Editorial

ANATOMY: THE MOST MODERN OF ANCIENT SCIENCES

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Knowledge of the form, size, position and relationships is the basis for knowledge of the function, purpose, "what for". This also has to do with that which is frequent, usual, distinguishing from, and contrasting with that which varies, which appears modified to the point of functioning differently, poorly or not at all.

In this very unique manner, Anatomy appears on the horizon as a science focusing on humans, animals, vegetables, the macroscopic (Gross Anatomy), the microscopic, the comparative, the evolutionary, the developmental, the forensic and the clinical, among others. Anatomy harbors, by means of its principles and content many other sciences which profit from, depend on and evolve from it.

Despite its long and fruitful history, research and study results continue to abound in the anatomical field. Many are the modern paths that our ancient Anatomy currently follows. The publication of a beautiful study about the human head using anatomical network analysis (AnNA), stemming from nodes representing anatomical units and links representing their physical articulations, is one of such modern paths. This study uncovers new anatomical and functional modules of the human head and sheds new light on the symmetry/asymmetry of facial expression and how the use of facial muscles is crucial in non-verbal and oral communication (Esteve-Altava et al, 2015).

There is more concerning the head and face, now in light of evolutionary anatomy: a study related to the functional integration of the nasopharyngeal boundaries with the facial skeleton and external basicranium over the course of development in human and nonhuman hominoids, demonstrated that human adults are distinct from all groups in possessing a relatively shallow nasopharyngeal roof and shorter, more flexed external basicranium (Pagano and Laitman, 2015). Human and non-human skull measurements have been recorded many times, but the methodological approach employed, along with three-dimensional landmark coordinates, digitized and analyzed via the program Morphologike 2, were able to remove isometric size differences among specimens, although allometric shape variations remained and were measureable, permitting access to results presented with utmost elegance and reliability.

The use of Computed Tomography (CT) Scans, Magnetic Resonance (MRI), fMRI and all the important different kinds of anatomical/functional images techniques opened doors to ever more daring scientific flights with surprising results.

Some projects and research using CT Scan and vídeo-fluoroscopy, directed towards child Anatomy, with special interest in the development of the face, larynx, nasal cavities and aerodigestive tract are very illustrative in this line of anatomical research by imaging (Meaike et al, 2016; Curcio et al 2014; Curcio et al 2015).

When it is a question of microscopic Anatomy, a world of enormous possibilities opens up, in methodological aspects, immunohistochemistry, *in situ* hybridization and others, as well as in tridimensional reconstruction using the appropriate software. An interesting study on the Granulocyte colony-stimulating factor's (G-CSF) positive effects on muscle fiber degeneration (Simões et al, 2014) made use of an electron tomography 3D reconstruction of a malformed myelinated, which can be accessed by the link https://www.dropbox.com/sh/7yowuptdiru0l3p/AADBmMow_UCRcYGl6kJazntGa.

Attent to these technological requirements and the resources stemming from the "anatomy by image", our group in the Department of Morphology strove to find answers to the morphovolumetric issues, above all the abdominal wall and cavity, in conjunction with the Surgery Department of Santa Casa of São Paulo. Graduate students, using the OSIRIX MD Software, are performing the ongoing research with image reconstruction through computerized tomographies with submillimetric cuts, directed at 3D reconstructions of the normal and herniated abdominal cavities.

The advances in the understanding of brain circuitry underlying mental disorders contributed to the development of new therapeutic strategies, such as Noninvasive Brain Stimulation Techniques (NIBS). NIBS are techniques that might aid in overcoming some of the current challenges related to pharmacotherapy. Ideally, NIBS should be not only as effective as pharmacotherapy, but also present a low rate of adverse effects, thereby increasing treatment adherence. Neuromodulation techniques include novel techniques, such as trigeminal nerve stimulation (TNS) and transcutaneous vagus nerve stimulation (tVNS).

Our research group at Santa Casa of São Paulo School of Medical Sciences is formed by morphologists and psychiatrists, and this interaction brings to us a very productive and integrative way to obtain results.

Recently, we undertook a proof-of-concept study to evaluate both the safety and potential clinical efficacy of a Trigeminal Nerve Stimulation (TNS) protocol for treating Panic Disorder using an external neurostimulator to deliver electric current transcutaneously through the orbital branch of the trigeminal nerve (Trevizol et al, 2016a); TNS protocol for treating Major Depressive Disorder in the Elderly (Trevizol et al, 2016b); TNS for the treatment of Irritable Bowel Syndrome (Trevizol et al, 2015c) and TNS for a Major Depressive Disorder in Pregnancy (Trevizol et al, 2015d), all of which presented amelioration of patients symptoms.

We know that trigeminal nerve can modulate the activity of the *Locus Ceruleus* and nucleus of the solitary tract to affect psychophysiolgical arousal, the activity of the sympathoadrenal medullary axis, biochemical stress responses, and the dorsal motor nucleus of the vagus. Neuro-signaling pathways should be mechanisms for the regulation of cortical gain control and optimization, influencing a broad variety of neurophysiological and cognitive functions, as well as primary sympathetic responses to environmental stress (Tyler et al, 2015). But many doubts remain concerning neural pathways which are effectively stimulated or inhibited by TNS and the effects on neuronal activity and plasticity which might be caused.

Vagus nerve stimulation (VNS) is a neuro-modulation strategy first developed in the 1980s for epilepsy. More recently, growing efforts in clinical research have been underscoring possible clinical benefits of VNS for different medical conditions such as epilepsy, major depression and anxiety disorders. Vagus nerve stimulation is most commonly used by the implantation of a current-carrying electrode around the nerve in the cervical region. The electrode is connected to a battery-operated generator that is implanted in the chest wall.

More recently, a nonsurgical method of VNS known as transcutaneous VNS (tVNS) has been developed, in which the auricular branch of the VN is stimulated by electrodes placed on the outer ear (Kreuser et al, 2012). But, an important piece of anatomical information limited the stimulation, because the right vagal nerve has efferent fibers to the heart, so tVNS is safe to be performed only in the left ear.

Interestingly, once our group observes potential clinical benefits of VNS and tVNS, it is reasonable to infer that stimulating other specific areas innervated by the VN would also relate to hypothetical neuromodulatory effects. Another site of interest is the skin over the mastoid process, which has not been evaluated hitherto. This posterior region is innervated by the auricular branch of the VN (also called Alderman's nerve).The interest of targeting this specific area over the mastoid process for tVNS trials relies both on (a) the feasibility of easily placing tVNS electrodes over the skin in this area and (b) stimulating a more specific site innervated exclusively by the VN — rather than the outer ear which is also innervated by other cranial nerves.

Following the rationale of VN anatomy and cranial innervation presented above, we then hypothesized that the transcutaneous placement of electrodes over the mastoid process could be a useful study protocol for future tVNS trials (Trevizol et al, 2015a). We hereby present the first case of tVNS with electrodes positioned over the mastoid process. In this report, we describe a 38-year-old male patient diagnosed with major depressive disorder who successfully underwent a tVNS intervention protocol, Ten consecutive daily tVNS sessions were performed. After two weeks of the intervention protocol, we found clinical amelioration of depressive symptoms with complete clinical remission. The patient remained stable after a two-month follow-up period (Trevizol et al, 2015b). Again, the anatomical approach was the golden opportunity for a new protocol for a clinical study.

The integrated multidisciplinary approach in conjunction with the insertion of modern methods of obtaining and analyzing data presents itself as an advanced strategy for gleaning new results in the field of anatomical research.

Innovation in Anatomy is not only based on the inclusion of modern technological methods, but also on the flexible conceptual structure which Anatomy as a science provides.

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