Pulverized human skull in pharmacological preparations: Possible evidence from the “martyrs of Otranto” southern Italy, 1480

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Abstract

Ethnopharmacological relevance

Ever since the Late Medieval Ages historico-medical literature has attested the use of cranium humanum as an ingredient in pharmacological preparations for the treatment of epilepsy. Some authors suggest the use of pulverized bone obtained from individuals who died a violent death and were not buried.

Materials and Methods

The skeletal remains of hundreds of male inhabitants from Otranto, killed by the Ottomans in a mass execution on 14 August, 1480, are preserved in the Chapel of Martyrs in Otranto Cathedral (Apulia, southern Italy). The so-called “martyrs of Otranto” were beatified in 1771 and canonized by Pope Francis on 12 May, 2013. A cranial vault with 16 holes of different sizes, with regular rounded shape, was noticed among the skeletal remains, symmetrically arranged behind five large rectangular windows. Eight of the 16 holes, which exposed the diploe without reaching the endocranial surface, are incomplete perforations, while 8 holes are complete perforations; no evidence of bone reaction is visible.

Results

The lesions are the result of a multiple trepanation performed by using an instrument equipped with a large rounded tip. This tool could not produce bone discs, but only bone powder. It is impossible to establish with certainty the reasons for these multiple trepanations, but several hypotheses can be advanced, ranging from experimental surgery to a procedure designed to obtain relics. However, saint bones are very likely to
have been regarded as having medicinal properties. As a matter of fact the martyrs of Otranto died a violent death and were not buried, and the pulverized bone obtained from their skulls might have been considered a particularly powerful ingredient for pharmacological preparations, as attested in the historico-medical literature.

Conclusions

The skull of Otranto might represent a unique evidence of multiple trepanations carried out to obtain bone powder as ingredient for therapeutic preparations.

Keywords: Apulia; Renaissance; Trepanation; Cranium humanum; Epilepsy; Therapy
1. Introduction

Curious and unusual substances attributed with particular curative properties were frequently used in ancient pharmacological preparations. Cranium humanum, consisting in pulverized human skull, has long been an ingredient in several remedies prescribed in particular to treat diseases with no clear explanation and possibly caused by magical or demonic influences such as paralysis, stroke, and epilepsy. Pulverized human skull has been cited as an ingredient since the Late Middle Ages and is described in numerous pharmacopoeias of 16–8th centuries. For centuries, flasks labeled Cranium humanum occupied the shelves of pharmacies, and were used in order to drive out evil spirits in convulsive disorders (Fig. 1). The ingredient was then abandoned as a drug with the scientific development of medicine in the 18th century (Arnott et al., 2003).

![Pharmaceutical vessel labeled CRAN(IUM ) HUM(A)N(UM) P(RE)P(ARA)T(UM) dated back to 18th century. Courtesy of the Museum of Pharmacy, Cracow.](image)

Starting from the Middle Ages healing powers were attributed to vegetable, mineral and animal substances through the omnipotence of God. The human body was considered as the God’s masterpiece within the animal kingdom and especially the head was considered the most distinguished part of the human body. The principle of action of the Cranium humanum was in the invisible spiritual life forces, that remained active even after death.
On the basis of these considerations, it is clear why the skull was used as an ingredient for the preparation of medicaments (Bernscheider-Reif and Gruber, 2011). For example, according to the Flemish chemist Jean Baptist van Helmont (1579–1644) the skull was the most efficacious of all the human bones because, after death, “…all the brain is consumed and dissolved in the skull”; it is “by the continual… imbibing of [this] precious liquor” of dissolved brains that “the skull acquires such virtues” (Van Helmont, 1650, p. 30). Cranium humanum was often used as a synonym for other bones of the human skeleton that have been used for healing purposes. The bones required for drug preparation came mostly from executed persons. As well as cranium humanum also mumia and human fat (axungiaAxungia hominis) were often listed as medicinal substances of human origin in historical pharmacopoeias (Bernscheider-Reif and Gruber, 2011). In this article we discuss the possible direct evidence of powdered Cranium humanum that was obtained from the skull of one of the hundred “martyrs of Otranto”.

2. Material and methods

On 28 July 1480 an Ottoman army, commanded by Gedik Ahmed Pasha, landed below the walls of Otranto, in Apulia (southern Italy). The city strongly resisted the Ottoman bombardment but, on July 29, the inhabitants abandoned the city and retreated into the citadel. After a 15-day siege the Ottomans captured the citadel, killing the men who were older than 15 and gathering the women and children to be sold into Albanian slavery. After reaching the Cathedral, where the clergy and the survivors took refuge, Gedik Ahmed Pasha ordered them to renounce their Christian faith, but having received a flat refusal, he broke into the Cathedral with his men and captured the refugees. On August 14, 800 of the city’s male inhabitants were taken to a place called the Hill of Minerva, later renamed “Hill of the Martyrs”, and were executed. According to legend, the Otrantines were killed by impalement or, mainly, by decapitation (Gianfreda, 2007; Ricciardi, 2009). The city was later retaken in the spring of 1481 by Alfonso of Aragon, son of King Ferrante I.

One year after the Martyrdom most of the Otrantine bodies were transferred into the crypt of the Cathedral, whereas the others, about 250, were taken by the King in the church of St. Mary Magdalene of Naples (called the church of the Martyrs) and then church of St. Catherine in Formiello. Since 1711 the bones of the Martyrs have been preserved in five large glass cabinets in the Chapel of Martyrs of the Cathedral of Otranto. On 14 December 1771 Pope Clement X IV beatified the 800 martyrs and authorized their cult. The martyrs were canonized on 12 May, 2013 by Pope Francis. They are the patron saints of the city of Otranto and of the Archdiocese of Otranto.

The bones are commingled and symmetrically arranged behind five large rectangular windows; in particular, the crania, separated by other bones, are placed in horizontal rows, with the splanchnocranium turned towards the visitors (Fig. 2).
There are a few exceptions to this arrangement: in a low row of the central window a cranium is positioned with the face towards the ceiling and the cranial vault towards the visitors (Fig. 3). The specimen was probably arranged in this manner so as to show a series of holes on the cranial vault.

Fig. 3 Cranial vault with evidences of multiple trepanation.
The window could not be opened nor could the skull be removed for study. Therefore, the cranium had to be examined in situ and photographically documented, and radiologic or histological examination impossible to perform. The cranium cannot be related to any post-cranial bones belonging to the same individual. Only some features could be evaluated to determine sex and age at death according to standard anthropological methods (Meindl and Lovejoy, 1985).

3. Results

According to tradition, the martyrs of Otranto were all males. The absence of frontal bossing in the cranium with the holes seems to suggest male sex (Ferembach et al., 1977–79). As for age at death, only the synostosis degree of cranial sutures can be applied (Meindl and Lovejoy, 1985), even if this method has been criticised (Hershkovitz et al., 1997); only the coronal, sagittal and lambdoid sutures are observable, and seem to suggest that the individual was an adult.

The cranial vault reveals a series of holes of different size and depth, but with a regular rounded shape. In particular, 7 holes are on the frontal bone, 1 is on the left coronal suture close to the bregma, 5 on the right and 3 on the left parietal bone, for a total of 16 holes. Their size varies greatly, ranging from 0.5 to 3 cm in diameter. Of the 16 holes, 8 are incomplete perforations with a regular hemispheric shape that exposed the diploe without reaching the endocranial surface. The remaining 8 holes are complete perforations, which involved the bone in all its thickness, producing a rounded conical shape hole; the edges of the trepanations are not vertically oriented, but have rounded walls (Fig. 4).

Fig. 4 Detail of the trepanned defects.
These holes are the result of a trepanation performed with the drilling technique characterized by the continuous tip rotation of a trepan. The trepanations show no evidence of healing, since there is absence of bone reaction at the edge of the incisions and the spongy diploe is open and visible.

4 Discussion

4.1 Trepanation technique

Trepanation is considered to be the most ancient surgical procedure; evidence of this practice comes from all continents and ranges from prehistory to present times, and still attested in some African tribes (Margetts, 1967). Several trepanation techniques have been developed over time and space, but the most frequently used in Europe is grooving. This technique consists in drilling the bone with a sharp and hard stone or with a metallic element, by exerting pressure and repeatedly drawing and redrawing the groove. As a result, a troncoconical hole, with circular outline, is obtained (Campillo, 2007).

Although a hard sharp stone is sufficient for this technique, two types of drill bit have been known since Greek and Roman times, as reported by Hippocrates in his *De vulneribus capitis* (Vegetti, 1965) and by Celsus in his *De medicina liber* (Mazzini, 1999): a standard drill bit, called *trypanon* by Hippocrates and *terebra* by Celsus, and a hollow drill bit, called *prion* by Hippocrates and *modiolus* by Celsus. The first allowed us to obtain bone powder, whereas with the latter bone discs were achieved. Both tools leave the same regular cylindrical hole (Germanà and Fornaciari, 1992), but the holes on the Otranto cranium have rounded, not vertical walls. The incomplete perforations also demonstrate a perfectly cupped shape, suggesting the use of a particular type of trepan with semi-lunar shaped blade or rounded bit, like the ones illustrated in the 16th century surgical treatise of Dalla Croce (1583) (Fig. 5). Furthermore, the different dimensions of the holes hypothesize the use of rounded bits of different sizes to achieve complete and attempted trepanations. In any case, this kind of tool could not have produced a bone disc, but only bone powder.
Fig. 5 Different types of rounded drill bit as illustrated in the *Cirugia universale* of Giovanni Andrea (Dalla Croce, 1583).

4.2 Purposes of the trepanation of the Otranto skull

Trepanation was practiced by past populations for different reasons, i.e. for therapeutic reasons, experimental surgery, and ritual purposes. Although it is not possible to establish with certainty the reasons for the multiple trepanations observed in the skull of Otranto, several hypotheses can be made.
4.2.1 Torture

There are no signs of healing in the cranium of the Otranto martyrs, but this does not necessarily mean that trepanation was practiced post-mortem. In fact, it is impossible to distinguish a peri-mortem from a post-mortem surgical procedure, as in both cases the lesion presents an absence of bone remodeling (Sauer, 1998). The distinction between peri and post-mortem injuries in osteoarchaeology is sometimes supported by differences in color continuity between drilled and intact bone. In this case color homogeneity would suggest a post-mortem procedure. The tradition linked to the Otranto martyrs reports on a particularly savage massacre, with episodes of torture, such as decapitation and impalement, but there is no reference to trepanation (Gianfreda, 1991, 2007). Cranial trepanations were largely practiced in Anatolia since the Aceramic Neolithic period; in particular, drilling was used for cranial surgery until the Late Ottoman period (Erdal and Erdal, 2011). In this case, however, the lack of reference to trepanation in the detailed tradition of the Otranto martyrs, the use of variable-size bits, possibly used at different times, and the probable post-mortem origin of the lesions suggests to exclude torture to explain the multiple trepanations.

4.2.2 Therapy

Some paleopathological evidence demonstrates that trepanation was used for therapeutic purposes, as it was found in association with various pathologies, especially of traumatic origin (Parker et al., 1986; Germanà and Fornaciari, 1992; McKinley, 1992a, 1992b; Mariani-Costantini et al., 2000; Powers, 2005; Mays, 2006; Weber and Wahl, 2006; Rubini, 2008); in these cases the skull was trepanned to remove bone fragments from cranial fractures. It has also been hypothesized that trepanation was used to treat migraines caused by high intracranial pressure or to cure cerebral disturbances, in particular related to vascular pathologies (Facchini et al., 2003). Therefore, it is possible to relate trepanation with therapeutic purposes in presence of traumas or other pathologies. The absence of signs of trauma and the probable post-mortem origin of the lesions allow us to rule out a therapeutic purpose to explain multiple trepanations on the cranium from Otranto.

4.2.3 Experimental surgery

An explanation for post-mortem trepanation, even if very difficult to demonstrate, is the practice of surgery on cadavers. A number of cases of multiple post-mortem trepanations were interpreted as cases of experimental surgery. (Campillo, 1993, p. 62, Fig. 1) described a skull with seven holes, dated to 5th century BC from Son Real (Spain), as post-mortem trepanation by drilling. A case from Perge (Turkey) and dated back to the Roman period shows eight holes in two rows on the right half of the frontal bone (Erdal and Erdal, 2011). A case from Natividad, Peru, and dated back to the Late Intermediate Period (1000–1250 AD) has been documented recently; a middle adult male showed complete trepanation made from 74 bore holes on the
right frontal and parietal bones, and an additional 19 discrete bore holes that penetrated only the external table (Kurin, 2013). For these cases the authors concluded that the respective trepanations were aimed at skill training or practice. The Otranto cranium presents similar characteristics, but an experimental surgical procedure should be excluded, considering the aura of sacredness of these human remains.

4.2.4 Procedure to obtain relics

A possible explanation for the multiple Otranto trepanations is connected to ritual purposes. Trepanation may have had a ritual significance, especially when practiced post-mortem (Lisowski, 1967). According to Campillo (1984), post-mortem trepanations undoubtedly had a ritualistic character, especially the cases showing multiple openings with no signs of healing. Evidence of cranial discs extracted from the dead to be worn as amulets is dated back mainly to prehistoric times and have been discussed by several authors since the late 19th century (Prunières, 1874; Broca, 1877; Fletcher, 1882; Munro, 1897). The practice is still attested among modern African populations (Merbs, 1989).

The cranium from Otranto belongs to the skeletal remains of martyrs, who have been the object of veneration and cult since Renaissance times. Trepanation performed to obtain bone powder as a relic is worth considering (Freeman, 2011). However, the employment of such a complex technique, requiring experienced practitioners, to obtain bone powder to be used as a relic seems unlikely, considering the availability of hundreds of bones belonging to the martyrs of Otranto.

4.2.5 Procedure to obtain Cranium humanum

The possibility that saint’s bones were thought to have medicinal properties should be considered. The history of medicine supports this hypothesis, since several ancient medical authors refer the use of the bone skull as an ingredient in pharmacological remedies, in particular in the treatment of epilepsy. With regard to the “sacred diseases”, already in Roman times the human bone is recommended by the father of Western medicine, Galen (129–c. 200/2 16AD). However, the physician does not specify which bone should be used: “I know that some of our people have cured epilepsy and arthritis in many cases by prescribing a drink of burned (human) bones, the patients not knowing what they drank lest they should be nauseated” (Galen, 182 1, III, 9, p. 336, III, 9, p. 336).

Even Arabic medicine suggests the use of human bones for treating epilepsy and other diseases. Avicenna (980–1037) attributes the power to cure epilepsy to human bones; he probably copied this information from Greco-Roman sources without questioning its legitimacy in religious terms. The pharmacist, botanist and physician Ibn al-Baytar (1197–1248) quotes Galen, and reports the power of human bones to dry surplus humors in the body. Al-Damiri (1344–1405), an Egyptian naturalist, prescribes human bone, without specifying which one, to treat nasal hemorrhoids (Alkhateeb Shehada, 2012).
Late Medieval authors transmitted this tradition, inherited by classical authors through the influence of Arabic medicine. For example, John of Gaddesden (1280–1361), author of *Rosa medicinae*, reports on the use of burned and powdered human bones to treat apoplexy and epilepsy (Lennox, 1939). The use of pulverized human skull appears in medical prescriptions to treat epilepsy in authors of the Late Middle Ages. In the *Breviarium practicae medicinae* (chapter XXII) Arnold of Villanova (1240–1312/1313) prescribes burned human bones and says: “For epilepsy make this approved powder: take of the bones of the human head, and especially from the anterior part, burned, … and give them in drink”; again: “bones of the skull of a man long dead, three ounces” (Von Storch and Von Storch, 1938). Antonius Guaimerius (1440/1445) in the *Opera medica* (tractatus 7) states: “There are some things from animal parties which we can use only in powdered form, such as [...] the human skull. For a male patient, take the skull of a man, for a woman, that of a woman”; he includes powder of the human skull among the simples suitable for epilepsy producing a wonderful and even divine effect (Lennox, 1940). In the Renaissance and in the Modern Age the beliefs related to the powers of the human skull are further strengthened. Paracelsus (1493–1541) prescribes a remedy called *Arcanum vitrioli* to treat epilepsy. *Rasure cranei* is cited among the ingredients, which need to be crushed and pulverized. Paracelsus affirms: “We consider that Arcanum vitrioli is sufficient to heal all epileptics” (Sigerist, 1941, p. 172). In the fundamental work of Pietro Andrea Mattioli (1501–1578) the drinking of human skull bone is considered to be an effective remedy to treat epilepsy, colic and renal pain (Mattioli, 1573, p. 111). The French Jean Fernel (1497–1588) recommended powdered human skull to treat epilepsy in his *Consiliorum medicinalium liber* (Fernel, 1582, advice 8). Another French physician, Jean Taxil, wrote an entire book on epilepsy titled *Traicté de l’épilepsie* (1602). The work summarizes the knowledge of his time on epilepsy, according to which human cranial bones were believed to possess special curative powers. The bones were prescribed in different forms, including shaving, powders, and cinders, and could be applied to the coronal sutures, administered as potions or pills, or suspended around the neck in a small sac (Taxil, 1602, pp.149–159). During his last days of life King Charles II of England (1630–1685) underwent the best treatments Europe could offer to a monarch. Among the remedies, the “spirit” of the human skull was administered to treat convulsions (Crawford, 1909).

In a medical treatise written at the beginning of the 18th century, chapter 14 is reserved to remedies against epilepsy, and it is said : “...put them in a glass alembic, add above them scraping of the human skull” (Saint-Hilaire et al., 1709, p. 37–38) However, the most interesting references to *Cranium humanum* are reported by the Neapolitan Giuseppe Donzelli (1596–1670) and the French Nicolas Lemery (1645–1715). In his *Teatro farmaceutico, dogmatico, e spagirico* (1675) Donzelli writes: “Oil of distilled human skull. You’re going to polish two or three human skulls, died violently, and with glass retort obtain oil, and water. Properties and use. It is really useful against epilepsy, and it is to be taken at the beginning of the paroxysm in the amount of a scruple” (Donzelli, 1675, p. 161).

In his *Pharmacopée universelle*, a truly comprehensive work on pharmaceutical compositions (which appeared in 1697 and was translated into several languages
including Italian), Lemery refers about a significant use of human skull bones: the human skull “is good against epilepsy, paralysis, stroke, and other illnesses of the brain. The dose is from half scruple up to two scruples. The skull of a person who died of violent and sudden death is better than that of a man who died of a long illness, or who had been taken from a cemetery: the former has held almost all of his spirits, which in the latter they have been consumed, either by illness or by the earth” (Lemery, 1720, p. 59). And later: “To obtain the magisterium of the human skull, the skull needs to be calcined; it is subtly pulverized, then proceed as in the magisterium of coral […]; but this so-called magisterium is nothing else that a dead head devoid of virtue. You will much better use in his stead, the skull of a young man who died a violent death. (Lemery, 1720, p.159)” To prepare cinnabar powder “you have to use the human skull of a man who died of violent death and has not been buried” (Lemery, 1720, p. 139) (Fig. 6).
CRANIUM HUMANUM.

Craniun humanum, francösisch, Crâne humain, teutsche, ein Menschen-Schädel, ist als wie eine Hälfte oder Schachtel von Rein, welche das Gehirn beim Menschen in sich enthält, und ihm gleich wie Schranken, oder als wie eine Decke über alle höhe Luft und andere Dinge von ausßen bie- net. Er wird zur Steine gebraucht.

Man soll sich einen erwecken, von einem jungen Menschen, gutem Tempeaments, welcher eines seelsel- samen Todes gestorben, und nicht todt, worin willst du, tiefer, und nicht eatenen und verbrennen, so wie es die Völker haben woltet: dann durch das brentnet nicht das flütige Salz hinweg, vorinno doch die beste Kracht behielt.

Er dient wider das höhe Weis, wider den Schlag, und andere Zufälle des Gehirns: unver- schießt bem gilt, hilft die unermessliche Aus- dünnung oder Transpiration befördert, und hemmet den Durchfall.

Die dos ist von einem halben Ecrupel bis auf zwee Ecrupel.

Craniun von un-ders, gleiel einer Steinru- haube, oder ein Helm, eine elterne Hütte: dieje der Schädel zu dem Gehirn bedeckt, als wie der Helm denstopf eines Kriegsmanns.

CREA.

Creta, francösisch, Craye, teutsche, Areide, ist eine in etwas fette Ede, überaus weich, sandlich leicht, und hat ihren Namen von der Insel Creta oder Candies begeffen, welches so ihrer die Menschen jetzt. Die zu Paris gebraucht werden, kommen insgemein aus Champaigne, allweil auch sie auch in andre Menge gefunden werden. Die sperrbare Gîte des Champaigne Wines soll, wie man sagt, guten Theil haben kommen, daß die Weinberge auf Kreidensand angebaut werden.


CRISTA GALLI.

Crissagalli, Lob. Dod.
Crissagalinae, Dod. Gal.
Crissagallia mat et forma, J.B.
Alborelahos, Ang.
Pedicularia lutea, Tab.
Pedicularia campestris, s. Trag.
Pedicularia procera, lutea, vel crissagalli, C.B.
Pic. Tournef.
francösisch, Crête de coq. teutsche, Zahnfellam.

ist eine Gattung Pedicularis, oder ein Kraut, welches Johann. Bumgin in zwei Bhstücke abges- theilt, in Männlein und in Weiblein.

viererzigt und hol, theiset sich in ähnliche Zveigleit.


Das andere ist von dem ersten darinne unterschie- de, weil es viel niedriger, und ein Theil nicht so starr ist, die Blätter sind gleichfalls viel schlanker, die Blüten auch ein gitz Theil klein. Diebe wachsen auf dem Feld, und in den Wiesen; zur Steine werden sie gar nicht gebraucht.

Crista galli heisst es, dieviel die Blätter an dieser Kraute bey nabe eine Eröth haben, als wie ein Hau- nenfamm.

CRITHUM.

Crithum, francösisch, Bacille et Fenuil mar- ron, teutsche, Meeresfelche, Meierpeterlein, Bacillen, ist ein Gemüse, dessen es zwei Sorten siebet, eine grosse, und eine klein.

Die erstes heisst

Crithum, five Forniculum marinum majus, sa- re Api, C.B. Pit. Tournef.

Crithum, five Forniculum marinum grandus, cu fucus luteus, J.B. Jaxi Hilt.

Crithum Sutulum, Bactile alterum genus ex Scithia, Casalp. Boccioni.

Crithum marinum majus, Park.

francösisch, Meeresfenchel, Meierpeterlein.

Sie treibt andershafte far lange Tangel, die sind hellig, die und holzig, liegen insgemein auf dem Boden, bießen aber stehen sie harnische in die Höhe.

Die Blätter sind zur Schul und dann starken spitz, weit und hollig, immer in drei Theile getheilt, riechen wie Spitzich, und schmecket hollisch.


Die andere heisst

Crithum, Ang. & Herba S. Petri, Dod. Gal.
Crithum, vulgo Cretes, seu Salsana marina, Gal.

App.
Fig. 6 A page of the work of Nicolas Lemery Vollständiges Materialien-Lexicon (Johann Friedrich Braun, Leipzig, 1721) with the description of Cranium humanum.

The pharmacological use of powdered human skull is clearly attested also in Southern Italy, as demonstrated by an ancient Apulian manuscript containing pharmacological prescriptions titled “Capaccio” of Nicol’Angelo Meola, dated back to 1750. This manuscript reports that the powder of the skull of a man who died a violent death, infused into the spirit of wine, is used to treat the falling sickness admirably (De Filippo, 2010). Finally, the use of human skull to be drunk in water is still attested as a remedy against epilepsy in 19–20th century popular medicine (Tagarelli et al., 2013).

The persons technically prepared to carry out the trepanations on the skull of Otranto were probably physicians or surgeons but, as the procedure was done post-mortem, also an apothecary could have attempted to perform the operation. There are no elements to consider this skull as belonging to a martyr of particular interest or importance, so it is not possible to know why this particular skull was chosen to obtain bone powder.

It is impossible to ascertain when the trepanations in the Otranto cranium were performed, whether soon after the death of the martyr or later. It might be dated to the late 17th-beginning of 18th century, when the theories about the use of cranium humanum in pharmacological preparations were well attested in medical literature. In particular, it was probably performed during the arrangement of the bones in the glass cabinet, which took place in 1711.

5 Conclusions

A cranial vault with 16 holes of different sizes and of regular rounded shape was noticed among the skeletal remains of the Otranto martyrs. The trepanations were probably carried out post-mortem, as demonstrated by the absence of healing. The perfectly cupped shape of the incomplete perforations leads to hypothesize the use of a particular type of trepan, with semi-lunar shaped blade or rounded bit; a tool of this type could not produce bone discs, but only bone powder.

Although it is impossible to determine with certainty the reasons of the multiple trepanations observed in the cranium of Otranto, the most likely hypothesis is that the procedure was performed post-mortem to obtain bone powder as ingredient in pharmacological preparations. Cranium humanum is in fact reported by several authors, starting from the Late Middle Ages, as efficacious remedy against some diseases, in particular epilepsy.

Some prescriptions of the 1717th century recommend the use of pulverized bone obtained from individuals who died a violent death and were not buried, as is the case of the martyrs of Otranto. These bones are very likely to have been regarded as having medicinal properties. Therefore, the skull of Otranto may represent a unique evidence of multiple trepanations carried out to obtain bone powder as ingredient in pharmacological preparations.
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