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Clinical Anatomy of the Extradural Neural Axis Compartment: A Literature Review

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Key words
- Cavernous sinus
- Extradural neural axis compartment
- Intervertebral foramen
- Lateral sellar compartment
- Orbit
- Spinal epidural space
- Tumor growth

Abbreviations and Acronyms
CN: Cranial nerve
CSVS: Cerebrospinal venous system
EDNAC: Extradural neural axis compartment
IAP: Intra-abdominal pressure
ICP: Intracranial pressure
IOP: Intraocular pressure
ISP: Intraspinal pressure
JF: Jugular foramen
LSC: Lateral sellar compartment
LSOJ: Lateral sellar orbital junction
SOF: Superior orbital fissure

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■ OBJECTIVE: **The extradural neural axis compartment (EDNAC) is an adipovenous zone located between the meningeal and endosteal layers of the dura and has been minimally investigated. It runs along the neuraxis from the orbits down to the coccyx and contains fat, valveless veins, arteries, and nerves. In the present review, we have outlined the current knowledge regarding the structural and functional significance of the EDNAC.**

■ METHODS: **We performed a narrative review of the reported EDNAC data.**

■ RESULTS: **The EDNAC can be organized into 4 regional enlargements along its length: the orbital, lateral sellar, clival, and spinal segments, with a lateral sellar orbital junction linking the orbital and lateral sellar segments. The orbital EDNAC facilitates the movement of the eyeball and elsewhere allows limited motility for the meningeal dura. The major nerves and vessels are cushioned and supported by the EDNAC. Increased intra-abdominal pressure will also be conveyed along the spinal EDNAC, causing increased venous pressure in the spine and cranium. From a pathological perspective, the EDNAC functions as a low-resistance, extradural passageway that might facilitate tumor encroachment and expansion.**

■ CONCLUSIONS: **Clinicians should be aware of the extent and significance of the EDNAC, which could affect skull base and spine surgery, and have an understanding of the tumor spread pathways and growth patterns. Comparatively little research has focused on the EDNAC since its initial description. Therefore, future investigations are required to provide more information on this under-appreciated component of neuraxial anatomy.**

INTRODUCTION

Parkinson,[1,2] in 2000, was the first to formally describe the extradural neural axis compartment (EDNAC) in his seminal account of this region. He had portrayed it as an elongated, slender, adipovenous compartment in the neuraxis that is extradural in nature, being interposed between the meningeal and endosteal layers of the dura mater.[1,2] The EDNAC spans from the orbital fossa, back into the cavernous sinus, along the clivus, through the foramen magnum, and into the spine before terminating at the coccyx.[1-4] The EDNAC has aptly been referred to as an "anatomical continuum" and is perhaps the longest single anatomical compartment known to date.[5-7] Epidural fat is the characteristic and major component of the EDNAC.[7] Contained within this fatty matrix are plexuses of small valveless, epidural veins, allowing bidirectional flow of blood.[1,2,4-6,8-13] This epidural adipovenous tissue is irregularly distributed and varies in amount throughout the length of the EDNAC. In certain locations, the EDNAC also transmits nerves, in addition to arteries and larger veins, before they continue on their extracranial or extraspinal course.[1] Although it has been asserted that the EDNAC is recognized by skull base surgeons, a relative paucity of EDNAC data has been reported, and only a few studies have investigated this compartment specifically or made reference to it.[7] In 2000, Parkinson[2] comprehensively reviewed the history of the EDNAC and found that previous anatomists and physicians, although likely aware of the nature of the EDNAC, had never explicitly discussed it in their reports. He further proposed organizing the EDNAC into 4 distinct segments.[2]

In the present review, we have summarized the current research pertaining to the anatomy and function of the EDNAC and commented on the relevant aspects of clinical significance.

METHODS

A comprehensive review of the reported data in the narrative style was conducted to identify the key reports and supporting data regarding the EDNAC. All the studies were from the English body of reports, save for one seminal report, which was in French.[14] The EDNAC was illustrated on paramedian and median sagittal plastinated slices from a 77-year-old male cadaver (Figure 1) and 4 anteroposterior coronal plastinated slices from an 81-year-old female cadaver (Figure 2).

DISCUSSION

Overview

The cavernous sinus within the skull was first recognized by Taptas[14] in 1949 as an extradural zone that he incorporated into his "interperiosteodural concept," which also included all intracranial dural sinuses.[15] This notion laid the groundwork for Parkinson[1,2] to propose and promote the concept of an "extradural neural axis compartment" or the EDNAC.[11] In essence, the concept of the EDNAC is a development of the interperiosteodural concept and comprises a lengthy, multifarious, anatomical complex with 4 segmental enlargements containing fat and neuro vascular elements.[1,2,4-7,10,16] The EDNAC extends throughout the axial skeleton from the orbit to the coccyx.[1,2,4-7,10,16] A fatty matrix and small valveless venous plexuses are the characteristic and major components of the EDNAC.[1,2,4-6,8-13] Therefore, except for those in the skull base, most intracranial dural sinuses (e.g., the superior and inferior sagittal, straight, transverse, and sigmoid sinuses) reside in the interperiosteodural space but might not be in the EDNAC, because they are not imbedded in a fatty matrix.[17,18] The methods used by investigators to investigate aspects of the EDNAC have included anatomical microdissection, vascular injections and/or casting, epoxy sheet plastination, histological examination, and even electron microscopy.[7]

The EDNAC is intimately associated with the dura mater, or pachymeninx, and runs between the endosteal layer adherent to the bone, which forms the "floor," and the meningeal layer, which forms the "roof" of the compartment. Thus, the EDNAC is effectively cocooned and, for the most part, limited by these 2 dural sheets within which the adipovenous contents are packed.[16] The EDNAC can be subdivided into 4 segments according to the differences in regional anatomy along its length.[2]

Orbital Segment

The most rostral segment of the EDNAC is located in the orbital fossa (Figures 1A and 2A). The orbital segment resides between the periosteum of the orbit (known as the periorbita) and the optic nerve sheath and contains abundant orbital fat, which supports the eyeball, large valveless ophthalmic veins, ocular muscles, and other smaller vessels and nerves.[1,2,11,12,19,20]

Lateral Sellar Orbital Junction

In 2009, Froelich et al.[6] conceived the term "lateral sellar orbital junction" (LSOJ) to describe the transitional zone between the orbit and the lateral sellar compartment. The LSOJ is located within the wide, medial portion of the superior orbital fissure (SOF; Figures 1A and 2A).[6] This intermediate region of the EDNAC represents an adipose corridor between the meningeal and periorbital dura, which transmits the lacrimal and frontal branches of the ophthalmic nerve (CN V_1), trochlear nerve (CN IV), and superior ophthalmic vein and fat and orbital veins from the orbit to the lateral sellar compartment.[3,6,21,22] The central structure of the LSOJ is the annular tendon of Zinn from which the 4 rectus muscles originate.[6] Liugan et al.[23] in 2017 also provided evidence that an adipose space surrounds the ophthalmic artery within the optic canal. However, how this fat is related to the LSOJ is unclear, because the optic canal is separate from, and medial to, the SOF. Communication between this sleeve of adipose tissue and the orbital EDNAC might also be reduced because the meningeal dural fibers from the optic nerve sheath blend with the periosteum in the optic canal.[23] At this rostral region of the EDNAC, it is important to remember the pterygopalatine fossa, which is located deep to the LSOJ (Figures 1A and 2A). Although this compartment possesses a significant mass of fat and contains a number of neurovascular structures, it is roofed by the orbital muscle of Müller and communicates with the cavernous sinus via the foramen rotundum. Thus, it is not considered an anteroinferior extension of the EDNAC.[6,24]

Lateral Sellar Segment

Passing back through the SOF, the EDNAC opens out into its second segment: the cavernous sinus or lateral sellar compartment (LSC).[20,22,25,26] The LSC contains a rich meshwork of discrete, very delicate veins imbedded within a fatty matrix, which also transmits CNs III, IV, and VI, the V_1 and V_2 divisions of CN V, and the internal carotid artery (Figures 1A and 2B).[1,2,7,10,14,16,27] The venous anastomoses between the orbital veins, superior petrosal sinus, and petroclival venous confluence are also embedded in the LSC.[16,28] Inspired by the quantity and variety of structures contained within the LSC, Parkinson[19,29] quaintly described this region as "an extradural, anatomical jewel box." Parkinson[1,2] also made a case against the use of the traditional, yet anatomically inaccurate, label "cavernous sinus," noting that no single venous cavern exists but, rather, a plexus of separate, discrete veins is present. Parkinson[1,2] appealed for the use of the term "lateral sellar compartment" (LSC) instead. Because the latter is more true to the anatomy of the region, the LSC has gained support in the reported data and has been used henceforth in the present report to describe the "cavernous sinus."[6,21,26,30] At the posterior margin of the LSC resides Meckel's cave, an evagination of the meningeal dura that envelops the trigeminal ganglion and the proximal divisions of CN V. This protruding dural pouch is associated with the EDNAC but is not strictly an EDNAC component.[31,32] François et al.[10] also reported that the LSC contains less adipose tissue compared with the other regions of the EDNAC, such as the orbit or spine. Using novel epoxy sheet plastination technology (similar to that shown in Figure 1), Liang et al.[33] and Diao et al.[34] reported on the fine architecture of the matrix and the medial and lateral walls of the LSC. Within the LSC, a trabecular dural framework deriving from the meningeal dura of the middle cranial fossa and Meckel's cave acts to suspend the traversing CNs and vessels. This meshwork then fans out to continue with the adipose matrix. The fat deposition in the LSC is mainly concentrated medially to the traversing nerves and exhibits a dumbbell-shaped morphology on a transverse orientation.[33] The EDNAC might even communicate with the potential space between the intracranial nerves and their surrounding

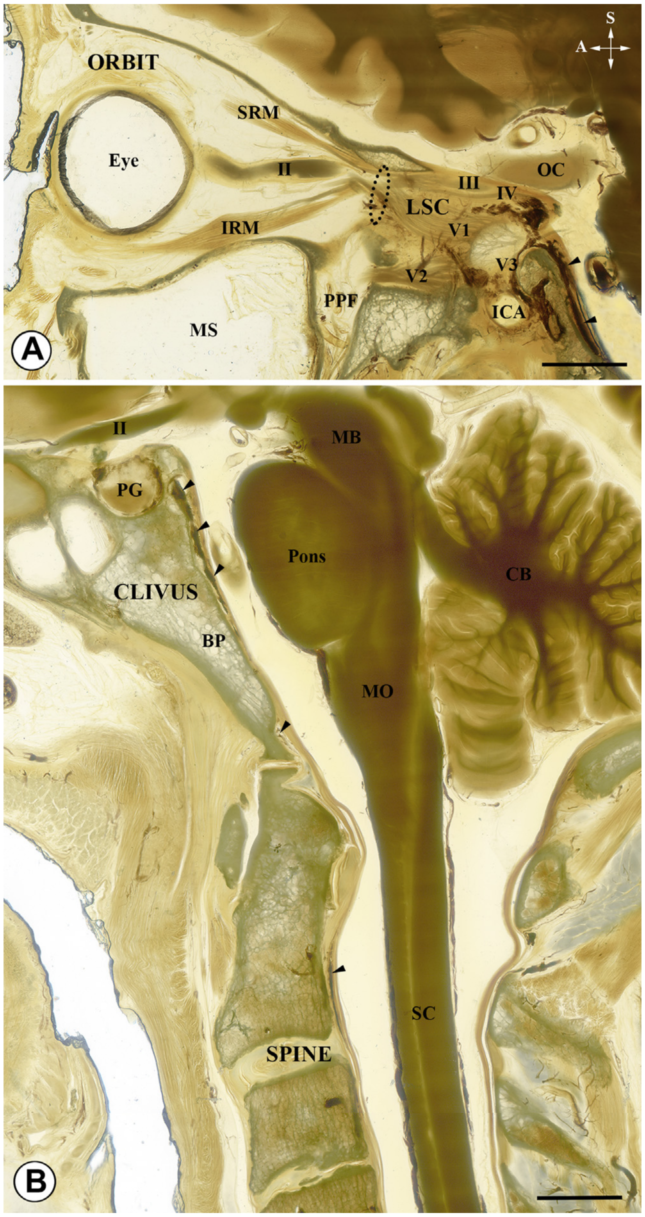

Figure 1. (**A**) Paramedian and (**B**) median sagittal plastinated slices illustrating the orbital, lateral sellar, clival, and spinal parts of the extradural neural axis compartment (EDNAC) and their continuation along the neuraxis. The *dashed circle* indicates the lateral sellar orbital junction, which connects the orbital segment with the lateral sellar compartment (LSC). The *single arrowheads* point to the epidural veins running through the EDNAC. A, anterior; BP, basilar process; CB, cerebellum; ICA, internal carotid artery; II, III, IV, V1, V2, and V3, second, third, fourth, and fifth cranial nerves; IRM, inferior rectus muscle; MB, midbrain; MO, medulla oblongata; MS, maxillary sinus; OC, optic chiasm; PG, pituitary gland; PPF, pterygopalatine fossa; S, superior; SC, spinal cord; SRM, superior rectus muscle. Scale bar = 2 cm.

sheaths. It has been demonstrated that within the LSC, the meningeal dural fibers surround the traversing CNs, forming the epineurium of the nerves, and then gradually fan out to continue with the adipose tissue of the EDNAC.[33]

The comparative anatomy of the LSC in different primate species has been explored in several studies. Kehrli et al.[15] found that in the olive baboon (*Papio anubis*), the overall architecture of the parasellar region, including the interperiosteodural arrangement, is similar to that of humans. They described the parasellar space as being occupied by large anastomosed sinuses, instead of a fine venous meshwork, and also reported that the baboon has a deposition of fat in the anterior LSC, similar to that observed in humans.[15] Using histological examination and electron microscopy to investigate the LSC anatomy in the crab-eating macaque (*Macaca fascicularis*), Rajendran and Ling[35] described a single main venous channel running in the LSC. They concluded that the simian LSC is, for the most part, similar to the human LSC.[35] In another early study in 1944 by Eyster[36] on Rhesus macaques (*Macaca mulatta*), the venous component of the LSC was also reported to comprise a single venous sinus that was minimally interrupted by trabeculae located medial to the internal carotid artery.

Clival Segment

Moving posteroinferiorly along the skull base, the EDNAC extends down the length of the clivus—a shallow intracranial depression on the basilar process of the occipital bone (Figures 1B and 2C). The EDNAC thins out markedly in the clival segment and is reduced to scant patches of adipose tissue bestrewn among plentiful veins.[2] These veins include Breschet's veins, which are continuations of the venous channels in the LSC.[5,12,19] The clival segment also contains the basilar venous plexus, anterior condylar veins, and inferior petrosal sinus, in addition to their anastomotic connections.[9]

Spinal Segment

After it exits the foramen magnum, the EDNAC once again broadens out, and fatty tissue amply fills the epidural space along the length of the spinal canal (Figures 1B and 2D).[2,11] This caudal spinal portion is the fourth segment of the EDNAC and transmits the epidural veins of Batson, which anastomose extensively with Breschet's veins in the suboccipital region.[1,3,5,12] This fourth segment is also the interface between the neuraxial, epidural veins and their drainage out into

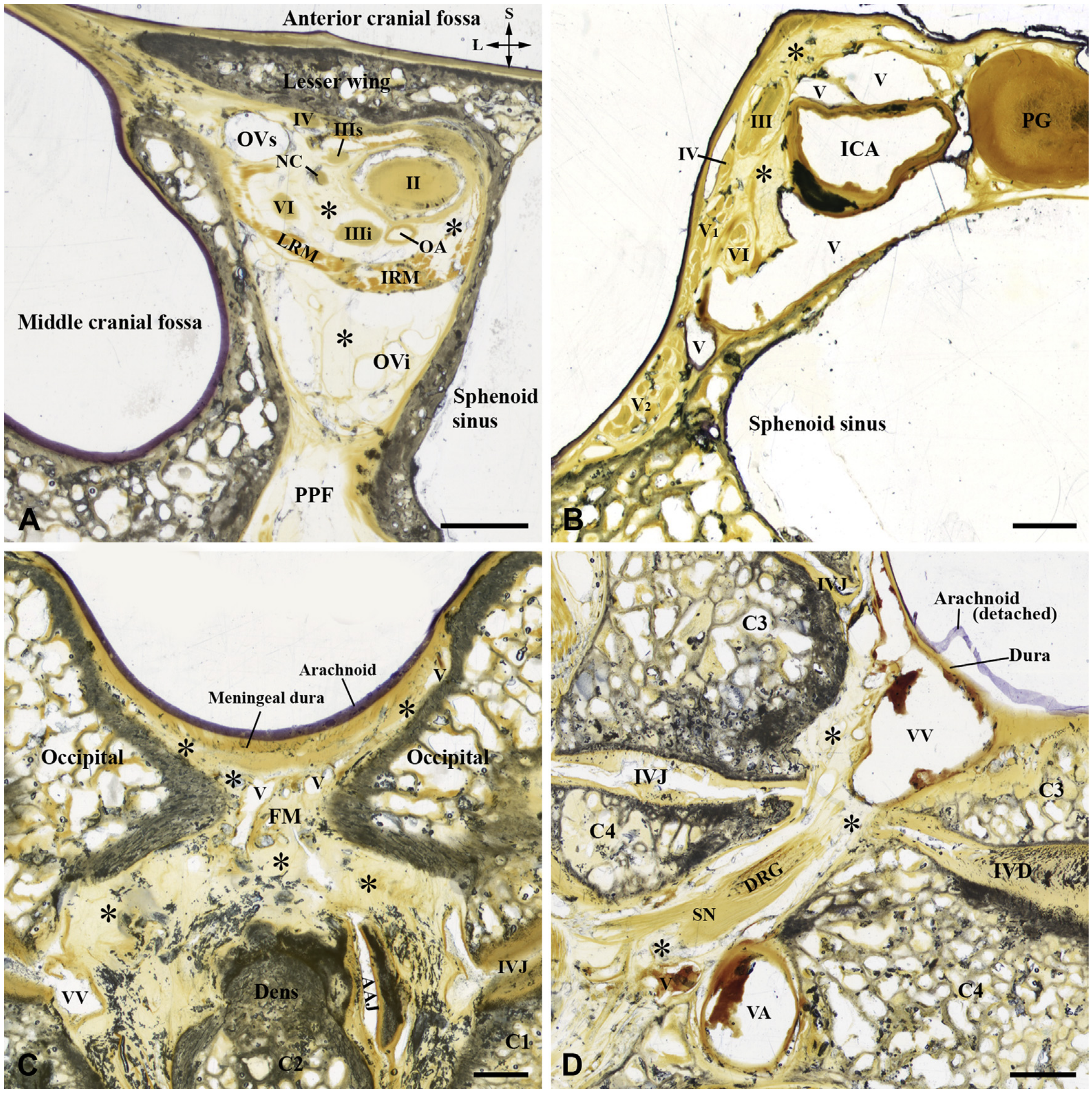

Figure 2. Plastinated coronal skull base and upper cervical sections showing the 4 main segments of the extradural neural axis compartment (EDNAC). From anterior to posterior, these include the (**A**) posterior orbit, (**B**) lateral sellar compartment, (**C**) clivus, and (**D**) spine. The adipovenous EDNAC matrix, which supports the traversing structures, is highlighted with *asterisks*. AAJ, atlantoaxial joint; C1, C2, C3, C4, cervical vertebrae 1, 2, 3, 4; DRG, dorsal root ganglion; FM, foramen magnum; ICA, internal carotid artery; II, optic nerve; III, IIIs, IIIi, oculomotor nerve, superior and inferior divisions; IRM, inferior rectus muscle; IV, trochlear nerve; IVD, intervertebral disc; IVJ, intervertebral joint; L, lateral; LRM, lateral rectus muscle; NC, nasociliary nerve; OA, ophthalmic artery; OVs, OVi, superior and inferior ophthalmic veins; PG, pituitary gland; PPF, pterygopalatine fossa; S, superior; SN, spinal nerve; V, vein; V1, V2, ophthalmic and maxillary nerves; VA, vertebral artery; VI, abducens nerve; VV, vertebral vein. Scale bar = 3 mm.

the extra-axial venous systems.[11] These interconnected, valveless epidural veins within the EDNAC have been grouped into what has been called the cerebrospinal venous system (CSVS): a continuum of venous plexuses and anastomoses including the orbital ophthalmic veins, LSC veins, Breschet's veins and surrounding networks, petroclival veins, Batson's veins, internal vertebral venous system, and terminal coccygeal veins.[5,9,12,13] The spinal EDNAC has 4 partitions demarked by the lateral margins of the thecal sac: the central anterior and posterior parts and the 2 lateral parts. The lateral spinal canal portion of the EDNAC also extends out into the intervertebral foramen (Figure 2D).[37]

Peripheral Extensions

The EDNAC may follow the neurovascular structures and extend peripherally into the spaces in the skull base and between the vertebrae. The intervertebral foramen is a well-known example illustrating the peripheral extension of the EDNAC (**Figure 2D**).[37,38] In the skull base region, Bernard et al.[4] verified the presence of the EDNAC within the jugular foramen (JF) in a cadaveric dissection study. The foraminal EDNAC is so significant it was incorporated as a feature of their new tripartite compartmental model of the JF.[4,39] They reported that the vicinal sigmoid and inferior petrosal sinuses appeared to course within the EDNAC before entering the foramen.[4] Liang et al.[40] also reported a venous plexus within the JF suspended in an adipose matrix, consistent with the adipovenous nature of the EDNAC.

Other than the JF, no peripheral extensions of the EDNAC in the skull have been studied. Some likely candidates for future investigation include the foramen rotundum (transmits CN V_2) and foramen ovale (transmits CN V_3 plus an accessory meningeal artery and emissary vein). It is likely that an EDNAC presence exists in these foramina considering 1) their proximity to an EDNAC expansion in the LSC, and 2) that the foramen ovale transmits both neural and vascular structures supported by an adipose matrix (**Figure 1A**). Taptas[27] attested that the 2 first divisions (V_1 and V_2) of the trigeminal nerve run within the EDNAC of the LSC. However, whether the EDNAC terminates before reaching these 2 foramina has not yet been determined. It is highly likely that the hypoglossal canal (transmitting CN XII, the posterior meningeal artery, and the anterior condylar vein) could also contain an extension of EDNAC because it is immediately adjacent to a significant deposition of fat in the spinal epidural space.

Boundaries

Defining the margins and limits of the EDNAC can be difficult in places because this compartment resides between 2 dural layers, which have varying configurations. The "interior" EDNAC boundary is relatively straightforward because it is demarcated by the inner, meningeal dura. The "exterior" limits of the EDNAC are defined by the endosteal dura and, when the EDNAC extends into a foramen, by the extracranial foraminal margins. Within the orbit, the EDNAC boundaries are well defined by the orbital bony margins and eyeball and optic nerve coverings. At the LSC, an encasement of meningeal dura forms the roof, lateral wall, and anterosuperior medial wall of the LSC to limit the EDNAC.[33,34,41] In contrast, the posteroinferior medial LSC wall is composed of a meshwork of loose fibers from the LSC that attach to the pituitary capsule, and the floor of the LSC comprises the endosteal dura.[34] At the clival segment, the EDNAC is contained by a roof of meningeal dura and an endosteal dural floor. It is unclear, however, how far the EDNAC extends laterally in this region. It might extend with the inferior petrosal sinus along the petro-occipital fissure. The spine has a well-defined EDNAC component that is limited interiorly by the meningeal dura surrounding the spinal cord. The endosteal dura forms the exterior border intraspinally. However, exteriorly, the EDNAC opens into the paravertebral adipose space via the intervertebral foramen (**Figure 2D**). Xu et al.[37] delineated the exterior EDNAC boundary in the spine as a line extending from the posterolateral margin of the vertebral body or intervertebral disc to the most lateral aspect of the intervertebral joint.

Functions

The fat in the orbital enlargement of the EDNAC contributes to eye function, specifically, by facilitating triaxial movement.[7,10] In the spine, this fat is thought to facilitate movement of the meningeal dura during flexion and extension of the vertebral column.[16] In the skull base, the filling of adipose tissue apparently acts to enhance minute movement between the 2 opposing sheets of dura.[10] Elsewhere, such as the foramina and channels in the skull base and the intervertebral foramina, the main function of the EDNAC is to cushion the neurovascular structures as dural fibers contribute to their coverings.[37] Considering the EDNAC's distribution, it is evident that it tends to be more substantial and enlarged in areas transmitting major neurovascular elements, as exemplified by the expansions in the orbit, LSC, and spine. As previously described, the EDNAC also sends an extension into the JF, and a fatty pocket is a noticeably significant feature that surrounds the nerves and inferior petrosal sinus within the anterior foramen.[4,40] Although hardly described in reported studies, it is likely that the adipose component of the EDNAC also acts to support and protect the nerves and vessels within the orbit, LSC, spine, and JF.

Pressure Transduction

Another important clinical implication regarding the EDNAC has been discussed by Depauw et al.[13] They described the relationship between its venous contents and the transmission of intra-abdominal pressure (IAP), intraspinal pressure (ISP), and intracranial pressure (ICP).[13] This hemodynamic interaction influences the CSVS pressure through 2 mechanisms. First, an increased IAP will generate a pressure gradient that shunts blood back through the pelvic venous plexuses into the spinal column veins, causing congestion of the spinal venous blood and increasing the ISP, which can extend up into the cranial venous systems, increasing ICP. A raised IAP can also generate an elevated intrathoracic pressure, and the resulting backpressure will hinder drainage of intracranial cerebrospinal fluid and blood via the jugular veins, which will ultimately lead to an increased ICP. The surgical complications of increased ISP and ICP can include intraspinal venous clogging, brain prolapse, and swelling during posterior fossa surgery, as well as potentially severe perioperative bleeding that will obscure the visual field working area.[13] Because of the EDNAC's pivotal role as a venous pressure conduit, Depauw et al.[13] advised that patients should be positioned prone for procedures on the spine or brain and have their abdomen hanging free using thoracolumbar supports to minimize or prevent a pressure increase in the spinal and/or intracranial compartments.

Insufflation of the abdomen during laparoscopic surgery is another method by which the IAP can become elevated, which, in turn, will increase the intrathoracic pressure, ISP, and ICP, as outlined previously. Perioperative visual disturbance or loss has been reported as an uncommon side effect after such a procedure.[42-46] This presumably results from the transmission of IAP along the spine into the skull base EDNAC segments and then through into the orbit, causing increased intraocular pressure (IOP). Adisa et al.[45] reported that the resultant intraocular venous congestion in the orbital EDNAC segment can manifest as perioperative visual impairment via ischemic optic neuropathy or retinal vascular occlusion.

This phenomenon of an elevated IOP can be further exacerbated by patient positioning during operations, particularly in the steep Trendelenburg and prone jackknife positions where the effects of gravity, in tandem with an increased IAP, can further elevate ICP and IOP.[44,45,47-49] Such a prolonged head-down orientation during surgical procedures should best be avoided for fragile patients (e.g., those with a diagnosis of coronavirus disease 2019). A number of recent reports have emphasized the use of the prone position for surgery in this patient group as this position will minimally alter IAP and IOP.[50-53] Nonetheless, some anesthetic medications, in particular, propofol, have been reported to mitigate an increased IOP and its sequelae during surgery even in the presence of an increased IAP and steep patient positioning.[54-58]

Controversy

It has been claimed that all of the cranial sinuses lie in the "interperiosteodural space."[14,15] Although some general features characterize the periosteal and meningeal dural layers, the border between them is not distinct.[59] The walls of the dural venous sinuses are only composed of dural fibers lined with endothelium.[17] Therefore, the inter periodural space might not be equivalent to the EDNAC, which has been defined as an adipovenous space.[1,2,16] Several points of disagreement also exist regarding the EDNAC in reported studies. François et al.[7] contradicted the 4-segment subdivision of the EDNAC described by Parkinson,[2] instead reporting an orbital (rostral), LSC (middle), and spinal (caudal) portion. However, their alternative model failed to include the clivus, which has clinical implications in the spread of tumors.[7] Bernard et al.[4] also reported that the EDNAC "sometimes" contains fat. In contrast, François et al.[16] described ubiquitous fat tissue as "a primary condition for the interperiosteodural concept." In a microdissection study of 14 specimens, Kehrli et al.[25] reported that the LSC holds "widely anastomosed sinuses, and not veins," in disagreement with the reports of distinct veins described by Parkinson[1,2] and others.

Pathological Entities

The vast majority of EDNAC-related pathologies are cancerous in nature and can affect any segment of the EDNAC. A variety of extradural and intradural tumoral lesions associated with the EDNAC have been reported in the orbit,[60,61] LSC,[62,63] clivus,[64] and spine.[65] Terrier et al.[66] described irregular spheno-orbital meningiomas that had sent extensions into the periorbital region, likely by spreading along the adipose corridor of the EDNAC. Angiolipomas are especially rare types of neuraxial tumors that arise directly from the EDNAC adipose tissue. They are contained by the 2 dural layers, and therefore illustrate the EDNAC concept rather well.[16,67,68] These fatty lesions are much more prevalent in the spine compared to the skull base because there exists a significant, stabilizing fatty matrix.[69] The valveless CSVS in the EDNAC can also be used for dissemination by metastatic cancer. Rao et al.[12] reported a cervical carcinoma that had infiltrated the clival EDNAC via the hematogenous CSVS route. In another report, Gasco et al.[5] described the spread of a prostate adenocarcinoma up through the CSVS into the skull base, which formed a tumor within Meckel's cave, lateral to the LSC. The JF, with its significant anterior pocket of fat, represents a typical example for invasive growth of extrinsic tumors or expansion of intrinsic tumors into the EDNAC. JF tumors such as paragangliomas and schwannomas frequently exploit the soft adipose matrix of the EDNAC as a conduit for infiltration, following the paths of least resistance.[16,70] Paragangliomas are the commonest JF tumors and are unencumbered by a capsule, allowing for aggressive invasion of EDNAC pockets to produce extensive, irregular lesions.[70-72] Direct expansion of tumors within the EDNAC will be influenced by a number of elements, including the EDNAC arrangement, dural fibrous network configuration, restrictive bony walls, and mechanical barriers formed by crossing neurovascular structures.

Another pathological entity associated with the EDNAC is epidural hemorrhage of the occupying blood vessels, leading to bleeding between the dural layers.[73,74] Known as a spinal epidural hematoma, it involves rupture of the epidural vessels (Batson's veins) in the spinal segment of the EDNAC along the thoracocervical or thoracolumbar spine.[75,76] This condition is thought to be due to trauma, vascular malformations, and anticoagulants, among others, and results in hematoma formation within the epidural space, causing compression of the spinal cord and concomitant neurological symptoms.[77-81]

CONCLUSIONS

The present narrative review of the reported data has shown that the EDNAC is a relatively obscure compartment with a multitude of roles and functions. The EDNAC is an intricate, extradural, neuraxial continuum consisting of adipovenous tissue, epidural veins, and traversing neurovascular structures. It can be subdivided into 4 segments (i.e. orbital, lateral sellar, clival, and spinal) and 1 transitional zone (LSOJ); (**Figure 1**). Peripherally, the EDNAC extends into the intervertebral foramina[37] and JF[4,39,40] however, no research has yet investigated the presence of the EDNAC in other skull base foramina. The precise borders of the EDNAC have not been fully elucidated, and are still somewhat vague in places (e.g., the clival segment and dural venous sinuses).

The EDNAC is responsible for eyeball movement, facilitating movement between the 2 dural layers, and supporting major nerves and vessels. The spinal segment of the EDNAC also has a noteworthy role as a venous pressure conduit that transfers IAP into the spinal and intracranial compartments.[13] Perhaps the most pertinent function of the EDNAC from a clinical perspective is that it represents a soft tissue corridor throughout the neuroaxis that cushions the neurovascular dural sheathes as they traverse the skull base and vertebrae, and can function pathologically as a conduit for tumor expansion. The EDNAC also plays a role in perineural tumor spread, which is a recognized pattern of tumor dissemi nation occurring along the potential space between the nerve and its coverings, and has been associated with the risk of tumor recurrence and greater morbidity and mortality.[82] It is therefore vitally important for clinicians to be aware of the EDNAC in terms of both its anatomical arrangement and its functional roles. This understanding could influence surgical plans for regions with a significant EDNAC presence and will help with appreciating the patterns of extradural tumor expansion and optimizing surgical approaches. This review has also shown that the EDNAC has many facets to its anatomy and function that remain to be unveiled and clarified by future investigations.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Jacob D. Bond: Conceptualization, Methodology, Data curation, Investigation, Formal analysis, Writing - original draft, Critical revision, Writing - review & editing. **Ming Zhang:** Conceptualization, Methodology, Funding acquisition, Data curation, Formal analysis, Critical revision, Writing - review & editing, Approval of final version, Supervision.

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