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Pain and Nociception in the Clinical Context

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Pain and nociception in the clinical context

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Two subjects will be discussed: (i) the changes brought about in the central nervous system by a noxious input; (ii) certain states of consciousness in which human beings do not feel pain.

Examples will be given of a pattern of neural activity being latent in the central nervous system after a period of localized pain. When this region is stimulated, even after a period of years, the previous pain is felt. Also, stimulation of the sensory cortex and thalamus in conscious patients shows permanent changes induced by constant pain.

Studies from the literature are reported of human beings inducing trance states in themselves so as not to feel pain. In all of these states there is a great increase in sympathetic activity and an increase in the theta-activity in the electroencephalogram.

1. Memory traces left in the central nervous system

I shall first tell you about two of my patients and then consider other cases.

Mr A had had his left leg amputated above the knee as it had been shattered in the Korean war. When he came to me, I was investigating the pains associated with amputations. During one day, I had been injecting concentrated saline into neuromata of the stump and had induced paraesthesiae in the stump. These manoeuvres had caused pain in the stump, which went off within an hour. The next day the patient said that something extraordinary had happened during the night. He had been woken by a pain in his phantom leg, but this was not the pain I had been inducing. He told me that a few years before his amputation he had been playing ice-hockey in Canada, had fallen, and one of the players had skated over the outside of his leg, the skate cutting open the skin and damaging the muscles. What he felt during the night were the identical sensations in his leg that he had had five years before. It was not that he remembered having such sensations; the sensations were present once again.

Mrs C came to us to have a cordotomy for the pain of carcinoma of the cervix. After this operation, there is sometimes a form of reference of sensation on being stimulated that I have described elsewhere (Nathan 1956). In this patient stimulation in the more cranial regions of the body that had been rendered analgesic or hypoalgesic by the cordotomy was felt in the right knee. But what the patient felt was not just a sharp pain as might have been expected from a repeated pinprick. She said that six years before she had had a car accident and had had a comminuted fracture of the right patella. This had been very painful and had been followed by excision of the patella, which was also painful. On being stimulated, she felt the identical sensation in the knee that she had had six years previously.

Where are these memory traces laid down in the nervous system? I don't think we know. In neurology, we tend to hope that things are more peripheral and more distal than at higher levels of the central nervous system, because we know more about the physiology of such levels and find it easier to think about them.

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This phenomenon has been described before; and during World War II, two Americans had investigated it. Pilots in the semi-pressurized planes of that time would get pain in the face during high-altitude flying; and it was noted that different pilots had them at different places in their faces. Hutchins and Reynolds (Hutchins & Reynolds 1947; Reynolds & Hutchins 1948) noted that these facial pains were related to teeth that had been treated within previous years. They then investigated these memory traces in the following ways. One of them carried out routine dental treatment, such as fillings and a few extractions. Ten to sixteen days later, the other one stimulated the nasal mucosa by needle prick. This pain was felt locally and it was also felt in the tooth that had been treated a few days earlier. The one who pricked the nasal mucosa did not look into the mouth and did not know which tooth had been treated. Their further investigation showed that the phenomenon still occurred when the dental treatment was carried out under general anaesthesia; and so it was clear that consciousness was not a necessary factor to produce the effect. But when they carried out the dental treatment with a local anaesthetic block, on one side, the phenomenon never occurred on that side but it did occur on the side treated without a local anaesthetic block.

This is, I am sure you will agree, an important phenomenon, wherever the traces are laid down. In these dental cases, it could have been in the 5th nerve nucleus, and/or higher in the neuraxis.

The memory trace is re-activated by a new painful input; had it not been, we would never have known that anything had been laid down for years, perhaps permanently. I think this phenomenon belongs to the group of neural activities called learning; when learning has occurred, there are changes in synapses, dendrites and the spines on dendrites.

How long does a pain have to go on to cause a change in a group of neurons? In my cases it was a few weeks. In a case seen by my colleague Dr John Bates at the National Hospital for Nervous Diseases, a change had been induced after ten days of toothache. In a patient being operated on under local anaesthesia, the thalamus was stimulated. This patient had been having toothache for ten days. Normally on stimulating the thalamus during the operation for Parkinsonism, there is no pain. But when the thalamus was stimulated in this patient, the toothache was reproduced.

There is a moderately large literature on stimulation of the brain giving rise to pain in the presence of a painful lesion somewhere in the body, whereas that stimulation never causes pain when there is no painful lesion. These are all cases being operated upon under local anaesthesia and the stimulation is of the thalamus, the white matter between the thalamus and the cortex, and the cortex. Doubtless there are many more case where this has been seen, for once a thing has been established, one does not write papers to say that one has seen further cases illustrating the phenomenon. This experience has been summarized by Obrador & Dierssen (1966) as follows: 'We have never been able to produce a real sensation of pain by stimulation of the subcortical sensory pathways...in patients that did not suffer a painful disorder, while pain could easily be evoked under the same conditions of stimulation, in patients with a painful syndrome at subthalamic, thalamic and capsular levels.' In these cases, these parts of the brain have been changed by a continuing input of impulses causing pain. If we take the case of the post-central gyrus being stimulated in a patient with a painful lower limb, say an amputation or a long-lasting sciatic lesion, we may find two changes from the normal state. Normally neurons of the post-central gyrus do not cause pain when they are stimulated electrically in conscious subjects; they cause a tingling sensation or a numb feeling. But in these cases,

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stimulating of the neurons of the post-central gyrus causes pain. Moreover, stimulation of the neighbouring regions of the gyrus, for example the region subserving the upper limb, now gives rise to painful sensations in the lower limb when they are stimulated. Thus we learn that a continuing painful input has changed the function of these central neurons normally connected to the painful region of the body; and also that of the neighbouring neurons, which are not normally connected to that part of the body. These cortical neurons have come to have new peripheral fields as well as becoming activated by afferent impulses that usually would not affect them.

I suggest that it is the presence of pain that causes the change in function of the thalamic and cortical neurons. The evidence for this comes from the case of toothache, in which there was no denervation but just pain; and that it occurs in cases of causalgia, where the amount of denervation may be minimal.

We know from the work of Wall and his colleagues (Basbaum & Wall 1976; Millar *et al.* 1976) and from the more recent work by Merzenich *et al.* (1983) that various sorts of denervation cause a changed organization of the receptive neurons at many and perhaps all levels on the afferent pathway, including the cortex.

The kind of reorganization is different in these pain cases and in the denervation examples. For instance, take the experiments on monkeys by Merzenich and his colleagues: they cut the median nerve and then found that the cortical areas of the superficial radial and ulnar had spread to the previous median area of the cortex. But in the pain cases, the region of the painful peripheral part, say the hand, has spread on to the neighbouring cortical area, say that of the lower limb. And so the one case could be the result of deprivation of an input and the other the result of an excessive input.

2. How not to feel pain

Research on pain used to consist of learning how one feels pain, which tissues are sensitive to which kinds of stimulation and which nerve fibres convey the impulses to the posterior horns. Outstanding in this work was Sir Thomas Lewis. In the last 25 years research has been concerned with how one does not feel pain.

The two events that started these investigations were the discovery by Reynolds (1969) of stimulation-produced analgesia and the discovery of the neuropeptides that have actions related to pain.

I shall now discuss ways human beings have of not feeling pain. The main way I shall be reporting on is the induction of a trance state. Most of what I will be saying is taken from Schmerz by Larbig (1982) who works at the Psychological Institute of the University of Tübingen. Larbig's two sources of material are shown in figures 1 and 2.

Figure 1 is a photograph of Greek fire-walkers. As a part of the practice of their religion, these people practise going into a certain psychological state in which they walk on red-hot coals without feeling any pain.

Figure 2 is a photograph of a fakir in Larbig's laboratory being investigated. The history of this fakir was that he had had a great deal of painful illness as a child. At the age of 10, he discovered that when he looked at a hole in the wall and concentrated his entire thinking on that hole, he entered a state in which he felt the pain less. He practised this technique and used steel knitting-needles through his forearms. He first appeared doing such things in public

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at the age of 18, and later gave an act lasting half an hour at night-clubs. He also taught himself to raise and lower his blood pressure and pulse rate. The technique he used to get into this state was to concentrate his thinking on one theme, putting all other thoughts out of his mind. If he was worried about anything, he could not do this. This intense concentration on one theme would go on to a phase of thinking about nothing, an absence of thinking. It was this state that he called his trance state. During it, acoustic and visual stimulation produced far less sensation. The preparation to enter the state lasted 2–3 hours. During the entire time, he manifested no evidence of pain, and, incidentally, no bleeding.

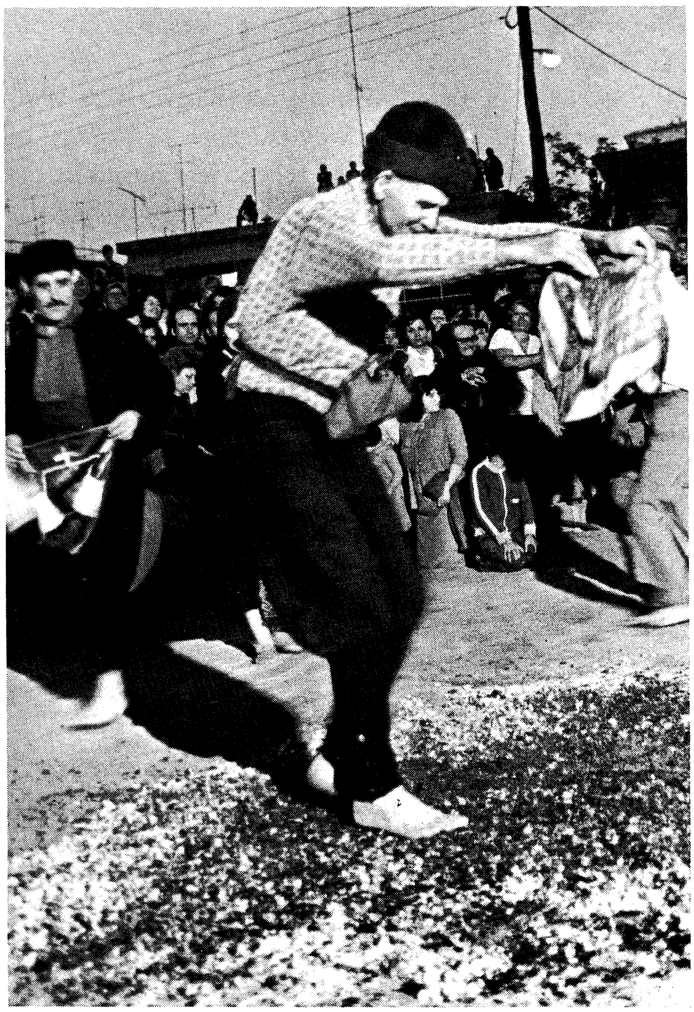

FIGURE 1. A Greek fire-walker. The red-hot coals appear black in the photograph. He is holding a holy relic; a similar Christian relic is more clearly seen in the hands of the fire-walker on the left.

What was particularly interesting in this fakir was that when he was not in a trance state, he had a low pain threshold. For instance, he winced when venepuncture was performed and he was one of those people who considered that the pressure of the blood-pressure cuff on his arm was painful.

If the fakir or the Greek fire-walkers were suddenly painfully stimulated, as a surprise, they

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felt the pain normally. In these cases, then, the pain has to be anticipated, whether it is self-inflicted or inflicted by someone else, in order not to be felt.

The fakir explained that in order not to feel pain he has to induce a trance state. He does this by thinking of nothing, he concentrates on keeping his mind a blank. In this state he is largely unaware of visual and auditory stimuli. During the investigation of the fakir, it was seen that he could easily pass in and out of the trance state into a normal state of being fully awake. In the trance state, his vision was fixed on a distant point; there was no blinking of his eyelids during a period of five minutes or more.

Figure 2. A fakir under investigation in Larbig's laboratory. The sword through the tongue and daggers below the left breast and in the left lower abdomen and through the neck, near the jugular vein and the trachea, are seen.

There were two measurable physiological accompaniments of the trance state: an increase in theta activity in the electroencephalogram and heightened sympathetic activity.

Although the e.e.g. has been a disappointing test in clinical neurology, it is useful from a physiological standpoint; for it is a manifestation of a person's state of consciousness; it correlates with his vigilance and his paying attention to a sensory input.

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Four German volunteers tried to learn fire-walking and two succeeded. In these two and in the fakir, there was a large increase in the power spectrum of theta, 3, 5–7 Hz, in the e.e.g. In these two volunteers, the change in the e.e.g. occurred before they stepped on the hot coal and remained as long as they were on it. The fakir, also, whenever he applied a painful stimulus to himself or was warned that he was going to be given one, induced this large amplitude theta activity during the period of anticipation as well as during the period of likely pain.

Larbig and his colleagues noted that their clinical judgement of the trance state corresponded with the increase in the e.e.g. theta activity.

Increased theta activity is usually associated with drowsiness. But it also occurs in some other states, such as selectively inactivating certain cortical areas and increasing the activity of others. This occurs when one's attention is concentrated on one field, such as intense mental work entailing the solution of mathematical problems within a limited time. Examples are given in Larbig's (1982) book. The most striking example is that reported by Adey *et al.* (1967) of the e.e.g. of the astronaut Frank Borman. For a few minutes before take-off and just before landing there was a great increase in temporal, parietal and occipital theta. This was interpreted as an extreme focusing of attention on the situation.

Larbig concluded from his investigations: 'One can learn to narrow the field of attention, which leads to a trance-like change in consciousness; with this is associated an e.e.g. change consisting of large amplitude theta waves; and with this state there is an inhibition of pain.' Stated like that, it appears to be easy, but Larbig points out that the selective focusing of attention is an active intellectual achievement. This is often done by focusing vision on a distant point; that was how this fakir learned to do it in childhood. Larbig adds that a part of this skill includes learning not to fall asleep.

The other measurable change found was increased sympathetic activity; this may be the cause of the lack of bleeding. During the demonstration of his trance state, there was a rise in blood pressure; the cerebrospinal fluid adrenaline, noradrenaline and dopamine before and after one demonstration are given in table 1. The increase in adrenaline and noradrenaline are clearly shown; the fall in dopamine is doubtless due to all the dopamine's being converted to adrenaline and noradrenaline.

TABLE 1. BIOCHEMICAL DATA ON FAKIR

	adrenaline	noradrenaline	dopamine
	pg ml^{-1}	pg ml^{-1}	pg ml^{-1}
before demonstration	115	140	624
after demonstration	800	304	0

There is increased sympathetic activity in all trance states, deep hypnosis, among the fire-walkers, and in Zen Buddhist monks' trance states, whenever it has been examined. The blood pressure is increased, not decreased as it is in states of relaxation. The German volunteer fire-walkers said that they felt excited and euphoric.

The various ways in which trance states are induced seem to me to have one psychological common feature: one must be able to detach oneself from everyday life. The fakir said that he could not do his performance if he was worried and preoccupied. The fire-walkers cannot walk up to the hot coals and just walk on them. They prepare themselves for weeks, during which they concentrate attention on religious objects and detach themselves from the events

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of everyday life. This is the same with other religious sects in which they mutilate their bodies in various ways. Also Zen Buddhist monks detach themselves from worldly cares by going off to monasteries away from their friends and relations, where they have nothing to think about except the induction of such psychophysiological states.

These methods of not feeling pain are used for acute pain, the pain from being noxiously stimulated. I do not know how well they can be used for chronic pain; neither do I know if they could be used for central pain, pain arising in the central nervous system, such as thalamic pain. It is likely that this way of not feeling pain is using the descending inhibitory pathways, which we have learned about in species other than man, the raphe-spinal and/or the reticulo-spinal pathways and/or the pathways originating in the locus coeruleus going to the 5th nerve nuclei and the spinal cord. It may be that learning to induce this kind of trance state includes learning to activate this kind of inhibitory mechanism.

There are other states in which pain is not felt, for instance hypnosis. There have been physiological investigations of this state; and both increased and decreased blood pressure have been recorded. The sympathetic activation may depend on the depth of the hypnotic state, there being increased sympathetic activity with deeper hypnosis. Perhaps this is not surprising for there is increased sympathetic activity in REM sleep.

Twenty years ago Halliday & Mason (1964) examined the cortical evoked responses to electrical stimulation of the fingers under hypnosis. They were unchanged, even though the subjects did not feel the electrical stimulation nor natural stimuli and heard clicks to a diminished degree. Thus the analgesia and anaesthesia induced by hypnosis is not due to decreasing or stopping the input. In terms of signal detection theory, it is probable that the effect is due to a change in the report criterion, rather than a change at the neurosensory level.

I think that it will be rewarding to investigate such cases as these, and to examine their cortical evoked potentials during trance states. The question to be answered is, in cases such as these and in hypnosis, how far into the central nervous system do the relevant afferent impulses penetrate. And when the answer to that question has been obtained, what form of inhibition, originating where, is causing the absence of the expected sensation?

We know something of the cortical anatomy of tactile and kinaesthetic sensibility; but we do not have similar knowledge regarding chronic or even acute pain. We do not understand how afferent impulses needed for the programming of movement continue to arrive normally into and within the cortex while afferent impulses subserving pain in the same region of the body no longer cause pain.

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FIGURE 1. A Greek fire-walker. The red-hot coals appear black in the photograph. He is holding a holy relic; a similar Christian relic is more clearly seen in the hands of the fire-walker on the left.

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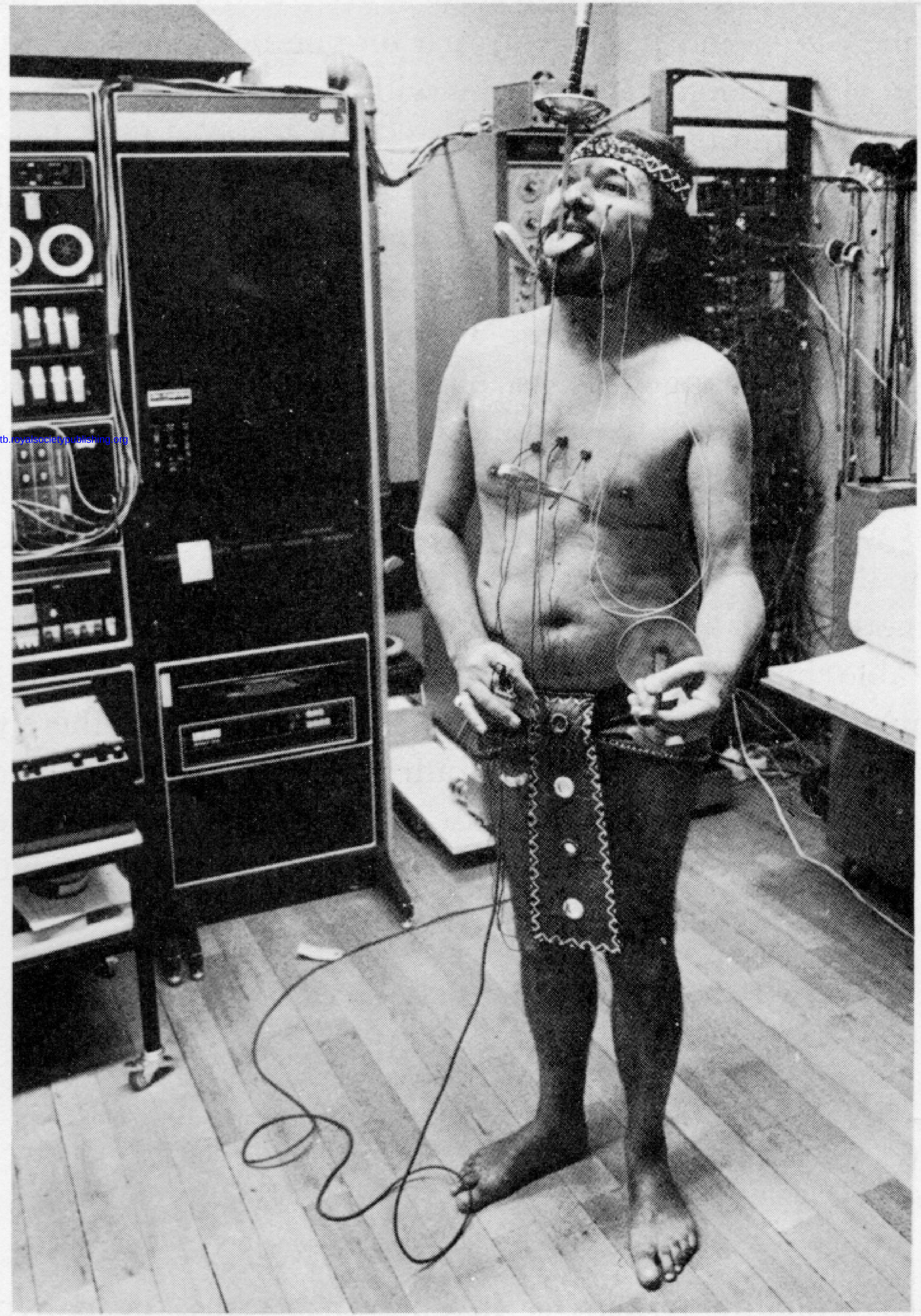

'IGURE 2. A fakir under investigation in Larbig's laboratory. The sword through the tongue and daggers below the left breast and in the left lower abdomen and through the neck, near the jugular vein and the trachea, are seen.