# Exploring fetal pelvic neuroanatomy: a deep dive into understanding nerve pathways, endometriosis, and pain

Pelvic innervation has been a subject of investigation for many years. In the late 19th century, surgeons Mathieu Jaboulay and Giuseppe Ruggi independently described neuroanatomical techniques for the surgical disruption of pelvic autonomic nerves to relieve severe dysmenorrhea (1). Although we continue to advance technologically, our research and knowledge of pelvic innervation have not seemed to grow at the same rate. We are still far from understanding pelvic nerve pathways and the implications thereof.

The study by Pinsard et al. (2) provides the first 3-dimensional (3D) reconstruction model of uterine innervation in a fetus model. Studies such as this may shed light on the physiology of pelvic pain pathologies and strategies for better treatment of these conditions.

When thinking of the current surgical therapies for the treatment of chronic pain, 2 procedures come to mind that specifically target nerve bundles: presacral neurectomy and laparoscopic uterosacral nerve ablation (LUNA).

In 1924, M.G. Cotte defined the proper anatomical location for presacral neurectomy to achieve the best results for the treatment of midline pelvic pain (1). Since that time, there have been several techniques described for the interruption of pelvic autonomic nerves; however, the basic principles of a presacral neurectomy are still the same as described by Cotte (1).

During a presacral neurectomy procedure, the superior hypogastric nerve plexus is skeletonized at the "triangle of Cote" and a segment of the nerve fibers and ganglions in this area is resected (1). In patients with centralized pelvic pain, studies have shown that this method results in decreased pain, dysmenorrhea, and dyspareunia (1, 3). However, with LUNA, the nerve pathways located in the uterosacral ligaments are disrupted. In a randomized controlled trial from 2009, patients who underwent LUNA did not have any significant improvements in pain, dysmenorrhea, or dyspareunia compared with laparoscopy without pelvic denervation (4). On the contrary, in a randomized controlled trial by Chen et al. (3), the long-term efficacy of presacral neurectomy for dysmenorrhea was significantly better than that of LUNA.

The work by Pinsard et al. (2) may be giving us a clue into understanding why there are differing rates of success with these 2 methods of pelvic denervation. In this study, functional mapping of uterine innervation showed that nerve fibers have a centripetal path with rich innervation next to the parametrium and paracervix (2). Therefore, it makes sense that a procedure such as LUNA, which interrupts the Frankenhauser plexuses, would not be as effective as those that work on more centralized nerve pathways, such as presacral neurectomy. If we can understand the location and density of nerves in the pelvis, we can better tailor treatments to these pain conditions.

We can consider supracervical hysterectomy as another example of how this study could change our approach with certain pathology. As this study has shown, the paracervix and parametrium are the most richly and densely innervated regions compared with the uterine body (2). To this, we must add the well-known fact that patients with endometriosis have altered uterine and pelvic innervation (1). By understanding these 2 premises, one may wonder that leaving the cervix in patients with endometriosis and pelvic pain who undergo hysterectomy may not be the best method for managing pain. Indeed, in our personal experience, patients with endometriosis who undergo supracervical hysterectomy do not seem to have as significant of pain relief as those who undergo total hysterectomy.

It should be noted that Pinsard et al. (2) used human fetuses as the model in their studies, which is an established method of studying pelvic neuroanatomy. However, as the investigators themselves stated, this does not allow for the possibility of neurophysiological changes brought about by hormones (2). Previous research has confirmed the presence of ectopic endometrium in human female fetuses through autopsy analyses (5). Similar to the tissue analysis performed by the investigators, through specific histologic staining and immunolabeling, the anatomical sites of the endometrial structures in fetuses have been shown to be close to the posterior wall of the uterus, posterior cul de sac, and rectovaginal septum and in the rectal tube and the wall of the uterus (5).

The investigators demonstrated skillful implementation of advanced software, which, through stacking and alignment of 2-dimensional sections, resulted in a 3D model. This model opens a world of possibilities, including potential endometriosis mapping with staining for cancer antigen 125, cytokeratin 7, and cluster of differentiation 10 as well as estrogen and progesterone receptors, a process that could aid in the validation of the theory of embryonic cell remnants as one of the causes of endometriosis (5).

Pinsard et al. (2) provide an invaluable addition to the scarce literature on the neural pathways of chronic pelvic pain. Even more promising is the methodological advances brought by this study, particularly the possibilities of the methods for adult neuroanatomy proposed by the investigators for their future studies. As we dive deeper into our understanding of pelvic innervation, we develop a new understanding of our current pathologies and procedures. To our knowledge, this is the first study to generate a comprehensive model of uterine innervation in physiological conditions and provide a solid base for studying uterine innervation in pathological situations. Few studies have described the uterine human innervation with such depth of detail. The investigators have highlighted the strengths and limitations involved with fetal analyses and have opened our eyes to a realm of potential histologic studies using section-based 3D models.

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