
THE MECHANISM OF ACUPUNCTURE AND CLINICAL APPLICATIONS

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This study presents the result of the studies explaining the effects of acupuncture on various systems and symptoms. It has been determined that endomorphin-1, beta endorphin, enkephalin, and serotonin levels increase in plasma and brain tissue through acupuncture application. It has been observed that the increases of endomorphin-1, beta endorphin, enkephalin, serotonin, and dopamine cause analgesia, sedation, and recovery in motor functions. They also have immunomodulator effects on the immune system and lipolytic effects on metabolism. Because of these effects, acupuncture is used in the treatment of pain syndrome illnesses such as migraine, fibromyalgia, osteoarthritis, and trigeminal neuralgia; of gastrointestinal disorders such as disturbance at gastrointestinal motility and gastritis; of psychological illnesses such as depression, anxiety, and panic attack; and in rehabilitation from hemiplegia and obesity.

Keywords acupuncture, beta endorphin, endogen opioids, enkephalin, serotonin

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INTRODUCTION

The term “Acupuncture” consists of two words from the Latin: *acus*: needle and *puncture*: insertion. It is a treatment procedure in which, generally, steel, silver, or gold needles are inserted into specific acupuncture points.

Traditional Chinese Acupuncture has a history of over 3,000 years (Ullet et al., 1998). Although the history of acupuncture dates back to ancient times, it has not lost its popularity. On the contrary, it has gained popularity recently. Acupuncture is applied especially in pain syndrome illnesses, in rehabilitation of hemiplegia, and in the treatment of psychological illnesses and obesity.

ACUPUNCTURE POINTS AND ITS CHARACTERISTICS

Application is made to the skin and muscle tissue under the skin. The skin and muscle tissue under skin are affected by every kind of stimulation during the application. It has been determined that 70–80% of all acupuncture points are the same as the trigger points (Melzack et al., 1977) and that most of the acupuncture points are also the same as muscular motor points (Liao, 1975).

Acupuncture points have low electrical resistance (Shang, 1989). The acupuncture points themselves can be regarded as energy concentrating points, comparable to electric batteries in which, up to a certain extent, physical energy is stored. This can be proven with a high-ohm galvanometer, which will show increased electric potential at acupuncture points (Leonhardt, 1980).

Generally, needle insertion to acupuncture points stimulates skin receptors that are slowly adapted. It has been determined that there is a close relationship between the location of the acupuncture points and the receptors of the acupuncture points. For example: when a needle is inserted into the Shangyang (LI 1), Zhongchong (P 9), and Shaoshang (L 11) points, it stimulates the receptors of touch and pressure, which are two sense receptors. When the needle is inserted into the Neiguan (P 6) and Yuji (L 10) points, it stimulates the muscle fibers because these points are located deep in tissue, which has a lot of muscle fiber. Accordingly, when a needle is inserted into the Daling (P 7) point it stimulates the receptor of the golgi tendon and/or pressure receptors (Wang & Liu, 1988).

At the histological level, a study of large numbers of microtomed preparations originating from 34 skin areas, including 11 acupoints and a number of “neutral” skin areas, revealed 2 types of acupoints: receptor and effector (Kellner, 1966). This was based on the difference in the distribution of the somatosensory receptors and a number of free nerve endings. These include

Meissner's corpuscles, Krause's end-bulbs, glomus-bodies, and smooth muscle (Kho & Robertson, 1997).

THE EFFECT MECHANISM OF ACUPUNCTURE

Neurophysiological Effects

A low frequency, dense current causes muscle contraction. It has been observed that in humans (Chiang et al., 1973) and in rats (Takeshige et al., 1980) that the stimulation of muscle that lies under the acupuncture point, with such a current, creates acupuncture analgesia. However, the same current when applied to another place does not create analgesia. The analgesia resulting from the stimulation of the acupuncture point occurs through inhibition of the neural activity of the dorsal periaqueductal gray region and the reticular formation of the brainstem. It has been observed that this acupuncture analgesia can be stopped by application of hypophysectomy and beta endorphin antiserum to the third ventricle (Takeshige et al., 1992).

A pain controlling system is activated to inhibit the pain signals that come into the nervous system. This controlling system is called the analgesia system. When the acupuncture needle is inserted, it stimulates the pain receptors (nerve endings) and causes the secretion of endogen opioids. These play a role in pain control. When the pain controlling system is activated, the neurons that originate from mesencephalon, periaqueductal gray substance in the periventricular region send their stimuli to the nuclei of rafe magnus and nucleus reticular paragigantocellularis (RPGC). Then these stimuli go to the dorsolateral column of the medulla spinalis with its pain inhibiting complex. In the analgesia system there are neurotransmitters like endorphin, enkephalin, and serotonin. Enkephalin is secreted by most of the nerve fibers originating in periaqueductal gray substance and the nucleus of the periventricularis and terminate in the rafe magnus nucleus. Enkephalin shows high affinity to opioid receptors delta and μ (Chen et al., 1996). Enkephalin, which is secreted by pain stimulation, is connected to the μ receptors and creates supra-spinal analgesia. It is also connected to the delta receptors and creates spinal analgesia. The stimulus of pain causes secretion of serotonin from nerve fibers that originate in the rafe magnus nuclei and terminate in the dorsal horn of the medulla spinalis. It also causes the secretion of enkephalin from local neurons of the medulla spinalis. It is believed that secreted enkephalin causes the presynaptic and post synaptic inhibition at the places where the C and A δ type nerve fibers synapse in the dorsal horn (Guyton & Hall, 2001).

It has been determined that electroacupuncture (EA) application causes the secretion of endorphin, which plays a role in producing the analgesic effect of hypophysis (Takeshige et al., 1992). It also plays a role in the increase of the endorphin level in plasma and the central nervous system (Jin et al., 1996; Fu, 2000). It has been observed that secretion of beta endorphin and ATCH from the anterior lobe of the hypophysis (Pan et al., 1996) and their plasma level increases (Malizia et al., 1979) with EA application. It has also been observed that there is a strong relationship between the endorphin level in the brain tissue and analgesic effect especially as a result of EA (Ullet et al., 1998). Concerning analgesic effect, EA application is more effective than traditional acupuncture (Wang et al., 1992). It has been determined that these endogenous opioids are connected to the opioid receptors, which are located in the central nervous system and the surface membrane of *nociceptors*, and they produce an analgesic effect. It has been observed that the analgesia that is produced by electroacupuncture is inhibited by naloxan (Pomeranz et al., 1977) and hypophysectomy (Takeshige et al., 1992).

Zhao (1995) observed in his study on rats that the analgesic effect of acupuncture decreases in the lesions of the reticular paragigantocellularis (RPGC), but the electrical stimulation of the RPGC increases the analgesic effect of acupuncture. In this study, he also determined that the beta endorphin and leucine enkephalin (LE) secretion in rats' RPGC increases with EA application. He concluded that beta endorphin and LE, which are secreted by the RPGC, play an important role in acupuncture analgesia.

In the study by Hardebo et al. (1989) it was observed that the low level of methionine enkephalin (ME) in the cerebrospinal fluid of the patients with type cluster headaches was increased by the application of acupuncture to the St 2, St 5, St 6, GB 14, Gb 20, and Ex 2 points on one side and point Liv 4 bilaterally for 30 min, once a week. The period of treatment was five weeks.

It has been determined that the level of enkephalins, which increases in the central nervous system and plasma with the application of acupuncture, has a role in the arrangement of psychological behaviors. It is known that enkephalins have antidepressant, anticonvulsant, and anti-anxiety effects (Plotnikoff et al., 1985). It has been observed that in addition to endogenous opioids in the brain tissue, the level of serotonin increases with the application of acupuncture (Li et al., 1982). It is also known that serotonin has an effect on feeling well, producing happiness, being pleased, producing a normal level of appetite and sexual stimuli, and achieving psychomotor balance (Guyton & Hall, 1996).

An effect bringing improvement in motor functions has been observed

through acupuncture. Because of this effect, acupuncture has been applied in the rehabilitation of cases of hemiplegia (Wong et al., 1999).

It has been observed that acupuncture application affects the nervous system (Fu, 2000) and causes changes in the concentrations of K^+ , Na^+ , and Ca^+ in the neurons (Deng, 1995), and the amount of neuropeptides like beta endorphin, leucine, enkephalin, and neurotransmitters like aspartate in the central nervous system (Fu, 2000). Researchers strongly support the opinions that the effect of acupuncture is arranged by the brain (Futaesaku et al., 1995) and that EA application causes a great change in the action potential of nerve cells (Fu, 2000).

Effects on the Immune System

It is believed that the effect of acupuncture on the immune system is related to the effects of beta endorphin, methionine enkephalin, and leucine enkephalin on this system. It has been noted that leukocyte has proopiomelanocortin mRNA. Because of this, leukocytes can synthesis ACTH and beta endorphin from promolecules. Besides this, endogen opioid receptors have been found on B lymphocytes, T lymphocytes, natural killer cells, granulocytes, monocytes, platelets, and complement terminal complex. It has been observed that there were chemical and physical similarities between neuroendocrin system opioid receptors and immune system opioid receptors (Khansori et al., 1990).

It has been determined that alfa, beta, and gamma endorphins have different immune functions. Whereas alfa endorphin like metionin encephalin and leusin encephalin play a role in the production of antibodies, gamma endorphins have no such effect (Jankovic, 1994). In this study, when methionin encephalin was applied into the cerebral cavity, it was observed that it had a stronger immunomodulator effect than periferic application. It was determined that methionin encephalin had a repairing effect on the immune system of aged rats. When 5 mg/kg of methionin encephalin was injected into the cerebral cavity, there was a decrease in T helper lymphocytes. But when 0.001 mg/kg methionin encephalin was injected into the same area, an increase in T helper lymphocytes was determined (Jankovic, 1994).

Yu et al. (1997), in their study performed on rats, applied electroacupuncture to the Zusanli (St 36) acupuncture point for 60 min per day over 3 days. The electroacupuncture application was performed with 1–5 mV, at 1 Hz electrical current for 1 ms. It was determined that the levels of interleucin-2, interferon gamma; and the activity of natural killer cells of the spleen increased with this application.

In another study on rats, Yu et al. (1998) applied electroacupuncture to the St 36 point for 30 min over 3 days and they observed that the activity of natural killer cells of the spleen and levels of beta endorphin and interferon gamma increased. The acupuncture application was performed with 3.5–5 mV, 1 Hz electrical current for 0.05 ms. When 10 mg/kg of naloxan was injected before electroacupuncture, it was noted that the increases in natural killer cell activity and interferon gamma were less than before. It was concluded that electroacupuncture applications increased the spleen beta endorphin secretions. As a result of this, natural killer cell activity and the level of interferon gamma increased.

It has been determined that endorphin and enkephalin increase the activity of natural killer cells, the generation of cytotoxic T lymphocyte, the chemotaxis of monocytes, and the production of interferon gamma, interleucin-1, interleucin-2, interleucin-4, and interleucin-6. In the studies on this subject (Jankovic, 1994; Millar et al., 1990), it has been concluded that endogen opioids create an immunomodulatory effect. In these studies, the immunomodulatory effect of acupuncture application was connected with the increase in levels of endogen opioids with acupuncture application.

Effects on Metabolism

It is thought that beta endorphin, one of the endogen opioids, also plays a role in the effect of acupuncture on metabolism. In the beginning, the studies that showed the lipolytic activity of beta endorphin were performed on animals as in vivo and in vitro. Later, these studies were performed on human fatty tissue as in vitro.

The studies that were carried out on rabbits as in vivo and in vitro indicated that beta endorphin has a lipolytic effect (Richter et al., 1983). Vettor et al. (1993) observed the lipolytic effect of beta endorphin on isolated human fatty tissue.

Electroacupuncture application on the Ren 12 point caused hypoglycemia in diabetic mice and increased beta endorphin levels. It was presumed that the increase of beta endorphin in plasma was caused by the increase of insulin in the plasma of diabetic mice (Chang et al., 1999).

Effects on the Gastrointestinal System

In gastroenterology, acupuncture has been used successfully to treat different gastrointestinal disorders, but only recently have scientific studies (Jin et al., 1996; Li et al., 1992) evaluated its effect. Both Chinese and Western studies

(Maciocia, 1989; Li et al., 1992; Jin et al., 1996) support the efficacy of acupuncture in the regulation of gastrointestinal motor activity and the secretion of opioid and other neural pathways. It has been observed that acupuncture applications depress the gastric acid secretion after food intake. It is thought that the increase of BE with acupuncture application leads to this condition (Jin et al., 1996). It has been noted that the tone of the smooth muscle of the stomach increases by stimulation of the auricular branch of the nervous vagus with auricular acupuncture application (Richards & Marley, 1998).

CLINICAL APPLICATIONS OF ACUPUNCTURE

In Diseases with Pain Syndrome

Nowadays acupuncture is a method of preference in most of the pain clinics. Acupuncture is applied to one million patients with pain syndrome a year in the United States (Paramore, 1996). In their study, Ahonen et al. (1984) observed that acupuncture application was effective in stress headache treatment and this effect continued throughout their 28 weeks of study. Pintov et al. (1997) determined that the opioid system of children with migraines activated following acupuncture application and the frequency and the intensity of pain decreased.

In the treatment of some diseases with pain syndrome like dysmenorrhea, osteoarthritis, fibromyositis, trigeminal neuralgia, and post-operative ache, acupuncture has been used and different degrees of recovery have been observed (Helms, 1987; Crocetti et al., 1998; Creamer et al., 1999; Marteleto & Fiori, 1985).

In the Rehabilitation of Patients with Hemiplegia

Wong et al. (1999) divided 128 patients with hemiplegia into two groups and they applied only a classic and detailed rehabilitation to the first group and the same treatment including acupuncture application to the second group. The neurologic and functional recovery of the patients in the second group was better than the first group's and their hospitalization period was shorter.

In the Treatment of Psychological Diseases

Acupuncture application increases the level of serotonin and enkephalin in the central nervous system and plasma. As a result, it is known to be effective in the arrangement of psychological condition. Because of this effect,

acupuncture may be used successfully in the treatment of anxiety and depression (Ullet et al., 1998).

In the Treatment of Obesity

Although diet application in obesity treatment brings weight loss, it has no effect on the suppression of appetite (Richards & Marley, 1998). It has been determined that acupuncture application has some distinct and certain effects on appetite and metabolism in obesity treatment (Mulhisen & Rogers, 1999). Asomoto and Takeshige (1992) explained that auricular acupuncture activated the satiety center in the hypothalamus. Because of this, it could help to control the sense of hunger. Furthermore, it has been determined that auricular acupuncture suppresses the appetite by stimulation of the auricular branch of nervous vagus (Richards & Marley, 1998).

CONCLUSION

Acupuncture has been used thousands of years to treat a variety of diseases and symptoms. The mechanisms of acupuncture's effects are not completely understood. Nevertheless, as a result of the efforts of many scientists, it has been recently understood that levels of neurotransmitters such as endomorphin-1, beta endorphin, enkephalin, and serotonin increase in plasma and brain tissue through acupuncture application. It has been observed that the increases of endomorphin-1, beta endorphin, enkephalin, Serotonin, and dopamine cause analgesia, sedation, and recovery in motor functions. Furthermore, they also have immunomodulator effects on the immune system and lipolytic effects in metabolism. Because of these effects the use of acupuncture is gradually increasing worldwide in the treatment of pain syndrome illnesses, gastrointestinal disorders, psychological illnesses, disorder of motor function, and metabolic diseases.

REFERENCES

- Ahonen, E., Hakumaki, S., Pantanen, J., Riekkinen, P., & Sivenius, J. (1984). Effectiveness of acupuncture and physiotherapy on myogenic headache: A comparative study. *Acupuncture and Electro-Therapeutics Research*, 9(3), 141–150.
- Asomoto, S., & Takeshige, C. (1992). Activation of the satiety center by auricular acupuncture point stimulation. *Brain Research Bulletin*, 29(2), 157–164.
- Chang, S. L., Lin, J. G., Chi, T. C., Liu, I. M., & Cheng, J. T. (1999). An insulin-

- dependent hypoglycemia induced by electroacupuncture at the Zhongwan (CV12) acupoint in diabetic rats. *Diabetologia*, 42(2), 250–255.
- Chen, Z., Hendner, J., & Hedner, T. (1996). Substance P induced respiratory excitation is blunted by delta-receptor specific opioids in the rat medulla oblongata. *Acta Physiologica Scandinavica*, 157(2), 165–173.
- Chiang, C. Y., Chang, C. T., Chu, H. L., & Yang, L. F. (1973). Peripheral afferent pathway for acupuncture analgesia. *Scientia Sinica*, 16, 210–217.
- Creamer, P., Singh, B. B., Hochberg, M. C., & Berman, B. M. (1999). Are psychosocial factors related to response to acupuncture among patients with knee osteoarthritis? *Alternative Therapies in Health and Medicine*, 5(4), 72–76.
- Crocetti, E., Crotti, N., Feltrin, A., Ponton, P., Geddes, M., & Buiatti, E. (1998). The use of complementary therapies by breast cancer patients attending conventional treatment. *European Journal of Cancer*, 34, 324–328.
- Deng, Q. S. (1995). Ionic mechanism of acupuncture on improvement of learning and memory in age mammals. *American Journal of Chinese Medicine*, 23(1), 1–9.
- Fu, H. (2000). What is the material base of acupuncture? The nerves! *Medical Hypotheses*, 54(3), 358–359.
- Futaesaku, Y., Zhai, N., Ono, M., Watanabe, M., Zhao, J., Zhang, C., et al. (1995). Brain activity of a rat reflects apparently the stimulation of acupuncture. A radioautography using 2-deoxyglucose. *Cellular and Molecular Biology*, 41(1), 161–170.
- Guyton, A. C., & Hall, J. E. (2001). *Textbook of Medical Physiology*. Philadelphia: WB Saunders.
- Hardebo, J. E., Ekman, R., & Eriksson, M. (1989). Low CSF met-enkephalin levels in cluster headache are elevated by acupuncture. *Headache*, 29(8), 494–497.
- Helms, J. M. (1987). Acupuncture for the management of primary dysmenorrhea. *Obstetrics and Gynecology*, 69(1), 51–56.
- Jankovic, B. (1994). *Neuroimmunomodulation: The state of the art*. New York: The New York Academy of Sciences.
- Jin, H. O., Zhou, L., Lee, K. Y., Chang, T. M., & Chey, W. Y. (1996). Inhibition of acid secretion by electrical acupuncture is mediated via beta endorphin and somatostatin. *American Journal of Physiology*, 271, 6524–6530.
- Kellner, G. (1966). Bau und function der haut. *Dtsch. Ztschr. Akup.*, 3, 1–31.
- Khansori, D. N., Murgu, A. J., & Golt, P. W. (1990). Effects of stress on the immune system. *Immunology Today*, 11, 170–175.
- Kho, H., & Robertson, E. N. (1997). The mechanisms of acupuncture analgesia: Review and update. *American Journal of Acupuncture*, 25, 261–281.
- Li, S. J., Tang, J., & Han, J. S. (1982). The implication of central serotonin in electroacupuncture tolerance in rat. *Scientia Sinica*, 25(6), 620–629.
- Li, Y., Tougas, G., Chiverton, S. G., & Hunt, R. T. (1992). The effect of acupuncture on gastrointestinal function and disorder. *American Journal of Gastroenterology*, 87(10), 1372–1381.

- Liao, S. J. (1975). Acupuncture points: Coincidence with motor points of skeletal muscles. *Archives of Physical Medicine and Rehabilitation*, *56*, 550.
- Maciocia, G. (1989). *The Foundations of Chinese Medicine*. New York: Churchill Livingstone.
- Malizia, E., Andreucci, G., Paolucci, D., Crescenzi, F., Fabbri, A., & Fraioli, F. (1979). Electroacupuncture and peripheral beta endorphin and ACTH levels. *Lancet*, *2*(8141), 535–536.
- Martelete, M., & Fiori, A. M. (1985). Comparative study of the analgesic effect of transcutaneous nerve stimulation; electroacupuncture and meperidine in the treatment of postoperative pain. *Acupuncture and Electro-Therapeutics Research*, *10*, 183–193.
- Melzack, R., Stillwell, D. M., & Fox, E. J. (1977). Trigger points and acupuncture points for pain correlation and implication. *Pain*, *3*(1), 3–23.
- Millar, D. B., Hough, C. J., Mazorow, D. L., & Gootenberg, J. E. (1990). Beta endorphin's modulation of lymphocyte is done, donor and time dependent. *Brain Behavior and Immunity*, *4*, 232–242.
- Mulhisen, L., & Rogers, J. Z. (1999). Complementary and alternative modes of therapy for the treatment of the obese patient. *Journal of the American Osteopathic Association*, *99*, 8–12.
- Pan, B., Castro-Lopes, J. M., & Coimbra, A. (1996). Activation of anterior lobe corticotrophs by electroacupuncture or noxious stimulations in the anaesthetized rat, as shown by colocalization of fos protein with ACTH and β -endorphin and increased hormone release. *Brain Research Bulletin*, *40*(3), 175–182.
- Paramore, L. (1996). Use of alternative therapies: Estimates from the Robert Wood Johnson Foundation national access to care survey. *Journal of Pain and Symptom Management*, *13*, 83–89.
- Pintov, S., Lahat, E., Alstein, M., Vogel, Z., & Barg, J. (1997). Acupuncture and the opioid system: Implications in management of migraine. *Pediatric Neurology*, *17*(2), 129–133.
- Plotnikoff, N. P., Murgu, A.J., Miller, G. C., Corder, C. N., & Faith, R. E. (1985). Enkephalins: Immunomodulators. *Federation Proceedings*, *44*(1), 118–122.
- Pomeranz, B., Cheng, R., & Law, P. (1977). Acupuncture reduces electrophysiological and behavioral responses to noxious stimuli: Pituitary is implicated. *Experimental Neurology*, *54*(1), 172–178.
- Richards, D., & Marley, J. (1998). Stimulation of auricular acupuncture points in weight loss. *Australian Family Physician*, *27*(2), 73–77.
- Richter, W. O., Kerscher, P., & Schwandt, P. (1983). Beta endorphin stimulates in vivo lipolysis in the rabbit. *Life Sciences*, *33*(1), 743–746.
- Shang, C. (1989). Singular point organizing center and acupuncture point. *American Journal of Chinese Medicine*, *17*(3–4), 119–127.
- Takehige, C., Sato, T., & Komugi, H. (1980). Role of peri-aqueductal central gray in

- acupuncture analgesia. *Acupuncture and Electro-Therapeutics Research*, 5, 323–337.
- Takeshige, C., Nakamura, A., Asamoto, S., & Arai, T. (1992). Positive feed-back action of pituitary beta endorphin on acupuncture analgesia afferent pathway. *Brain Research Bulletin*, 27(1), 37–44.
- Ullet, G. A., Han, S., & Han, J. S. (1998). Electroacupuncture: Mechanism and clinical application. *Biological Psychiatry*, 44(2), 129–138.
- Vettor, R., Pagano, C., Fabris, R., Lombardi, A. M., Macor, C., & Federspil, G. (1993). Lipolytic effect of beta-endorphin in human fat cells. *Life Sciences*, 52(7), 657–661.
- Wang, J. Q., Mao, L., & Han, J. S. (1992). Comparison of the antinociceptive effects induced by electroacupuncture and transcutaneous electrical nerve stimulation in the rat. *International Journal of Neuroscience*, 65(1–4), 117–129.
- Wang, K., & Liu, J. (1988). Needling sensation receptor of an acupoint supplied by the median nerve—studies of their electro-physiological characteristics. *American Journal of Chinese Medicine*, 17(3–4), 145–155.
- Wong, A. M., Su, T. Y., Tang, F. T., Cheng, P. T., & Liaw, M. Y. (1999). Clinical trial of electrical acupuncture on hemiplegic patients. *American Journal of Physical Medicine and Rehabilitation*, 78, 117–122.
- Yu, Y., Kasahara, T., Sato, T., Asano, K., Yu, G., & Fang, J. (1998). Role of endogenous interferon-gama on the enhancement of splenic NK cell activity by electroacupuncture stimulation in mice. *Journal of Neuroimmunology*, 90(2), 176–186.
- Yu, Y., Kasahara, T., Sato, T., Guo, S., Liu, Y., Asano, K., & Hisamitsu, T. (1997). Enhancement of splenic interferon-gama, interleukin-2, NK cytotoxicity by S36 acupoint acupuncture in F344 rats. *Japanese Journal of Physiology*, 47(2), 173–178.
- Zhao, L. (1995). Role of opioid peptides of rat's nucleus reticulari paragigantocellularis lateralis (RPGL) in acupuncture analgesia. *Acupuncture and Electro-Therapeutics Research*, 20(1), 89–100.