PAIN AND SUFFERING

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In 1940, Hardy, Wolff and Goodell devised an apparatus for imposing radiant-heat stimulation upon the skin surface, and proceeded to define the threshold for pain with a precision impossible in earlier methods. Their book[1] summarizes the excellent series of experiments carried out by them in the next 10 years. It is now a standard text, and I propose only to take two major points from it that are specially relevant for further research.

The first point is that the authors claim a physiological uniformity of pain threshold in man, provided that all extraneous variables, such as the temperature of the skin, and the attitude or expectation of the subject (which includes his emotional state) are controlled. Such uniformity, however, is achieved only where normal subjects have been carefully trained and instructed how to distinguish between sensations of heat and the end-point of pain as defined by the experimenter. I have reviewed the evidence on uniformity and variability factors elsewhere,[2] and it is only necessary here to point out the significance of their work in possibly establishing objectively a kind of base-line in relation to which degree and kind of variation, in the individual subject, may be assessed.

These writers were convinced, on account of their own experimental findings and of the neuro-anatomical work they had reviewed, that pain was a specific sensory modality, having specialized terminal receptors and pathways to the central nervous system. Thus they adhered to the orthodox text-book account, and to the possibility that accessory fibres may contribute a sensory quality to the pain experience which enables the subject to distinguish the nature of the stimulus causing pain and to localize it.

The second point, however, is that Hardy *et al.* fully recognized the importance, in the normal pain experience, of conditioning and emotional factors that cause wide individual variation in reaction-type and reaction-level to a physically identical heat-stimulus. They refer briefly to the evidence afforded by prefrontal lobotomy as to alteration in the response to pain while the sensory threshold may remain unchanged.

Parallel to this outstanding physiological work, the very detailed and interesting histological and physiological studies of Weddell and his associates (recently reviewed by Oldfield[3]) has raised in new form the old controversy about pain as a specific modality or pain as an experience resulting from intense stimulation of other cutaneous receptor-fibre pathways. But the new form given to the von Frey-Goldscheider affair emerges in Weddell's conception of pain as a centrally interpreted spatio-temporal pattern of incoming impulses. This opens the way for experimental research on cutaneous sensibility or, rather, cutaneous perception, that need not confine itself to the 'either or' dilemma of specificity or intensity theory.

While the Weddell, and the Hardy, researches have each contributed outstandingly to the scientific data on pain, they have inevitably left virtually unexplored the problems of central representation and, more especially, a problem that should be a major topic for psychological experiment, viz. how an incoming pattern, whatever its peripheral origin may be, is related to previous experience and the emotional response system. In other words, it is widely recognized clinically, and on the basis of common experience, that pain is intimately related to anticipation, anxiety, suffering, and other complex determinants of individual behaviour during illness, before and after operation, or in response to minor traumata such as visits to the dentist, receiving an injection, or experiencing a headache.

It is the purpose of this article, therefore, to review and evaluate the chief kinds of evidence that have emerged in recent years on the nature of these complex determinants and their possible representation in the central nervous system.

THE PARIETAL LOBES

The largely negative evidence as to any specific representation of pain in the cerebral cortex is reflected in Head's account of pain and temperature as 'thalamic' sensations, only the 'epicritic' sensations of touch discrimination, localization, etc., being the concern of the somesthetic cortex. Penfield and Boldrey[4] likewise concluded that electrical stimulation of this region, as of other cortical regions, very rarely elicited an awareness of pain in their patients. Critchley's review[5] of the parietal lobes reaches a similar negative conclusion, and he points out that epileptic seizures rarely produce pain experience. The evidence from stimulation studies is therefore negative, but it may not be conclusive, because this form of stimulation may be biologically irrelevant for the cortex.

Investigation of the effects of lesions in the temporo-parietal areas has given variable results. Schilder and Stengel[6] long ago described a few cases of lesions affecting these areas of the dominant hemisphere where a syndrome of 'asymbolia' for pain was prominent. Their findings have been confirmed in later series, the syndrome usually consisting not of complete insensitivity to a noxious stimulus but of a generalized inability to respond appro-

priately, by word or action, to threat of danger or damage. The syndrome is therefore a complex one and, as its name implies, consists essentially of an inability to relate an incoming pattern to its experience-category and hence to its normal output-behaviour.

Cases of focal lesion in the parietal area producing clearly defined cutaneous sensory dissociations have, however, been reported, notably in Marshall's bullet-wound series.[7] He reported 3 such cases where pain sensibility (as tested by pin-prick and intramuscular injection of hypertonic sodium chloride) was lost, while other modalities were intact. He also reported a case where thermal sensitivity was lost, while pain remained intact. I have myself examined similar cases of dissociation, where there seemed no doubt of the separate loss of pain or temperature, but the obvious difficulty lies in the interpretation of how such loss, even if temporary, is related to cerebral structure and function. Marshall gets round this difficulty by supposing that sensory awareness of pain is a complex function of two-way circuits between thalamus and cortex. Thus, a lesion in the parietal area may not be such as to disrupt these circuits. It is inferred, therefore, that a pattern of impulses is only consciously appreciated as pain when the double relay of pattern to cortex and back to thalamus is completed. Neither thalamus nor parietal cortex are independently concerned with pain representation.

Individual variation in the function to which the parietal cortex may be put is interestingly suggested by Lewin and Phillips.[8] They carried out a partial removal of the post-central gyrus in 3 patients suffering from very severe intractable pain from the phantom limb of an amputation. They located the apparently affected areas of somesthetic cortex by exploratory electrical stimulation, and removed those areas from the appropriate hemisphere, giving relief from the pain in all 3 cases. In contrast to the great majority of phantom-limb pain cases, these were reported to be reasonably well-adjusted, non-neurotic individuals. To account for the discrepancy between their results and those obtained by Penfield and others, they suggest that a differential conditioning factor, due to the special experience and associations of the pain, must be assumed. Thus, although their findings may have no bearing upon the 'normal' representative function of these areas, they seem to imply some kind of reverberation or generalization of signals when the original pain was associated with intense emotional experience.

The problem of pain representation in the parietal cortex is complicated, not only by the multiple connections of the thalamic nuclei, the mutual dependence of thalamus and cortex, and the apparent variability of projective function caused by traumatic association. It is further complicated, as Walker[9] points out, by evidence from hemispherectomy cases (the operation being carried out exclusive of the basal ganglia) and from other sources, which suggests that there may be some ipsilateral, as well as contralateral representation for pain.

PREFRONTAL LOBOTOMY AND RESTRICTED OPERATIONS

The striking alterations of emotional behaviour consequent upon the standard bilateral lobotomy operation when carried out on psychotic or chronic neurotic patients led Freeman and Watts,[10] and others, to test its value for relief of intractable pain of chiefly organic origin. In most of the series of cases studied, it is reported that sensory awareness of pain is unaltered, but that the 'affective' component of suffering is abolished. Thus, typically, the patient is described as no longer being acutely miserable, apprehensive, afraid of dying, unable to sleep without sedation, but able to regard the pain of his illness with equanimity or indifference. Le Beau[11] considers that such suffering, or 'psychalgesia' as Freeman and Watts called it, may develop in 2 types of case: (1) Where the patient has been emotionally normal and well adjusted, but where the pain from his illness has been so intense, and above all continuous, that it leads to a sustained and heightened awareness of the condition, and (2) where the patient has been emotionally unstable (over-anxious or hypochondriacal) before the illness, so that the pain of his illness is assimilated directly into the conditioned emotional response system, and becomes a focal point of that system. In either sort of case, the effectiveness of the operation would probably be ascribed, as by Bonner, Cobb, Sweet and White,[12] to the surgical isolation of the pain impulses from the possibility of their cortical elaboration in relation to previous conditionings and anticipations about the future.

The drawback of the standard operation, however, was that it reduced much more than the suffering of the patient. It tended to reduce him intellectually and emotionally to a deteriorated condition; so that the next step was to find some form of restricted technique which would relieve the suffering without producing such drastic associated after-effects. Two such restricted techniques, at least, seem to have had some initial success. Thus, Le Beau[13] carried out a bilateral topectomy, in which areas 9, 10 and 46 were excised. He reported good results on 25 cases of intractable pain, a practically complete relief being claimed, on the basis of clinical criteria, in 19 of them. He was much impressed, indeed, by the close parallel between establishment of anxiety and unbearable pain, and their simultaneous disappearance after the operation. The 'suffering' function of the brain, compounded of organic pain impulses and anxiety, he considers may be regulated through a circuit defined by at least 3 relays: dorsomedial nuclei of the thalamus, granular prefrontal cortex, and hypothalamus.

Grantham's restricted bimedial technique,[14] whereby a precisely determined and limited section of white matter is destroyed on each side, appears to have been about equally successful, in that 14 out of his 21 cases were said to be 'near-perfect' results. These patients no longer complained spontaneously of pain, and sometimes even denied that the pain of their illness was present, while they showed no personality deterioration.

These, and other similar results, have demonstrated how the emotional quality and experience-context of a pattern of pain impulses may be radically changed by operative techniques on the frontal lobes and their connections. Associated with such change, there may be a deterioration of those intellectual and emotional characteristics that are the highest forms of socially acquired human behaviour. We shall return to the possible significance of this association later, but it is now only necessary to point out that the clinical accounts of these changes still require a detailed experimental verification and elaboration.

The possibility of a restricted surgical excision relieving suffering without causing any but minor intellectual changes has led Fulton,[15] Maclean[16] and others to examine closely the anatomical and physiological basis for this finding. Fulton seems to consider that the effectiveness of the various techniques employed in the relief of intractable pain depends upon whether or not the limbic system connections have been severed. This system is described as phylogenetically primitive, and, in man, overlaid by the neopallium or discriminative or 'intellectual' cortex. It has anatomical connections with nuclei of the thalamus and hypothalamus, and work referred to by Maclean appears to have demonstrated that conspicuous electrical reactions can be recorded from the pyriform area in response to noxious stimuli such as pinching the ear or foot. The effectiveness of the standard lobotomy operation for relief of suffering was thus ascribed by Fulton to the severing of connections with the limbic system, while its adverse effects upon intellectual function were attributed to the extensive bilateral encroachment upon connections with the neopallium.

Fulton's is an interesting supposition, but it seems unjustifiable, in the present state of knowledge, to assume any discrete functional localization of affective and cognitive behaviour in the cortex, for such functions are closely dependent one upon the other for efficient coordination of behaviour—a dependence arising inevitably from the parallel developments, in ontogeny, in emotional and intellectual training. It may still, therefore, be, as Scarff's unilateral lobotomy procedure for pain relief suggested,[17] that effectiveness is proportional to the extent of disconnection rather than to the specific region in which such disconnection takes place.

CONGENITAL UNIVERSAL INDIFFERENCE TO PAIN

It will be apparent so far from our discussion of central representation for pain that there is much to be said for retaining a distinction between pain and suffering, and between pain sensitivity and the pattern of reactions aroused by a pattern of incoming impulses. The rare cases reported in the medical and psychological literature where, in an otherwise normal person, there is an apparently congenital universal indifference to pain (CUIP) are of great interest because they seem to suggest a central, probably cortical, origin for the defect. Critchley[18] has recently reviewed most of the available case reports, and has tabulated the 'indifference' symptoms for each case. He points out that such cases usually retain 'cognitive', 'discriminatory' perception of stimuli, such as pin-prick, temperature changes, and so on, while being

completely unaware of any 'affective tone' or 'emotional reactions' normally associated with pain. He believes that there is no evidence of (1) peripheral sensory defect, (2) spinal-cord defect or (3) thalamic defect. Although there is no autopsy evidence (and he points out that, even if there were, it might well be negative) he considers that the syndrome suggests a high-level defect having some resemblance to 'asymbolia' and to the effects of frontal lobotomy where sensitivity is retained while pain-quality and reactivity are deficient or altered. Individuals may lie on a continuum with respect to perception of pain and reaction to it, these 'congenital' cases being at one extreme of the hyposensitivity scale, the hypersensitives (e.g. constitutional anxieties) being at the other end.

As this type of case may not be generally familiar, it is worth quoting briefly from a report by Cohen *et al.*[19] The subject of this study was a 19-year-old college girl, with the usual history in such cases of burning, breaking, and other injury without reporting pain. The result of careful psychological, physiological and neurological studies showed the girl to be not in any significant degree emotionally, socially, or intellectually abnormal, nor did she show neurological signs or histological evidence indicating nerve pathology at periphery or cord or above; nor was there any evidence of central 'blocking' such as may be presumed to occur in cases of hysterical anaesthesia. On sensory examination, not only was deep and superficial pain absent, but there was defective warmth and cold sensitivity, except at extremes of temperature. She appeared to have achieved highly adequate alternative methods of identifying 'painful' (i.e. potentially harmful) stimuli.

In the evaluation of this type of case material, the writers may use the terms 'insensitivity' and 'indifference' to pain as if they were synonymous and, in fact, there can be no useful reason for making a distinction between them, for a congenital case of this kind cannot, *ipso facto*, know what pain is either as a defined sensory phenomenon or as a complex experience for which, in the normal person, some form of avoidance behaviour is adaptive. In the prefrontal-lobotomy cases, it is inferred that the patient is not sensorily impaired in that he continues to report a quality of sensation arising from noxious stimulation or from his illness, which he 'knows', from past experience, to have been painful. Critchley's comparison of the CUIP case with the lobotomized patient may or may not be strictly valid. Rather, the special interest of such cases lies simply in the suggestion of a complex, unknown, presumably cortical basis for insensitivity, indifference, or both.

CONDITIONING AND LEARNING FACTORS

I have already referred to the fact that 'uniformity' of sensory threshold for a noxious stimulus is only found under strict laboratory conditions, where normal subjects, clearly instructed and experienced in the type of reporting required, are used in the experiments. In freer experimental situations, a wide range of variation, both in the verbal reports of pain and in the reactions to the stimuli, is commonly found, because each subject tends to have his own personal 'standard' or 'schema' by which to judge a stimulus as painful or not, and because each subject's reactions to such stimuli are governed by conditioned emotional responses that have been developed from early childhood.

The evidence to show the major factors accounting for such variability is still far from complete, but it is possible to make some preliminary conclusions from clinical observation and from experimental work on animals and man.

1. Attitude, expectation or 'set' may determine the individual's perception of and reaction towards a particular form of stimulation. Thus Hall and Stride[20] have shown that the response to 'pain' stimulation is likely to vary with the form of instruction given to the patient. The expectation aroused by the word 'pain', when the patient is, for example, told, 'I want you to report as soon as you feel the stimulus to be painful', may set in readiness a conditioned avoidance response. Thus, anxious patients, where such instruction is given, tend to report as painful, and to withdraw from a stimulus of low physical intensity. Where, however, such patients are merely instructed to report on the nature and quality of each sensation they experience, their verbal and reaction thresholds will be raised.

At the other extreme, however, severely depressed patients may have a very high pain tolerance, and may describe the sensation of a high-intensity stimulus as, for example, 'burning hot, but not painful'. Indifference to pain, perhaps very similar to that of the CUIP cases, is sometimes shown by schizophrenic patients, but the indifference of the hysterical anaesthesia case may usually be distinguished from these other two categories by the fact that the hysteric does respond autonomically to pain, though not at a voluntary motor or verbal level.

These, and other observations on the effects of suggestion, distraction, and so on, demonstrate the importance of central factors in determining normal and abnormal variability of behaviour in response to noxious stimulation.

2. Conditioned emotional reactions may determine persistence and severity of 'spontaneous' pain or 'psychalgesia'.

The phenomenon of accentuation of the pain experience without apparent physical cause is very striking in the phantom-limb cases of intractable pain, as well as in some cases of hypochondriacal pain. Kolb[21] has made a valuable analysis of the former category of case, where he points out that, in a series of 2,284 amputees seen in an American army hospital during World War II, only 8 patients complained of a painful phantom limb (although the 'phantom' occurs in as many as 95% of amputees). All these 8 cases were described as suffering from severe psychopathological disturbances. Kolb's analysis of the cases is interesting in showing that their complaint of pain (and accompanying emotional behaviour) may be intermittent, and may occur in relation to emotionally significant episodes in the patient's life, whereas it may not occur during psychiatric interview until such episodes are discussed. In other words, the 'suffering' may be directly associated, through learning, with the amputated limb, but, at least in some cases, the major discomfort is clearly emotional and not due primarily to sensory impulses from the stump.

It is, of course, important to appreciate that the 'suffering' in such cases, as in cases of hypochondriacal pain, may itself be the product of a vicious circle, or feed-back of impulses from the autonomic reactions and tensions of the skeletal musculature. These may build up a central excitatory state in relation to which minimal external stimulation, or minimal stimulation from some organic focus, may be reported as painful because of its special conditioned context of emotion.

3. Conditioned variation of response: experimental studies of animals.

In Pavlov's laboratories,[22] the classical conditioned withdrawal experiment shows how the dog, standing in the conditioning frame, reacts to the unconditioned stimulus of electric shock on the paw by violent struggling. Equally violent attempts to escape follow the sound of a metronome when used as the 'neutral' signal preceding, but overlapping with, the shock. However, when the dog is fed, sometimes forcibly, upon numerous occasions after the shock, very strong shocks or even burning of the skin cause the animal to salivate, wag its tail, and turn towards the food dish. Thus the 'meaning' of the shock stimulus has been transformed through learning so that it has become a 'neutral' conditioned stimulus arousing reflexes preparatory for ingestion of food.

Perhaps the most striking examples of conditioned variation come from the North American studies of environmental restriction. Thus, Nissen, Chow and Semmes[23] observed the effects of restricting opportunity for tactual, kinesthetic and manipulative experience on the behaviour of a chimpanzee, comparing performance with that of other nursery infant chimpanzees reared under normal conditions. When the restricted animal was tested after 31 months, it appears that, on being pricked with a pin, he showed no behaviour indicative of pain or discomfort—often, in fact, he was reported to 'pant' as chimpanzees do when they are being tickled. The implication of this study was that the animal has to learn, in the free environment, how to discriminate particular signals as potentially harmful rather than pleasurable or neutral.

Confirmation and elaboration of these observations has come from a recent study by Melzack and Scott,[24] in which the behaviour of 2 groups of Scottish terriers in a variety of noxious stimulation situations was compared. The one group had been reared in isolation from the time of weaning till they were 8 months old, being thus restricted from acquiring normal sensory and social experience. The other group was reared normally in private homes and in the laboratory. Comparison of the behaviour of the two groups to electric shock, pin-prick, burning, etc., produced some interesting results. The isolated group, though show-

ing reflex twitches and movements of the body area stimulated, tended to learn appropriate avoidance reactions extremely slowly and, even 2 years after being released to a normal environment, still had difficulty in avoiding noxious stimuli. When the experimenter held a lighted match up to the dog's nose, preventing it running away but leaving it free to turn its head away, 7 out of 10 'isolated' dogs made no attempt to escape even during stimulation, and it was not even necessary to hold them. The authors describe the dogs' behaviour as follows: '. . . they moved their noses into the flame as soon as it was presented, after which the head or whole body jerked away, as though reflexively; but then they came right back to their original position and hovered excitedly near the flame . . . . In contrast, the normal dogs moved their heads so rapidly that it was often impossible to hit their noses with the flame' (p. 158).

These experiments reveal very clearly the importance of early environment in determining the animal's behaviour to noxious stimulation, and it is suggested that, if the animal is deprived of the opportunity of acquiring the appropriate conditioned avoidance responses at the critical phase in its development, it may have considerable difficulty in forming the necessary adaptive habits thereafter, however free the sensory and social environment.

Such experimental results on animals fit in well with Livingston's clinical observations of young children.[25] He says: 'The pain that a child experiences is often conditioned by the fears, attitudes and afflictions of his parents. Indeed, parental influences may be decisive factors in determining the amount of pain their children will suffer from minor injuries throughout the rest of their lives' (p. 64). Thus, not only will restricted opportunity lead to a potentially dangerous indifference or inappropriateness of behaviour, but the reverse process of heightening the degree of anticipation, apprehensiveness, and therefore suffering, may equally well be primarily the product of early social training.

The implication of all the studies reviewed in this section is that pain, as an elementary sensation, is a physiological artefact—a useful one, indeed, but one that has little relevance for our understanding of the complex pain experience, its emotional context of suffering, and the behaviour indicative of suffering in high or low degree. The personal, social factor affecting experience of pain is understandable in this frame of reference. Relief of suffering, in child or adult, is not uncommonly experienced by the patient who is in sympathetic contact with the physician or nurse, and may certainly be experienced even from the fact of the physician being able to diagnose and 'name' the patient's disorder, thus reducing the anxiety derived from the uncertain origin of the pain.

DISCUSSION

The link between pain and suffering has become more clearly defined as a result of recent neurosurgery, clinical observation of special types of case, and experimental study of animals and Man. The sensory input to the brain may not necessarily be initiated by stimulation of specialized receptors, but the controversy over the nature of the peripheral events, and the new form given to it by the work of Weddell and his associates, may not be directly significant for our understanding of the central factors.

Whatever the origin of the impulses eventually experienced as pain, it is generally agreed that the input pattern will be modified and elaborated at different levels of the central nervous system. The pain experience is thus a product, not only of the pattern derived from some cutaneous or internal focus, but of incoming impulses from other sensory modalities and other regions of the body. It is complicated, even at the lower levels of integration, by the fact that a part of the spinothalamic bundles does not decussate spinally, most of the ipsilateral fibres being apparently of viscerogenic origin (see Bremer's very able review[26]). Bremer goes on to cite the recent evidence of comparative anatomy on the important function of the reticular formation of the brain stem in the upward transmission of pain impulses, showing that the existence of a direct spinothalamic tract is a relatively recent acquisition in the course of mammalian evolution, perhaps first appearing in the primates. Such lower-level complexity prepares one for the consequent difficulty of tracing the cortical destiny of the 3rd-order sensory axones, and thus of defining with any precision the 'representation' of pain in the cortex. Indeed, the anatomical, as well as the physiological, neurosurgical and psychological evidence, points to diffuse rather than specific representation, and to individual variation rather than any uniformity in localization.

The very extensive work of White and Sweet[27] dealing chiefly with neurosurgical treatment of intractable pain leads to the same kind of conclusion. Although considerable success is reported for various techniques of relieving such conditions, two major implications of this work stand out from the rest. One is the extreme complexity of the course of the pain pathways at both cord and higher levels, and the other is the individual variation that occurs in response to what is, as near as is technically possible, an identical operation. There are a number of possible factors accounting for this variation, including unintended difference in the surgical interruption of pathways and anatomical difference in the course and decussation of the pathways, but the major factor would seem to arise from highest-level variation in the individual's experience and habitual emotional responses.

The idea of diffuse representation seems to be supported by the evidence of stimulation, excision and lesions of the parietal cortex. Possibly only when a specific area is physiologically abnormal, perhaps through concentrated or persistent conditioning, as in the Lewin and Phillips cases,[8] will excision result in reduction of a pain experienced to a tolerable level. The 'asymbolia' cases are of great interest, but suggest an agnosia, even a categorical defect, rather than a simple reduction in sensory intensity or discrimination. Marshall's bullet-wound series[7] provides the chief evidence that a dissociated loss of pain sensitivity can occur with a lesion apparently restricted to the parietal cortex, but he himself interprets the phenomenon as due to interruption of maintaining circuits between cortex and thalamus rather than to any specific localizable representation of pain in the somesthetic cortex; and, further, the phenomenon of dissociated loss is usually temporary.

We are thus faced, even before proceeding to discuss the role of the prefrontal cortex and limbic system, with a considerable variability of findings that indicates the present impossibility of generalizing about parietal or lower-level function in this respect. Rather do we see the need to suppose a variation and a diffuseness in the functions which these areas may play in the integrated action of the individual brain.

In examining the evidence from prefrontal lobotomy—standard and restricted techniques—we come upon changes in the reported pain experience and behaviour of patients the significance of which is very great. We can see how the whole character of the pain experience is altered when the capacity to elaborate the incoming patterns by relating them to conditioned emotional responses is reduced. Yet we are very far from being able to conclude, on present evidence, that this elaboration is invariably the function of special areas, such as 9, 10 and 46, or that it is inevitably the function of parts of the limbic system to coordinate pain impulses with responses, and the feed-back from such responses, of the autonomic nervous system through the hypothalamus and other subcortical regions. Again there seems the possibility of diffuse, rather than specific, representation, which would correspond with the diffuse nature of the pain experience when it achieves that dominant quality of suffering. So many variations are possible in the exaggeration or inhibition of pain impulses that we should be unwise to attempt to simplify the problem by proposing a localization that may apply to one case but not to another.

The special significance of the CUIP cases is that, although proving nothing, they demonstrate the possibility that a congenital cerebral defect may prevent the patterns from noxious stimuli ever being elaborated in relation to normal conditioned, or even unconditioned, avoidance behaviour. The cerebral origin of this defect, in otherwise normal people, remains a mystery, but the history of such cases does not, contrary to Critchley's view,[18] indicate that we have overemphasized the biological significance of pain. Such cases have to be taught by those who do know its significance to use alternative cues from other sensory modalities in order to avoid irreparable damage or death. We do not argue that the biological significance of vision is overemphasized simply because the congenitally blind can be educated to a high degree of social usefulness.

The effects of restricting environmental opportunity of learning appropriate avoidance behaviour in animals run parallel with the evidence of the CUIP cases where the restriction is, of course,

absolute. The evidence shows very clearly the great importance of normal conditioning and learning in establishing the consistent patterns of individual behaviour in response to noxious or potentially noxious stimuli. The concept of a critical phase in development, during which this kind of learning is chiefly established, is a specially interesting one, and may fit in well with Russell's view of the developmental functions of the prefrontal areas in Man.[28] He considers that these areas are of special significance in the forming and elaborating of normal conditioned emotional responses in the early years of a child's life. If these areas are damaged during this period, as by encephalitis, normal maturity of emotional behaviour may be established with difficulty.

This review may, I hope, bring out some of the fascination of the task of trying to work out the relations between the simple and artificially definite input patterns of pain and the enormously complex modification and elaboration of these patterns at the different levels of central nervous integration. The clinician is fully aware of the complexity of the pain experience and of the degree and quality of variation that he encounters in individual patients, in different age-groups, and possibly in different social or racial groups. But scientific research on this complexity and on the major factors accounting for individual variation has scarcely proceeded beyond a reasonably systematic descriptive phase, chiefly because pain has for so long been treated as exclusively a problem of sensory psychophysiology rather than as a major problem in perceptual learning and motivation. The very factors that distinguish Man's complex social behaviour from that of the lower animals give him pre-eminently the capacity to elaborate and prolong his experience of pain so that it achieves that unenviable higher status of suffering. Whether or not there may eventually turn out to be any 'specific' representation for pain in the cerebral cortex, there is no doubt at present of its diffuse and generalized representation through conditioning, learning and memory. The major research tasks in this field lie in putting to experimental test the many hypotheses about individual variation that can be derived from the work reviewed in this paper.

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