Original scientific article
Izvorni znanstveni članak

Acta Med Hist Adriat 2026; 24(1);9-26
https://doi.org/10.31952/amha.24.1.1

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ON THE HISTORY OF THE TERMS *SUBSTANTIA ALBA* AND *SUBSTANTIA GRISEA* AND OTHER TERMS FOR COLOURED BRAIN SUBSTANCES

O POVIJESTI POJMOVA *SUBSTANTIA ALBA* I *SUBSTANTIA GRISEA* TE DRUGIH POJMOVA ZA OBOJENE TVARI U MOZGU

František Šimon[*], **Ema Pavľáková**[**], **Mária Šibalová**[***]

SUMMARY

This study explores the historical development of neuroanatomical terms that describe coloured brain substances, particularly substantia alba (white matter) and substantia grisea (grey matter), from a terminological perspective. Through a narrative review of major anatomical sources from antiquity to the early modern period, it traces how colour descriptors entered anatomical terminology and gradually came to denote distinct brain structures. While ancient anatomy lacked colour-based distinctions in brain anatomy, Arabian and Salernitan traditions introduced the idea of the brain being white. The earliest known use of the phrase substantia alba appears in 1502 in the printed version of a medieval pseudo-Galenic text De anatomia vivorum, but it could also be a later editor's interpolation of the text. Vesalius (1543) was the first to distinguish brain matter by colour, introducing terms corresponding to substantia alba and an early version of substantia grisea. By the

[*] Department of Classical Languages, Faculty of Arts, P. J. Šafárik University, Košice, Slovakia. ORCID: https://orcid.org/0000-0003-2094-1425.
[**] Institute of Medical Terminology and Foreign Languages, Faculty of Medicine, Comenius University, Bratislava, Slovakia. ORCID: https://orcid.org/0009-0009-6389-843X.
[***] Institute of Medical Terminology and Foreign Languages, Faculty of Medicine, Comenius University, Bratislava, Slovakia. ORCID: https://orcid.org/0009-0004-7943-5337.
Correspondence Address: František Šimon, Katedra klasickej filológie FF UPJŠ, Moyzesova 9, 04001 Košice, Slovakia. E-mail: frantisek.simon@upjs.sk.

late 18th century, multiple colour-based terms had been introduced to reflect distinct brain structures. Despite evolving anatomical knowledge, colour descriptors remained stable linguistic signs, often preceding or outlasting conceptual shifts.

***Keywords**:* substantia alba, substantia grisea*, colours, brain matters, anatomical terms*

Introduction

The earliest anatomical terms referring to macro-level parts of the human body are typically motivated by the shape of the anatomical structure, its position, or its relationship to other anatomical structures. One of the features used in naming was also the colour of the structure, as perceived by the pioneers of anatomical dissection. Examples include *medulla flava ossis* (yellow bone marrow), *pulpa rubra* (red pulp), and *corpus luteum* (yellow body). In the nervous system, examples also include *substantia alba* (white matter) and *substantia grisea* (grey matter). At the time these terms were coined, they served merely as a visual distinction within gross (macroscopic) anatomy, as these terms are "based on their appearance in freshly dissected material observed with the naked eye" (Swanson, 2015, p. 285). Differences in microscopic structure and function remained unknown to scientists for centuries after the earliest terminology for white and grey matter had been introduced. It is now recognised that *substantia grisea* "is grey because only a sparse amount of … myelin is present in it," whereas *substantia alba* is characterised by a high myelin content, which underlies its white appearance. (Feneis, 2000, pp. 292, 406). These now well-known facts are the result of scientific research in the 18th and 19th centuries, when a number of foundational discoveries were made in what would later become the field of neuroscience. Researchers identified myelin as the substance responsible for the whitish appearance of white matter and described the structure of nerve fibres (Boullerne, 2016, pp. 432–434). As a consequence of these advances, the distinction between *substantia grisea* and *substantia alba* ceased to represent a merely macroscopic, descriptive observation and came to designate two histologically distinct tissues.

Research on the histological structure of brain matter culminated in the late 19th century in the work of Santiago Ramón y Cajal, whose demonstration of the neuron as the fundamental structural unit of the nervous system laid the foundations of modern neuroscience (Carlos & Borrell, 2007, pp. 12–13). Since then, the development of neuropathology and the advent of neuroimaging technologies in the 20th century – including computed tomography and magnetic resonance imaging – have allowed the definition of increasingly precise relationships between individual clinical syndromes and the selective involvement of grey or white matter. Among them, at least the diagnosis of multiple sclerosis should be mentioned,

which relies to a significant extent on the observation of lesions in the white matter (Montalban et al., 2024, p. 852). Through clinicopathological correlations like this, the terms white matter and grey matter have undergone further semantic expansion: they have become clinical and diagnostic categories for classifying disorders of the nervous system. Their function has thus evolved from descriptive anatomical labels to histological labels and finally to clinically relevant concepts important to modern neurology, neuropathology, and neuroradiology. This trajectory demonstrates the continuing relevance of these historically rooted terms and the research on them in contemporary medical science.

Terminology evolves alongside knowledge; original terms often referred only to an approximate notion of concepts that were later defined more precisely. According to the theory of terminology, a term has linguistic form and content that represent the concept. A concept is a unit of content consisting of a set of characteristics (Cabré, 1998, p. 95). The terms are not fixed; they transform with the development of knowledge, leading to a continuous change in concepts. The phonetic form of the designation, the formal aspect of the term, is more constant (Drozd, 1973, p. 46). A linguistic label for a concept, a term, or part of a term, might have appeared before anatomy had arrived at its current understanding. A term may have referred to something that only approximated the later concept.

Colour as a descriptive feature in anatomical terminology appeared in brain anatomy long before anatomists began to distinguish brain structures based on their structure and function. The development of the understanding of the concepts *substantia alba* and *substantia grisea* from an anatomical perspective is presented by Clarke & O´Malley (1968) and Schmahmann & Pandya (2007).

The purpose of this terminological study is to examine the use of colour names in neuroanatomical terms, to supplement and clarify current knowledge about the development of names for the coloured parts of the brain from a terminological perspective. The screening question was whether colour codes, white and grey, or their synonyms were used in the description of the brain. The method used is a review of neuroanatomical terminology in major anatomical works from antiquity to the earliest international anatomical nomenclatures. The data were collected either directly from the works of important anatomists in the history of neuroscience, according to books on this topic (Finger, 1994; Clarke & O´Malley, 1968), or using search engines such as Google Books, HathiTrust, Internet Archive, and the Bium Paris databases. In addition to Greek texts and translations of medieval Arabian medicine, the review includes mainly Latin literature. This literature later formed the basis for unified anatomical nomenclatures, including those used

today. A distinct component of the source base consists of historical anatomical dictionaries.

Historical anatomical dictionaries

Sources that help answer the question of the origin of anatomical terms include medical dictionaries, particularly historical ones. However, there is no consensus in the most relevant dictionaries regarding the origin or authorship of these terms. Hyrtl (1880) and Marcovecchio (1993) do not include entries for these terms in their dictionaries. Barcia Goyanes attributes the terms *substantia alba* and *substantia grisea* to Malpighi in 1665 (1985, p. 356), and the term *substantia nigra* to Vicq d'Azyr in 1786 (1985, p. 361). Swanson, under the entries "grey matter" and "white matter," cites Meckel in 1817, but also mentions an earlier synonym by Gordon from 1815 (2015, pp. 285–286, 766–767). Swanson does not include the Latin forms *substantia alba* and *substantia grisea*, as he claims that the preferred language for anatomical standard terms is English with American spelling (Swanson, 2015, p. 4). However, the Latin term *substantia nigra* is included in his dictionary, with authorship attributed to Soemmerring in 1791, and an earlier synonym from Vicq d'Azyr in 1784 (Swanson, 2015, p. 644). Burdach also provides a historical overview of opinions and terms, starting with Piccolomini's work *Anatomicae praelectiones* from 1586 (1820, pp. 249–253).

Antiquity

Regarding ancient medicine, there is no evidence of anatomical investigation of the brain in the Hippocratic corpus (primarily 430–350 BC). Aristotle (384–322 BC) does not appear to have dissected the brain in as much detail as he did other organs. Herophilos from Kos (330–250 BC) is considered the father of neuroanatomy, and his innovative anatomical nomenclature survived, but few fragments of his work itself have been preserved, none of which concern the overall description of the brain. (Staden, 1989, pp. 155–160, 195–201). Galen (129–210 AD) did deal with brain substance, but only in terms of its consistency (Rocca 2003, pp. 28, 30, 82–86). Differentiation between white and grey brain matter has not been preserved in any ancient medical text.

The Middle Ages

In Arabian medicine, colour was already used as a descriptor in brain descriptions. The first to refer to the brain as a white organ was the Persian physician Haly

Abbas (930–994) in his book *Al-Malaki* (The Royal Book), from around the year 980 (*Trois traités*, 1903, pp. 278–279). The younger Persian physician, Ibn Sina (Avicenna, 980–1037), in his *Canon of Medicine* from 1025, distinguishes brain matter by its hardness and softness, but not by colour (*Trois traités*, 1903, p. 414). In fact, he does recognise white and grey matter, but he refers to them as covering and medullary matter (Mazengenya & Bhikha, 2017, p. 68).

Haly's *Royal Book*, translated by Constantinus Africanus (1020–1087), became part of the foundational medieval medical text *Pantegni*, around 1080 (Keil, 2005, p. 1096). As a result, the idea that the brain is white also appears in some of the four known anatomical works of the Salernitan medical school, the so-called *Salernitan anatomical demonstrations*. These are short treatises from the 12th century based on pig dissection (Corner, 1927, p. 44). The first, *Anatomia Cophonis* or *Anatomia porci*, describes the brain but does not mention its colour (Corner, 1927, pp. 48–50). The *Second Salernitan demonstration* already contains the statement *cerebrum …, quod album est,* "the brain …, which is white" (Benedict, 1920, p. 36). The *Anatomy of Maurus of Salerno* (1130–1214), in the Vatican manuscript Pal. Lat. 1097, Bl. 122, does not mention the colour of the brain (1921, p. 10), but in another manuscript of the same work, preserved in the 14th-century *Peneth Codex*, it is stated that the brain is white (Maurus, f. 106v). The *Fourth Salernitan demonstration*, attributed to Urso of Calabria (died in 1225), contains a similar phrase: *Est autem cerebrum album,* " the brain is white" (Sudhoff, 1928, p. 41).

From the period between 1130 and 1180 likely comes the *Anatomia Ricardi (Salernitani)*, also of Salernitan origin. It was also based on the *Pantegni*, and the phrase: *cerebrum est … subtile, molle, album, rotundum*, "the brain is subtle, soft, white, round", appears in its description of the brain (Ricardus, 1907, pp. 54–56, 82).

The pseudo-Galenic text *De anatomia vivorum*, dated to 1225 and erroneously attributed to Richardus Anglicus, represents a move beyond Salerno, as it likely originated in Paris or western Germany (Corner, 1927, p. 87). Terminologically, it marks a shift: whereas previous texts merely state that the brain is white, here, colour appears as an attribute. The edition based on manuscript No. 1634 of the Austrian National Library in Vienna includes the expression *nucha alba* (white spinal cord): *nerui qui sunt tanquam virgulta orta a cerebro et a nucha alba nuntia seu vicaria,* "nerves that emerge like little twigs from the brain and the white spinal cord as messengers or deputies" (Ricardus Anglicus, 1902, p. 1). However, the first printed edition of this anatomy modifies the phrase slightly: *nerui qui sunt tanquam virgulta orta a cerebro et a nuca a substantia alba nuntia seu vicaria,* "nerves that emerge like little twigs from the brain and from the spinal cord, from

the white matter, as messengers or deputies" (Pseudo-Galenos, 1502, p. 589). The adjective *alba* appears in the margin as a variant from another manuscript, and this could be considered the first known occurrence of the term *substantia alba* in anatomical texts, but it could also be an interpolation by a later editor of the text. This view would be supported by the several centuries' time difference between this use and the next one (Vesalius).

Another French author, Henri de Mondeville (1260–1320), known primarily as a surgeon who also performed human dissections, is the author of a work titled *Anatomie*. In his description of the brain, he returns to the Salernitan style: *cerebrum est membrum ... album,* "the brain is a white structure" (1889, p. 36).

Early renaissance pre-vesalian anatomy

Some pre-Vesalian anatomists did not concern themselves with the colour of the brain. The first among them was Mondino de Luzzi (1275–1326), born, educated, and active at the University of Bologna. His *Anathomia* from 1316 is a landmark in the history of anatomy (Clarke & O´Malley, 1968, p. 22). While Mondino discusses the brain substance in his work and refers to it as *substantia medullaris*, he does not mention its colour. This also applies to Alessandro Achillini (1463–1512), a professor of philosophy in Bologna with anatomical interests. In his anatomical work *Annotationes anatomicae*, the *substantia cerebri* carries no colour descriptor (1520, p. XIIr).

Another group of anatomists returned to Haly Abbas and his statement that the brain is white. Among them was Hieronymo Manfredi (1430–1492), a professor at the University of Bologna, who stated in his *Anothomia* from c. 1485 that "the brain is of the substance like marrow, white" (1917, p. 108). Niccolò Massa (1499–1569) also stated that the brain substance is white and soft (1536, p. 83v). Similarly, the most prominent pre-Vesalian anatomist, Jacopo Berengario da Carpi (1460–1530), who also worked in Bologna for a time, emphasised this view in his *Commentaria cum amplissimis additionibus super Anatomia Mundini* (1521, p. 433r). Gabriele Zerbi (1445–1505), in his anatomical work *Anatomia corporis humani et singulorum illius membrorum*, explicitly refers to Haly Abbas (1502, p. 114v). Both Berengario and Zerbi also explain why the brain is white: Berengario says it is *nutritur sanguine flegmatico,* "nourished by phlegmatic blood," while Zerbi explains it is because the brain is a *membrum spermaticum,* "a spermatic part."

French anatomist Charles Estienne (1504–1564) also belongs to this group. Although he published his *De dissectione partium corporis humani* two years later than Vesalius, it still belongs content-wise to the pre-Vesalian period, because

the plates and text were mostly completed by 1539 (Choulant 1920, p. 152). Nevertheless, Estienne did notice variations in brain matter, writing that the brain substance is *interius … candidior quam exterius*, "whiter on the inside than on the outside" (1543, p. 243).

Vesalius

Andreas Vesalius (1514–1564), the author of the foundational work of modern anatomy, was the first to distinguish two types of brain substance by colour. In the first edition of *De humani corporis fabrica* from 1543, he wrote: "What is enclosed by the lines here is the yellow or slightly pale substance [*s. grisea*] of the brain as marked by the D's (i.e., lines). What stands outside the lines is the white substance [*s. alba*] of the brain, marked with E's." (1543, p. 612; 2014, p. 1238). For *substantia alba*, he uses the Latin adjectives *albus* (white) and *candicans* (approaching white); for *substantia grisea*, the adjectives *subpallidus* (somewhat pale) and *fulvus* (brown). In the second edition, he added: "this difference is seen also in the colour of the cerebral substance" (1555, p. 763; 2014, p. 1238). Thus, in Vesalius, we already have two terms: *substantia alba* and *substantia subpallida*, the latter being lexically closest to the modern term *substantia grisea*.



Figure 1. A. Vesalius De humani corporis fabrica. 1543 e-rara, the platform for digitised rare books from Swiss institutions (https://www.e-rara.ch/bau_1/content/zoom/6299666).

A. Vesalius De humani corporis fabrica. 1543 e-rara, the platform for digitised rare books from Swiss institutions.


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ut tertij cerebri uentriculi, seu communis dextri sinistriq; uentriculorum concauitatis sedes in conspectum melius ueniret, una cum eius cauitatis meatibus.

A,A Cerebri substantiæ adhuc in caluaria reliquæ dextra pars.

B,B Cerebri substantiæ adhuc in caluariæ asseruatæ sinistra pars.

C,C,C Lineæ hic passim conspicuæ illis correspondẽt, quas tres modo præcedentes figuræ similiter eõ monstrarunt. Verum quia huiusmodi lineæ substantiæue cerebri diuersitas, inibi duntaxat consistunt ubi cerebrum tenui membranæ uicinius est, præcedentes figuræ eas solum in lateribus ostẽderunt. hæc autem quum hic tanta cerebri portio ablata sit, ut tam apparens superficies in basi non procul à tenui membrana distet, etiam lineæ in basi spectantur. Quod itaque lineis hic intercipitur, siluam seu subpallidam cerebri notat substantiam: quemadmodum sedes D,D,D insignitæ. Quod uero extra lineas consistit, alba est prorsus, candicans cerebri substantia, hic

D,D· E,E & E insignita.

E,E,E.

Figure 2. A. Vesalius De humani corporis fabrica. 1543 e-rara, the platform for digitised rare books from Swiss institutions (https://www.e-rara.ch/bau_1/content/zoom/6299667).

Post-Vesalian anatomy

Some anatomists, even after Vesalius, continued to mention only the white matter. Gabriele Falloppio (1522–1562) refers to a very white substance, *substantia candissima,* of the brain (1561, p. 13r). He was the first to use the adjective *candidus* (shining white), although Estienne had used the comparative *candidior* and Vesalius the participle *candicans*. Matteo Realdo Colombo (c. 1515–1559), professor in Padua, refers only to *substantia alba* (1559, p. 190), as does André du Laurens (1558–1609), professor of anatomy in Montpellier (1595, p. 532).

The Spanish anatomist Juan Valverde (1525–1587) was the first to compare the colour of grey matter to ash. In his Spanish anatomy text, he describes the outer brain matter as *casi de color de ceniza,* almost the colour of ash, while the rest of the brain is *blanquissimo,* very white (1556, 7p. 9). In a later Latin translation, grey matter is *subcinericii coloris* (ashen-coloured) and the rest of the brain is *albissimum* (very white) (1607, p. 241). The Swiss anatomist Felix Platter (1536–1614) also distinguishes two brain colours: *albus* (white) and *cinereus* (ashen). Platter did not use the terms *substantia alba* or *substantia cinerea* but stated that the brain is either white or ashen in colour (1583, p. 46).

The adjective *cinereus* (later appearing as *cinericius* in post-classical Latin) was first introduced in anatomy at this time and continued to be used as an attribute of *substantia*. The Italian anatomist Archangelo Piccolomini (1525–1586), personal physician to several popes, clearly distinguished between white and grey matter (Clarke & O´Malley, 1968, p. 387). However, from a terminological perspective,

these were not yet the modern terms. He referred to the *cerebrum* as *candidum corpus* (white body) and the medulla as *corpus cineritium* (ashen body) (1582, p. 252). Piccolomini was the first to use the positive form of *candidus* (shining white), which would later become widespread. Swiss anatomist Caspar Bauhin (1560–1624) echoed Piccolomini and was the first to use the term *cortex* in reference to the brain (1605, p. 580). Adrian van de Spiegel (1578–1625), a Flemish professor of anatomy and surgery at the University of Padua, in his posthumous edition of *De humani corporis fabrica*, also claimed there were two brain substances: the cortical substance was *colore subcinericia* (ashen) and the medullary part was white (1627, p. 316).

Microscopical anatomy of the 17th and 18th centuries

Marcello Malpighi (1628–1694), an Italian anatomist and pioneer of microscopy, was the first to discover that white matter was composed of fibers (Clarke & O´Malley, 1968, p. 580). Like Caspar Bauhin, he referred to Piccolomini, asserting that Piccolomini had significantly advanced brain research. Malpighi also named two substances: *corpus cineritium* and *corpus candidum* (1665, p. 6). These adjectives were also adopted by other anatomists, such as Caspar Bartholin Sr. (1585–1629) (1611, p. 208) and Ysbrand van Diemerbroeck (1609–1674) (1672, p. 352–353). Another Danish anatomist, Niels Stenon (1638–1686), lamented that when he opened the brain, he could see very little, two substances, grey, *griseatre* in the original French, and white, *blanche,* and that was all he could say about them (1669, p. 3).

Gradually, however, more detailed characterisations emerged. Raymond de Vieussens (1641–1716), in his *Neurographia* from 1684, was the first to demonstrate the continuity of white matter fibres from the *centrum ovale* to the brainstem. He showed that white matter is not homogeneous but a complex structure (Vergani, et al. 2012, p. 2012). Vieussens used the terms *substantia cinerea* and *substantia alba* (1684, p. 54); the terms *substantia cineritia corticalis* and *substantia alba medullaris* also occurred (Heister, 1717, p. 77). The German physician and alchemist, Christoph Heinrich Keil (1680–1736), also included the terms *Substantia corticalis cineritia* and *Substantia medullaris alba* in his anatomical dictionary (1730, pp. 77–78).

In the 19th century, the Latin term *substantia grisea* emerged for grey matter. The adjective *griseus* is not from classical Latin but derived from French *gris* (Gabler, 1857, p. 108). It had been used in other anatomical systems, for example, Danish anatomist Frederik Ruysch (1638–1731) used *substantia grisea* in descriptions of the kidney (1721, p. 17). In neuroanatomy, the term first appeared in the inaugural thesis of Dutch physician Anton J. M. van Heusden (1789–?) (1821, p.

17), but Vicq d'Azyr used the French form *substance grise* as early as 1786 (p. 80). From the late 18th/early 19th century onward, the terms *substantia grisea* and *substantia alba* became a stable terminological pair in neuroanatomy, as evidenced by numerous anatomy textbooks from this period.

Vernacular terms

In the 18th century, vernacular languages began to be used in the writing of anatomical works. But non-Latin works used vernacular terms inconsistently, often labelling only one of the two brain substances by colour. English philosopher David Hartley (1705–1757), who worked in psychology, used the terms *white medullary substance* and *cortical substance*, i.e., the latter without a colour adjective (1749, pp. 7, 16). Scottish anatomist Charles Bell (1774–1842), who discovered the distinction between sensory and motor nerves, used *medullary substance*, without colour, and *cineritious substance* (1802, p. 9). Gall and Spurzheim used the German equivalents *graue* and *weisse Substanz* (1809, p. 136), as did Meckel (1815, p. 253). The French anatomist Félix Vicq d'Azyr (1748–1794) used *substance blanche* and *substance cendrée,* ashen, or *corticale* (1784, pp. 585, 600).

Further colours in terminology

By the late 17th century, anatomists began to believe there were more than two brain substances. Pierre Dionis (1643–1718), a French author of a highly successful and often translated anatomy, wrote in the first edition that the brain consists of three substances: the first one is the cortical substance, also called the ashen body, the second is the medullary body, and the third is the cornified substance or *corpus callosum*. These differ not only in colour but also in consistency: the greyish substance, *substance grisâtre*, is soft, and the whitish medullary substance, *substance blanchâtre,* is less soft (1690, p. 381). In the third edition, however, he revised his view to only two substances: the cortical, ashen, body and the medullary body or *corpus callosum* (1698, pp. 491–492).

By the late 18th century, other coloured substances were appearing in anatomical descriptions. The first sign of multiple colours in brain terminology was noted by Swiss polymath Albrecht von Haller (1708–1777). In his physiology work, he described the cortex as ashen, red, and (pale) yellow (1762, p. 22). German anatomist Johann Christoph Andreas Mayer (1747–1801), observing a yellowish "third substance," asked whether Haller had already known the cortex was tricoloured (1794, p. 94). Haller referred to Johann Friedrich Meckel Sr. (1724–1774), a founder of a dynasty of anatomists, who dissected a black man and observed his cortex

to be greyer than in white individuals (in French, *une couleur plus cendrée*; Latin, *fuscus*) (Meckel 1759, p. 69).

Thirty-eight years after the death of Italian anatomist Giovanni Domenico Santorini (1681–1737), his student Michael Girardi (1731–1797) published Santorini's *Septemdecim tabulae*, expanded from his unpublished notes. In the supplemented text on the brain, Girardi wrote that between the cerebral crura, a substance exists that is no longer *cinerea* but *fusca* (dark-coloured) (1775, p. 14).

Three years later, in his dissertation, Samuel Thomas von Soemmerring (1755–1830) recognised a third substance: besides *substantia cinerea* or *corticalis* and *substantia medullaris*, there is a medium substance described as *colore fusco flavescenti* (a dark yellow colour) (1778, p. 63). In 1782, the young Italian anatomist Francesco Gennari (1750–1797) described a structure that, as he noted, no one had previously observed. Considering it a third substance in addition to the cortical and medullary, he named it *subalbida* (whitish) (1782, p. 72). The structure is now known as the "line of Gennari" or *stria occipitalis* of the cortex (Bakkum, 2015).

Two years later, French anatomist Félix Vicq d'Azyr described more coloured structures. In the midbrain, he identified the *substantia nigra*, which he called in French *tache brune* (brown spot) and in Latin *locus niger crurum cerebri*, referencing Santorini. He also observed a *tache rougeâtre,* a reddish spot, surrounded by a white circle in the optic layers (1784, pp. 556, 607). Burdach noted he meant an ashen substance located at the lower part of the thalamus, first described by Girardi in Santorini's work in 1775. Burdach called it *rother Kern* (red nucleus), and was the first to describe it in detail (Meyer, 1970). The Latin term *nucleus ruber* appeared later. Vicq d'Azyr also mentioned *substance noirâtre* (a blackish substance), on both sides of the *calamus scriptorius* (1784, p. 585). Later anatomists, including the Wenzel brothers in 1812, referred to it as *loculi caerulei* (blue or blue-green spots) (1812, p. 341). German anatomist Friedrich Arnold (1803–1890) later named it *substantia ferruginea* (dark purplish substance) (1838, p. 26). Along with other substances like *substantia gelatinosa* (gelatinous substance) and *substantia nigra*, he regarded them as subtypes of grey matter (1838, p. 55).

Thus, by the late 18th century, Soemmerring in the first edition of his German anatomy textbook listed four brain substances: *cinerities* (*graue Substanz*), *medulla* (*Marksubstanz*), *substantia intermedia* (*gelbliche Substanz*), and *substantia nigra* (*schwarze Substanz*) (1791, p. 25). German anatomist Georg Friedrich Hildebrandt (1764–1816), in his German work, provided German names with Latin equivalents in parentheses: *graue Substanz* (*substantia cinerea*), *Rindensubstanz* (*substantia corticalis*), *weiße Substanz* or *Mark des Gehirns* (*substantia medullaris*

sive medulla cerebri), and *gelbliche Substanz* (*substantia subflava* or *subalbidum*), leaving one term without a colour in the term itself (1792, p. 272).

During the 19th century, anatomists disagreed on the number of brain substances and often used various terms. British physician Robert Hooper (1773–1835), author of the influential *The Anatomist's Vade-Mecum*, did not mention brain substance in the first three editions, but from the 4th edition onward included three brain substances: *substantia medullaris,* of a … white colour, *substantia corticalis,* also called *cineritia*, and *substantia nigra* (1811, p. 223). German anatomist Johann Friedrich Meckel Jr. (1781–1833), grandson of the aforementioned Johann Friedrich Meckel Sr., acknowledged white matter, *substantia medullaris,* and grey matter, *substantia cinerea* or *corticalis*, while considering two others, yellowish, *substantia flava,* and black, *substantia nigra,* to be modifications of the same matter (1815, p. 253). Scottish anatomist John Gordon (1786–1818) used terms for three substances, white, grey, and brown, as well as *cortical* or *cineritious matter* or *medullary matter* (1817, pp. 18–28).

German neuroanatomy pioneer Karl Friedrich Burdach (1776–1847) used *graue* and *weisse Substanz*, as well as *markige* and *Marksubstanz*. He noted that both substances maintain a characteristic colour across all structures. In his historical commentary, he also mentioned *gelbe Substanz, substantia flava*, and *schwarzgraue Schicht, stratum nigrum* (1822, p. 249). Burdach criticised the terminology: "The naming of these two forms of nervous substance is, like our entire system of names in neurology, still very inappropriate. Grey and white matter refer only to colour, i.e., to what is less essential, and even then, not in a suitable way, because grey matter as a whole is reddish" (1819, p. 167). Nevertheless, for clarity, he retained the traditional terms, a convention that continues to play an important role in terminology theory today.

Nomenclatures

At the end of the 19th century, when the first unified international anatomical nomenclature, Basle Nomina anatomica, was created, most neuroanatomical terms with adjectives indicating colour were included in this nomenclature (His, 1895) and are also found in subsequent revisions, as well as in the currently valid Terminologia Anatomica 2. These include: *substantia alba*, *substantia grisea*, *substantia nigra*, *nucleus ruber, nucleus caeruleus*, and *tuber cinereum*, which, however, is only in the obscure column "others" (FIPAT, 2019). Even special Terminologia neuroanatomica (FIPAT, 2017) and the latest attempt at a generally accepted nomenclature, Terminologia anatomica humana (TAH), which is still in process, contain these "coloured" terms (FIPAT, 2024).

Conclusion

While the conceptual understanding of various "coloured" brain substances gradually evolved, enriched by important structural and functional insights, the terms reflecting their external characteristic, colour, persisted. Historians studying these terms must consider the evolving content associated with each term, which helps explain the differing opinions about their origins. From a terminological point of view, these terms are an example of how even in the case of a change in content, their linguistic form can continue to function as a sign.

Based on the analysis of primary literature sources, it was possible to identify the first recorded use of the specific term referring to the coloured substance in the brain, including the work in which the term appeared and its original author, as shown in Table 1.

Table 1. The first occurrence of the terms for white and grey matter.

year / term	980	1225	1543	1556	1561	1582	1821
brain is white	Haly Abbas						
corpus candidum/ cinereum						Piccolomini	
substantia alba		Pseudo-Galenos?					
substantia alba/ pallida			Vesalius				
substantia candida					Fallopio		
substantia cinerea				Valverde			
substantia grisea							Heusden

Specifically, terms for white and grey matter, which initially served to visually distinguish and describe the macroscopic structure of the brain, have proven to be functional also for the histological description of the given structures, and their use has also spilt over into the clinical practice of contemporary neuroscience. Even when teaching and studying anatomy, colour helps students because it reflects one of the characteristics of a particular anatomical structure.

This small section of neuroanatomical nomenclature confirms the words of German medical historian Heinrich Schipperges (1918–2003): "Medical terminology is almost 3000 years old, its roots reach back many ways to ancient high cultures, its branches will continue to shade medicine in the 21st century, some things have been inoculated or cut off, some things have withered and fallen away completely, and all this is a fascinating process" (1976, p. 12).

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SAŽETAK

Ova studija iz terminološke perspektive istražuje povijesni razvoj neuroanatomskih naziva kojima se opisuju obojene tvari u mozgu, osobito substantia alba *(bijela tvar) i* substantia grisea *(siva tvar). Narativnim pregledom glavnih anatomskih izvora od antike do ranoga modernog doba prati se kako su deskriptori boja ušli u terminologiju anatomije i postupno počeli označavati različite moždane strukture. Dok antička anatomija nije razlikovala anatomiju mozga temeljenu na boji, arapske i salernske tradicije uvele su predodžbu o mozgu kao bijeloj tvari. Najranija poznata upotreba izraza* substantia alba *pojavljuje se u tiskanoj verziji srednjovjekovnog pseudogalenskog teksta* De anatomia vivorum *iz 1502., ali bi to mogla biti i kasnija urednička interpolacija teksta. Vesalius (1543.) bio je prvi koji je razlikovao moždanu tvar prema boji, uvodeći termine koji odgovaraju* substantia alba *i ranoj verziji* substantia grisea. *Do kraja 18. stoljeća uvedeni su višestruki termini temeljeni na bojama kako bi se prikazale različite moždane strukture. Unatoč razvoju znanja iz anatomije, nazivi koji označuju boju ostali su stabilni lingvistički znakovi te su često prethodili konceptualnim promjenama ili ih nadživjeli.*

Ključne riječi: substantia alba, substantia grisea, *boje, moždane tvari, anatomski termini*