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ORIGINAL ARTICLE

Labelling of individual ependymal areas in the third and fourth ventricle of the human brain: ependymal tables

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Abstract

The ependymal lining of the walls of the human brain third ventricle (3v), fourth ventricle (4v) and aqueductus cerebri (A) was studied. For a better localization of different ependymal areas, they were labelled by periventricular structures that represent a basic and stable part of brain nerve tissue and they are localized most closely to ventricle walls. Labelling of individual ependymal areas of the ventricle walls was composed of the number of a brain ventricle, letters: E – ependyma and abbreviation of a Latin name of the periventricular structure, e.g., the corpus mammillare is "CM". Labelling of ependyma over the corpus mammillare is" 3vE – CM "Results of labelling of ependymal areas were arranged in the form of tables called "ependymal table "(ET), i.e., ET for 3v; ET for 4v; ET for A. It is believed that labelling of individual ependymal areas according to periventricular structures could be useful for unambiguous labelling of ependyma of the ventricle walls and will help to a mutual comparison of the same types of ependymal areas studied by various authors.

Keywords Human central nervous system; walls of the third and fourth brain ventricles; cerebral aqueduct; ependymal areas; ependymal tables

Abbreviations

3v	Ventriculus tertius (third ventricle)
4v	Ventriculus quartus (fourth ventricle)
A	Aqueductus cerebri (cerebral aqueduct)
CA	Commissura anterior (anterior commissure)
cc	Canalis centralis medullae spinalis (central canal of spinal cord)
CF	Corpus fornicis (fornix body)
CHO	Chiasma opticum (optic chiasm)
CM	Corpus mammillare (mammillary body)
COI	Colliculus inferior (inferior colliculus)
CP	Commissura posterior (posterior commissure)
FI	Fossa interpeduncularis (interpeduncular fossa)
FIV	Foramen interventriculare (interventricular foramen)
H	Hypothalamus (hypothalamus)
I	Infundibulum (infundibulum)
Lv	Ventriculus lateralis (lateral ventricle)
NCT	Nucleus centromedialis thalami (centromedial nucleus of thalamus)
NH	Nucleus habenularis (habenular nucleus)
NMT	Nuclei mediales thalami (medial nuclei of thalamus)
NPI	Nuclei praeoptici (preoptic nuclei)
P	Pons (pons)
PC	Pedunculus cerebri (cerebral peduncle)
PCS	Pedunculus cerebellaris superior (peduncle cerebellar superior)
T	Thalamus, (thalamus)
TMT	Tractus mamillothalamicus (mammillothalamic tract)
VMS	Velum medullare superius (superior medullary velum)

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Introduction

Ependymal cells were discovered by Purkyne in 1836, and studied quite extensively in the human central nervous system as well as in various animals (Studnička 1900; Opalski 1934; Schimrigk 1966; Bruni et al. 1985; Del Bigio 1995; Barnabé-Heider et al. 2010; Hugnot and Franzen 2011; Jiménez et al. 2014; Haemmerle et al. 2015).

Ependymal cells are localized in the innermost part of brain "ventricle walls", and they represent an interface between two different physical environments, they are in the contact with cerebrospinal fluid (CSF) and on the other side with the brain nervous tissue.

In the literature, there is no uniform naming of various structural types of ependyma, e.g. standard type of ependyma, specific subtypes of ependyma, etc. (Leonhardt 1980; Hauwel et al. 2005; Mothe and Tator 2005 and others).

In this work, the expression "ependyma "stands exclusively for ependymal cells (Del Bigio 2010). The term "ventricular wall "stands for: 1 – ependymal cells, they form so-called ependymal component and 2 – non-ependymal components of the wall, e.g., nerves and glial cells, nerve fibres that are localized close to the ependymal cells.

In this work, it is intended to propose for easier reference (i) the labelling of ependymal areas of the walls of the human brain ventricles and (ii) summarize the results of labelling in the form of ependymal tables.

It is believed that the proposed labelling of ependymal areas will help to compare the same type of ependymal cells in health and pathology studied by individual authors and to get the answer, if the achieved results of study are valid only for one type of ependymal cells or for all ependymal cells in the studied part of the human ventricle system.

Material and methods

Five human brains from individuals of both sexes aged from 27 to 60 years were used for the study (Table 1).

The brains were removed by a standard procedure 24–48 h after death, the brains were fixed in 10% neutral formaldehyde for 30 days.

The fixed brains were sliced in the auxiliary device to obtain frontal brain slices of equal thickness (0.5 cm). They were numbered 1–19 (Fig. 1). The first brain slice

Table 1 Characteristics of the individuals whose brains were analysed

Age (years)	Sex	Cause of death
27	Female	Neoplasma renis
42	Male	Infarctus myocardii
50	Male	Morbus hypertonica
51	Female	Neoplasma mammae
60	Male	Embolia truncus pulmonalis

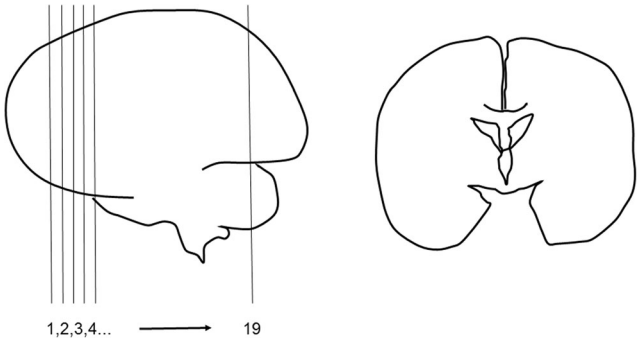

Fig. 1 **Right:** Sectioning of the brain in the frontal plane (sections 1–19). **Left:** Scheme of the frontal brain section

was performed in the distance 2 cm from the frontal pole of the brain. The distance of each following frontal brain slice was 0.5 cm from the previous one. Accordingly, the last (the nineteenth) slice was 11 cm distant from the frontal pole of the brain (Fig. 1). The third ventricle appeared in frontal sections 7–12, beginning in the region of chiasma opticum; the aqueductus cerebri in sections 13–15 (as a continuation of the lumen of the third ventricle); the fourth ventricle in section 15–16 (as a continuation of the lumen of aqueduct) (Fig. 2).

The brain sections were photographed by the standard technique.

From large brain slices, small pieces of ventricle wall were excised and embedded in paraffin 10 μm histological sections were stained with hematoxyline-eosine and cresyl blue dyes (Wolf 1966) and investigated under light microscopy. Based on results obtained by the light

Fig. 2 Scheme of the ventricle system. Lv-lateral ventricle, 3v-the third ventricle, A-aqueductus cerebri, 4v-the fourth ventricle, cc-central canal of the spinal cord. Arrow indicates foramen interventriculare

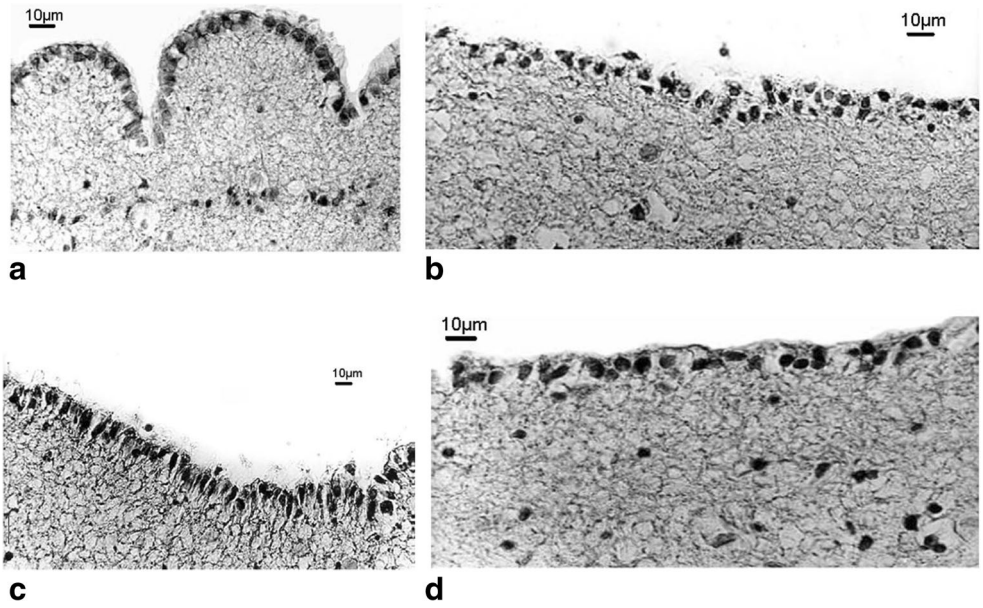

Fig. 3 Micrographs of some types of ependyma of the third ventricle in different ependymal areas (see also Fig. 5): **a** – regular cuboidal ependyma in 3vE-NPI, **b** – stratified irregular ependyma in 3vE-H, **c** – stratified tanycyte ependyma in 3vE-I, **d** – irregular cuboidal ependymal in 3vE-NCT

microscopy we divided the ependymal lining of various regions of the human brain ventricles into regular and irregular type of ependyma. Localizaton of nuclei of ependymal cells was the main criterion for classification. The type of ependyma where the size of nuclei and the distances between them were equal, we called regular. In contrast, the ependyma where the nuclei of ependymal cells are of different size and distances between them, we called irregular.

The periventricular structures were chosen as reference nerve tissue for labelling of the ependymal areas, and they were used for the creation of the labelling (naming) of individual ependymal areas. For better orientation the result of labelling of the individual ependymal areas was fitted into ependymal tables.

Results

The unpaired third ventricle is situated in the medial sagittal plane of the mesencephalon, and it spreads out as the hollow cavity around the circumference of the adhesio interthalamica.

In the preoptic region, the ventricle walls are lined with cuboidal ependyma. The cell nuclei are round or oval.

In the region of the frontal group of hypothalamic nuclei, the third ventricle on frontal brain section has a slot-like shape, and lateral walls are lined with cuboidal, stratified and tanycyte type of ependyma.

In the region of central groups of hypothalamic nuclei, the walls of the third ventricle are covered by cuboidal, stratified regular and irregular and tanycyte ependyma.

Table 2 Occurrence of individual types of ependyma in the third ventricle

Parts of 3v	Type of ependyma				
	Regular		Irregular		Tanycyte
	Cuboidal	Stratified	Cuboidal	Stratified	One-to stratified
Regio praeoptica: lateral walls	+			+	+
Hypothalamus (H): Anterior part of H lateral walls	+	+			+
Central part of H lateral walls	+	+		+	+
Posterior part of H lateral walls	+		+		+
Infundibulum: lateral walls					+

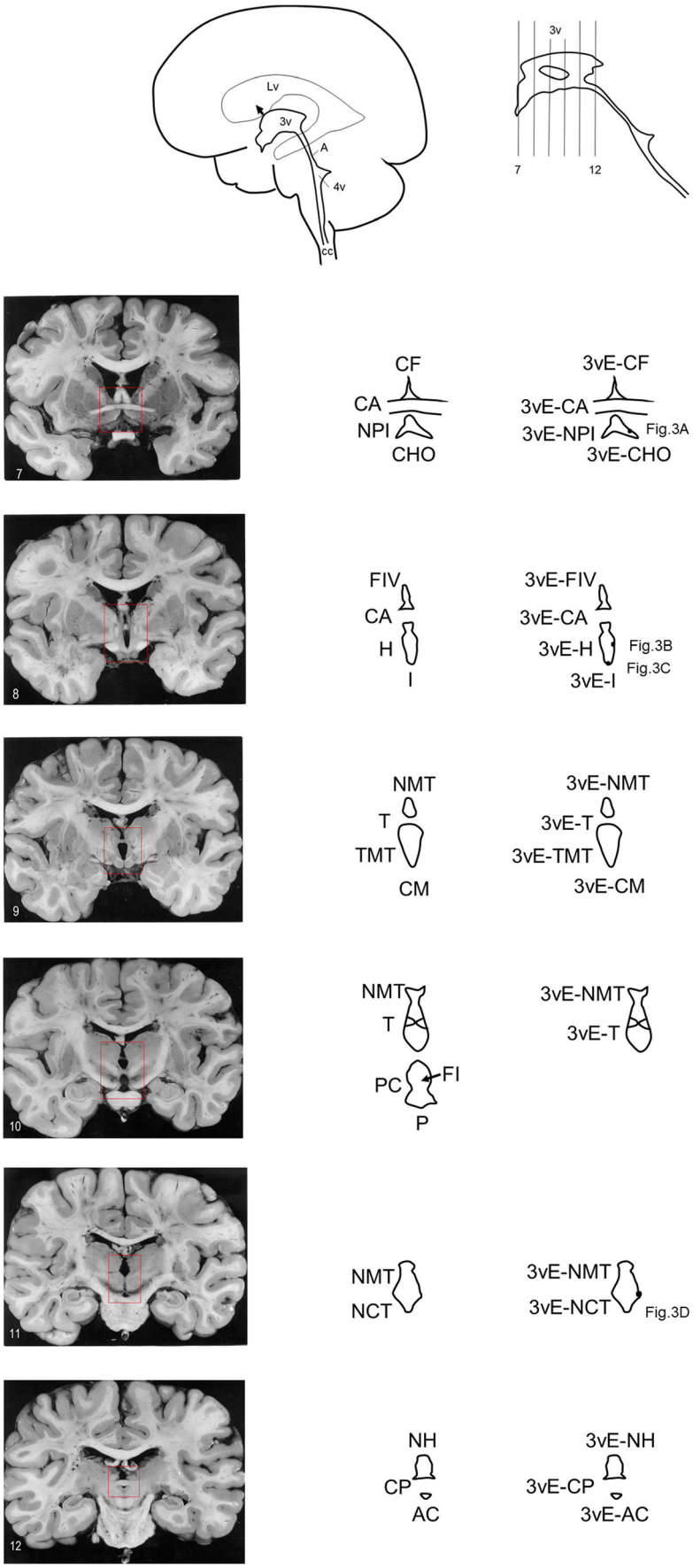

Fig. 4 **Top:** Scheme of the brain ventricle system and places of the brain frontal sections numbered 7–12 **Bottom:** frontal brain sections; cross sections of the third ventricle; abbreviation of periventricular structures; labelling of individual ependymal areas. Position of black dots correlate with the micrographs demonstrated in Fig. 3.

Table 3 Labelling of ependymal areas in the third ventricle

Third ventricle				
Brain section	Wall	Periventricular structure	Abbreviation	Labelling of ependyma
7	lw	Corpus fornicis	CF	3vE-CF
		Commissura anterior	CA	3vE-CA
	vw	Nuclei praeoptici	NPI	3vE-NPI
		Chiasma opticum	CHO	3vE-CHO
8	lw	Foramen interventriculare	FIV	3vE-FIV
		Commissura anterior	CA	3vE-CA
		Hypothalamus	H	3vE-H
	vw	Infundibulum	I	3vE-I
9	lw	Corpus mammillare	CM	3vE-CM
		Tractus mamillothalamicus	TMT	3vE-TMT
		Thalamus	T	3vvE-T
		Nuclei mediales thalami	NMT	3vE-NMT
10	lw	Nuclei mediales thalami	NMT	3vE-NMT
		Thalamus	T	3vE-T
		Pedunculus cerebri	PC	3vE-PC
	vw	Pons	P	3vE-P
11	lw	Nuclei mediales thalami	NMT	3vE-NMT
		Nucleus centromedialis thalami	NCT	3vE-NCT
12	lw	Nucleus habenularis	NH	3vE-NH
		Commissura posterior	CP	3vE-CP
		Aqueductus cerebri	AC	3vE-AC

In the caudal direction, in the posterior part of the hypothalamus, the wall lining consists of cuboidal and single to the stratified irregular type of ependyma. In the region of infundibulum, the ependymal lining is constituted of tanycyte cells. In the roof of the ventricle, plexus choroideus ventriculi tertii is situated.

Some types of ependyma (regular and irregular) localized in the human third ventricle are demonstrated in Fig. 3.

Localization of various structural types of ependyma present in the third ventricle is viewed in Table 2.

On studying the microscopic structure of the ependyma, it was ascertained that a certain type of ependyma as a part of the ventricle wall is bound to a certain region.

The labelling of ependymal areas in the third ventricle is composed of several letters. Letter of ventricle: 3v – third ventricle ;letter "E" (means "ependymal") and letters for the abbreviation of the Latin name of the periventricular structure (e.g., the corpus mammillare abbreviation is "CM"). The labelling of the ependymal area over the corpus mammillare is thus "3vE-CM".

The proposed labelling of the ependymal areas may offer several advantages: 1 – the labelling gives a name as well as localizes the ependymal areas; 2 – the labelling prevents the interchange of different types of ependymal areas; 3 – the labelling avoids a false interpretation in experiments.

Labelling and localization of ependymal areas of the third ventricle are shown in Fig. 4 and summarized in "ependymal table of the third ventricle" (Table 3).

Table 3 shows the number of a brain section, lateral wall (lw) and ventral wall (vw) of the third ventricle; the name of periventricular structures, its abbreviations; labelling of individual ependymal areas of the third ventricle.

Suggestion for labelling of non-ependymal structures (nE) of the wall of the third ventricle (3v), e.g., close to the hypothalamus (H) is 3v-nE-H.

The lumen of the third ventricle continues in aqueductus cerebri. The scheme of the aqueductus cerebri and frontal brain sections (13–15) is demonstrated in Fig. 5.

The walls of aqueductus cerebri are lined with regular and irregular cuboidal, and irregular stratified ependymal. The thickness of ependymal lining is different in various regions. In the caudal direction, the lumen of aqueductus cerebri extends in several foldings lined with cuboidal ependyma. Individual types of ependyma that line the walls of the aqueductus cerebri according to histological criteria are shown in Table 4.

For labelling and localization of individual ependymal areas of the aqueductus cerebri we used the periaqueductal nerve structures, as it is shown in Fig. 5 and summarized in "ependymal table of aqueductus cerebri "(Table 5).

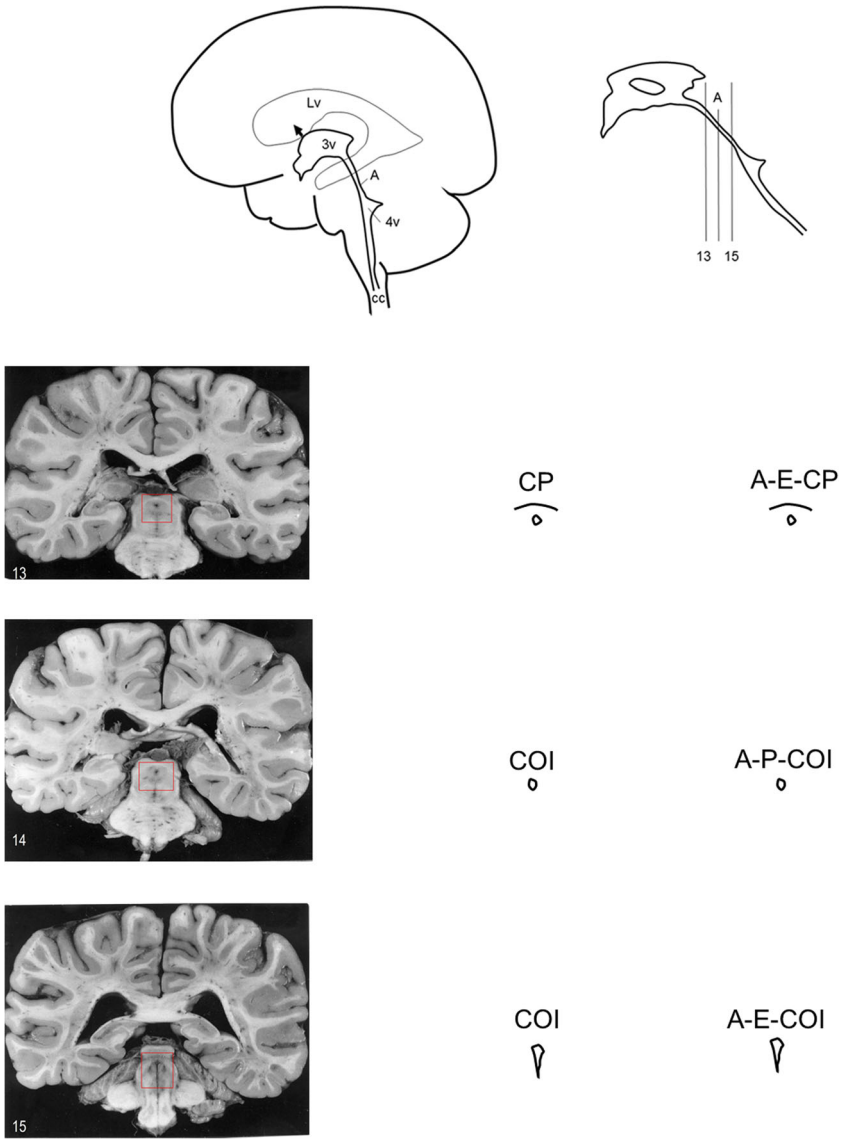

Fig. 5 **Top:** Scheme of aqueductus cerebri **Bottom:** Frontal brain sections (13–15); cross-sections of aqueductus cerebri, an abbreviation of periaqueductal nerve structures; labelling of ependyma in aqueductus cerebri

Table 5 shows the number of a brain section, lateral wall of aqueductus cerebri (lw), name of periaqueductal structures, abbreviations of periaqueductal structures, and labelling of ependyma of the wall of aqueductus cerebri.

Suggestion for labelling of non-ependymal structures (nE) of the wall of aqueductus cerebri (A) close to commissura posterior (CP) is, e.g., A-nE-CP.

Table 4 Types of ependyma in aqueductus cerebri

Cerebral aqueduct	Type of ependyma		
	Regular	Irregular	
	Cuboidal	Cuboidal	Stratified
Lateral walls	+	+	+

Table 5 Labelling of ependymal areas in aqueductus cerebri

Aqueductus cerebri				
Brain section	Wall	Periaqueductal structure	Abbreviation	Labelling of ependyma
13	lw	Commissura posterior	CP	A-E-CP
14	lw	Colliculus inferior	COI	A-E-COI
15	lw	Colliculus inferior	COI	A-E-COI

Table 6 Types of ependyma in the fourth ventricle

Parts of 4v	Type of ependyma			
	Regular	Irregular		
	Cuboidal	Cuboidal	Cuboidal to columnar	Stratified
Roof		+		
Lateral walls	+			+
Floor		+	+	

In the caudal direction, aqueductus cerebri continues in the fourth ventricle, ventriculus quartus. The ventricular floor comprises fossa rhomboidea with sulcus medianus stretched through it. The fourth ventricle leads to canalis centralis. The roof of the fourth ventricle is lined with irregular cuboidal ependymal. Lateral walls of the fourth ventricle are lined with monolayered ependyma, which in some areas continues in stratified ependyma. The floor of the fourth ventricle is lined with irregular cuboidal ependyma. The ventricle wall foldings are present in lateral walls. They are lined with irregular cuboidal to columnar ependyma.

Types of ependyma according to histological criteria localized on the wall of the fourth ventricle are listed in Table 6.

To reach more exact localization and specific labelling of individual ependymal areas of the walls of the fourth ventricle, the periventricular nerve structures localized most closely to the ventricular walls of the fourth ventricle were chosen as reference nerve tissue and their abbreviations were included in the naming of ependymal areas. The large brain sections of

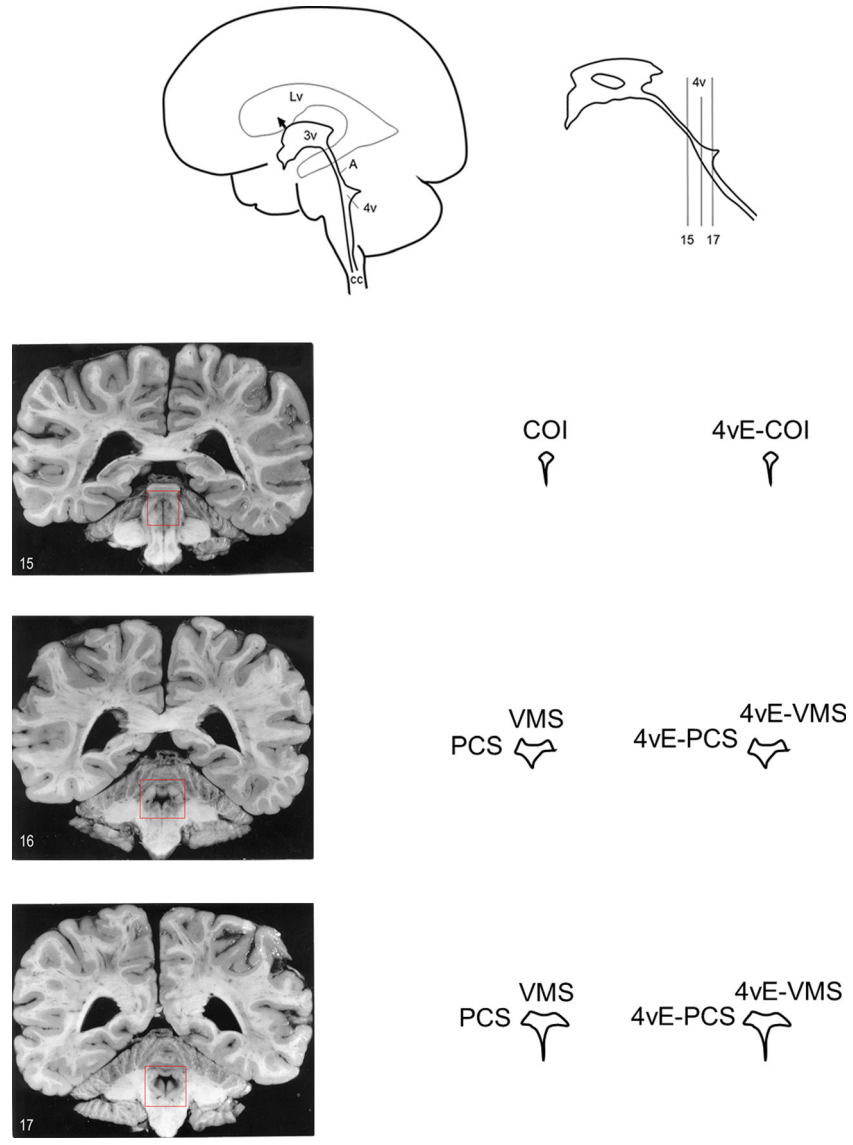

Fig. 6 **Top:** Scheme of ventriculus quartus (4v) **Bottom:** Frontal brain sections (15–17). Cross-sections of ventriculus quartus, abbreviation of periventricular structures; labelling of individual ependymal areas of the ventriculus quartus

Table 7 Labelling of individual ependymal areas in the fourth ventricle walls

Ventriculus quartus				
Brain section	wall	Periventricular structure	Abbreviation	Labelling of ependyma
15	dw	Colliculus inferior	COI	4vE-COI
16	dw	Velum medullare superius	VMS	4vE-VMS
	lw	Pedunculus cerebellaris superior	PCS	4vE-PCS
17	dw	Velum medullare superius	VMS	4vE-VMS
	lw	Pedunculus cerebellaris superior	PCS	4vE-PCS

the fourth ventricle and localization of labelled ependymal regions are demonstrated in Fig. 6 and summarized in "ependymal table of the fourth ventricle "(Table 6).

Table 7 shows the number of a frontal brain section (15–17), walls of the fourth ventricle: dorsal (dw), lateral (lw); the name of periventricular structures, their abbreviations, labelling of individual ependymal areas of the fourth ventricle.

Suggestion for labelling of non-ependymal structures (nE) of the fourth ventricle (4v) wall: e.g., the area near velum medullare superior (VMS) is 4v-nE-VMS.

Discussion

In the course of time and as a result of improving imaging techniques, the ependyma's morphology and functons are becoming more known. However, there are still numerous obscured connections related to the ependyma, which have to be revealed. Several authors presented comprehensive reviews of the ependyma's morphology and functions (Del Bigio 2010). Ependyma is often the subject of research because of its connection with the function and flow of the cerebrospinal fluid (Veening and Barendregt 2010). Deficient development of ependyma is linked to congenital hydrocephalus and other abnormal conditions (McAllister et al. 2017; Jiménez et al. 2014). These authors did not put stress on the heterogeneity of the human ependyma and did not specify particular regions of ependymal lining within the human brain ventricular system.

It is well known that the microscopic structure of the ependymal lining which covers the walls of human brain ventricles is not the same. Therefore, it is very difficult to denote some of the ependymal cell types studied, as being so-called "standard type of ependyma "of the human brain ventricles. Actually, each region of the ventricle system possesses a particular characteristic type of ependyma (Bruni et al. 1972; Scott et al. 1973; Mathen 2008). Therefore, when investigating the ependyma, it is necessary to specify not only the structure of the ependymal area, but also its location within the walls of human brain ventricles.

For easier reference we suggested labelling of individual ependymal areas not only according to their structures but also name (categorize) them according to localization with the help of periventricular nerve structures. The periventricular structures are stable part of brain nerve tissue. For this quality they were chosen as reference nerve tissue and they were used for the labelling (naming) of individual ependymal areas (Mitro 2014; Mitro et al. 2018).

The proposed method of the naming of ependymal areas can assist to obtain the answer whether certain pathological changes of ependyma are related to only one type of ependymal area or all types of ependymal areas in investigated human brain ventricles.

We believe that the suggested technique of labelling of the individual ependymal areas is universal and will fulfil the appointed goals, e.g., to compare the same type of ependymal cells in health and pathology.

Conflict of interest statement The authors declare that they have no conflict of interest.

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References

Barnabé-Heider F, Göritz CH, Sabelström H, Takebayashi H, Pfrieger FW, Meletis K, Frisén J (2010) Origin of new glial cells in intact and injured adult spinal cord. Cell Stem Cell 7:470–482. https://doi.org/10.1016/j.stem.2010.07.014

Bruni JE, Montemurro DG, Clattenburg RE, Singh RP (1972) A scanning electron microscopic study of the ependymal surface of the third ventricle of the rabbit, rat, mouse and human brain. Anat Rec 174:407–419

Bruni JE, Del Bigio MR, Clattenburg RE (1985) Ependyma: normal and pathological. A review of the literature. Brain Res 356:1–19

Del Bigio HB (1995) Ependymal reactions to injury. A review. J Neuropathol Exp Neurol 54:1–15

Del Bigio MR (2010) Ependymal cells: biology and pathology. Acta Neuropathol 119:55–73. https://doi.org/10.1007/s00401-009-0624-y

Haemmerle CA, Nogueira MI, Watanabe IS (2015) The neural elements in the lining of the ventricular-subventricular zone: making an old story new by high-resolution scanning electron microscopy. Front Neuroanat 9(134). https://doi.org/10.3389/fnana.2015.00134

Hauwel M, Furon E, Canova C, Griffiths M, Neal J, Gasque P (2005) Innate (inherent) control of brain infection, brain inflammation and brain repair: the role ofmicroglia, astrocytes, "protective" glial stem cells and stromal ependymal cells. Brain Res Brain Res Rev 48:220–233. https://doi.org/10.1016/j.brainresrev.2004.12.012

Hugnot JP, Franzen R (2011) The spinal cord ependymal region: a stem cell niche in the caudal central nervous system. Front Biosci 16: 1044–1059

Jiménez AJ, Domínguez-Pinos MD, Guerra MM, Fernández-LlebrezP P-FJM (2014) Structure and function of the ependymal barrier and diseases associated with ependyma disruption. Tissue Barriers 2(e28426):1–14. https://doi.org/10.4161/tisb.28426

Leonhardt H (1980) Ependym und zirkumventrikuläre Organe. In: Oksche A, Vollrath L (eds) Handbuch der mikroskopischen Anatomie des Menschen. Nervensystem 10 Teil: Neuroglia I. Springer - Verlag, New York

Mathen TC (2008) Regional analysis of the ependyma of the third ventricle of rat by light and electron microscopy. Anat Histol Embryol 37:9–18. https://doi.org/10.1111/j.1439-0264.2007.00786.x

McAllister JP, Guerra MM, Ruiz LC, Jimenez AJ, Dominguez-Pinos D, Sival D, den Dunnen W, Morales DM, Schmidt RE, Rodriguez EM (2017) Ventricular zone disruption in human neonates with intraventricular hemorrhage. J Neuropathol Exp Neurol 76:358–375. https://doi.org/10.1093/jnen/nlx017

Mitro A (2014) Method of labelling of individual ependymal areas according to periventricular structures of the rat lateral brain ventricles. Biologia 69:1250–1254. https://doi.org/10.2478/s11756-014-0421-5

Mitro A, Lorencova M, Kutna V, Polak S (2018) Labelling of individual ependymal areas in lateral ventricles of human brain: ependymal tables. Bratisl Lek Listy 119:265–271. https://doi.org/10.4149/BLL_2018_049

Mothe AJ, Tator CH (2005) Proliferation, migration, and differentiation of endogenous ependymal region stem/progenitor cells following minimal spinal cord injury in the adult rat. Neuroscience 131:177–187. https://doi.org/10.1016/j.neuroscience.2004.10.011

Opalski A (1934) Über lokate Unterscheide im Bau der Ventrikelwände beim Menschen. Z Ges Neurol Psychiatr 149:221–254

Schimrigk K (1966) Über die Wandstructur der Seitenventrikel und des dritten Ventrikels beim Menschen. Z Zellforsch 70:1–20

Scott DE, Kozlowski GP, Paull WK, Ramalingam S, Krobisch-Dudley G (1973) Scanning electron microscopy of the human cerebral ventricular system II. The fourth ventricle. Z Zellforsch 139:61–68

Studnička FK (1900) Untersuchungen über den Bau des Ependymas der nervösen Zentral-organe. Anat Hefte 15:303–430

Veening JG, Barendregt HP (2010) The regulation of brain states by neuroactive substances distributed via the cerebrospinal fluid; a review. Cerebrospinal Fluid Res 7:1. https://doi.org/10.1186/1743-8454-7-1

Wolf J (1966) Mikroskopická technika. SZN, Praha