Summary  Acupuncture research, especially the mechanistic investigations on acupuncture analgesia, has yielded abundant information showing that acupuncture signal, either generated by manual acupuncture or electroacupuncture (EA), remarkably influences the release, synthesis, reuptake, and degradation of the central neurotransmitters/modulators, including monoamines (e.g., serotonin, noradrenalin, and dopamine), acetylcholine (ACh), amino acids, orphanin FQ, substance P, prostaglandin, cholecystokinin-octopeptide-8 (CCK-8), somatostatin, and neurotrophic factors. In general, acupuncture enhances the activity of the endogenous opioid peptides, serotonin, dopamine, ACh, and inhibitory amino acids such as γ-aminobutyric acid (GABA), glycine, taurine, and lactamine, while it attenuates the activity of noradrenalin and excitatory amino acids including glutamate and aspartic acid. A prolonged period of acupuncture may induce excessive production of CCK-8 and deplete some pro-acupuncture substances, thus causing the so-called acupuncture tolerance. Acupuncture also regulates the expression and function of the corresponding receptors. However, the effects of acupuncture on the central neurotransmitters/modulators are dependent on the status of the organism and conditions of acupuncture (e.g., stimulation parameters and acupoints), and vary from region to region in the central nervous system. Although these data were largely obtained from the studies on acupuncture analgesia, it is reasonable to presume that acupuncture is capable of modulating the brain functions through the regulation of central neurotransmitters/modulators, because all the acupuncture-influenced neurotransmitters/modulators participate directly or indirectly in neural regulation in almost all aspects.

Keywords  neurotransmitters, modulators, monoamines, acetylcholine, amino acids
5 Effect of Acupuncture on Neurotransmitters/Modulators

5.1 Introduction

Acupuncture on the body can generate an afferent signal of the nerves, which has the ability to initiate the central signal process involving multiple neurotransmitters/modulators at different levels in the central nervous system (see Chapters 2 and 3). Because of the unique nerve distribution and afferent pathway (see Chapter 2), specific acupoints, when stimulated by acupuncture or other approaches, may activate/inhibit certain neurotransmitters and modulators in various pathways. Indeed, past investigations have shown that acupuncture could greatly influence the activities of many neurotransmitters and modulators, including endogenous opioid peptides, monoamines, acetylcholine (ACh), and amino acids. This chapter will summarize the progress in this field, except for the endogenous opioid peptides, which has been presented in Chapter 4. Owing to numerous earlier studies, we will make succinct description of the cited studies and present plumpish information in this short chapter.

5.2 5-hydroxytryptamine

Serotonin (5-hydroxytryptamine, 5-HT) is a monoamine neurotransmitter synthesized in the serotonergic neurons that are mainly located in the median regions of the brain. Its synthesis and metabolism are schematically shown in Fig. 5.1. Under normal conditions, the level of serotonin is dependent on the intake of tryptophan (TRP) and the degradation by monoamine oxidase (MAO). In the central nervous system, serotonin is believed to play an important role in the regulation of body temperature, mood, sleep, vomiting, sexuality, and appetite.

![Figure 5.1 Schematic representation of 5-HT synthesis and degradation pathway.](image)

TRP, Tryptophan; TPH, tryptophan hydroxylase; 5-HTP, 5-hydroxytryptophan; AADC, aromatic-L-amino-acid decarboxylase; 5-HT, 5-hydroxytryptamine; MAO, monoamine oxidase; 5-HIAA, 5-hydroxyindole-3-acetic acid.

Acupuncture has been shown to induce a therapeutic effect by increasing the activity of 5-HT system in the central nervous system. Early studies (Han et al. 1980) showed that acupuncture analgesia could be enhanced or attenuated by the increment or decrement of the 5-HT level, respectively, in the central nervous system. We (Xia and Li 1984; Xia et al. 1985) found that simulated EA (low-frequency and low-intensity stimulation of deep peroneal nerve) could attenuate sympathetic cardiac arrhythmia induced by hypothalamic stimulation, which was found to be associated with an increase in the 5-HT activity in the periaqueductal