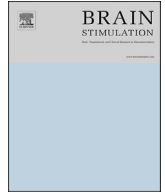




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Transcutaneous auricular vagal nerve stimulation (taVNS) might be a mechanism behind the analgesic effects of auricular acupuncture

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ABSTRACT

Background: Randomized clinical trials (RCT) demonstrated that auricular acupuncture (AA) is effective in treatment of acute and chronic pain, although the mechanisms behind AA are not elucidated.

Methods: The data concerning the localization of AA points, which are commonly used to treat pain, were extracted from the meta-analysis of 17 RCTs and evaluated using the anatomical map of auricular afferent nerve supply.

Results: Fifteen out of 20 specific AA points, used in the treatment of pain, are situated in areas innervated mostly by the auricular branch of the vagal nerve (ABVN), whereas sham stimulation was applied at the helix of the auricle, innervated by cervical nerves.

Conclusion: Considering the clinical data relating to the anatomy of neural pathways and experimental findings of the mechanisms of transcutaneous auricular vagal nerve stimulation, the analgesic effects of AA may be explained by stimulation of ABVN.

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Introduction

Auricular acupuncture (AA) is a complementary medicine technique based on a hypothesis that the entire human body is represented on the external auricle [1]. Randomized clinical trials (RCTs) have demonstrated that AA (including needling, acupressure and electrical stimulation of AA points) can reduce opioid requirement during and after surgery as well as pain intensity in acute and chronic pain conditions when compared to placebo and sham control procedures [2,3]. The mechanisms behind the analgesic effects of AA are not clearly understood. The theory of AA postulates that the dysfunction of the organs of the human body causes changes of the respective areas of the external auricle, which can be identified as painful spots with decreased tissue density/resistance (on palpation) and reduced electrical impedance of the skin [4,5]. Stimulation of these areas, connected to an organ with “pathology” is believed to improve the function of the organ or relieve the concomitant pain [1]. Thus AA is based rather

on the theory of reflexotherapy than on the Chinese system of energy circulation along the meridians, however no neuroanatomical pathways are known to connect the “diseased” body organs with the external auricle and explain the analgesic effects of AA [1]. In order to clarify the potential mechanism of AA, we aimed to evaluate the localization of AA points, which are commonly used to treat patients with acute and chronic pain with regard to contemporary knowledge on neuroanatomy of the external auricle.

Methods

This was a re-analysis of the data from the systematic review of Asher et al. [3]. This investigation analyzed 17 RCTs on the effectiveness of AA in treatment of patients with acute and chronic pain and remains the most comprehensive source of original research with sufficient methodological quality on this research topic [6].

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Table 1
Features of auricular acupuncture (AA) points in 17 randomized controlled trials included into systematic review on analgesic effects of AA (reference 3).

Nr.	AA points	Number of RCTs, where the AA point was used	Source of afferent innervation
1	Shenmen	12	ABVN, GAN
2	Lung	7	ABVN, GAN
3	Thalamus	5	ABVN, GAN
4	Cushion	4	GAN
5	Hip	3	ABVN, GAN
6	Knee	3	ABVN, GAN
7	Lumbar spine	1	ABVN, GAN
8	Toe	1	ABVN, GAN
9	Ankle	1	ABVN, GAN
10	Finger	1	GAN
11	Uterus	1	ABVN
12	Wrist	1	GAN
13	Elbow	1	GAN
14	Heart	1	ABVN, GAN
15	Tooth	1	ABVN, GAN
16	Mouth	1	ABVN, GAN
17	Valium	1	ATN, ABVN
18	Cingulate gyrus	1	ATN, ABVN
19	Point zero	1	ABVN, ATN
20	Cervical spine	1	GAN

AA: auricular acupuncture; RCT: randomized controlled trial; ATN: auriculotemporal nerve (from trigeminal nerve); ABVN: auricular branch of vagal nerve; GAN: great auricular nerve (from cervical plexus).

The data about the localization of AA points, which are commonly used to treat pain, were extracted from the main Table 1 and the papers included in the meta-analysis of Asher et al. [3]. The choice of specific AA points was based on empirical recommendations, described in detail in each RCT included in the meta-analysis. The choice of the areas for control procedures (AA at non-acupuncture points – sham acupuncture) was recommended after methodological investigation by an expert team [7]. All specific AA as well as the sham points were plotted over a schematic drawing of the pinna with an anatomical map of the auricular nerve supply (Fig. 1A & B). The data on the afferent nerve supply of the external auricle were taken from the original investigation of Peuker and Filler, 2002, who traced the complete course of auricular innervation using classical anatomic dissection of human cadavers under magnifying glasses and dyeing of nerves [8].

Results and discussion

Fifteen out of 20 AA points, which were used for treatment of pain in 17 RCTs, are situated in the areas innervated by cranial nerves exclusively or receiving mixed innervation by the auricular branch of the vagal nerve (ABVN) and cervical nerves (Table 1, Fig. 1). The AA points that were most frequently chosen to treat pain – Nr. 1 (Shenmen), Nr. 2 (Lung) and Nr. 3 (Thalamus) - are located in the area of afferent mixed innervation of ABVN and cervical nerves (Table 1, Fig. 1). Whereas the specific AA points are situated in areas innervated by cranial nerves only and in the areas of mixed innervation of ABVN and cervical nerves, sham stimulation was mostly applied at the helix and lobulus of the auricle, innervated by cervical nerves (Fig. 1B).

The AVBN provides the cutaneous afferent innervation of the external acoustic meatus and cymba conchae, whereas the peripheral regions of the auricle – helix and scapha are innervated by the cervical nerves [8]. According to Peuker and Filler (2002) the cavity of conchae is supplied by ABVN in 45% of cases and by

ABVN and the great auricular nerve (GAN) in 55% [7]. The afferent fibers of ABVN terminate in the brain stem nuclei of vagal and trigeminal nerves, including mainly the ipsilateral nucleus solitarius, principal sensory and spinal trigeminal nuclei [9].

Stimulation of the ABVN, but not cervical nerves of the external auricle, elicits cardiovascular responses, which could be abolished using the antagonist of muscarinic acetylcholine receptor atropine in experimental rodent investigation [10]. Experimental human investigations demonstrated anti-nociceptive effects of ABVN stimulation on experimentally evoked pain in healthy volunteers and in patients with chronic pelvic pain [11–13]. The functional magnetic resonance imaging (fMRI) investigations on the mechanism of ABVN stimulation in healthy volunteers confirmed the involvement of the neurons of the solitary tract and the locus coeruleus in the brain stem [14,15]. Moreover, decreases in fMRI signal in limbic structures were demonstrated, including the amygdala, hippocampus, parahippocampal gyrus and the cingulate cortex, suggesting that ABVN stimulation is targeting the regulation of emotional and autonomic components in cerebral processing of pain [16,17].

On the other hand, transcutaneous electrical stimulation of the auricular branch of the vagal nerve (ABVN), known as transcutaneous auricular vagal nerve stimulation (taVNS), is being increasingly used as a non-invasive method for treatment of neurologic and psychiatric disorders [18] but the clinical evidence of taVNS, based on few RCTs, is still too modest to make any recommendations for clinical practice [19].

Conclusion

Almost all empirically described specific AA points, which were used in randomized clinical trials to treat patients with acute and chronic pain, are situated in areas of the external auricle that principally receive afferent innervation from cranial nerves. Regarding the clinical data in connection with the anatomy of

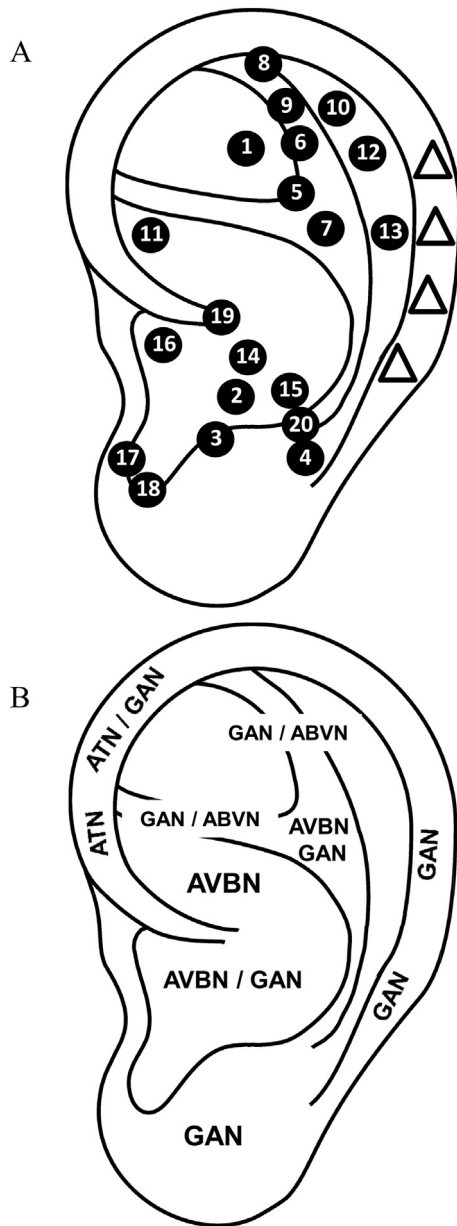


Fig. 1. A: Auricular acupuncture (AA) points, used for treatment of patients with acute and chronic pain in randomized controlled trials (RCTs) included into meta-analysis of Asher et al., 2010 (reference 3). Black circles with numbers: various specific AA, the nomenclature is given in Table 1; triangles: non-acupuncture points for sham acupuncture on the helix of the auricle as a control condition in several RCTs from the meta-analysis. B: Anatomic map of afferent nerve supply according to Peuker and Filler, 2002 (reference 7), where cymba conchae is exclusively supplied by the auricular branch of the vagal nerve (ABVN); cavity of conchae is exclusively supplied by ABVN in 45% of cases and by ABVN and the great auricular nerve (GAN) from the cervical plexus in 55%; tail of helix is exclusively supplied GAN; antihelix is exclusively supplied by ABVN in 73%, exclusively supplied by GAN in 18%, and supplied by ABVN and GAN in 9%; the crura of antihelix are supplied by GAN in 91% and ABVN in only 9%. ATN: auriculotemporal nerve (from trigeminal nerve).

neural pathways of the external auricle and experimental findings about the mechanisms of taVNS, we conclude that the analgesic

effects of auricular acupuncture can be explained by stimulation of ABVN.

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