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LITERATURE REVIEW

Olfaction and traumatic head injury - Is it possible to discriminate between malingering and patients with smell disorders based on nowadays knowledge?

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ABSTRACT

BACKGROUND. Olfaction is one the most important senses; however, even nowadays it is incompletely known in humans from an anatomical and physiological point of view, but also as concerns the assessment methods and treatment. The main causes for acquired olfactory dysfunctions involve inflammatory pathology (local or general) and head trauma. Olfactory impairment after traumatic head injury (THI) is more frequent than believed. Today there are a number of tests for assessing the loss of smell, but more studies are needed in order to establish standardized protocols for patients with such pathology after THI. This uncertainty is more and more exploited by malingerers.

OBJECTIVE. The aim of the paper was to find in literature the necessary information in order to permit a correct management of a patient with olfactory impairment after head trauma and to establish new protocols that may help identify malingerers when medico-legal implications exists.

MATERIAL AND METHODS. We studied an amount of works and studies in order to highlight the diagnosis options specialist have, if such a case is encountered (olfactory loss after THI).

RESULTS. Recent studies show that great progress has been made, but more scientific research is needed. Specialists still search correlation between all diagnosis methods.

CONCLUSION. Olfactory disorders are an important topic given their importance in patient quality of life, but also for the medico-legal implications.

KEYWORDS: olfaction, smell impairment, head trauma, olfactory cleft, malingerers

INTRODUCTION

Olfaction is even nowadays a mysterious sense. Olfaction plays an important role in our interaction with the environment, and its disorders can affect the quality of life in a significant way. The olfactory system may be considered an alarm system for the human being by detecting potential dangers in the environment, but also it influences our nutrition, interpersonal communication and well-being[1].

Smell disorders are common in the general population. Although loss of smell occurs increasingly often, these disorders are often overlooked by the medical community and, more interesting, by the majority of patients[1].

Viral infections, nasal causes (e.g. rhinitis, rhinosinusitis, polyposis, tumors - esthesioneuroblastoma, sinonasal carcinomas, benign or malignant brain tumours), trauma, neurological illnesses, systemic diseases, isolated organ deficiencies (kidney/liver failure) or iatrogenic causes (e.g. ENT procedures - septoplasty, polipectomy, ethmoidectomy, neurosurgical operations; radiotherapy, intake of medicines) could lead to smell dysfunctions[1].

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Olfactory impairment following traumatic head injury (THI) is increasingly often discovered. Nevertheless, we observe a lack of standardised assessment tests and diagnosis protocols. Thereby, olfaction dysfunctions represent an actual topic from medico-legal point of view, discriminating between the malingerers and the patients being quite a difficult task.

CURRENT KNOWLEDGE ABOUT OLFACTION

Anatomy and physiology

Main olfactory system

The olfactory epithelium in the roof of the nasal cavity is the place where the olfactory perception initiates.

This location is called olfactory cleft (OC) and it receives information from the ortho- and retronasal airflow. This means odours can reach the OC through the nostrils, by sniffing, or retronasally, by nasopharynx, when eating or drinking. Due to the localization of the olfactory receptors in the epithelium of the OC, olfaction is closely related to respiratory control and to the intranasal anatomy[2,3].

Olfactory receptor neurons (ORN) are located within the respiratory epithelium, being directly exposed to environmental factors. ORN location could be the reason why olfactory cells can regenerate continuously, according to several authors[4,5]. Before odours initiate excitation of the olfactory receptors, the odours must first diffuse through the mucus[6]. In the mucus, transport proteins for lipophilic odours that carry the molecules through the mucus to the receptor are dissolved[7,8]. The ORN axons reach the olfactory bulb (OB) through the cribriform plate. The receptors are not specific to only one odorant, but an odorant can bind to various receptor types.

ORNs carrying the same OR converge in the same area within the OB (glomerulus).

The activation of distinct types of receptors causes different excitation patterns in the OB. The quality coding of odours depends on the model of diverse excitation patterns. ORN axons synapse with the mitral cells in the olfactory bulb. Axons of the mitral cells follow the olfactory tract and split into two bundles. Most fibers project to the pyriform, entorhinal cortices and to the amygdalae (it could explain the emotional character of odours and the major role of odours in memory records)[9]; other fibers project through the thalamus into the orbito-frontal cortex.

Trigeminal system

Given the close connection, from an anatomical and physiological point of view, between the olfactory and the trigeminal system, a strong and continuous interaction is evident[10,11]. The trigeminal system ensures the somato-sensory innervation of the nasal mucosa, which means that, in most cases, it is co-activated in the perception of odours. This is due to the fact that almost all odorants exhibit trigeminal activation[12]. The fact that trigeminal stimulation can be localized has important consequences in the clinical assessment, the system supplying olfactory function by giving information on the temperature, pain, touch, irritation. Although in patients with olfactory impairment the trigeminal system is also weakened, there are extremely rare cases when patients have complete trigeminal loss[13-15].

Olfactory coding

Olfactory information encoding represents a topical subject. Several theories have been proposed. According to Mozzel, the odorants cross de mucous film to reach the specific receptors that are placed on the cilia of the olfactory neurons[16,17]. Another theory suggests that the olfaction recognition is mainly based on a few fundamental odours and what encodes the olfactory information is the combination of those[18,19]. The vibration properties of the odorants are the base for an old model. Another theory is based on the fact that odorants are chemical structures; therefore, a ligand-receptor interaction is implicitly involved. This theory was confirmed in 1991 when a family of seven transmembrane receptor proteins was discovered. They are peculiarly expressed in the olfactory epithelium. This finding led to a number of new discoveries, like topographical organization and distribution of ORNs within the olfactory epithelium. Furthermore, it was observed that every ORN expresses just one OR gene and that ORN axons with the same OR project into 2 glomeruli in each olfactory bulb. In conclusion, OR are not selective for only one odorant, but each odorant is recognized by more ORs[15,20,21].

Olfactory disorders

It is known that olfactory sensibility depends on age and even on gender. Presbyosmia, decreased ability to smell with increasing age, is quite frequent, but it seems that progressive loss is not noticed or complained of[15]. Women are superior to men in what the olfactory function is concerned[22]. The reason remains unclear; the hormonal effect has been associated with this fact, but it is still a matter of debate.

When speaking about olfactory dysfunctions, one must mention the quantitative and qualitative smelling disorders.

Quantitative smelling disorders are: anosmia, hyposmia and hyperosmia. Anosmia describes the disability to smell; the specific anosmia refers to the disability to smell a certain odour, but the rest of odours are distinguished; while functional anosmia is the ab-

sence of the capacity to smell although some olfactory sensations can be present[15]. Hyposmia is a reduced ability to smell (common condition), and hyperosmia refers to an improved capacity to smell (very rare).

Concerning the qualitative smell disorders, one must mention parosmia - the qualitative "wrong" perception of odours and phantosmia - the cognition of odours in the absence of an odour source. Parosmia is often associated with reduced olfactory sensitivity. Also, numerous patients with qualitative smell disorders are frequently suffering of depression[23].

The etiology of olfactory disorders

The most frequent causes of smell dysfunctions are: viral infections, nasal pathologies, sinonasal or head trauma, aging or neurological diseases (e.g. Parkinson's disease, Alzheimer's disease, Lewy-Body dementia, multi-system atrophy, Huntington's disease, heredoataxias and motor neuron diseases, etc.)[24,25-29].

Viral infections are incriminated to cause ORNs' damages[30]. It is not known which the agent is in this case: the virus, the bacteria or the local immune response. Inflammation is considered to be the major factor responsible for functional impairment of the mechanical access of the odour to the olfactory epithelium. Nasal polyposis, allergic rhinitis or chronic rhinosinusitis are often associated with mild olfactory impairments. Olfactory dysfunction after head trauma imply fila olfactoria injury or lesions of olfactory-related zones of the brain[31,32]. In what the neurological diseases are concerned, it has been observed that decreased olfactory sensitivity is one of the first symptoms, long before the pathognomonic symptoms appear.

Other causes of smell disorders are congenital anosmia (occurring isolated or within a syndrome – Kallmann syndrome)[33], exposure to toxic substances (e.g. cardiovascular drugs, anti- hypertensive drugs, antibiotics)[34-37], psychiatric diseases like schizophrenia, depression or epilepsy.

In certain systemic diseases (sarcoidosis, lupus erythematosus), endocrine disorders (hypothyroidism, diabetes) or isolated organ deficiencies (kidney/liver failure), dysfunctions are also encountered. Patients with different types of cranio-facial tumors (e.g. esthesioneuroblastoma, sinonasal carcinomas, benign or malignant brain tumours) may face smell disorders. In what iatrogenic causes of smell loss are concerned, different types of ENT procedures have been mentioned (e.g. septoplasty, polipectomy, ethmoidectomy), neurosurgical operations, radiotherapy, intake of medicines[1].

Assessment in olfactory disorders

Detailed patient's history is very important - daily habits like eating, drinking, smoking or use of medicines, also if the patients reports accidents or surgery interventions in the past, as well as if local symptoms that could indicate a local pathology (nasal obstruction, rhinorrhea, facial pain) in the near or distant past exist. Previous medical history related to mentioned pathologies or zinc, vitamin A or B12 deficiencies must be known.

ENT examination must assess the ability to breathe - must verify if any kind of pathology is present in the area of the middle turbinate or olfactory cleft region that may impede the odour molecules access to the olfactory neuroepithelium.

A neurological evaluation must be made in order to establish whether the condition is central or peripheral, or to find other lesions.

A MRI is often necessary to evaluate a possible sinonasal or brain pathology; moreover, MRI is considered to be the gold standard exam for assessing congenital smell disorders (aplasia, hypoplasia of OB). The OB volume varies depending on olfactory sensibility and is reduced in patients with olfactory impairment. An interesting fact is that the OB volume can grow during recovery, highlighting its plasticity[38]. MRI protocol implies coronal 2-mm-thick T2-weighted images. These images manage to evaluate the anatomical olfactory tract, the existence of any parenchymal lesions and the volume of the olfactory bulb[38]. Applying planimetric delineation in all frontal slices of the FSE T2-weighted sequence gives the possibility to measure the olfactory bulb volume as follows: the OB surface (in mm^2) is contoured, then the sum of the surfaces on all slices is calculated and, in the end, the result is multiplied by the thickness of the sequences. For healthy people under 45 years the average volume of the olfactory bulb is 58 mm^3, while for those aged over 45 years the minimum volume of the olfactory bulb is 46 mm^3.[38]

Psychophysical testing of orthonasal olfaction. There are several screening tests for orthonasal olfaction and specific examination procedures.

Screening tests must be able to differentiate a "normosmic" from a "hyposmic/anosmic". "Sniffin' Sticks" involves smelling 3, 5 or 12 odours and it can give a comprehensive outcome[39-41]. The odours are contained in felt-pen appliances. The odour is released when the cover is removed. Afterwards, the pen is held about 2 cm under both nostrils for 3 seconds. Patients are required to recognize the odour from a list of four choices. The procedure is based on a forced choice paradigm. The sum of all right answers represents the total outcome.

Moreover, for a detailed evaluation of olfaction, standardised tests have been developed. These special tests permit a correct estimation regarding the threshold identification for odours and the above-threshold odour concentrations rank, the capability to distin-

guish between them, or to explore the smell remembrance[1]. They are divided into 3 parts: threshold, discrimination and identification tests (TDI)[42]. The best-validated tests are the University of Pennsylvania Smell Identification Test (UPSIT), the Connecticut Chemosensory Clinical Research Center test (CCCRC-test) and "Sniffin' Sticks". The tests method is based on a forced choice paradigm as follows: the patient is submitted to an odorant and he/she has to recognize it from a list of odours. The odours concentration is above threshold.

The concentration at which the odour is certainly detected is also stated by the threshold tests. The patient is presented three sticks - one stick bears the odour, the other two contain the solvent without the odour.

The discrimination tests investigate patient's capacity to distinguish odours. The patient is also given three sticks - two of them have identical odour and one a different one. The subject must recognize the odd stick[1].

The identification test is similar to the UPSIT – the patient must answer 40 questions, 4 different 10-page booklets. On each page, there is a different strip and also a four-choice question. There is an answer column and the test is scored out of 40 items. The score is compared to scores obtained by normosmic subjects[1].

Psychophysical testing of retronasal olfaction. Nowadays, there is a reliable psychophysical test for the assessment of retronasal olfaction[43,44]. The test involves placing a taste powder in the mouth and asking the patient to detect and mention the taste from a list of four choices.

Electrophysiological procedures to study olfaction

- *Electro-olfactogram (EOG)*

The principle on which the electro-olfactogram is based is that the response to olfactory stimulation of the neuroepithelium is represented by electrical potentials. The EOG is the sum of these potentials.

Nevertheless, the electro-olfactogram has not been yet systematically used in patients with olfactory impairment, due to the topographical specificity of the responses. But the impediment to a correct analysis is that certain odorants are recorded only in some particular epithelial sites and, also, the presence of an electrical potential may not always represent an odorous sensation[15]. Therefore, the current medico-legal value is limited.

- *Olfactory Event-Related Potentials (OERPs)*

OERPs are a reliable technique that can be performed in order to evaluate the olfactory system. This method permits to objectively identify changes in the olfactory function. Moreover, the response does not depend on patient's partiality. In conclusion, OERP presence is an indicator of normal function of the olfactory system; also, the OERP absence is relevant for an olfactory dysfunction.

The activation of cortical neurons generating electro-magnetic fields is represented by poly-phasic signals[45]. In addition, OERP testing typically involves the recording of responses to all stimuli, whether they are olfactory or trigeminal[15]. Three electrodes are placed on the midline of the scalp (Fz, Cz, and Pz). Such disposition allows to detect the cortical regions activated by the stimuli and to establish the OERP topography.

OERPs are the representation of the activation of various brain areas, beginning from the OB, the olfactory tract, orbitofrontal and insular cortices, reaching into the rostrum-medial regions of the temporal lobe[46,47]. The main components of the OERP are N1 – a large negative wave and P2 – a large positive component. P1 and N2 are frequently undetectable. The N1 and P1 are the early OERP components. N1 and N2 are the representation of the exogenous cortical activity. N1 and N2 are correlated with the identification of sensory input detection and primary cognitive processing. P2 is a later OERP component; it reflects endogenous cortical activity related to secondary sensory processing[48,49]. The OERP's principal parameters are latency and amplitude. Latency of N1 and P2 measures the time needed for processing the sensory and cognitive characteristics of odour stimuli. Amplitude represents the significance of the odour stimulus and its contained information[49]. The latency of P2 gained high reliability. It can be observed from 530 to 800 ms after stimulus onset. N1 and P2 components have maximal amplitudes in Cz and Pz positions[50].The amplitude of N1-P2 lies between 4 and 20 μv[50]. It is one of the most important assessment methods in medico-legal questions.

- *Functional Magnetic Resonance Imaging (FMRI)*

FMRI uses the Blood Oxygenation Level Dependent Effect (BOLD Effect) to evaluate blood flow changes that may appear in the brain. This assessment method is based on the increased neuronal activity that raises the blood flow in this region. Beside determining when the activation occurs, it also indicates the cerebral area involved[51,52]. There are no standardised test protocols. Also, due to a great variability of the results obtained until now the test cannot be routinely used in a clinical setting.

- *Single Photon Emission Computed Tomography (SPECT)*

SPECT is an imaging method that measures the increase of cortical perfusion after sensorial stimulation. It is considered an objective method and a quantitative imaging assessment modality[53]. Some authors sustain the fact that SPECT may be more efficient than FMRI; for example, the orbitofrontal cortex is better visualized by SPECT than FMRI. Thereby, signal distortions could appear due to its location near the skull base[54].

Other techniques that may be useful are: positron emission tomography (PET)[55-57] and magnetic source imaging (MSI) based on magneto-encephalography[58,59]. However, these techniques await further standardization.

- *Biopsies from the olfactory regions*

Recent studies mentioned the importance of biopsies from the olfactory regions, but there are still many unanswered questions related to these tests[60-62].

TRAUMATIC HEAD INJURY AND OLFACTION

Olfactory dysfunction is known to be a sequel in traumatic head injury since the 19th century[63]. It is one of the most important causes of olfactory loss. The frequency of olfactory dysfunctions after THI oscillates within vast limits in performed studies. Authors reported percentages between 4 and 65%[63].

At first, the general belief was that the severity of the trauma was proportional with the degree of olfactory sensation loss. Nowadays, it is well known, though even minor THI could determine anosmia[64]. Within the reviewed clinical studies, the reported prevalence of patients with olfactory complaints among cases with "mild" THI was between 20% - 44%; among those with "moderate" THI: 37% - 68.4%; with "moderate to severe" THI: 49% - 56%; and with severe THI: 33% - 61%[65].

Occipital traumas are reported to be more often responsible for olfactory impairment than the lesions localized in frontal or parietal regions[63]. Still, other studies reported that frontal lesions were associated with worse performance on olfactory tests[65].

Olfaction may be impaired due to lesions situated at the olfactory nerve filaments, on the cribriform plate, on the olfactory bulb or the olfactory tracts. Also, the olfactory nerve filaments can get torn by fractures involving the cribriform plate of the ethmoid, can be sheared off by frontal or occipital injury, affected by acceleration or deceleration forces with secondary avulsion of the roots in contrecoup injuries, by fractures in the region that can lacerate the filaments. Olfaction dysfunction could appear in oedema, ischemia or haematoma. Closed head trauma in orbitofrontal and temporal lobes can generate dysfunction of olfactory recognition in spite of preserved olfactory identification[66].

Concerning the assessment of a patient with THI facing subsequent olfactory dysfunction, it must be said that there are not yet standardized protocols.

First, olfactory function tests are not the first intention in these cases. Thereby, almost all the patients with posttraumatic olfactory impairment become conscious of the dysfunction some day later. Often, they complain several days or weeks after the trauma, when the health status improves.

At this moment, a very detailed history of the patient must be reviewed. The following are important: traumatic head injury severity - often defined by the Glasgow Coma Score (GCS), the duration of post-traumatic amnesia (PTA), the moment when the loss of smell occurred and the duration of loss of consciousness (LOC) and also other investigations that the clinician can perform immediately following THI. Also, if the patient's health condition permits, following THI, it is recommended to evaluate the functional outcome (neuropsychological test performance, behavioural tests or other functional questionnaires)[65]. Additionally, one must insist on the olfactory status before the THI. However, the specialist knows that the patients' answers are not always reliable.

Moreover, another problem in evaluating patients with olfactory impairment – especially in cases where medico-legal issues are involved – is the difficulty of quantifying olfactory losses accurately. If a clinician encounters an anosmic patient following traumatic head injury, it would be recommended to search also the possible presence of a neurobehavioral disease or task-related deficits associated with damage to the frontal lobes.

Nowadays, even if the most sophisticated systems for measuring olfactory recognition - the "Sniffin' Sticks" or, more often, the University of Pennsylvania Smell Identification Test are used, they are still dependent on the patients' subjective responses.

With respect to the objective assessment methods, such as EOG, OERP, MRI, FMRI, SPECT, PET, MSI, the lack of studies and the absence of clinical data correlation make them still uncertain when distinguishing a malingerer from a real patient.

Concerning the OB volume, it would be ideal having a pre-THI MRI to compare it in order to exclude pre-existing conditions.

Another important fact is that, although functional neuro-imaging is sensitive to the presence of post-traumatic impairment of anatomical structures and function of the olfactory system, hypo-metabolic activity or decreased perfusion in the prefrontal regions is not necessarily a specific indicator of THI. It must be said that it is well known that there are other diseases with nearly the same characteristics on imaging.

Regarding the olfactory impairment after THI, many studies show that, although there may exist some improvement, most of the patients rarely regain total olfactory function. Also, olfactory dysfunctions after THI are considered permanent if recovery does not appear early in the evolution[63]. Thus, several studies reported that the recovery in THI is more often encountered in young patients compared with old age ones[63].

MALINGERERS OR PATIENTS WITH OLFACTORY DISORDERS?

Conscientiously assessing olfactory function is likely to be especially difficult, especially when medico-legal involvement exists.

Since reduced sense of smell is most often tested clinically by presenting odorants and obtaining a verbal report from patients, the olfactory dysfunction became subject to malingering in the context of litigation following head trauma.

A detailed and well managed history patient could guide de specialist regarding such an intention – an experienced practitioner may identify the intention to feign.

In what the psychophysical tests are concerned, malingerers could cheat on them since information is widely available. Nevertheless, one of the keys in this kind of tests could be the odours that stimulate the trigeminal system. Malingerers often do not identify these odours and their scores in the mentioned tests (UPSIT, Sniffin' Sticks test) are smaller than the ones obtained by the certificated anosmic persons.

In order to establish if it is the case, more objective tests, which depend less on the patients' cooperation, must be performed.

CONCLUSIONS

Olfaction is one of the main senses of the human being, but only recently has the scientific community commenced to give smell the amount of attention it deserves.

The olfactory sense is important for everyday activities (nutrition, non-verbal communication or simply to satisfy small pleasures like perfumery, etc.) but also in dangerous situations, when it functions like an alarm signal.

The loss of smell seriously affects the patient's quality of life. The most frequent causes for olfactory dysfunctions are viral infections, brain or nasal trauma, nasal diseases. In traumatic head injury, the smell assessment is not routinely performed; only after the vital danger has passed or if the patient complains about the loss of smell (days or even weeks after the incident). The percentage of patients that encounter this pathology in given circumstances (THI) varies greatly in studies. Likewise, it seems that not only the reported trauma (with certain gravity) can cause olfactory impairment, but also small and, initially, unimportant injuries.

Concerning the olfactory evaluation, nowadays psychophysical, electrophysiological and imaging methods are used. Yet, a standardized protocol for assessing this pathology does not exist.

Given the fact that THI represents one of the most frequent aetiologies of olfactory dysfunctions and often associates medico-legal implications, more attention must be paid in this field.

Malingering in olfactory disorders is, therefore, more frequently encountered in medico-legal litigation due to diagnosis methods that are not standardized. Thus, great progress has been made, more objective techniques of evaluation being lately developed. Nevertheless, olfaction receives an increasingly interest from researchers, becoming nowadays an important topic.

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