skin is endowed with two anatomically distinct systems—protopathic and epicritic—which regenerate at different rates after nerve injury. Occasional areas are naturally (the glans penis), or by chance (the triangle on Dr Head’s forearm), devoid of one or the other. Protopathic sensation depends on a punctate mechanism that responds to extreme stimulation of end organs for the detection of cold, hot or pain that are scattered and differ in their density; the responses they elicit have a high threshold, and are both unpleasant and diffuse. The second system responds normally to less extreme stimuli and at a lower threshold, and it can adapt. This epicritic sensation has localizing value and estimates separation and size with precision. It recovers more slowly than protopathic sensibility after nerve injury but restores awareness of touch and temperatures in the ambient zone when it does. ‘Epicritic sensation… must be present before the sensory complex resembles that from normal skin…an effective protopathic stimulus of low intensity…covering a large area may produce a sensation of greater apparent intensity than a more restricted stimulus of greater strength’. And on the questions of stimulus intensity and thresholds, ‘… the usual psychological view that an increased sensory reaction corresponds to a lowered threshold…is true in the strict sense only of epicritic and deep sensibility’.

Writing in 1908, 2 years after publication of Sherrington’s Silliman lectures, it is natural that Dr Rivers and Dr Head should seek to ‘integrate’ the anatomically distinct systems of deep, protopathic and epicritic sensation in their closing formulation. The afferent impulses transmitted by these peripheral pathways merge in the spinal cord to convey the summated sensations of temperature and pain to the highest centres after ‘undergoing redistribution from the elementary grouping to something simple and specific’. Integration involves not only sorting but also inhibition. ‘Sensation, the final end of the process, assumes forms simpler than any sensory impulses’. After nerve injury, the return of heat spots for pain at a time of impaired touch makes for an exquisite but temporary imbalance, and hence hyperaesthesia, from which relief is only obtained with the restoration (or preservation, for the small triangle on Dr Head’s forearm, see Fig. 4) of epicritic cutaneous sensibility. Diffuse discomfort returns during recovery if epicritic sensation is temporarily compromised by placing the affected part in an abnormal ambient temperature. Whereas Dr Rivers and Dr Head favour a peripheral mechanism for protopathic pain, von Frey has interpreted ‘protopathic sensibility [as] due to anatomical changes which have taken place within the central nervous system in consequence of the abnormal state of the injured nerve’—a concept of central adaptation in the context of peripheral nerve injury now explored in more detail by Keri Taylor and colleagues (page 3122).

Alastair Compston
Cambridge