Commentary: Auricular Neuromodulation: The Emerging Concept Beyond the Stimulation of Vagus and Trigeminal Nerves
Claire-Marie Rangon*
Head of Scientific Auriculotherapy Diploma, Faculty of Medicine, University of Paris-Saclay, 94276 Le Kremlin-Bicêtre, France

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*Correspondence
Dr Claire-Marie Rangon, Scientific Auriculotherapy Diploma, Département FMC, UFR Médecine Paris Sud, 63 rue Gabriel Péri, 94276 Le Kremlin-Bicêtre, France; Telephone No: +33 1 49 59 67 96; E-mail: cmrangon@gmail.com.

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Abstract
The ears are a potential gateway to the brain, mainly through their innervation. Transcutaneous stimulation of the vagus (tVNS) and trigeminal (TNS) nerves at the auricles is gaining ground in the field of non-invasive brain therapeutics.

The concept of Auricular Neuromodulation (AN), described in the article « Auricular Neuromodulation: The emerging concept beyond the stimulation of vagus and trigeminal nerves”1 is particularly interesting for neurologists, and might even help researchers to unravel fundamental mechanisms of brain functioning.

Introduction
Non-invasive brain neuro-modulation is an exciting, growing field2-6. There are mainly three efficient techniques that are available: magnetic, ultrasound and electrical stimulations. Among non-invasive electrical stimulations, transcranial Electrical Stimulation (tES ), is the most common approach7. Nevertheless, electrical bottom-up techniques are making their way, in particular, transcutaneous Vagus Nerve Stimulation tVNS and Trigeminal Nerve Stimulation TNS6. Interestingly, these two techniques can be carried out by the stimulation of the external ear1. In other words, the auricles may be considered as a free gateway to the brain.

The Auricular Neuromodulation (AN) concept, developed in the article « Auricular Neuromodulation: The emerging concept beyond the stimulation of vagus and trigeminal nerves”1, takes advantage of the three main nerve supplies of the ears, including the little-studied but promising superficial cervical plexus (SCP). This article aims to discuss why AN is particularly attractive in neurology, both for clinical and research purposes.

Auricular Neuromodulation is Ideal for Clinical Neurology

Among non-invasive techniques, there are at least three reasons to choose AN for treating chronic brain diseases. First, it is affordable. Second, it helps patients to stick to their treatments. Last, but not least, it takes advantage of a design by nature to reach the brain.

An affordable non-invasive neuromodulation
TNS and tVNS devices are easy to obtain by individuals via the world wide web. Moreover, they are affordable (a few hundred USD), depending on the brand, the number of electrodes, the quality of the
battery, and the size of the device. Many people without health insurance can afford them. Therefore, AN should be considered by governments as an opportunity to improve health care access.

An easy way to treat patients at home

Moreover, AN is a very easy technique that is suitable for patient home care. It functions as a Transcutaneous Electrical Nerve Stimulation (TENS) device targeting the ear. It involves putting electrodes on the ears, selecting the right frequency, intensity, and duration of the electrical stimulation. As with TENS therapy, which has become very popular among chronic pain patients, we can bet AN will achieve similar success among neurological patients.

Certainly, AN is no longer the only non-invasive neuromodulation technique offering home treatment. Transcranial Direct Current Stimulation (tDCS) is becoming more available thanks to a recently developed « Adjustable Helmet Frame »19. Nevertheless, the AN device is still more attractive because of its smaller size. Indeed, it complies with the anatomical shapes of the external ear. The tragus is easy to clip9 which makes this well-suited for everyday life. The latter is of capital importance since new AN devices can deliver continuous neurostimulation over several days while offering the patient a high degree of comfort and mobility (Primary Relief ™ by DyAnsys®). This advantage is particularly interesting when dealing with patients who have memory impairment or cognitive disorders10.

A nature-designed technique to heal the brain through the guidance of neural plasticity and neuroimmunomodulation

At last, as the ears are connected to the brain through their innervation, AN does not have to face either physical (i.e., the cranium) or chemical (i.e., the brain blood barrier) obstacles to treat brain disorders. The resulting stimulation is fast and brain-targeted.

A single electrical stimulation of the ear (250 Hz, 0.14-1.08mA, 3V, 4 minutes) is able to directly modulate the activity of brain areas, thereby modifying significantly and specifically resting state EEGs11.

The vagus nerve, and consequently AN, is also able to modulate the connectivity of brain areas; in other words, to guide neural plasticity12, as a « neural connectome »13. For instance, tVNS significantly reduces symptoms in depressed patients14 and decreases also the functional connectivity between the bilateral medial hypothalamus and rostral anterior cingulate cortex15. In a stroke, tVNS favors not only neural plasticity by enhancing rehabilitation16,17, but also seems to strike at the root of brain lesions by decreasing the angiogenic response18,19 and the infarct size20,21.

Finally, the vagus nerve, and therefore AN, can stimulate indirectly the brain, via the modulation of the immune system22,23. In epilepsy, a common neuroinflammatory disease, a randomized double-blind study including 76 drug-resistant patients24 showed a significant reduction of seizures after 20 weeks of tVNS (25 Hz, 4 hours daily; p = 0.034). Ear electrostimulation of kainic acid-induced epileptic rats confirmed tVNS efficacy against brain inflammatory mediators25,26.

Thus, AN is a promising method that is consistent with several expectations of neurologists. Neuroscientists as well might soon get interested in AN.

Auricular Neuromodulation is Promising for Brain Research

Unravelling brain hubs through mass ear recordings

An excellent review, published in April 2018, suggests that « non-invasive neuromodulation affects a brain network rather than just the local stimulation site targeted »27. In humans, the identification of the major brain hubs requires time and money to collect and compare using structural and functional neuroimaging studies28,29. No matter how many hundreds or thousands of neuroimaging studies are available in the data banks, it virtually impossible to get an exhaustive data collection that takes into account all the neurodevelopmental stages, all the genetic backgrounds, even all the epigenetic disturbances.

In contrast, electrical resistance recordings of the ears are much easier to get from millions of people than from functional neuroimaging studies, provided that the recording time is not too long, the procedure is accurate, painless, affordable and ideally easy to move. Besides, significant changes of the electrical resistance recorded on the auricules may also serve as early screening tests for specific brain diseases. For instance, for the early diagnosis of dementia30,31, auricular electrical resistance measurements would be much easier to carry out than vagus somatosensory potentials recordings.

Fortunately, this kind of device is already available! It is currently used by auricular acupuncturists to detect active acupoints. Interestingly, in an Austrian study, the ears of neonates suffering from neonatal abstinence syndrome were screened : one hundred percent of the neonates presented active acupoints, including in the ear area supplied by the SCP32. In addition, another auricular acupuncture randomized trial studying the efficacy of selected ear acupoints in migraine attacks concluded that the point located in the area supplied by the SCP was significantly more efficient than another point located above the concha33. This result was not surprising because, in auriculotherapy maps, the head is always represented within the earlobe, supplied by the superficial cervical
plexus (« the inverted fetus »). Furthermore, other clinical applications of auriculotherapy in neurology have been cited lately and provide an evidence-based medicine overview of this still little-known field of research\(^\text{14}\).

Likewise, up and coming basic neuroscience research should also pay attention to the detection and stimulation of the ear area supplied by the superficial cervical plexus. Optogenetics manipulations may turn out to be the best option to validate the hypothesis of the auricular brain map in animal models. Indeed, optogenetics, a revolutionary research tool based upon bioengineered light-sensitive proteins, can optionally stimulate or silence particular cell types and neuronal circuits with milliseconds temporal accuracy\(^\text{35-37}\). Therefore, optogenetics might represent an alternative cutting edge approach in term of Auricular Neuromodulation both for the validation of the “ear hubs” corresponding to the brain hubs, potentially through transdermal ear illumination\(^\text{38}\) and for unravelling the neural circuits involved in ear stimulation\(^\text{39,40}\). Finally, optogenetic manipulations may also contribute to optimize the ear stimulation parameters\(^\text{41}\).

**Optimizing ear stimulation parameters**

Aside from defining the ear points, the optimal characteristics of the electrical stimulation have to be precisely determined. First, the frequency is of capital importance, otherwise, the stimulation even of the right ear point will not trigger any significant improvement\(^\text{42,24}\). Along these lines, the intensity of the optimal current, the wavelength and the duration of the ear stimulation each require scientific evaluation.

Once more, sharing the experience of ear acupuncturists should help neuroscientists. For instance, semi-permanent needles are inserted into the ear according to the electrical charge of the acupoint (thereby indicating whether the acupoint is active or not), which is a technique that gives a sense of the magnitude of the necessary stimulation to apply. Laser stimulation parameters, applied to the ears of neonates, could also help researchers get a headstart\(^\text{43}\).

**Conclusion**

Auricular Neuromodulation is only in its early stages. So far, studies have concerned mainly tVNS. In view of the tremendous potential of the AN as an amazing concept, leading neuroscience research laboratories as well as other interested decision-makers should join in and show the way.

**Conflict of interest statement**

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