

Functional magnetic resonance imaging and swallowing: systematic review

Ressonância magnética funcional e deglutição: revisão sistemática

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ABSTRACT

Purpose: Evaluate the feasibility and safety of functional magnetic resonance imaging (fMRI) for the evaluation of cortical areas involved in swallowing. **Research strategy:** The search was conducted from April 2003 to April 2013, using the keywords “functional magnetic resonance imaging” or “fMRI” and “dysphagia” and “functional magnetic resonance imaging” or “fMRI” and “swallowing” in “PubMed” database. **Selection criteria:** Studies were reviewed by analyzing their titles and abstracts with the following inclusion criteria: research involving human subjects, use of neurofunctional tests, reference to swallowing function, adult and/or elderly population analysis and association with neurological disorders. **Results:** the search strategy resulted in 1167 citations, from which only 35 met the eligibility criteria. **Conclusion:** the functional magnetic resonance imaging was considered safe and feasible for evaluating cortical areas involved in swallowing. However, the reports of functional magnetic resonance usage differed between the reviewed studies and the variability in the methodology used, made meaningful comparisons difficult.

Keywords: Disorders of swallowing; Neuroimaging; Swallowing; Neurology; Neurological diagnostic techniques

RESUMO

Objetivo: Avaliar a viabilidade e segurança da ressonância magnética funcional para a avaliação de áreas corticais envolvidas na deglutição. **Estratégia de pesquisa:** Conduziu-se uma busca entre abril de 2003 e abril de 2013, usando as palavras chave “functional magnetic resonance imaging” or “fMRI” and “dysphagia” e “functional magnetic resonance imaging” or “fMRI” and “swallowing” na base de dados PubMed. **Critérios de seleção:** Os estudos foram revisados por análise de seus títulos e *abstracts* e os critérios de inclusão utilizados foram: pesquisas envolvendo seres humanos, utilização de exames neurofuncionais, referência à função de deglutição, análise de população adulta e/ou idosa, relação com patologias neurológicas. **Resultados:** A estratégia de busca resultou em 1167 citações, das quais apenas 35 preencheram os critérios de elegibilidade. **Conclusão:** A ressonância magnética funcional foi considerada segura e viável para a avaliação de áreas corticais envolvidas na deglutição. Entretanto, os relatos de utilização de ressonância magnética funcional diferiram entre os estudos revisados e houve variabilidade na metodologia utilizada, dificultando as comparações.

Descritores: Transtornos da deglutição; Neuroimagem; Deglutição; Neurologia; Técnicas de diagnóstico neurológico

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INTRODUCTION

Swallowing is one of the processes that ensure the human being survival and its disorders require global health care. Among its consequences are dehydration, malnutrition and pulmonary complications involving aspiration, pneumonia and deficits in the quality of life⁽¹⁾. Initially, research in neurophysiology swallowing restricted the process to functional mechanisms of the brain stem. Subsequently, however, thanks to advances in the use of functional neuroimaging techniques, the cerebral cortex contribution in the swallowing control has been better understood⁽²⁾.

The complexity involving swallowing is the result of a sequence of coordinated movements, including pressure balance, sensory processing of ingested food and synergistic movement of the muscles involved in the oral, pharyngeal and laryngeal regions. It is synchronized with other stomatognathic functions such as breathing and chewing and, when voluntarily performed, requires a cognitive processing and attention activation⁽³⁾. From the first swallowing component until the last stage of the solid bolus movement, multiple oral and perioral muscles are used⁽⁴⁾.

The knowledge of the swallowing neurophysiology, including understanding the role of different brain structures in the movement synergy, can bring new perspectives of dysphagia management and treatment. Studies in the fMRI brain field (functional MRI) in recent decades have helped to understand the brain spatial and temporal activities of swallowing by means of a noninvasive procedure. Although fMRI is an important tool for understanding the brain mechanisms involved in swallowing, the methodologies and paradigms used are varied.

PURPOSE

The purpose of this systematic review was to identify and compare brain activation during swallowing, analyzing the tasks used and stimuli provided to patients in healthy adults, elderly and with dysphagia.

Data collected for the functional MRI studies were analyzed in order to verify the safety and reliability of the findings, in a comparative way.

RESEARCH STRATEGY

To identify the swallowing and brain imaging studies, a search of publications available in PubMed and MEDLINE databases was conducted. In order to achieve a broad base of literature review, the research including studies published since 2003. The survey was conducted using the following keywords: “*functional magnetic resonance imaging*” or “*fMRI*” and “*dysphagia*” and “*functional magnetic resonance imaging*” or “*fMRI*” and “*swallowing*”.

SELECTION CRITERIA

The studies analyzed by two examiners independently, were selected according to the following inclusion criteria:

- Published between 2003 and 2013;
 - Original studies involving human subjects;
 - studies, whose objective was the evaluation of swallowing through the brain neuroimaging;
 - Analysis on adult or elderly population.
- Exclusion criteria used for this work were:
- Samples with animals;
 - Samples with fetuses, children and adolescents;
 - Evaluation of related functions such as speech, voice, among others;
 - Peripheral structures evaluation: larynx, pharynx, tongue, vocal folds;
 - No use of fMRI.

Full texts were classified according to the type of study (case study, meta-analysis, systematic review or experimental); type of protocol used to collect the cortical functioning of images; the sample size; the population characteristics and results found. The tests results were compared between two evaluators and the criteria classification was revalued in a consensus meeting, analyzing differences. Differences occurred in the articles classification exclusion. Therefore, the hierarchy among the topics for deletion was established and unselected items were reclassified.

The search for studies published between April 2003 and April 2013 resulted in 1167 articles, of which 397 were repeated. 728 abstracts were excluded for not using neurophysiology assessment techniques, studies not related to swallowing functions, anatomical functioning and/or functional studies sensory oral motor system, among others. 35 complete articles that met the proposed criteria for this systematic review were included.

Figure 1 shows the breakdown of the articles analysis.

DATA ANALYSES

Determining the recommendation degree and level of evidence

Articles framed in defined criteria were assessed by two researchers on the type of study, level of evidence and recommendation grade, according to the Oxford Centre for Evidence-Based Medicine Classification. In a consensus meeting, studies were organized (Figure 2).

RESULTS

Population studied

The number of subjects in the selected relevant studies ranged from 1⁽⁵⁾ to 56⁽⁶⁾. Scientific articles were categorized

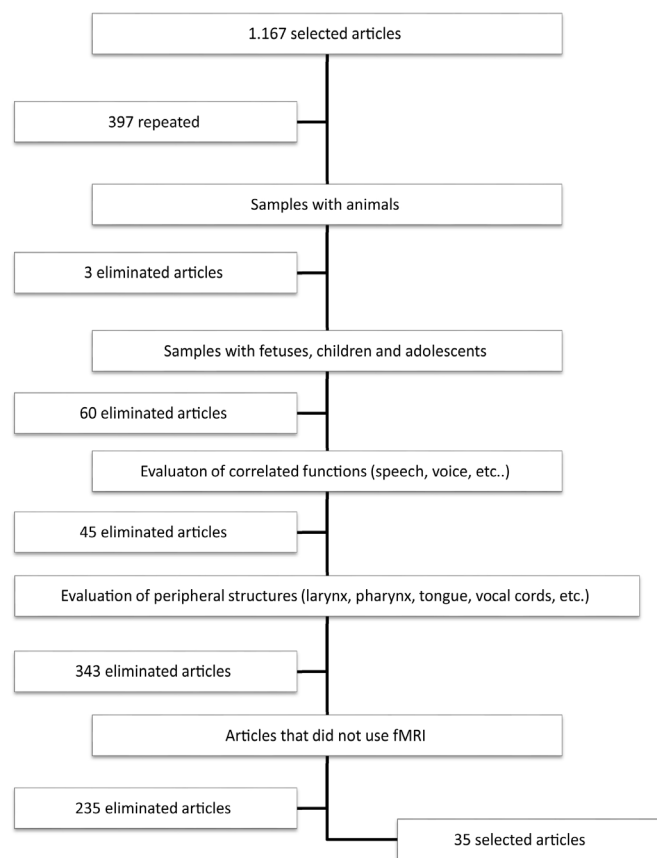


Figure 1. Selection of abstracts and articles complete texts

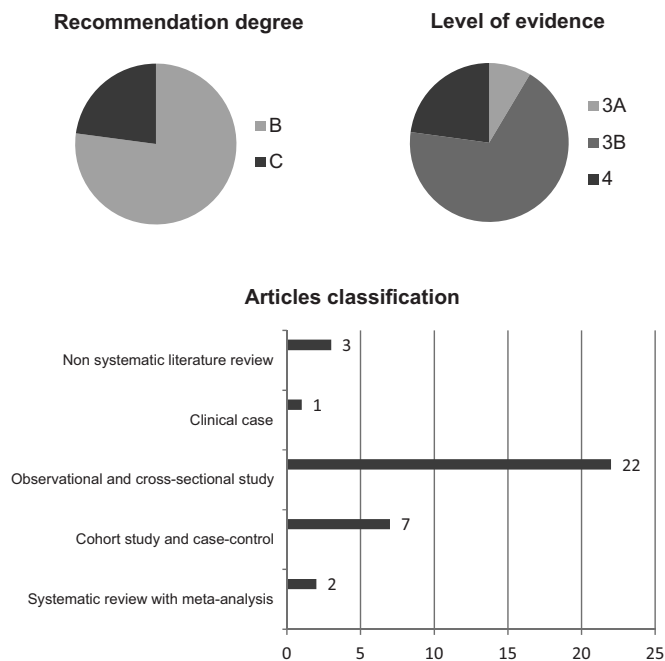


Figure 2. Distribution of items according to the recommendation degree, level of evidence (Oxford Centre for Evidence-Based Medicine) and its classification

and classified into clinical cases, meta-analyzis, systematic reviews and experimental studies.

Studies involving healthy volunteers aimed to search for

specific features to the swallowing cortical representation^(3,7-25). Research on elderly and patients with dysphagia underwent compared to control groups. There was a tendency to use healthy adults for comparison with elderly people^(1,26,27), except in two researches^(5,28). Studies involving dysphagia patients groups or patients with specific diseases were compared with those who evaluated healthy individuals, matched by chronological age and elderly patients^(6,29-32).

Tasks used

A chronological analysis of the presented studies, observed that initially the concern was the confirmation of cortical activation mechanisms for swallowing

Therefore, procedures such as saliva^(1,3,5,7,16-20,22,23,26,29-32), water^(5,11,12,17,24-26,28,29,31), barium^(5,26,29,31) swallowing were performed, comparing swallow and not swallow^(1,7,14,27). Later on, studies began to analyze differences in the cortical areas, responsible for each motor phase, differentiating the role of the structures involved. To this end, electrical stimulation⁽²⁴⁾, swallowing by means of air pulses in the oral cavity^(13,31), gustatory stimulation^(12,17,24), olfactory⁽⁹⁾ and stimulation of the esophagus^(1,6,15) were employed.

In an attempt to assess the representativeness of sensory-motor organs, the authors proposed an examination of cortical responses to movements used in rehabilitation procedures, such as orofacial exercises^(1,14,21,27) and maneuvers used in rehabilitation⁽¹⁸⁾.

Even on population with dysphagia, they used swallowing of different types of food, such as water^(5,29-31), barium^(5,29,31) and saliva^(5,29-32). In the case of food introduction, they were generally administered by positioning a catheter in different portions of the oral treatment, varying in time and food volume administration. Agar-agar seaweed⁽¹⁰⁾ was used as solid food, for being devoid of flavor, and chewing gum⁽⁸⁾ to evaluate the chewing and swallowing.

Stimulation type and swallowing monitoring

The motivation to study the stimuli used to trigger the swallowing process emerged as a result of competitive activation of stimuli on brain areas. The overlap of the swallowing task with the trigger for its elicitation makes it difficult to determine the areas truly activated during the swallowing act.

Researches show that tasks requiring attention activate a group of cortical regions related to the nature of the task (sensory, motor, cognitive, visual or auditory).

Guidance provided to different groups of surveyed subjects included visual^(3,7,8,10,14,16-19,23-28,30-32), hearing^(6,16,21,29) and sensorial clues^(5,9,11,13,15,17,19,24,29). In studies examining the food swallowing, its ingestion was the track for the patient to swallow, i.e., the absence of formal statement was a major factor, differentiating it from studies with other types of tasks.

The use of fMRI techniques provides high resolution anatomical images, which can detect human tissue variations⁽⁵⁾. The biggest advantage of this technique is related to security, for it is a non-invasive method of investigation of the human brain operating processes, capable of detecting relatively small signal changes, with high resolution reliability and location in areas used in the neuronal activity. Furthermore, it allows many brain areas to be analyzed with relative ease⁽⁵⁾.

The fMRI disadvantages making the swallowing operation depend on the examined patient positioning, who should be in a supine position during mapping, which means an unfamiliar position, making it difficult to search different food types, beyond saliva. It is assumed that swallowing without food intake, i.e., saliva only, when lying down, occurs in people's various everyday situations, either asleep, or awake. However, the authors agree that it is doubtful that the neural swallowing activation would vary according to body positioning^(3,14,33). Other factors that may influence the signal accuracy include the use of medication and its effects on the hemodynamic response of neural excitability, the motion artifacts required for certain motor tasks in assessment and the patient's degree of relaxation⁽⁵⁾. It is evident that the swallowing cortical representation involves various related fields, as a network of sequential or simultaneous activation, found in the pre-motor cortex, the sensory-motor, cingulate gyrus and some limbic regions⁽¹⁴⁾. Therefore, the clinical findings suggest that there may be the existence of a functioning network for swallowing⁽³⁾.

In an attempt to elucidate the activated locations contributions during swallowing, an experiment using the "swallow, not swallow" paradigm was designed aiming to compare these conditions. The tasks have been previously trained with patients and, for the swallowing task, saliva was used. The experiment was considered satisfactory and the suggested tasks suitable to achieve the proposed objectives⁽⁷⁾.

The orofacial exercises and tongue, lips and jaw movements have been used in order to monitor the activated cortical areas, serving as a control task for the swallowing analysis^(3,14,21,27). Movements involving the tongue mobility can be used to monitor the activated cortical areas, serving as an important comparative feature between the cortex regions.

The use of short air pulses directed to the posterior oral cavity and the oropharynx, monitored during fMRI, aimed to analyze that region processing during swallowing. The authors argue that the use of this type of stimulation useful for research is effective and well tolerated by the subjects, allowing exploring the oral and oropharyngeal sensory systems, increasing the swallowing frequency⁽¹³⁾.

Cortical regions activated

Current evidence on the cortical regions involved in swallowing have been obtained thanks to fMRI studies results

in humans⁽³⁴⁾. Multiple regions of the brain are seen as responsible for this task, however, the functional contributions of each region remain uncertain⁽³⁾. Studies suggest that the neuronal activity is located in different cortical regions, including pre-central, post-central gyrus and insula for saliva automatic swallowing, saliva voluntary swallowing and food bolus swallowing⁽¹³⁾. Meta-analysis studies show that networks involved in swallowing water and saliva are distributed and partially overlapping in the cerebral cortex⁽³⁵⁾.

The back of the oral cavity and oropharynx have a decisive role in the swallowing process. The experience of monitoring them concluded that their stimulation can activate a cortical network bilaterally distributed, which overlaps the regions previously involved in the pharynx sensory motor functions, as well as the tongue movement, chewing and swallowing. The direction of the food bolus through the oral cavity is preceded by the oral preparatory stage, which is highly dependent on the sensory motor cortical integration⁽¹³⁾.

In the meta-analysis articles, it is concluded that when swallowing water, there is greater activation in the sensory motor cortex, left parietal lobe and right anterior insula. For saliva swallowing, a higher activation in the left sensory motor cortex, right motor cortex and bilateral cingulate gyrus was found. The comparison between the two tasks revealed evidence of increased participation of cortical areas for water than for saliva swallow, in the inferior parietal lobe, right post-central gyrus and right anterior insula. The higher activation for saliva was found in the supplementary motor area, bilateral anterior cingulate gyrus and bilateral pre-central gyrus, which are crucial to the initiation and control of movement⁽³⁴⁾.

Combined techniques such as fluoroscopy video and fMRI were used to observe the oropharyngeal motor behaviors, associated with brain regions. Data were obtained through healthy adults' response analyses, who were passively watching to a movie. The fluoroscopy video use determined the beginning of swallowing and controlled the cortical activation analysis. The results found with fMRI were the activation of regions commonly identified as swallowing network areas. However, differences included the Brodmann activation areas 8 and 41 and precuneus, which may be related to the nature of the additional proposed task, requiring a visual demand⁽²⁰⁾.

The cortical activation result in response to auditory and sensory clues was investigated, in order to observe its effects on patients with dysphagia treatment. Through auditory, visual and audiovisual stimuli presentation of swallowing movements the brain areas, activated in healthy adult volunteers, were mapped. For visual stimulation, the primary and pre-motor areas of the right and left hemispheres as well as the pre-frontal area of the left hemisphere were activated. Concerning the auditory stimulus, answers in the supplementary area were observed and for the audiovisual stimulus, the pre-motor areas and prefrontal right and left hemisphere showed positive responses. It is concluded that the brain areas related to swallowing performance

and programming were triggered by visual, auditory and audiovisual stimuli provided⁽¹⁶⁾.

Studies showed no correlation concerning the lateralization aspects of the swallowing function in the cerebral cortex. The preparatory and oral stages have been linked by varying degrees of the bilateral cortical activation^(3,4). It was found that for the tongue lifting there is a preferred activation in the left cortex⁽⁴⁾. It is noted that this lateralization may be related to the dominance of the left hemisphere for language and lingual functions, including those associated to swallowing⁽⁴⁾.

The swallow and not swallow skills, tested in an experiment, suggest that pre-central, post-central gyrus and the anterior cingulate gyrus primarily contribute to the act of swallowing. However, contrary to what was expected, there was no difference in the cuneus and precuneus activation in both tasks, suggesting that these regions mediate the input signal of the swallowing process⁽⁷⁾.

Studies results suggest the occurrence of a bilateral activation in the neuronal extensive network, including pre-central gyrus (primary motor cortex) and multiple activations in the primary sensory motor cortex, supplementary motor cortex, prefrontal cortex, Heschl gyrus, cingulate gyrus, insula, Broca's area and superior temporal gyrus. The increased activation leads some researchers to suggest that these areas are not specific for swallowing, but indicate the location for related functions with the tongue, larynx, pharynx and face also⁽⁵⁾.

Hemispheric representation

The models of cerebral lateralization were analyzed using fMRI, by comparing preparing tasks for swallowing, swallowing, tongue pressure and clearing of oropharyngeal tract. The study included 10 young and 9 elderly people. The results showed that the hemispheric lateralization was more frequent in the young group for swallowing and planning and that the elderly people tended to combine laterality during swallowing and clearing the oropharynx⁽²⁷⁾.

Depending on each investigation's context, the swallowing lateralization may show different fMRI results. Comparing the cortical activation results, measuring water and saliva, it was concluded that there was initiation of the cortical activity, primarily in the right hemisphere for water and bilateral for saliva⁽⁴⁾.

It is noteworthy that the cortex primary sensory and motor areas are constantly driven in healthy adult subjects. Other activated areas also include the cingulate cortex and the insular cortex. When comparing saliva swallowing and the tongue lifting movements, it was found that approximately 60% of the subjects showed strong lateralization in post-central gyros for the left hemisphere, during the swallowing task. In 40% of the subjects, there was an activation similar to the language elevation, showing that there is no equivalence between the sensory motor oral cortex in different hemispheres, representing

a non equivalent functionality in the above mentioned tasks. Regarding the type of task requested, the study found that the activated regions for swallowing and the language movements are the same, being consistent with the pericentral lateral cortex, the front-parietal operculum and the anterior cingulate cortex, showing higher activation in the tongue mobility than for the swallowing task⁽³⁾.

Oral exercises have been widely used in the rehabilitation of patients with dysphagia, as it is believed that they affect nerve centers in various ways. Therefore, in a study analyzing the brain activity of eight healthy adults, performing labial contraction exercises, stretching lip, tongue protrusion, lateral movements of the tongue and roll a ball in the oral cavity, it was found that many regions increased their brain activity. The regions commonly activated during the lips and tongue exercises include the pre-central gyrus and cerebellum. The rolling the ball in the oral cavity activation activity was longer, compared with the other three exercises⁽²¹⁾.

The current trend in neuroimaging studies is to analyze the relationship between the cerebral cortex and sub-cortical regions, responsible for the swallowing task, in its different phases. The normal subjects fMRI during saliva swallowing and the tongue elevation showed that motor responses activate the pericentral lateral cortex, the anterior parietal cortex and the supplemental motor area adjacent, suggesting that these regions may serve both functions. However, the tongue elevation activates a larger volume of cortex than saliva⁽³³⁾.

To view the cortical activation of all swallowing stages, it was proposed to 10 healthy volunteers, responding to a visual stimulus, to perform the following movements: swallow, prepare to swallow, raise the tongue and throat clearing randomly. These movements were helpful to identify the neural location of various swallowing components. The more activated areas during the throat clearing, when compared to other tasks, were the posterior insula and small portions of the pre-central gyrus and post-central, bilaterally. The tongue elevation showed high activation in the pre-motor cortex portions, the primary sensory motor cortex and parietal lobes. Planning swallowing did not show greater activation of any particular region. When swallowing was compared to other tasks, there were more significant activation in the cerebellum, the thalamus, the cingulate gyrus and in all areas of the sensory motor cortex, bilaterally⁽¹⁴⁾.

DISCUSSION

Study of cortical representation in subjects with dysphagia

Studies on the neurophysiology of swallowing after neurological injuries can provide information on the brain operating implications, identifying the swallowing cortical representation⁽²⁾. For speech therapy, these studies are important for the understanding of normal and pathological physiology, to the

implications for rehabilitation. The motor aspects and sensory implications compose a set of monitored skills, due to its importance on the rehabilitation procedures⁽²⁾.

One study analyzing a eight weeks pre-treatment and post-treatment of a dysphagic patient with fMRI swallowing barium, water and saliva showed increased activation in the contralateral lesion, indicating plasticity related to treatment. To confirm these findings, muscle and dietary conditions were also considered, highlighting the patient food benefits⁽⁵⁾.

There is evidence of changes in swallowing cortical activation networks in healthy adults and patients with Alzheimer's disease (AD). In a study aiming to analyze swallowing through saliva, water and barium use, the control group subjects - healthy adults - showed higher cortical activation in the swallowing network than the group with AD, for water and saliva swallowing. There was great activation of the insula and operculum for the experimental group, in agreement with previous studies showing that these areas are activated with the swallowing onset. Patients need to make additional efforts to "bind" the swallowing centers, putting the function in a conscious alertness⁽³¹⁾. The study highlights that there is a preclinical condition of dysphagia in patients with this pathology, and therefore patients should be carefully evaluated⁽³¹⁾.

The comparison between subjects diagnosed with neurogenic dysphagia post stroke was performed using the saliva swallowing task during the fMRI procedure. The results showed activation opposite to the lesion, in areas related to swallowing, i.e., patients with lesions on the right hemisphere showed great activation on the left hemisphere and vice versa for patients with injury on the left side. These findings enable the analysis of cortical adaptation phenomenon of the neurological damage process⁽³²⁾.

Similarly to the previous study, patients with Amyotrophic Lateral Sclerosis (ALS), with and without dysphagia, were compared to healthy individuals. Results concluded that the non dysphagia group had neurophysiologic responses similar to the control group. However, dysphagic patients showed reduced signal, specifically in the primary motor sensory cortex⁽³⁰⁾.

The implications on neuroplasticity are particularly important in speech rehabilitation processes. In a case study with a dysphagic patient, the neural activation was compared for barium, saliva and water swallowing. The authors state that results should be analyzed with caution, but point out that, in neurofunctional post-treatment evaluations, more areas in both hemispheres, ipsilaterally and opposite to the lesion were activated⁽⁵⁾.

Studies with fMRI in populations of dysphagic patients have limited use in determining results due to difficulties related to patient's positioning, postural changes during the exam and its duration. However, these studies may have important information on adaptations of the brain in neurological damage in acute or chronic disease's phase⁽⁵⁾.

In studies with dysphagic patients, it is still necessary to

analyze the characteristics of neurological damages, such as location, size, etc. In neurodegenerative diseases, implications as the pathology diagnosis time, the intensity of symptoms and treatments provided to the patient may also produce variants to be studied.

The rehabilitation processes variables, such as time, intensity and treatment characteristics need to be carefully controlled, so that data can be generalized.

Study of aging and the swallowing cortical representation

It is reported that extra cortical activation is found in elderly, when compared to young adults, in swallowing the same type of bolus and it is believed that this difference may be related to the first group increased effort needed⁽⁵⁾. This activation increase was found in somatosensorial areas in both cerebral hemispheres and may be due to inaccuracy in swallowing, according to age. The effects on the swallowing physiology have been shown in all phases, but specifically the increase of the oral phase and the reduced pharyngeal sensitivity lead to difficulties in the swallowing reflex trigger^(1,5). Moreover, it is noted that the areas involved in the sensory processing, sensory integration and motor coordination, show limited cortical activity in elderly patients⁽³⁾.

Physiological changes in the functional behavior of the elderly swallowing are described in literature. Through water and saliva swallowing, the activation trigger of multiple cortical regions was found, including anterior cingulate cortex, perisylvian and pericentral lateral. The activation of the post-central gyrus was lateralized to the left hemisphere in swallowing of the two comparative situations. The activation relationship between saliva and water swallowing showed a fourfold increased volume for water related to saliva, particularly in the right hemisphere of the pre-motor and prefrontal cortex. This finding may suggest a compensatory response in water demand, compared to saliva, due to the sensory motor functional abilities decline related to age⁽²⁸⁾.

Comparing healthy adults and elderly in saliva, water and barium swallowing, through video-fluoroscopic and fMRI analyses, we found increased brain activity in elderly cortex regions, indicating they required greater effort to swallow. This factor may be related to the increased need of the sphincter response to swallow different bolus types and also an additional effort in memorizing tasks inherent to these procedures. The barium swallowing recruited more regions and saliva swallowing an increased number of activated areas, with non associated specific functions for this function, bilaterally⁽²⁶⁾.

In patients with Alzheimer's disease at an early stage, the mapping of cortical areas responsible for swallowing demonstrated less activation of regions traditionally identified as constituents of a working network. This also occurs in areas commonly affected by the disease typical clinical picture.

Therefore, authors point out that investigation with functional neuroimaging means showed that swallowing includes regularly cortical cognitive areas⁽²⁹⁾.

The effects and results found in the analysis of the selected studies are related to the ability to objectively measure the changes undergone in the cortical tissue and therefore, generalize this information to the rehabilitation process.

Different paradigms have been used by researchers and applied in different population groups and, just recently, research models have been applied in dysphagic patients. It is difficult to generalize the results obtained in researches, due to the variability of tasks and stimuli used that generate activation of non specific areas to swallowing, however related to the received stimulus. The establishment of guidelines for fMRI studies is suggested, in order to standardize and classify applied protocols, facilitating the comparison with similar studies.

CONCLUSION

The study of swallowing neurophysiology is a valuable method for understanding the normal and pathological physiology, which can contribute to the rehabilitation techniques innovation. Despite differences in paradigms used in the studies, it appears that the activated areas during swallowing are not specific, i.e., the swallowing cortical representation seems to be multifocal and overlapped to the motor areas responsible for controlling the oral motor gestures.

Therefore, an extensive field of research opens up in the swallowing neurophysiology and its rehabilitation, when the typical physiological mechanisms are understood, in aging and disease.

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ERRATUM

On page 167:

Which read:

“Ana Carolina Batezzini”

Read:

“Ana Carolina Battezzini”

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