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REVIEW

Sensory Perception in Leprosy-Neurophysiological Correlates[1]

ABSTRACT

The loss of sensation in skin lesions, and in a palm or sole that has been innervated by peripheral nerve trunks, is characteristic of leprosy. Detection of early nerve trunk involvement depends on demonstrating sensory loss. Newer developments in neurological sciences have made fresh interpretations of the observed sensory abnormalities in leprosy-affected persons possible. Some of these observations are described in this review, and their implications discussed.

RÉSUMÉ

Les pertes de sensibilité des lésions cutanées, ainsi que de la plante et la paume qui sont innervées par des troncs de nerfs périphériques, sont caractéristiques de la lèpre. La détections précoce de l'atteinte de troncs nerveux dépend de la démonstration de la perte de sensibilité de la paume et de la plante des pieds. De récents développements en neurologie ont permis de réaliser de nouvelles interprétations d'anomalies sensitives observées chez des personnes atteintes de lèpre. Certaines de ces observations sont décrites dans cet article et leurs conséquences, discutées.

RESUMEN

La pérdida de sensación en las lesiones de la piel y en la palma de la mano o en la planta del pie que han sido inervadas por troncos de nervios periféricos, es característica de la lepra. La detección de la afección temprana de los troncos nerviosos depende de la demostración de la pérdida sensorial en la palma de la mano o en la planta del pie. Los nuevos desarrollos en las ciencias neurológicas han permitido hacer nuevas interpretaciones de las anormalidades sensoriales en las personas con lepra. Algunas de estas observaciones se describen en este artículo y se discuten sus implicaciones.

Our five senses enable us to experience the world around us. They work in harmony, each contributing in varying degrees. Sensations are so well integrated that the contributions of any one becomes apparent only when that sense is not functioning. Absence of any one sensation may not be detrimental because those remaining usually try to compensate for the deficiency. The process of integrating data through senses seems to be rapid, almost subconscious to the observer, and likely to precede examination of details.

The hand is an important sensory organ. The nerve supply to the palm of the hand is relatively constant, though wider variations are described. The skin of the hand, particularly the palmar surface, is richly innervated and supplied with all types of skin sensory receptors. Receptors for touch, though present all-over the body, are concentrated in the palm of the hand. Fingernails can also judge textures and shapes in cases where skin sensations are absent ([3]). Based on information continuously provided by the hand and all its appendages, one can decide whether an object is of interest and safe or is uninteresting and dangerous. It is not until we are without the ability to experience tactile stimuli—hot or cold, pain or pressure, position or proprioception—that we realize the importance of touch in our lives.

Sense of touch is probably not given that much importance by those who have all their sensory functions intact, especially those with unimpaired vision. However, a blind person, who depends upon his hands to explore and appreciate his environment, has a different perception of surroundings compared to his sighted colleagues. He un-

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derstands how much the role of the hand as a sensory organ has been neglected ([1]).

Very few people realize the precision of perception of the fingertips and palm, and underestimate the acuity with which finer details can be appreciated through them. A sensate hand can give an instant picture of the overall shape, size, weight, and general texture of an object. Still finer details can be appreciated by feeling the vibrations produced by running the free ends of the fingernails across the surface or edge of an object ([3]).

These extraordinary sensory capacities of the human hands have a long evolutionary history. The hand, as a complex unit of muscles, tendons, and bones could not function properly, with its versatility, flexibility and power, without the ability to feel. Touch is far more than a means of observation; it is also a source of esthetic and sexual pleasure. Much beauty in objects can be appreciated by anyone through the sense of touch. Touch may reveal that some surfaces are genuinely ugly to the touch even if they appeal to eye, e.g., a beautifully carved nose with a rigid implant.

PHYSIOLOGY OF SENSORY PERCEPTION

Sensory modalities. Von Frey established the doctrine of four energies in the form of pressure, warmth, cold, and pain. The other senses are believed to be perceptual interactions of pressure and pain sensations. There are four primary modes of sensations: touch, pain, cold, and warmth. Pressure sensation may be derived from the activity of both cutaneous and deep sensory mechanisms, and therefore it is more of a concept than a primary sensation. The relation of pin-prick pain to light pressure is obscure. Normal skin does not respond to temperature variations within ± 5°C of the existing skin temperature.

Two-point discrimination (2-PD) is a judgment and depends, to some extent, upon a patient's intelligence. The presence of 2-PD is related directly to precision grip and probably determines fiber density, and thus helps in judging the number of fibers re-innervated during the recovery process.

Receptors. It has been suggested that receptors merge into one another at a morphological level and are constantly being replaced. Their precise morphology is determined by the stress patterns to which the hand is subjected. Immobilization of the hand results in retrogressive changes in the receptors. The stimulus of normal use probably helps to differentiate new sensory receptors ([2]).

Receptors can respond to more than one type of stimulus depending upon its strength. No cutaneous receptor has an absolute specificity; rather, they have a high degree of selective sensitivity, i.e., a lower threshold for a particular type of stimulus. A single stimulus excites different receptors to varying extents due to the overlapping of receptive fields of a number of different nerve fibers. In 1 cm^2 area, 3000 end organs are present. Any stimulus will therefore activate several of these end organs, and several types of receptors may get stimulated.

It is not the particular receptor that is stimulated which, alone, determines what is felt, but also the temporal and spatial patterns of activity in the various receptor types stimulated. Coding depends upon the frequency of the discharge, the interval between pulses, the total duration of the discharge, and the spacing of individual bursts. Further, it depends upon the firing of actual numbers of nerve fibers, the density of those fibers within the receptor field, and their sequential activation. Impulses generated in this manner can be modified-inhibited or facilitated, pre or post-synaptically.

The process of sensory perception is dynamic. There are no modality specific cells in the dorsal horn, but there is a different firing pattern in a single cell in the spinal cord when activated by touch, temperature, skin damage, or hair movement. Convergence-divergence, summation-inhibition, and facilitation occur at one or several levels\places, thus sensation depends upon the firing patterns, and receptors vary according to the demand made on them. This combination forms the basis of sensory re-education.

Three quarters (75%) of small, thinly myelinated alpha and delta fibers respond to innocuous mechanical and thermal stimuli, and the remaining 25% respond only to damaging stimuli. Of nonmyelinated C fibers in dorsal roots, 50% supply mechanoreceptors responding to innocuous stimuli, 20% to mechanical nociceptors, and 30% to thermal nociceptors ([2]). Some of each of these are polymodal and can have a lower threshold for hours, and fire for minutes after a single stimulus. Even though C fibers are activated by painful stimuli, these fibers also respond to other stimuli like pressure and touch.

After complete denervation, receptors disappear completely in 2 to 3 yrs but can be created if re-innervation (growing nerve terminals) reaches the dermal level. In this way, protective sensations may reappear. During the recovery phase, the presence of only protective sensations probably means that there are fewer fibers per unit area and conduction speeds are slower—both of these distorting the spatial and temporal patterns. There is no direct connection between the regained functional ability and the number of nerve fibers regenerated. It is important that the fibers that have recovered are put back to use.

Process of sensory perception. Sensory function involves several steps: sensory perception leading to discrimination, followed by localization, and finally grading according to previous experiences. Age, occupation, intelligence, and callus formation affect the sensitivity of receptors.

For touch perception, two variables are involved: the force variable and the displacement variable. Skin deformation occurring due to mechanical shear stress after applying pressure with a nylon monofilament stimulates receptors, and at a certain threshold level impulses are generated that are transmitted onwards. Quickly adapting end organs give clues or signals to slowly adapting end organs, and vice versa.

Stereognosis is a function of sensory discrimination. When one wishes to ascertain the texture or nature of an object, it is moved intimately between the fingers and thumb setting up spatial and temporal patterns of impulses, thereby coding mechanisms for sensations. It is impossible to tell the nature of an object if it is merely placed on the fingertip and allowed to rest there, without being handled by the fingers and thumb.

The most natural way, therefore, to test sensations is by assessment of function, i.e., recognition of texture, shape etc. Abnormalities of sensations can be more realistically described and assessed in terms of slowness or inaccuracy in recognition. Due allowances need to be made in the presence of motor palsies.

TESTS FOR SENSORY FUNCTIONS

A simple test is usually employed when information is desired for personal use. Here, the procedure and records are simple and intra-observer reliability is good. For communication to other people, detailed testing is required where the procedure is more complex and records are extensive. It is practically impossible to control the multiple variables involved in a given situation for sensitivity testing, therefore inter-observer reliability is reduced.

Any sensitivity testing has a two-fold objective: (a) an assessment of any actual disability, and (b) a patient's ability to function in his present state so that suitable modifications can be made to improve the situation ([4]).

Actual acuity, i.e., the potential to function, must be determined along with the patient's ability to function with that level of acuity. It is therefore likely that two sets of tests are required: academic and functional. Academic tests require a high degree of cooperation, intelligence, and patience on the part of the subject.

Light touch and protective sensations are measurable as specific forces in a spectrum ranging from light touch to deep pressure. While testing vibration perception, it is essential to ask the patient to describe the feeling, otherwise it will merely be pressure testing. Tests using moving point or 2-PD pose problems of force of application and velocity. Semmes-Weinstein monofilament nylons, to some extent, control the force of application, but a consistent tip size is not available. However, comparative results in a serial study with nylon filaments reveal the changing status in patients ([5]). In addition, it should be noted that sensory innervation and sweat distribution are by no means always the same ([6, 7, 8, 9]).

SENSORY PERCEPTION AND PLASTICITY OF BRAIN

Sensory perception is a central nervous system experience. The brain is a complicated neural network, which continuously remodels itself as a result of changes in sensory inputs. Such synaptic reorganizational changes may be activity-dependent, based on alterations in hand activity and tactile experiences. Surgical procedures on the hand are always accompanied by synaptic reorganizational changes in the brain cortex, and the outcome of many hand surgical procedures is largely extent dependent upon brain plasticity ([10]).

The relationship between hand and

brain. The hand and brain functions are intimately linked together, and the hand occupies a very substantial part of the somatosensory cortex of the brain. Receptive fields of different areas of the skin on the hand slightly overlap, and the extent of overlapping may change in different locations, as may the activity of tactile discrimination.

The tactile information generated by active touch forms the basis for further processing and cortical interpretation of a sensory message. The sublime discriminative capacity of the hand is a result of a sophisticated interaction between the central nervous mechanism and a large number of nerve endings, and mechanoreceptors in fingertips responding to various types of sensory stimuli. Nerve transection and repair leads to a very significant functional reorganization in the corresponding cortical areas, as a result of aberrant innervation of peripheral skin areas ([11, 12, 13]).

Synaptic plasticity of brain. Synaptic plasticity can be defined as the ability of synapses to change as circumstances require. Synapses may alter function by increasing or decreasing their sensitivity, or by increasing or decreasing in actual numbers. This is a general phenomenon involving both cortical and subcortical representation. These synaptic changes are activity-dependent, occurring in response to peripheral inputs, and are seen in both sensory and motor cortices ([14, 15]). It can be presumed that any behaviorally important use of the hand requiring delicate sensory feedback and discrimination would have an impact on the details of the corresponding cortical representation, as well as the size of the receptive fields in the fingers. There are reasons to believe that such improvement in skill and capacity may be due to practice-induced cortical representational changes. It has been shown in humans, that the cortical functional reorganizations can also take place as a result of changes in peripheral sensory performance and experience.

Overlapping areas of cortical representation for sensory perception. In sudden transections of nerve, the areas innervated by the cut nerve are taken care of by the expanding cortical representations of adjacent nerves. If there is no regeneration, this increased cortical representation persists. If regeneration occurs, these reorganizational changes in the brain revert back to the original state depending upon the innervation achieved ([17, 16]). Over a long period of observation, these fields change continuously. Nerve transection, therefore, results in both immediate and progressively developing changes in the cortical map of the skin surface ([18, 19]).

NERVE DAMAGE IN LEPROSY

Patients with leprosy can have reduced sensations, either because of end organ invasion by bacilli, or by nerve trunk invasion. The nerve damage becomes clinically manifest when 25% to 30% of the nerve fibers in a nerve trunk become nonfunctional ([20, 21, 23, 22]). All nerve fibers are not destroyed in leprosy; some functional fibers remain even in badly damaged nerves. Regeneration of nerve fibers has been demonstrated histologically proximal to the nerve swellings ([24, 25]). Even if the motor nerve conduction velocity is zero, the sensory nerve conduction velocity is never zero on surface recording. In cases of complete sensory loss, it is around 25% of control values (Unpublished data).

Which sensory modalities are lost. All modalities of sensations may be lost except joint position sense, probably because the nerves subserving joint sensations travel via a tendon and not through the nerve trunks at the wrist. It is usually a coarse appreciation. The nails seem to retain sensitivity ([26, 27, 28]), even in established cases of sensory damage, probably through distal inter-phalangeal joints.

The zone of sensory loss. The most reliable way of getting an accurate idea of the area of sensory loss is to ask the patient to map out the area himself with the other hand, if possible. This holds true for leprosy-affected persons also ([29]). The anesthetic area in the palm contracts with time, especially in cases of ulnar nerve palsies where the median nerve fibers take over the functions of some ulnar innervated area. The finger circumference is reduced due to soft tissue atrophy.

In an area of sensory loss, the outer zone reveals reduced sensitivity and the inner area shows complete sensory loss. In a study of ulnar nerve damage (up to 1 yr), it was revealed that the loss of nylon filament perception was in a wider area compared to that of temperature and pain, in that order ([29]).

Monofilament nylon perception thresholds. Nylon monofilament perception thresholds in the hands and feet of normal persons are approximately 0.217 gm/mm^2 and 2.35 gm/mm^2, respectively. The level of protective sensitivity is double the value of normal threshold values ([30]). It might prove more logical to test the distal or middle pulps first with moving point or 2-PD, followed by graded nylons to detect evidence of early nerve damage.

The recovery process. During recovery, pin-prick is the first sensations to be felt, followed by the vibration of 30 Hz, followed by moving touch, static touch, and finally 256 Hz. Area localization indicates the actual level of return, whereas point localization indicates tactile discrimination, which requires cortical participation and probably the development of new sensory pathways.

The phenomenon of cross innervation during recovery. Even though the neural lesions in leprosy are in continuity, the possibility for cross innervation exists. Cross innervation between the facial and trigeminal nerves has been widely documented in leprosy ([31]), but such events have not been noticed in the hands even in cases of combined ulnar-median palsies which have fully recovered.

Phantom limb phenomena are believed to be due to rapid cortical reorganization, with the expansion of adjacent areas into the area previously activated by inputs from the amputated limbs ([17, 18, 32, 34]). In leprosy, sensory loss probably results in the shrinkage of those affected areas and synaptic reorganization, and there exists a "Physiological amputation." The corresponding cortical blood flow may also be reduced. A state of "confusion" probably prevails and, as a consequence, when the affected limb is actually amputated, there is no rapid reorganization, and no phantom pain. The gradual, slow absorption of the fingertips is probably accompanied by a simultaneous reorganization process, which does not result in phantom limb or phantom pain phenomena. Further, the adjacent digits or parts are also anesthetic, and their representation areas are shrunken. This rules out the possibility of reorganization in nearby areas, or triggering the amputated part zone in the brain by the stimulation of adjacent parts.

SENSORY SUBSTITUTION

There are no substitutes for touch deficiency at present such as those we have for acoustic disability, (i.e., hearing aids). Surgical techniques have attempted to address the loss of sensitivity, as has sensory re-education. All patients must be taught how to prevent damage to the body integument ([2, 33]).

Sensory re-education is the reprogramming of the brain in a re-learning process where items of increasing difficulty are touched and experienced with the eyes open or closed. An alternate sense (vision) is used to improve the deficient sense. Little is known about the synaptic events taking place during sensory re-education. The training may force the mind to cope with the new, more or less permanent, cortical reorganization in the somatosensory area, thereby regaining a capability to understand shapes, forms, and textures.

Sensory training involves the reorganization of central connections so that a new central pattern is laid down. The central nervous system has high degree of plasticity, which probably decreases with age but still exists in older persons too. A growing number of studies reveal that remodeling of cortical representation is, to a great extent, a function of the behavioral state and behavioral training. These changes progress gradually over a relatively slow daily improvement schedule ([12, 14]).

All those cases that have loss of protective sensations can be re-educated for sensory perception using suitable modalities. Sensory re-education exercises should be carried out in a positive environment with full attention of the performer. Following nerve lesions, sensory re-education to facilitate and improve the necessary cortical functional reorganization in the somatosensory cortex combined with drug therapy, may improve the clinical outcome.

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