综 述

针刺镇痛机制研究的过去与未来

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大家都知道，针灸是一项古老的医疗技术，它起源于中国，经过历代的发展，形成了我国几千年来保障人民健康的重要手段之一。它的重要性，可以说是和中草药方剂并驾齐驱的。

但是在满清统治时期，针灸遭到了厄运，因为它被认为是伤害皮肉，有损机体，曾被禁止使用。虽然在民间仍然很流行，但在上层社会里，从不认为是正统医学。这种情况，清楚地反映在清代的文学作品里。例如，在红楼梦一书里，有多处关于生病吃药的描写，但在任何地方都没有提到针灸。可见那时在上层贵族阶级，并不认为针灸是正派的、有效的医疗技术。有时甚至把针灸看成为惩罚人的一种手段。这完全是不公正的。例如，在清朝另一名著聊斋志异一书里，曾描写一个妇女，忌妒成性，残暴异常以伤人为乐，后来受到上天的惩罚，把她从一个残暴的色情狂者（Sadist）转变为一个受虐色情狂者（*Masochist*），甘愿接受针灸的痛苦，甚至以针刺穴位为乐。“聊斋”作者认为这是她作恶多端反应得的报应。可见针灸在清代是如何受到歪曲和贬损的。总之，在清朝以及清朝被推翻后总共长达三百多年这一历史时期内，针灸没有得到公正的待遇，针灸学也没有什么新的发展。

1958年，人们发现：针刺某些穴位，不仅能够治愈各种疾病，而且还可以用到外科手术上，以代替药物麻醉，收到镇痛的效果。这就为针灸的推广应用开辟了一个新的领域，也为针刺镇痛原理的研究开创了一个新时代。在这个新时代里，科学工作者企图用现代的科学方法来解释针刺镇痛机制，同时对传统的针灸理论基础——经络学说——进行了重新评价。在这期间发表了大量的科学论文，绝大部分是关于针刺麻醉神经生理学和神经内分泌学方面的研究。

在现在这个信息交流十分迅速的时代，任何一门学科的新发明、新发展、都会立即影响到其它学科。针刺镇痛的研究也不例外。这个研究课题的历史虽然不长，前后总共也不过只有二三十年，但其变化却是迅速而巨大的。从研究的侧重点来看，似乎大体上可以分为两个时期。在前一个时期，即1965到1975这十年间似乎是侧重于神经生理学机制和一般化学因素的研究；第二个时期，即1975以后这段期间，研究重点逐渐转移到针刺与内源性吗啡样物质关系方面；至于第三个时期——即从最近开始的若干年内，很可能会进入一个神经生理与神经化学等多学科相结合的细胞下水平深入研究的时代。

在六十年代到七十年代这段期间，针刺镇痛机理的研究作用是从神经系统电生理学的角度去进行。认为针刺之所以有镇痛作用，主要是由于针刺穴位引起的感觉传入与痛觉刺激引起的传入信号在中枢神经系统内相互作用，使痛觉信号受到抑制的结果。从这种角度进行研究，很自然地会牵涉到痛觉定量测定的问题，痛觉信号在中枢内传递途径的问题，痛觉信号

与针刺引起的感觉信号在脑内整合调制的问题等等，实际上都是神经生理学上的基本问题。因此，我国的神经生理学在这一时期得到了意外的发展。

我们不应当忘记，在被用作镇痛的一种手段以前，针灸本来是一种普遍的医疗技术，主要有用以治疗各种疾病。因此很早就有人认为：针灸之所以有疗效，可能是由于针刺时体内产生了某种化学变化，因而改变了机制的内环境，有利于健康的恢复。因此，我国在很久以前，就有一支比较强大的力量投入到针灸疗效化学基础的研究，特别是对于针灸治疗机理的科学解释方面，作出了巨大贡献。

关于针刺镇痛的化学机制方面，从一开始就有人设想：也许针刺激活了体内某种化学变化，产生了一种镇痛物质，是这种化学物质缓解了疼痛。因此想用交叉灌流的方法来验证这种设想的正确性。尽管当时这类实验可能是比较粗糙，还存在着一种缺点和不足之处，但这种设想本身是合理的值得加以认真考虑的。必须承认：在当时人们只是揣想针刺可能会使体内产生一种镇痛物质，至于这种物质究竟是什么，人们并没有一个清楚的概念。恰好在这个时候，一些与针灸研究毫无关系的药物学家，独立地证明了：体内的确存在着一种内源性吗啡样物质。它是一种化学结构比较简单的多肽，它的镇痛效应比吗啡还要强大多少倍。这立即引起人们的注意。人们自然会问：在针刺过程中，是否在体内也产生了吗啡样物质。实验证明的确是这么一回事。这就为针刺镇痛机制的研究又开辟了一条新的途径。因为受内源性吗啡样物质发现的影响，我国针刺镇痛研究工作者，在神经化学和神经药理学方面，进行了大量工作，发表了大量论文，事实上成了八十年代我国针刺镇痛研究的作用潮流。沿着这条路走下去，不可避免地会要求了解：与内源性吗啡样物质相类似的化学物质还有多少，它们与其它化学物质，例如各种内分泌物和神经性药物的关系是什么，它们又是如何相互影响的等等问题。这样，这会带动一大片科学领域的发展，这是毫无疑问的。但是，这样下去，能否使我们更加深入地了解针刺镇痛的基本机制，现在还很难预测，估计可能会遇到一些困难，除非我们能把化学的药理学的研究深入到细胞水平或甚至细胞下水平，而且同其它学科结合起来进行。这种困难主要来自一般化学或药理学固有的特点。无可否认，痛觉信息在中枢神经系统内的传递是有一定的途径的，并经过一定的神经结构。这些信息必须经过各种过程进行选择，过滤、加强、减弱、分析、整合，最后送到大脑皮层，进入意识领域，它的加工程序像一架精制的电子计算机一样，要经过无数的特定线路和构件，有秩序地在运转着，在任何一个环节上都不能有丝毫混乱。

从以上这种观点来看，惯常使用的那种化学分析方法，似乎仍然显得过于粗糙，往往不能对于痛觉的精细机制作深入细微的分析。例如，在很多研究针刺镇痛神经化学机制的实验室里，往往作所谓微量注射，把某种化学物质注射到中枢神经系统内某一部位，然后观察行为的变化。在这种情况下，即使注射量共有九个微升之微，对于受影响的神经元精细结构来说，仍然是非常之大的。如果再考虑到液体弥散的效果，那就更是大得不得了啦，何况，像脑脒肽等各种神经肽之所以能够产生特殊效应，必须依赖于相应的受体的存在。受体，实际上分布在神经细胞膜上的一种蛋白质，它的分布有高度的部位选择性，并非到处都有。

为了适应这种新形势，神经科学工作者正在发展各种更加精细的新技术来进行细胞水平或细胞下水平的化学和药理学研究。在这方面，澳大利亚堪倍拉学派一直是走在前面的。很多年以前，他们就发明了离子微电泳技术，利用这种技术可以测定几微毫克化学物质对于一个单个神经细胞的作用。最近他们又发明了一种抗体微电极探测技术，使神经化学和药理学

武库中又增添了新的武器，利用这种武器可以探测，例如P物质在生理活动过程中在脊髓背角内释放的精确部位。这在未来的针刺镇痛机理研究中必将发挥重大作用。

除新技术新方法之外，还有一个促进痛觉研究发展的重要因素，就是新的神经肽及其受体的不断发现，以及神经肽与经典递质的共存与相互作用，这些化学物质，或者直接影响痛觉的接受，或者通过对于致痛物质或镇痛物质性能的改变而间接地影响痛觉。现在已经知道：各种神经肽都有其各自的特别受体，而各种受体又各有其不同的生物效应。某种化学物质（例如多巴胺），它的受体与配基相结合后可以激活或抑制细胞内蛋白磷酸化过程，因而打开或关闭某种离子通道，使神经细胞产生兴奋或抑制。对这些机制的深入研究，无疑会使我们对痛觉与镇痛机制的了解，大大地深入一步。

总之，在未来的若干年内，我们很可能进入一个新时代，在这个新时代里我们会更多的新技术、新方法涌现出来，使我们有可能从物理、化学、生理学、解剖学、行为学等多方面对于痛觉机制进行多学科的研究，进一步提高我们对于痛觉机制的认识水平，使我们不再“画地为牢”，把自己束缚在一个狭隘的陈旧的学说之内，到那时我们的思想会得到大大的解放。我们最终一定会找到一种新的控制痛觉最有效的方法。

A COMMENT ON PAST AND FUTURE OF ACUPUNCTURE ANALGESIA RESEARCH

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Acupuncture is known as an age-old healing art originated and developed in China. It has constituted one of the major means to protect the health of the people for many years, and it is regarded as important as as herb medicine in combating diseases in china. However, acupuncture suffered a serious setback during the Ching Dynasty when acupuncture was denounced as being harmful to the human body and was prohibited by the Manchu rulers. Although widely used privately among the general population, acupuncture was not accepted by the high class society as orthodox medical art. This situation was reflected in the classical literatures during this period. For instance, in “红楼梦”, the famous novel written by Cao Sue-Chin, a desolute aristocrat in early Ching dynasty, acupuncture was never even mentioned, although many stories about medical treatment were, meticulously deseribed. Acupuncture was even denouced unjustly as a cruel torturing trick for punishment. In another Ching classic “聊斋志异”, for instance, it was described how a jealous and cruel women who had enjoyed torturing the other girls was eventually punished by God

in turning her from a sadistic into a masochistic person, who would enjoy being acupunctured by others. In a word, acupuncture had not been correctly and justly treated during the past 300 or more years.

It was found in the late 1050s that acupuncture could be used in surgery to relieve pain in place of drug anaesthesia. Thus, a newarea of application was found for acupuncture and also a new era began for the study on the principles of acupuncture analgesia, during which many scientific workers attempted to interpret the mechanisms of acupuncture analgesia in term of modern science and, at the same time, to re-evaluate the meridian theory on which the traditional Chinese medicine and acupuncture is based. Numerous papers have been published since then in regard particularly to the neurophysiological aspect of acupuncture analgesia. With the advances of modern communication, new discoveries and advancements made in any branch of science will readily influence the development of its sister sciences. It is just what has happened with the research of acupuncture analgesia. Although the history of acupuncture research from the modern scientific point of view has lasted only a little more than 20 years there have quite rapid and numerous changes in ways of thinks and in trends of study.

From the relative preponderance in research two period may be divided. In the first period (ca. 1965—75), the large majority of the studies were confined to the neurophysiological and humoral aspects of acupuncture. In the next ten or twenty years, however, the interest of study was shifted gradually to the material relationship between acupuncture and endogenous morphine-like substances. Obviously, the discovery of the endogenous penlo-peptides has exerted a great influence on the frame of mind of the research workers in acupuncture. The third period, i.e., a number of years from now on, may be one in which the acupuncture research will be carried out with emphasis on the multidisciplinary subcellular or molecular approach.

During the period ranging from the early sixties to the seventies of the century, studies on the mechanism of acupuncture analgesia were carried out mainly with the electro-physiological techniques. It was believed that the analgesic effect of acupuncture is essentially the result of interaction in the central nervous system between the afferent impulses from the point of pain and those from the point of acupuncture so that the pain afferents are inhibited or prevented from reaching the realm of consciousness by the afferent impulses caused by acupuncture. Studies of this kind will inevitably involve the quantitative measurement of pain, determination of the pain pathways in the central nervous system, the manner in which the pain related impulses and the impulses produced by acupuncture are integrated, etc. are all practically the basic porblems

in neurophysiology. Therfore, neurophysiology in China got an unexpected chance of development as a result of the intensive interest in acupuncture research during this period.

Since acupuncture has been originally a popular healing art used exclusively for various ailments before it was found applicable to surgery as a substitute for drug anaesthesia, it is natural to think that the process of acbpuncture may involve some chemical changes in the body so as to have modified the internal melieu of the organism which is beneficial to the recovery of health. As a consequence we have a relatively strong force engaged in the study of chemical basis of acupuncture, and especially in interpreting the effect of acupuncture treatment in clinical practice.

In regard to the themrcal approach to the mechanism of acupuncture analgesia, people tend to think from the very beginning that acupuncture may perhaps be able to initiate within the body kinds of chemical processes which result in the formation of some kind of analgesic substance. To test the validity of this proposition cross transfusion experiments have been performed. It was hoped that the blood of the donor which received acupuncture would produce analgesic effect in the recipient animal. Although the original experiments were regarded as rather primitive in many ways, the rationale of the experiments was nevertheless correct and worthy of serious consideration. It was admitted by the pioneer workers that they could only assume the existence of some analgesic agents following acupuncture, but they had no clear idea as to what exactly it is. It was just at about the same (ca. 1975) several groups of pharmacologists, who had nothing to do with acupuncture discovered the existence of endogenous morphine-like substance, namely the leu-enkephalin and met-enkephalin which are structurally rather simple polypelides with powerful analgesic action. The discovery caught immediately the attention of those who were interested in acupuncture analgesia and wondered whether the same or similar substances were indeed produced during acupuncture. It proved to be true, Ther. a new was opered leading to the onderstanding of the puzzle of acupuncture analgesia. A large number of scientific and medical workers have been involved in investigation of acupuncture from this point of view and obtrined interesting results. In fact, the neurochemical and neuropharmacological approach is becoming currently one of the main strategies to the understanding of the mechanism of acupuncture analgesia in China. Proceeding along this road it will inevitably lead to a point where one would want to know how many more other endogenous substances analogous to enkephaling there are in the body followsng acupuncture, what the relations of these endogenons substances are to the hormones and other neurotropic agents, and the mamer in

which these chemical substances interact on each other etc. Further researches like this will undoubtedly create a new area of research and promote the development of science in general.

However, it seems to remain unpredictable whether we can understand further the very basic mechanism of acupuncture by adopting such a strategy. There may be obstacles lying ahead, unless we can bring the chemical and pharmacological studies to the cellular and subcellular level and make some combined effort with other disciplines. Difficulties may come from the limitations of the currently available traditional chemical and pharmacological methods, which appear inadequate for probing the very delicate and highly circumscribed certain predetermined neuronal pathways and relayed through certain nuclear stations in the central nervous system and are subjected to various processes of selection, filtering, facilitation, attenuation and integration and finally sent into the realm of consciousness. The course of message processing is very much like a signal transmission system in a compter, must go through numerous fixed circuits and specific electronic parts. Any slight trouble at any place will bring caos and failure.

From the above point of view, the chemical method of analysis as ordinarily used appears to be too crude to reveal the delicate neuronal mechanisms pain. For instance, we used to use the socalled micro-injection method to administer as little as possible certain substances into the central nervous system in order to observe its effect on changes of pain behavior. Under this circumstance the amout of the injected substance, even if it amounts only a few picrograms, would appear to be still too much for the delicate structures of a neuron, regardless of the fluid diffusion effect of the substance. Furthermore, it must be consieered that the specific biological action of most neurotropic substances, enkephalins for instance, depends on the existence of coaresponding receptors, which are in fact proteins distributee on the cell membrane of the neurons. Since the topographical distribution of certain receptors is known to be very highly specific, it would be very difficult to analyze the subtle action of the concerned substances with the ordinary chemical methods.

For coping with the present situation it is imperative to develope a more refined new technique to carry out the neurochemical and neurowharmacological study at the subcellular level. In this respect, the Canberra School in Australia seems to stand always at the front. Many years ago, they developed the method of micro-iontophoresis which permits administer a controlled amount of chemical substances to a neuron or even a specific part of a neuron. More recently, a novel antibody microprobe was again invented with one can determine rather precisely the localized distribution of cer,ain endogenous neurotro-

pic chemical substance, substance P for instance, in the central nervous system. It is undouctedly a new addition to the armentarium in the field of neuropharmacological research and will play an important role in the study of acupuncture analgesia in the future.

Besides the new techniques and methods, there is another factor which is highly important for promoting the development of pain research, namely the discovery of ever-increasing number of new neuropeptides and their receptors which may affect nociception either directly or through their action on the characteristics of the nociferous or analgesic agents. It is knhwn that different neuropeptides have their own specific receptors which have in turn their own specific biochemical action. A certain chemical substance, dopamine for instance, has its specific receptor or receptors (D1 and D2) which may activate or inhibit the process of protein phosphorilation within the cell so that certain ionic channels may be opended or closed and as a result the excitability of the neuron may be raised or decreased. An intensive study of this kind will enable us to make a big step forward to the understanding of the mechanism of pain.

In conclusion, it is quite possible that in the next one or two decades we will probably enter into a new era when the problem of pain may be tackled from different angles so as to raise our understanding of the mechanism of pain and its control to a high level. We should not confine ourselves within a selfimposed confinement and should liberate ourselves from the shackles of the outdated theory. We will eventually find the best way to relieve the sufferings of the people from the agony of pain.