


REVIEW

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Impact of anxiety and depression on the swallowing process among patients with neurological disorders and head and neck neoplasia: systemic review

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Abstract

Background Dysphagia is associated with depression and anxiety due to the severity, impact of symptoms itself or secondary to the underlying cause. This is more recognizable to brain diseases that has consequences common to the neural supply of the swallowing act and the cognition and behavior. Limited data are available to explore, quantitate and monitor these neurological outcomes. Our aim of this research to review the literature pertinent to depressive disorders, anxiety, and/or the quality of life (QoL) and psychological well-being. Search of Medline and Google Scholar databases for relevant articles had revealed a total of 1568 citations; 30 articles met the inclusion and exclusion criteria.

Results Data about the direct effect of dysphagia on psychiatric aspects are limited. Studies of the relationship between severity of dysphagia and depressive symptoms demonstrated that several evaluation tools are available for objective and subjective assessment. The severity and progression of dysphagia was significantly associated with increased depressive symptoms.

Conclusion Dysphagia is associated with and positively correlated to depression and anxiety scores observed in Parkinson disease (PD), multiple sclerosis (MS) and stroke. Similar association is observed in patients with head and neck cancer, tongue cancer and oral cancer. A bidirectional positive correlation exists with a vicious circle that loops between dysphagia and psychological disease. Moreover, the severity of dysphagia shows correlation with depression and/or anxiety scores (Fig. 1, Graphical abstract).

Keywords Dysphagia, Depression, Major depressive disorder, Quality of life, Review, Psychological well-being

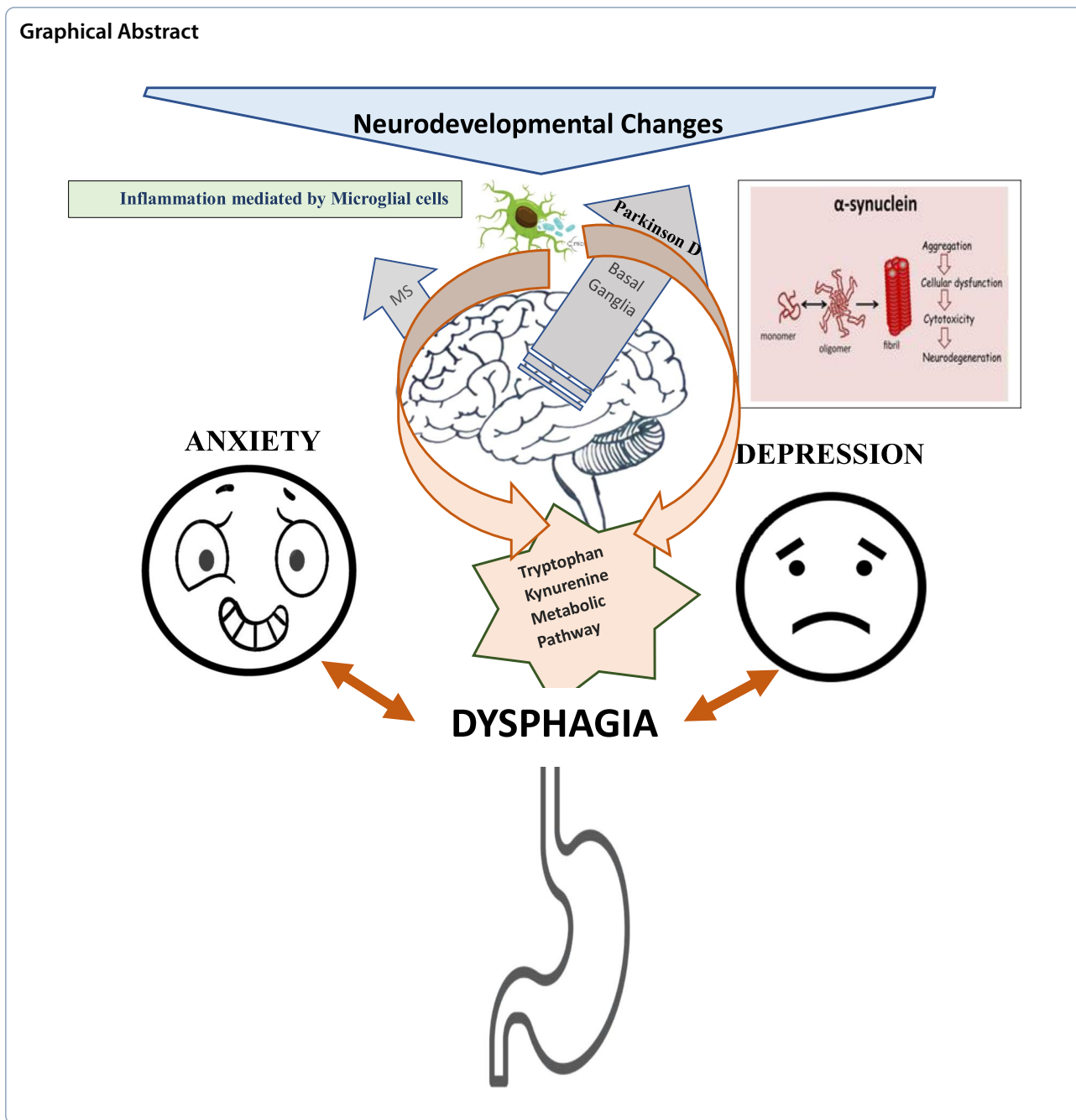
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Introduction

Dysphagia definition

Swallowing is a complex process that involves the integration of more than 30 muscles and nerves in a collective smooth action [1]. In a three-phase sequential process the food bolus is moved from the oral cavity to the pharynx, esophagus and then to the stomach [1]. The three phases are the *oral* (subdivided into oral preparatory stage and oral propulsive stage), *pharyngeal* and *esophageal* phases [2]. Any abnormality occurring

in any one of these phases is referred to as dysphagia [1, 3]. Dysphagia is a Greek term, derived from the words ‘dys’ meaning disorder and ‘phagein’ meaning eating [4]. Dysphagia, therefore, refers to the difficulty either in the process of oral food preparation prior to swallowing or in the food passage from the oral cavity to the pharynx, esophagus and stomach [1, 3]. Dysphagia is clinically recognizable as either oropharyngeal or esophageal dysphagia [5]. Oropharyngeal dysphagia is characterized by the difficulty to initiate a swallow, whereas esophageal

dysphagia is characterized by the difficulty experienced through swallowing several seconds immediately after the initiation of a swallow as well as the sensation of food being obstructed in its passage [5].

Epidemiology of dysphagia

Epidemiology of dysphagia is underestimated. Its Incidence among individuals above the age 50 in several European and US populations was 16 to 22% based on survey studies in the early 1990s [6–9]. However, more recent studies explored the epidemiology of dysphagia in adults reported rather different values. In USA, the incidence of dysphagia that occur at least twice weekly was 3% in both males and females, in a population-based cohort of 7640 individuals [10]. Furthermore, a population-based study in Iceland, revealed an estimated annual incidence of esophageal food impaction in adults to be 25 in 100,000 persons with the prevalence increases with age, particularly after the seventh decade [11]. The prevalence was broad in different countries and geographical regions, ranging between 3 to 27% [10, 12]. Dysphagia was found to be more prevalent in the male (male-to-female ratio 1.5:1) [11, 13] and elderly populations [12].

Etiology of dysphagia

As the etiologies of dysphagia are diverse, they can be classified as *nervous system-related causes*, *gastrointestinal-associated causes* or *causes induced by muscular, endocrinological, iatrogenic (surgical), pharmacological, mechanical, and psychogenic disturbances* [14–17]. Swallowing is a vagal nerve mediated process under balance of sympathetic and parasympathetic balance, it is demonstrated that fear conditioning in humans as demonstrated by spectral heart rate variability that refers to variations in length between consecutive heart beats may add easily performed in a less invasive assessment for neurologically mediated swallowing process. Heart rate variability may serve as a biomarker of the inhibitory prefrontal–amygdala fear network [18, 19]. Neurogenic dysphagia secondary to central nervous system disorders (CNS) including upper motor and autonomic centers responsible for controlling the swallowing process or the peripheral nervous system (PNS) including neuropathies, neuromuscular junction disorders, and muscle diseases [20]. Altered neuronal circuits in cerebral regions such as (cingulate cortex, amygdala, basal ganglia) may ultimately lead to psychopathological and functional symptomatic expressions. Among CNS disorders with gut manifestations including dysphagia is Parkinson's disease (PD) which is the second most common neurodegenerative disorder. Other CNS disorders are neurodevelopmental process abnormalities, cerebrovascular stroke, CNS neoplasms, degenerative disorders, and multiple sclerosis

[21]. Notably, Increased expression of serotonergic genes occurs with activation of the serotonergic system and subsequently, elevated anxiety levels on animal models [22]. Health resilience has drawn increasing attention to one of the etiological factors of illnesses from molecular to social levels. Less mitochondrial stress resilience, the disturbance of thiol homeostasis, and contemporary lifestyles may reportedly contribute to the pathogenesis of neurological and psychiatric diseases, multiple sclerosis, and mental illnesses, respectively [23]. It is believed that the pathogenesis of several diseases related to dysphagia is mediated by tryptophan (Trp)–kynurenine (KYN) metabolic system, Tanaka and colleagues discussed the Trp–KYN metabolic system with special emphasis on its interaction with the immune system, including the tolerogenic shift towards chronic low-grade inflammation, additionally explored the linkage between chronic low-grade inflammation, KYN metabolites, and major psychiatric disorders, including depressive disorder, bipolar disorder, substance use disorder, post-traumatic stress disorder, SCZ, and autism spectrum disorder [24]. Accelerated tryptophan metabolism is observed in conditions such as infection, inflammation, cancer, aging, neurodegenerative diseases, and psychiatric disorders [25]. Neurodegenerative processes that take place in CNS are mediated by microglial cells that participate in acute inflammatory state that is consequently resort either to a neuronal recovery or development of a low-grade inflammation. This biological mechanism explains the underlying pathobiology of dysphagia manifested in these disorders [26]. Analysis of levels of neurotoxic KYNs and neuroprotective KYNs revealed higher levels of neurotoxic KYNs and higher ratios of neurotoxic KYNs in neurodegenerative and psychiatric diseases, however, these levels and ratios of the neuroprotective KYNs are not clearly understood yet [25]. Animal models showed that in high doses of KYNA (20–40 µg/2 µL) there is a significantly decreased the avoidance latency, whereas at a low dose of KYNA (0.5 µg/2 µL) significantly elevate it compared to controls, Therefore, a low dose of KYNA would enhance memory function [27]. A major role of Neurodevelopmental pathology ought to explain the pathogenesis of other mental illnesses and neurological diseases. Schizophrenia (SCZ) has a substantial neurodevelopmental basis in the pathogenesis; likewise, bipolar disorder (BP), anxiety disorder, obsessive compulsive disorder (OCD), and Tourette syndrome are reported to have the neurodevelopmental backgrounds[28].It is caused by brain insults at stages of brain growth and development during late first or early second trimester as well as early postnatal period, leading to the emergence of neuropsychiatric manifestations during early life, which tend to last for lifetime. The earlier the age of

onset and the higher the severity and persistence of the genetic, cognitive, sensorimotor, and psychopathological dysfunction, the greater the overall neurodevelopmental impairment [29]. Clinical manifestations of altered KYN metabolism include impairments in memory and learning, poor planning, defects in set-shifting, adapt behavior to the environment, impaired working memory, emotional regulation, and altered executive function, which are common in neurological and psychiatric diseases that correlate with a typical cognitive pattern observed in frontal lobe dysfunction [29].

Movement disorders characterized by early accumulation of abnormal alpha-synuclein (α -SYN) containing inclusions (Lewy neurites) at the enteric nervous system (ENS) and at the dorsal motor nucleus of the vagus (DMV) both in PD and in incidental Lewy body disease (ILBD) [30–32] when compared to supranuclear palsy alpha-synucleinopathy were significantly more measurable compared to tauopathies related to progressive supranuclear palsy [33, 34]. Upon studying the full thickness of the upper gastrointestinal tract of Parkinson's postmortem findings that showed that Lewy pathology affects mucosal sensory axons in specific regions of the upper gastrointestinal tract and may be related to Parkinsonian type esophageal dysphagia [35]. Furthermore, detection of Synucleinopathy in the pharyngeal nerves using an immunohistochemical method for phosphorylated α -synuclein, Parkinson patients with dysphagia noted to have a higher density of α -synuclein aggregates in the pharyngeal nerves [35, 36]. Among common PNS and muscle disorders with dysphagia manifestations include Guillain–Barré syndrome, myasthenia gravis, polymyositis, and facioscapulohumeral muscular dystrophy [37]. These conditions affect the motor function of the upper gastrointestinal tract and impair swallowing [38]. Among the common causes of dysphagia are disorders that occur in the gastrointestinal tract [37]. Infrequently, swallowing disorder arise without a discernible abnormalities in the anatomy of the upper aerodigestive tract and/or in the swallowing physiology [13, 39–41]. Dysphagia is attributed to visceral conditions, most often related to gastroesophageal reflux disease (GERD) [10, 42, 43]. Autoimmune syndromes may present with systemic as well as gastrointestinal symptoms and dysphagia such as Sjögren's syndrome [44] in whom three-quarters of the patients were reported to have it [45–47]. Several studies have explored the relationship between GERD and dysphagia [42, 43]. In a population-based study of 926 individuals Eslick et al. reported that GERD was independently correlated with dysphagia (OR = 2.96, 95% CI: 1.76–4.98) using a regression analysis [42]. Similarly, in a national population Argentinian residents reported that frequent GERD symptoms were

connected with dysphagia (OR = 2.12, 95% CI: 1.27–3.54) [43]. Dysphagia can also arise from surgical (iatrogenic) causes, such as laryngectomy or head and neck surgeries [48, 49]. It can be caused by cancer of the oral cavity, tongue, or head and neck region [48, 49]. It can also result from an adverse effect of certain medications such as neuroleptics, cholesterol-lowering agents and anticholinergic drugs [50–52]. The aging process may also be a cause for dysphagia, and is associated with increased risk of mortality and morbidity [53–56]. However, the aging process gives rise to mild abnormalities of esophageal motility, which are rarely symptomatic [55]. Psychogenic dysphagia is a diagnosis of exclusion, detected only after thorough knowledge of patient history and full investigations [57]. For dysphagic patient morbidity and mortality rates are attributed, in part, to the higher risk of aspiration pneumonia [58, 59] and partly ascribed to the resultant states of malnutrition and dietary deficiencies [60].

Psychiatric aspects of dysphagia

Dysphagia is a distressing symptom that exerts several negative consequences on the patient's general state and health-related quality of life [57]. Combined with the negative consequences of the original diseases and/or conditions causing dysphagia, the difficulty in swallowing itself increases the morbidity and sometimes even the mortality rates of the causative disorders [58, 59, 61, 62]. Phenotypically, anxiety, depression and cognitive changes such as dementia were demonstrated to be inter-related to each other in a form of cross talk between each other [63]. To explain the rule of emotions and affection, emotions are noted to impact several brain executive processes, such as action inhibition. However, the complex interplay between emotional stimuli and action control is not clear. Inhibitory control measurement is done by the stop-signal task (SST) [64]. It is demonstrated and proved by Battaglia et al. that vicarious fear learning has a remarkably affect the cognitive abilities, making a neutral image as threatening as phylogenetically innate negative stimuli and hence impact behavioral control [64]. Moreover, it is noted by the prior author that observation of positive and negative body postures enhanced the ability to suppress an ongoing action compared to a neutral body posture. Concluding that emotional valence independent stimuli facilitate action control and explains that a trigger would increase sensory representation and/or attentional processing which promotes stop-signal processing and hence improved inhibitory performance [65]. In fact, one-third of the major sequelae of dysphagia are their negative consequences [57]. Dysphagic patients are reported to have high risk for depression and anxiety; however, due to the complexity of the dysphagia etiology, such psychological symptoms are generally studied

more in connection with the chronic comorbidities than with the swallowing dysfunction itself. Only limited review data are available on the relationship between depression and/or anxiety, quality of life and dysphagia itself. The aim of this research was to review the published studies available in the literature that focused on the major depressive disorders, anxiety, and/or the quality of life (QoL) in dysphagic patients.

Methods

Data sources and searches

This review is performed as a systemic review of the English language literature with inclusion criteria of adult age groups with no geographical location restriction. We searched the literature between January 1980 to December 2020 for neurological and psychiatric aspects along with their impact of these disorders on swallowing and dysphagia manifestation on quality of life (QoL) in various medical conditions mainly but not exclusively for the neurological disorders which neurodegenerative, neurodemyelinating and neurovascular disorders as well as for psychiatric disorders which are depression, anxiety and stress. An advanced search was conducted using the major search engines which are PubMed, Cochrane Library, and Google Scholar with MESH keywords of combination 'dysphagia', 'swallowing disorders', 'Parkinson', 'cancer', 'multiple sclerosis', 'depression', 'anxiety', 'major depressive disorder', 'psychological', 'surgery', 'Stroke', 'elderly', 'dementia' and 'quality of life' in a variety of combinations. The inclusion was non-restrictive of the type of publication or the setting of the study whether outpatient or hospital-based studies. Exclusion criteria are studies of non-English language and pediatric population studies. Literature that discussed dysphagia related to gastrointestinal diseases, functional non-organic disorders and neoplastic disorders was excluded.

Results

Figure 1 depicts the steps involved in the search conducted to choose the articles selected for review. First, the titles were screened, and then the abstracts of the selected articles were reviewed. The full texts of the relevant articles were then carefully read. The initial search revealed 1568 articles. After screening of the titles and elimination of the duplicates, 406 articles were selected for further assessment. After reading the abstracts of the remaining articles, 30 articles were chosen for final review for their relevance to the topic of study in the present manuscript [10, 42, 53, 54, 66–88] (Table 1).

Characteristics of the studies included

While all the 30 studies reviewed were observational, barring a single interventional non-randomized controlled

trial [81], most of the observational studies (total cohort=16) were cross-sectional [10, 43, 54, 66, 68–71, 77–79, 82, 83, 86–91]. Six were prospective cohort studies [53, 80–82], three were retrospective cohort studies [68, 69, 73], and two were case control studies [66, 79]. All the studies were exclusively inpatient, except for four; one was both mixed inpatient (hospital-based) and outpatient (community-based) [71], while the other three were community-based studies [10, 53, 77]. The studies included in this review evaluated dysphagia of several etiologies. The commonest etiologies were Parkinson disease assessed in six studies [70–72, 75, 76, 78] and old age evaluated in six studies [53, 54, 77, 88–90]. Dysphagia resulting from head and neck cancer was evaluated in five studies [68, 69, 79, 80, 82], while dysphagia due to oral [74] and tongue cancers [84] were evaluated in one study each. The remaining studies evaluated dysphagia in MS (total cohort=1) [66], stroke (total cohort=1) [81], total laryngectomy (total cohort=1) [73], and anterior cervical spine surgery (total cohort=1) [91]. Dysphagia of different etiologies was estimated in six studies [10, 42, 67, 83, 85, 87], and medically unexplained oropharyngeal dysphagia (MUNDO) was evaluated in one study [86]. Although most of the studies did not focus specifically on investigating the association between the psychological status and dysphagia, relevant findings were reported in their results. Only six of the studies reviewed included a specific aim in their objectives to evaluate the association between psychological status and anxiety [10, 42, 78, 83, 86, 89]. The objectives of the rest of the studies were directed mainly towards studying the prevalence of psychological dysfunction and dysphagia in certain comorbidities, and then further investigated their impact on each other in the context of their findings. The detailed findings of all the studies reviewed are described in Table 1. Quality assessment of the studies using CONSORT (Table 2) and STROBE assessment (Table 3) guidelines are performed.

Evaluation of dysphagia

A variety of methods of evaluating dysphagia were observed among the studies reviewed. The vast majority of the studies used only subjective measurement tools like questionnaires or patients' self-reporting of swallowing problems [10, 42, 67, 70, 73–80, 82, 84, 90, 91]. Physical examination performed either by a neurologist, an otolaryngologist (ENT) or a speech and language pathologist (SLP) was used to assess the dysphagia in eight studies [53, 54, 66, 71, 88, 89]; objective evaluation adopting the modified barium swallow examination (MBS) [68, 69], fiber-optic endoscopic evaluation of swallowing (FEES) [72, 83, 85, 86] or video-fluoroscopic swallowing study (VFSS) [81,

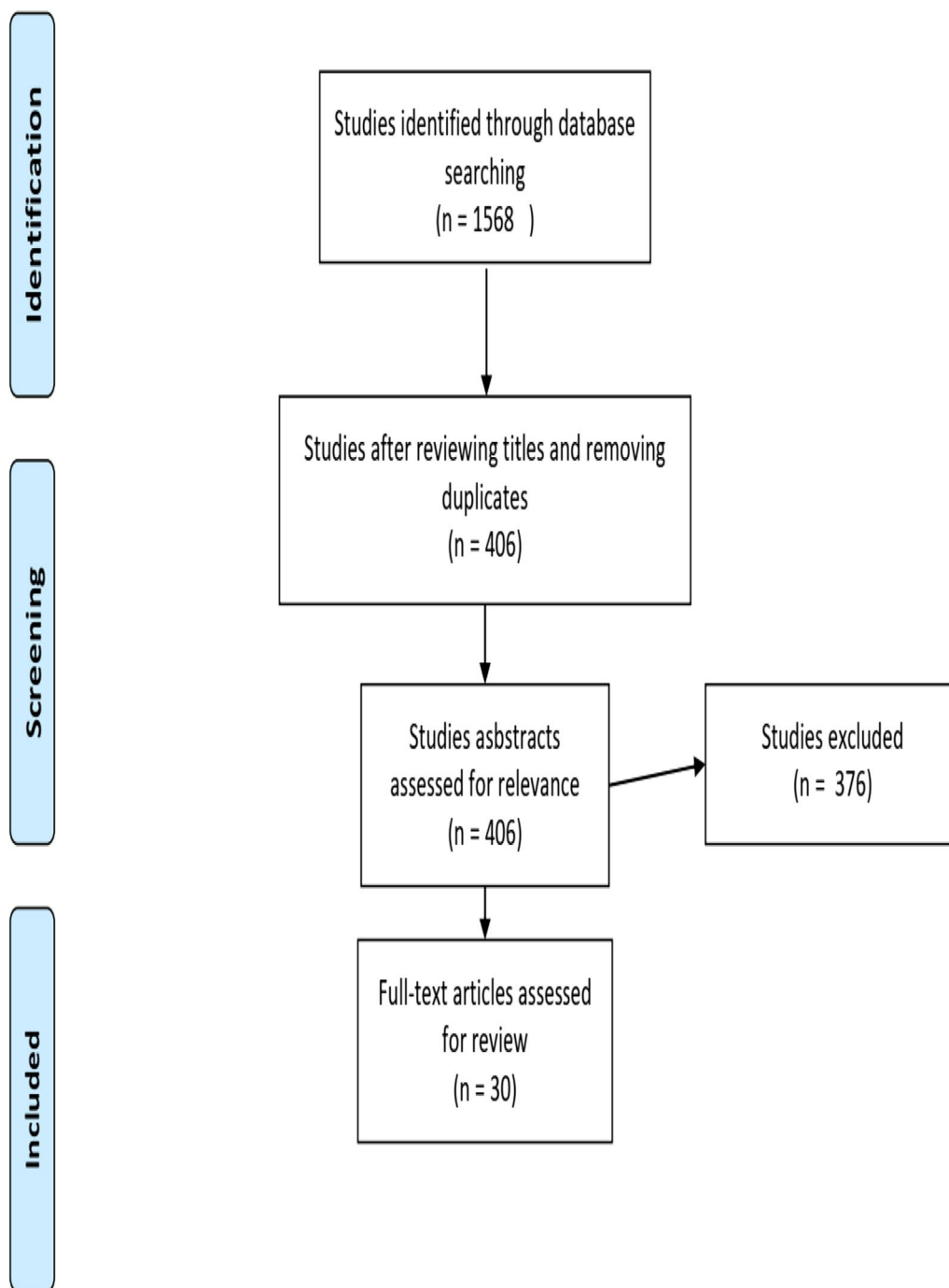


Fig. 1 Graphical abstract shows a schematic representation of the role of anxiety and depression and its interaction with dysphagia. Neurodevelopmental disorders exert a direct influence on the brain and through processes to cause movement disorders by Parkinson disease and multiple sclerosis (MS), synuclein has a central role as a mediator for generalized gut dysfunction and dysphagia. Tryptophan (Trp)–kynurenine (KYN) metabolic system and its metabolites are involved in pathogenesis and monitoring of inflammatory and neurodegenerative disorders of the brain and involved in manifestation of dysphagia

83, 87] was used only in eight studies. The commonest questionnaires/scales for assessment of dysphagia included the Unified Parkinson Disease Rating Scale

(UPDRS) adopted in three studies [70, 75, 78]; the MD Anderson Dysphagia Inventory (MDADI) employed in two studies[79, 80], the Swallowing Disturbance

Table 1 Study characteristics and outcomes

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
1	Thomas et al. [73]	25 Aug 1999	Dysphagia and nutritional status in MS	Case-control	79	MS	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ Timed swallowing test 	<ul style="list-style-type: none"> - To assess the incidence of dysphagia in MS - To evaluate the relationship between dysphagia, disability and nutritional indices range 	Abnormal swallowing was associated with a more depressed mood ($p < 0.001$)
2	Ekberg et al. [74]	17 April 2002	Social and psychological burden of dysphagia: its impact on diagnosis and treatment	Cross-sectional	360	Not specified	Psychological handicaps and QoL [Questionnaire of Gustafson and Tibbling (Modified version)— Face-to-face interview]	<ul style="list-style-type: none"> ■ Questionnaire of Gustafson and Tibbling (Modified version)— Face-to-face interview 	<ul style="list-style-type: none"> - To evaluate the effects of dysphagia on QoL - To investigate the relationship between psychological handicaps and dysphagia frequency 	<ul style="list-style-type: none"> - 55% of patients did not feel that eating is an enjoyable experience - 41% of patients experienced anxiety or panic during mealtimes
3	Lin et al. [42]	6 Sep 2004	Depressive symptoms in long-term care residents in Taiwan	Cross-sectional	315	Elderly	Depression [GDS]	<ul style="list-style-type: none"> ■ Self-report of swallowing difficulty ■ Neurological exam, Timed swallowing test 	<ul style="list-style-type: none"> - To investigate the prevalence and risk factors for depression in the elderly in association with dysphagia, functional disability and socio-demographic factors in long-term care facilities 	<ul style="list-style-type: none"> High incidence of depression (52.05%) - 64.6% of depressed elderly have had impaired swallowing ($p < 0.001$)

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
4	Nguyen et al. [75]	15 Feb 2005	Impact of dysphagia on QoL after treatment of head and neck cancer	Retrospective cohort	104	Head and neck cancer	Anxiety depression, and QoL [HADS and UW QoL scale]	<ul style="list-style-type: none"> ■ MBS exam 	<ul style="list-style-type: none"> - To evaluate QoL associated with dysphagia after head and neck cancer treatment 	<ul style="list-style-type: none"> - Lower HADS score in dysphagia group ($p=0.0005$) - Higher HADS score in moderate ($p=0.005$) and severe ($p<0.0001$) - In moderate-to-severe dysphagia, lower Anxiety (OR 0.23; 95% CI 0.07–0.69; $p=0.0005$) - In no/mild dysphagia, lower depression (OR 0.15; 95% CI 0.04–0.45; $p=0.0001$)
5	Nguyen et al. [76]	12 June 2007	QoL following chemo-radiation and postoperative radiation for locally advanced head and neck cancer	Retrospective cohort	101	Head and neck cancer	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ MBS exam 	<ul style="list-style-type: none"> - To estimate the impact of chemo-radiation and postoperative radiation on patients' QOL 	<ul style="list-style-type: none"> - Severe dysphagia requiring long-term tube feeding or repeated dilations was the most common complication - HADS were greater in patients who developed complications following treatment ($p=0.001$, $p=0.0001$, respectively)

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
6	Althaus et al. [77]	15 April 2008	Frequency and treatment of depressive symptoms in a PD registry	Cross-sectional	226	PD	Depression [MARDS (face to face)]	■ UPDRS	- To assess the prevalence of depressive symptoms PD patients	- Prevalence of depressive symptoms among PD patients was 35.4% - Dysphagia was a significant predictor for depressive symptoms (B = 3.06, R ² = 0.289)
7	Eslick et al. [30]	5 March 2008	Dysphagia: epidemiology, risk factors and impact on QoL—a population-based study	Cross-sectional	926	Population	Anxiety, depression, neuroticism, and QoL [Self-reporting and GDS]	■ Validated self-reporting questionnaire of dysphagia [prevalence, frequency and severity], anxiety, depression, neuroticism, QoL during last year	- To investigate the magnitude and impact of dysphagia in the general community	- Intermittent dysphagia was significantly associated with anxiety (OR = 1.09, 95% CI: 1.01–1.19) - The progressive dysphagia was significantly associated with depression (OR = 1.34, 95% CI: 1.07–1.67)
8	Miller et al. [78]	26 Nov 2008	Swallowing problems in PD: frequency and clinical correlate	Community and hospital-based	137	PD	Depression [GDS]	■ Timed swallowing test	- To identify prevalence of dysphagia in PD and the relationship between swallowing performance and indicators of disease progression	- Swallowing problems are frequent in PD (32%) - Patients with poorer swallowing rates had significantly greater depression symptoms compared to patients who had not (p = 0.01)

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
9	Manor et al. [53]	17 Dec 2008	Anxiety, depression and swallowing disorders in patients with Parkinson's disease	Cross-sectional	69	PD	Anxiety and depression [TAI and BDI]	<ul style="list-style-type: none"> ■ SDQ, FEES by an ENT and SLP 	- To establish the association between swallowing disorders and the PD affective state	<ul style="list-style-type: none"> - Patients with dysphagia experienced increased anxiety and depression - Anxiety and depression ranges demonstrated that the most anxious ($r = 0.472$, $p < 0.0001$) and depressed ($r = 0.357$, $p < 0.003$) patients reported more swallowing difficulties
10	Maclean et al. [54]	1 Sep 2009	Dysphagia following a total laryngectomy: the effect on QoL, functioning, and psychological well-being	Retrospective cohort	110	Patients with total laryngectomy	Anxiety, depression, stress, and QoL [WHOQoL-Bref, UW-QoL, and DASS]	<ul style="list-style-type: none"> ■ Self-reported questionnaire for dysphagia 	- To evaluate effect of dysphagia on QoL, functioning, and psychological well-being including depression, anxiety, and stress, of people who have undergone a total laryngectomy	<ul style="list-style-type: none"> - Dysphagia had a negative impact on psychological well-being - Laryngectomies with dysphagia had significantly higher levels of depressive symptoms ($z = -2.58$; $p = 0.01$), anxiety ($z = -2.94$; $p = 0.003$) and stress ($z = -2.139$; $p = 0.032$)
11	Airoldi et al. [55]	27 July 2010	Functional and psychological evaluation after flap reconstruction plus, radiotherapy in oral cancer	Cross-sectional	36	Oral cancer	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ Dische morbidity recording scheme evaluation and VAS for dysphagia 	- To investigate impact of flap reconstructive surgery with adjuvant radiotherapy (RT) on QoL and psychological functioning	<ul style="list-style-type: none"> Patients with severe dysphagia demonstrated increased anxiety and depression symptoms ($p < 0.05$)

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
12	Walker et al. [56]	4 Dec 2010	Self-reported dysphagia and its correlates within a prevalent population of people with Parkinson's disease	Cross-sectional	75	PD	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ UPDRS 	<ul style="list-style-type: none"> - To evaluate prevalence of dysphagia in PD patients - Assess correlations between dysphagia and motor function 	<ul style="list-style-type: none"> - Swallowing problems were significantly correlated with anxiety ($r=0.249$; $p=0.033$) - Depression symptom scores ($r=0.281$, $p=0.016$) - Participants were divided into four groups according to their BDI score then compared the PD patients with SDQ scores of ≥ 11 and with the SDQ cores of < 11 regarding depressive categories - OR (95% CI) of depression on dysphagia were: 3.28 (0.93–11.55) for mild depression symptom; 13.44 (3.10–58.16) for moderate depression symptom; 30.35 (5.65–162.97) for severe depression symptom, that suggesting a strong association between depression symptoms and dysphagia in PD
13	Han et al. [57]	28 Feb 2011	Relationship between dysphagia and depressive states in patients with PD	Cross-sectional	127	PD	Depression [BDI]	<ul style="list-style-type: none"> ■ SDQ 	<ul style="list-style-type: none"> - To determine relationship between depressive states and dysphagia in PD patients 	<ul style="list-style-type: none"> - SDQ scores of ≥ 11 and with the SDQ cores of < 11 regarding depressive categories - OR (95% CI) of depression on dysphagia were: 3.28 (0.93–11.55) for mild depression symptom; 13.44 (3.10–58.16) for moderate depression symptom; 30.35 (5.65–162.97) for severe depression symptom, that suggesting a strong association between depression symptoms and dysphagia in PD

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
14	Holland et al. [58]	10 March 2011	Prevalence and symptom profiling of oropharyngeal dysphagia in a community dwelling of an elderly population: a self-reporting questionnaire survey	Cross-sectional, community-based study	634	Elderly	Depression [GDS]	<ul style="list-style-type: none"> ■ Sydney swallow questionnaire 	<ul style="list-style-type: none"> - To identify the factors that predict age-related dysphagia 	<ul style="list-style-type: none"> - 11.4% reported symptoms indicative of significant dysphagia - Dysphagia severity was directly correlated with subject age ($r=0.11$, $P=0.007$) - Depression was strongly and independently associated with dysphagia symptoms ($P=0.002$)
15	Perez-Lloret et al. [59]	2 April 2011	Oro-buccal symptoms (Dysphagia, dysarthria, and sialorrhoea) in patients with PD: preliminary analysis from the French COPARK cohort	Cross-sectional	419	PD	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ UPDRS 	<ul style="list-style-type: none"> - To evaluate the frequency of orobuccal symptoms at baseline in patients with PD and to assess their correlations with patients' demographics, clinical characteristics, and drugs consumption 	<ul style="list-style-type: none"> - Logistic regression showed that dysphagia was related to higher depression symptom scores ($p=0.001$)
16	Chan et al. [60]	5 June 2011	The relationship between depressive symptoms and initial quality of life and function in head and neck cancer	Case-control	77	Head and neck cancer	Depression [BDI Fast screen]	<ul style="list-style-type: none"> ■ MDADI 	<ul style="list-style-type: none"> - To determine the incidence of depression in head and neck cancer patients and the effect of depression on baseline head- and neck-specific measures of QoL and function 	<ul style="list-style-type: none"> - Depression symptom scores were significantly associated with the functional ($\beta=17.31$; $p=0.009$), physical ($\beta=14.99$; $p=0.032$) and emotional ($\beta=11.60$; $p=0.049$) domains of the MDADI

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
17	Lin et al. [61]	3 April 2012	The relationship between depressive symptoms, quality of life and swallowing function in head and neck cancer patients one year after definitive therapy. Laryngoscopes	Prospective cohort	46	Head and neck cancer	Depression [BDI] Fast screen]	<ul style="list-style-type: none"> ■ MDADI 	<ul style="list-style-type: none"> - To evaluate the prevalence of depression in head and neck cancer patients following definitive treatment - To determine the correlation between depression and head and neck specific measures of QoL and function 	<ul style="list-style-type: none"> - Incidence of depression in head and neck cancer patients was 20% - Logistic regression analysis shown significant associations between depressive symptoms and MDADI ($\beta = -21.8, p = 0.038$) - A Significant association between depressive symptoms and a swallowing related question were found ($\beta = -23.9, p = 0.035$)
18	Kang et al. [62]	15 Sep 2012	The effect of bedside exercise program on stroke patients with dysphagia	Non-randomized controlled trial	50	Stroke	Depression [BDI]	<ul style="list-style-type: none"> ■ Physical examination ■ VFSS ■ Modified VFSS scale 	<ul style="list-style-type: none"> - To test the effects of a bedside exercise program on the recovery of swallowing after a stroke 	<ul style="list-style-type: none"> - Significant improvement in swallowing function scores in bedside exercise program compared to control group ($p < 0.05$), that showed consequently lesser depressive symptoms and better QoL ($p < 0.05$)

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
19	Crossen et al. [63]	1 Nov 2012	Computerized monitoring of patient-reported speech and swallowing problems in head and neck cancer patients in clinical practice	Prospective cohort	67	Head and neck cancer	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ EORTC QLQ-H&N35 swallowing subscale 	<ul style="list-style-type: none"> - To identify computerized monitoring of speech and swallowing outcomes and its impact on QoL and emotional well-being in head and neck cancer patients in an outpatient clinic 	<ul style="list-style-type: none"> - Dysphagia was associated with anxiety and depressive symptom scores at time of diagnosis ($r = 0.52; p = 0.001$) as well as at time of follow-up ($r = 0.46; p = 0.001$)
20	Nogueira et al. [64]	2 March 2014	Swallowing disorders in nursing home residents: how can the problem be explained?	Cross-sectional	266	Elderly	Depression [GDS]	<ul style="list-style-type: none"> ■ Dysphagia self-test ■ Timed swallowing tests 	<ul style="list-style-type: none"> - To estimate the incidence of swallowing disorders in nursing home residents - To analyze the relationship between self-perceived swallowing disorders, cognitive functions, autonomy, and depression - To assess which variables explain the score of dysphagia 	<ul style="list-style-type: none"> - 40% showed signs of dysphagia among nursing home population - Depression symptom scores had significant effect on the Dysphagia Self-Test scores ($p = 0.05$)
21	Yang et al. [41]	18 Oct 2013	Oropharyngeal dysphagia in a community-based elderly cohort: the Korean Longitudinal study on health and aging	Prospective cohort; Population-based study	415	Elderly	Depression [Based on DSM-IV diagnostic criteria for depression]	<ul style="list-style-type: none"> ■ Standardized swallowing assessment 	<ul style="list-style-type: none"> - To identify the occurrence of dysphagia and assess the association of dysphagia and activities of daily living in an elderly population residing in an independent living facility 	<ul style="list-style-type: none"> Major depressive disorder was significantly correlated to dysphagia [OR 3.0 (CI 1.149–7.962), $p = 0.022$]

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
22	Verdonschot et al. [65]	5 Nov 2013	Symptoms of anxiety and depression assessed with the Hospital Anxiety and Depression Scale in patients with Oropharyngeal dysphasia	Cross-sectional	96	OD	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ ENT examination ■ Logopedic observation of oral intake ■ FEES ■ VFSS ■ Functional oral intake scale ■ DSS ■ MDADI 	<ul style="list-style-type: none"> - To assess the presence of anxiety and depression and their severity in outpatients with OD 	<ul style="list-style-type: none"> - High prevalence of anxiety and/or depression symptoms (43.7%) in patients with OD - MDADI scores were significantly associated with depressive symptoms ($p = 0.05$)
23	Mentz et al. [66]	23 Nov 2013	Homozygosity in the ApoE 4 poly-morphism is associated with dysphagic symptoms in older adults	Cross-sectional	634	Elderly	Depression [GDS]	<ul style="list-style-type: none"> ■ Sydney swallow questionnaire 	<ul style="list-style-type: none"> - To investigate if ApoE 4 would be predictive of dysphagia symptoms in older adults 	<ul style="list-style-type: none"> - Swallowing score was significantly related to age ($R = 0.107, p < 0.007$) - Depression symptom scores were significantly related to the total swallowing scores ($r = 0.133; p < 0.001$)
24	Zhang et al. [67]	6 June 2014	Effect of swallowing training on dysphagia and depression in postoperative tongue cancer patients	Prospective cohort	59	Tongue cancer	Depression [Zung depression scale]	<ul style="list-style-type: none"> ■ Timed swallowing test 	<ul style="list-style-type: none"> - To demonstrate the effect of swallowing training on dysphagia and depression in postoperative tongue cancer patients 	<ul style="list-style-type: none"> Lower levels of the swallowing test score were associated with decreased depression level
25	Kang et al. [68]	1 Aug 2014	The association between Psychiatric factors and the development of chronic dysphagia after anterior cervical spine surgery	Prospective cohort	72	Anterior cervical spine surgery	Anxiety and depression [Zung anxiety scale and Zung depression scale]	<ul style="list-style-type: none"> ■ Bazaz-Yoo scale ■ Telephonic assessment of presence/severity of dysphagia 	<ul style="list-style-type: none"> - To estimate the occurrence of psychiatric factors and the development of chronic dysphagia in patients after anterior cervical spine surgery 	<ul style="list-style-type: none"> The presence of psychological disorders prior to surgery was the only significant predictor of chronic dysphagia ($p = 0.005$)

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
26	Cho et al. [10]	8 Nov 2014	Prevalence and risk factors for dysphagia: a USA Community study	Cross-sectional, community-based study	3669	General population	Depression [Antidepressant medications taken in medical files]	<ul style="list-style-type: none"> ■ A validated study survey: Bowel Disease Questionnaire including a single dysphagia question 	- To assess the prevalence and risk factors for dysphagia in USA population	<p>- GERD was the most common underlying disease identified in this community subjects but many cases remain undiagnosed</p> <p>- Antidepressants class was one of the most commonly taken medications by the dysphagia groups when compared to the no dysphagia group, but the association was not statistically significant</p> <p>- High prevalence of anxiety and depression symptoms in patients with dysphagia (43%)</p> <p>- A significant relationship found between anxiety symptoms and piecemeal deglutition ($p = 0.026$) and Post-swallow vallecular pooling ($p = 0.015$)</p> <p>- No significant relationship found between depression symptoms and any specific FEES variable</p>
27	Verdonschot et al. [69]	10 Oct 2015	The relationship between FEES outcome and symptoms of anxiety and depression in dysphagic Patients	Prospective cohort	107	OD	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ FEES ■ Two experts assessed patients' performance on 4 visuoperceptual FEES-variables independently 	- To identify the relationship between the severity of OD and affective symptoms	<p>- A significant relationship found between anxiety symptoms and piecemeal deglutition ($p = 0.026$) and Post-swallow vallecular pooling ($p = 0.015$)</p> <p>- No significant relationship found between depression symptoms and any specific FEES variable</p>

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
28	Verdonschot et al. [70]	7 June 2018	MUNOD at the University Hospital ENT Outpatient clinic for dysphagia: A Cross-sectional cohort study	Cross-sectional	14	MUNOD	Anxiety and depression [HADS]	<ul style="list-style-type: none"> ■ FEES ■ DSS ■ Two blind examiners scored 5 visuo-perceptual ordinal FEES variables 	- To determine the association of MUNOD with psychiatric conditions	<ul style="list-style-type: none"> - 42.8% had clinically relevant affective symptoms of anxiety and/or depression - The DSS scores did not differ significantly between patients with and without anxiety/depression - Relevant anxiety or depression symptoms are not correlated to the severity of MUNOD symptoms
29	Kim et al. [71]	9 March 2019	The mediating and moderating effects of meaning in life on the relationship between depression and QoL in patients with dysphagia	Cross-sectional	90	Not specified	Depression [CES-D developed by Radloff]	<ul style="list-style-type: none"> ■ Dysphagia test ■ VFSS 	- To identify whether meaning in life has moderating and mediating effects on the relationship between depression and QoL in patients with dysphagia	<ul style="list-style-type: none"> - High prevalence of patients experienced depression (62.2%) - Only 3% of the participants had a definite purpose of life, while the 63.3% had lost meaning in life - Meaning in life was found to mediate the relationship between depression as well as QoL in patients with dysphagia; however, the index of moderation was not statistically significant

Table 1 (continued)

Studies	Author	Year	Title	Study design	Total cohort	Dysphagia etiology	Psychiatric aspects evaluated [and tools]	Dysphagia measurement tools	Aim	Related results
30	Aguado et al. [72]	21 June 2019	GI comorbidity and symptoms associated with depression in patients aged over 6 years	Cross-sectional	13,361	Elderly	Depression [From computerized medical files]	<ul style="list-style-type: none"> ■ From computerized medical files 	<ul style="list-style-type: none"> - To assess the prevalence of GI diagnoses and symptoms associated with depression 	<ul style="list-style-type: none"> - Dysphagia has had a statistically significant association with depressive symptoms [OR 1.72 (1.30–2.28)]

Table 2 CONSORT 2010 checklist of information to include when reporting a randomized trial

Section	Topic	Item number	Checklist item	Kang 2012
Title and abstract		1a	Identification as a randomized trial in the title	Missing
		1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	Missing
Introduction	Background and objectives	2a	Scientific background and explanation of rationale	1,2
		2b	Specific objectives or hypotheses	2
Methods	Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Missing
		3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	Missing
	Participants	4a	Eligibility criteria for participants	2
		4b	Settings and locations where the data were collected	Missing
	Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	3
		Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b		Any changes to trial outcomes after the trial commenced, with reasons	Missing
	Sample size	7a	How sample size was determined	Missing
		7b	When applicable, explanation of any interim analyses and stopping guidelines	Missing
	Randomization Sequence generation	8a	Method used to generate the random allocation sequence	Missing
		8b	Type of randomization; details of any restriction (such as blocking and block size)	Missing
	Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Missing
		Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
	Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	Missing
		11b	If relevant, description of the similarity of interventions	3
	Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	4
		12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	Missing
Results	Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome	3
		13b	For each group, losses and exclusions after randomization, together with reasons	Missing
	Recruitment	14a	Dates defining the periods of recruitment and follow-up	2
		14b	Why the trial ended or was stopped	Missing
	Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	3
	Numbers analyzed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	4,5
	Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Missing

Table 2 (continued)

Section	Topic	Item number	Checklist item	Kang 2012
		17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Missing
	Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Missing
	Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	Missing
Discussion	Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	7,8
	Generalizability	21	Generalizability (external validity, applicability) of the trial findings	Missing
	Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	6,7,8
Other information	Registration	23	Registration number and name of trial registry	Missing
	Protocol	24	Where the full trial protocol can be accessed, if available	Missing
	Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	Missing
Overall CONSORT score (out of 37)				12

Questionnaire (SDQ) used in two studies [72, 76], and the Sydney Swallow Questionnaire was utilized in two studies [77, 90]. The rest of the questionnaires/scales included the Dysphagia Severity Scale (DSS) (total cohort=1) [86], European Organization of Research and Treatment of Cancer Quality of Life Core Questionnaire for head and neck cancer, version 35 (EORTC QLQ H and N35) (total cohort=1) [82], Self-Reporting Questionnaire of Dysphagia (total cohort=1) [73], Questionnaire of Gustafson and Tibbling (total cohort=1) [67], bowel disease questionnaire total cohort=1 [10], Bazaz–Yoo dysphagia severity scale total cohort=1 [91], and Dische morbidity recording scheme with Visual Analog Scale (VAS) total cohort=1 [74].

Evaluation of psychiatric aspects and QoL related to dysphagia

The three commonest questionnaires used included the Hospital Anxiety Depression Scale (HADS) total cohort=10 [66, 68, 69, 74, 75, 78, 82–84, 86], Geriatric Depression Scale (GDS) total cohort=6 [42, 54, 71, 77, 89, 90], and Beck Depression Inventory (BDI) total cohort=6 [72, 76, 79–81]. The less commonly used scales were the Depression Anxiety and Stress Scale (DASS) total cohort=1 [73], Montgomery Asberg Depression Rating Scale (MARDS) total cohort=1 [70], Center for Epidemiological studies-Depression (CES-D) [87], Trait Anxiety Inventory (TAI) [72], Zung anxiety and Zung Depression Scale total cohort=2 [84, 85]. In only one study, the Diagnostic and Statistical Manual

of Mental Disorders criteria, version IV (DSM-IV), was used for the diagnosis of depression [53]; however, two studies used the hospital files of the patients to select individuals diagnosed with depression and/or taking antidepressant medications [10, 88]. Questionnaires for assessment of the quality of life included the University of Washington Quality of Life scale (UW QoL) total cohort=1 [68], World Health Organization Quality of Life-Bref (WHOQoL-Bref) total cohort=1 [79], and the Questionnaire of Gustafson and Tibbling total cohort=1 [67].

Discussion

This review aimed at assessing the association between dysphagia and psychological well-being in the earlier literature. To date, this association has not been evaluated in randomized controlled trials. All the studies reviewed were observational and only one single non-randomized clinical trial was found and reviewed. Although the absence of well-designed randomized controlled trials reduces the strength of the evidence of the results, the large majority of the observational studies which focused upon the relationship between dysphagia and the psychological status reported consistent findings. From the majority of the studies, it appeared that anxiety and/or depression were independently and positively associated with dysphagia. Further, dysphagia and the psychological state seemed to be correlated in a vicious circle which is dysphagia could increase the psychological disturbance, and the psychological disturbance could worsen the dysphagia.

Table 3 STROBE statement—checklist of items that should be included in reports of observational studies

Section	Topic	Item number	Recommendation	Airoldi 2010	Althaus 2008	Chen 2011	Cho 2015	CNumbersen 2012	Ekberg 2002	Eslick 2008	Han 2011	Holland 2011	Kang 2014	Kim 2019	Lin 2004	
Title and abstract		1a	Indicate the study's design with a commonly used term in the title or the abstract	Missing	1	1	Missing	Missing	1	Missing	Missing	1	1	1	Missing	
		1b	Provide in the abstract an informative and balanced summary of what was done and what was found	1	1	1	1	1	1	1	1	1	1	1	1,2	1
Introduction	Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	1	2	1	2	2	1,2	2	1,2	1,2	2	3,4	2	
		3	State specific objectives, including any pre-specified hypotheses	2	2	1	2	2	2	2	2	2	2	2	4	2
Methods	Study design	4	Present key elements of study design early in the paper	Missing	2	Missing	Missing	2	Missing	Missing	Missing	2	2	2	4,5	Missing
		5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	2	2	2	2	2	2	Missing	Missing	2	2	Missing	5,6	2,3

Table 3 (continued)

Section	Topic	Item number	Recommendation	Airoidi 2010	Althaus 2008	Chen 2011	Cho 2015	CNumberssen 2012	Ekberg 2002	Eslick 2008	Han 2011	Holland 2011	Kang 2014	Kim 2019	Lin 2004
	Participants	6a	<i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up. <i>Case-control study</i> —Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls. <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	2	2	2	2,3	2	2	2	2	2	2	5	2
		6b	<i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed. <i>Case-control study</i> —For matched studies, give matching criteria and the number of controls per case	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
	Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give Number of criteria, if applicable	2,3	2	2	3,4	2,3	2,3	3	2	Missing	2	5,6	3

Table 3 (continued)

Section	Topic	Item number	Recommendation	Airoldi 2010	Althaus 2008	Chen 2011	Cho 2015	CNumbersen 2012	Ekberg 2002	Eslick 2008	Han 2011	Holland 2011	Kang 2014	Kim 2019	Lin 2004
	Data sources/measurement	8	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	2,3	2	2	3,4	2,3	2,3	2,3	2	2,3	2	5,6	3
	Bias	9	Describe any efforts to address potential sources of bias	Missing	Missing	Missing	3	Missing	3	Missing	Missing	Missing	Missing	Missing	Missing
	Study size	10	Explain how the study size was arrived at	Missing	Missing	Missing	2,3	Missing	2	Missing	2	2	Missing	5	Missing
	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	3	2	2	4	3	Missing	Missing	2	3	2	5	4
	Statistical methods	12a	Describe all statistical methods, including those used to control for confounding	3	2	2	4	3	Missing	3	2	Missing	2	6	4
		12b	Describe any methods used to examine subgroups and interactions	3	2	2	4	Missing	Missing	Missing	2	Missing	2	6	Missing
		12c	Explain how missing data were addressed	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	5	Missing

Table 3 (continued)

Section	Topic	Item number	Recommendation	Airoidi 2010	Althaus 2008	Chen 2011	Cho 2015	CNumberssen 2012	Ekberg 2002	Eslick 2008	Han 2011	Holland 2011	Kang 2014	Kim 2019	Lin 2004		
Results	Partic- pants	12d	<i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	6,7	Missing	Missing	
		12e	Describe any sensitivity analyses	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
Results	Partic- pants	13a	Report numbers of individuals at each stage of study—e.g., numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	2	2	3	4	Missing	Missing	2	2	2	2	2	7	2	2
		13b	Give reasons for Numbersn-participation at each stage	2	Missing	3	4	Missing	Missing	2	2	2	Missing	2	Missing	2	2
Results	Partic- pants	13c	Consider use of a flow diagram	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	3	3
		14a	Give characteristics of study participants (e.g., demographic, clinical, social) and information on exposures and potential confounders	2	3	2	4,5 and 13	3	3	3,4,5	2	2	Missing	3	7	7	4

Table 3 (continued)

Section	Topic	Item number	Recommendation	Airoldi 2010	Althaus 2008	Chen 2011	Cho 2015	CNumberssen 2012	Ekberg 2002	Eslick 2008	Han 2011	Holland 2011	Kang 2014	Kim 2019	Lin 2004
		14b	Indicate number of participants with missing data for each variable of interest	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	7	Missing
		14c	Cohort study—Summarize follow-up time (e.g., average and total amount)	2	Missing	Missing	Missing	3	Missing	Missing	Missing	Missing	Missing	8	Missing
	Outcome data	15	Cohort study—Report numbers of outcome events or summary measures over time Case-control study—Report numbers in each exposure category, or summary measures of exposure Cross-sectional study—Report numbers of outcome events or summary measures	4,5,6,7	3,4,5	2	4,5 and 12,13,14	4	4	3,4	2	3,4	3	8	5
	Main results	16a	Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (e.g., 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Missing	Missing	3 and 5	5 and 15	Missing	Missing	4,5	2	Missing	3	8	5
		16b	Report category boundaries when continuous variables were categorized	Missing	Missing	Missing	Missing	Missing	Missing	3	2	Missing	Missing	Missing	Missing

Table 3 (continued)

Section	Topic	Item number	Recommendation	Airoldi 2010	Althaus 2008	Chen 2011	Cho 2015	CNumberssen 2012	Ekberg 2002	Eslick 2008	Han 2011	Holland 2011	Kang 2014	Kim 2019	Lin 2004
		16c	If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
	Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Missing	Missing	4 and 6	15	Missing	Missing	5,6,7	2	Missing	Missing	11,12	Missing
Discussion	Key results	18	Summarize key results with reference to study objectives	8	4,5	4	5,6,7	4	5,6	6	2,3	4	3,4	8	4
	Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	9	5	Missing	7	5	6	8	2	Missing	4	10,12	6,7
	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8,9	4,5,6	5,6,7	5,6,7	5,6	6,7	6,7,8	2,3	4,5	3,4	9,10	7
	Generalizability	21	Discuss the generalizability (external validity) of the study results	Missing	Missing	Missing	7	Missing	Missing	Missing	Missing	Missing	Missing	9,10	Missing

Table 3 (continued)

Section	Lin 2012	Maclean 2009	MaNumberr 2009	Mentz 2015	Miller 2008	Numbergueira 2013	Nguyen 2005	Nguyen 2007	Perez-Lloret 2012	Thomas 1999	Verdonschot 2013	Verdonschot 2015	Verdonschot 2019	Walker 2011	Yang 2015	Zhang 2014
Results	Missing	3,4	Missing	3	Missing	4	2	Missing	3	Missing	Missing	Missing	3	2	2	2
	Missing	4	Missing	Missing	Missing	4	Missing	Missing	3	Missing	Missing	Missing	Missing	2	2	Missing
	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
	3,4	4	2	3	2	4	2	2	3	3	2,3	2 and 4	4	2,3	3	3
	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	3	Missing	Missing	Missing	Missing	Missing	Missing	Missing
	Missing	Missing	Missing	Missing	Missing	Missing	2,3	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
	3,4	5,6	2	5	2	4,5	3,4,5	2	3,4	2	2,3	3,4	5,6	3	3,4	3
	5	Missing	3	Missing	Missing	Missing	4	Missing	5,6,7	Missing	3	4,5,6,7	5	Missing	3,4	Missing
	Missing	Missing	Missing	4	Missing	Missing	4	Missing	2	Missing	Missing	Missing	Missing	Missing	3	Missing
	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing	Missing
	6	Missing	Missing	Missing	Missing	Missing	4	Missing	5,6,7	Missing	3	Missing	Missing	Missing	Missing	Missing
Discus- sion	4	5	3	4	3	6	5,6	4,5	Missing	5	3,4	5,6,7,8	4,5	3	4	Missing
	4,6,7	5,6,7	3	5,6	3	Missing	6	4,5	4	5	4	8	7	4	5	3,4
	6,7	7	3	5,6	3	5,6	4,5,6	4,5	4 and 8	Missing	3,4	5,6,7,8	5,6,7	3,4	4,5	4
	Missing	Missing	Missing	Missing	3	Missing	Missing	Missing	4	5	Missing	Missing	Missing	Missing	Missing	Missing
Other informa- tion	Missing	7	Missing	6	3	Missing	Missing	Missing	9	5	Missing	Missing	Missing	Missing	Missing	4
	21	18	15	17	13	16	23	16	23	14	17	17	18	17	23	18

Dysphagia and its association with psychological well-being

Dysphagia was reported to have a significant association with the psychological state of the patients in a number of diseases such as MS [66], PD [70], stroke [81], head and neck cancer [68], oral cancer [74], tongue cancer [84], and aging [54]. In patients with MS, abnormal swallowing was strongly linked to a more depressed mood ($p < 0.001$). Both depression and dysphagia are a common occurrence in PD patients [70, 71]. Poor swallowing was observed to have some correlation with depression and anxiety, in several cross-sectional and population-based studies of PD [71, 72, 75]. Similarly, lower swallowing rates were significantly correlated with depression scores in patients with tongue cancer [84], while those with oral cancer having severe dysphagia demonstrated symptoms of increased anxiety and depression [74]. Dysphagia is one of the most common complications noted in the treatment of head and neck cancer [69], and the depression and anxiety scores on the HADS were significantly higher in the dysphagic patients who experienced it as a treatment-induced complication, compared with patients who had no dysphagia [69]. Concurring with this observation, Cnossen et al. [82] in their prospective cohort study using 67 patients with head and neck cancer, reported that dysphagia was significantly linked to anxiety and depressive symptom scores, not only at time of diagnosis but on follow-up as well. The link between dysphagia and psychological well-being was also investigated in patients who had undergone total laryngectomy. In a retrospective cohort study involving 110 patients receiving total laryngectomy, dysphagia was found to exert a negative impact on the psychological well-being, exhibited as higher rates of depression, anxiety, as well as stress [73].

Regardless of the etiology of swallowing, patients with oropharyngeal dysphagia expressed higher rates of anxiety and panic during eating [67], were less likely to enjoy eating [67], and exhibited markedly higher rates of depression and general anxiety scores [83, 85]. Similar findings were reported in dysphagia that accompanies aging. The prevalence of the swallowing problems among the elderly was in the 11.4–40% range in elderly living in the community [77, 89], and 52% in long-term care residents [54]. The severity of dysphagia was seen to increase with age [77]. In this population, dysphagia was identified to be strongly linked to depression [77, 89]. Above two-thirds of depressed elderly patients living in long-term care facilities were reported to experience swallowing problems, significantly more than their counterparts who lacking depression ($p < 0.005$) [54].

Although there were wide variations in the study designs, population studies, measurement tools and

patient characteristics in the studies cited earlier, they all concurred on the fact that dysphagia is directly related to the psychological well-being of the individual. However, three out of the 30 studies reviewed failed to identify any relationship between these two parameters. The first was a cross-sectional study conducted in the Netherlands [86] on 15 patients with MUNOD, at the University Hospital, ENT Outpatient clinic, for dysphagia. Although depression and anxiety were widespread among those patients (42.8%), the DSS scores showed no significant difference between the patients with and those without anxiety/depression [86]. Similarly, *Kim and colleagues* in their cross-sectional study performed using 90 patients with dysphagia (regardless of etiology), reported no significant connection between dysphagia and depression, despite the high incidence of depression among the patients investigated (62.2%) [83]. One important fact to be noted here is that the results of both the studies must be given due consideration because they both adopted objective methods for the dysphagia evaluation (that is FEES or VFSS) [86, 87]. In contrast, most of the prior studies that reported a strong relationship between dysphagia and the psychological state employed either questionnaires or self-reporting of symptoms by the patients, which possibly render them highly subjective [10, 42, 67, 70, 73, 75–80, 82, 84, 90, 91]. Depressed patients might be more likely to report organic symptoms like dysphagia, hence making the association biased. Another important argument is that the disease causing the dysphagia might be a confounding factor in this association, and the only study that addressed the link between dysphagia and the psychological state in MUNOD patients failed to identify any significant association [86]. Therefore, caution is needed when interpreting the results, and the need for well-designed randomized controlled trials continues to account for these variables remain a priority. A third study that failed to discover a relationship between dysphagia and the psychological state was a large cross-sectional, community-based US study, conducted by Cho et al. using 3669 patients with dysphagia [10]. It used the validated bowel disease questionnaire which included only one question regarding dysphagia, and explored the association between dysphagia and the use of antidepressant medications (prescribed in the patients' medical records). Data from this study revealed gastroesophageal reflux disease (GERD) as the commonest etiology for the dysphagia, and antidepressants were one of the medications routinely taken by patients with dysphagia. However, their usage was not significantly unlike those who had no dysphagia [10]. In their discussion, Cho et al. argued against the association between dysphagia and depression [10]. They reported that despite the positive association reported between GERD and depression in

previous literature [42], they failed to find such an association in their results. They attributed their findings to the different methods they had adopted for the evaluation of depression; they only considered the use of antidepressant medications rather than the diagnosis of depression [10].

The severity of dysphagia and its correlation with psychological well-being

Dysphagia was found to be associated not only with the psychological state, however the severity of the dysphagia correlates as well. In a retrospective analysis of 104 patients who received treatment for head and neck cancer, Nguyen and colleagues assessed the severity of dysphagia through a modified barium swallow examination and studied its correlation to the QoL, depression, and anxiety using the UW QoL questionnaire and HADS. They reported that the anxiety, depression, and QoL scores were significantly higher in patients experiencing moderate-to-severe dysphagia compared with those having No to mild dysphagia [85]. Similar data were reported by Chan et al. in their study on 77 patients with head and neck cancer; they stated that the depression scores on the BDI were significantly correlated with dysphagia, assessed by the MDADI score ($\beta = -17.31$; $p = 0.009$) [73]. The severity of dysphagia was also reported to bear correlation to depression and/or anxiety scores in patients with PD. In a hospital and community-based, cross-sectional study using 137 PD patients, those with poorer swallowing rates evaluated by the timed swallowing test showed significantly higher depression symptoms compared with patients having better swallowing ($p = 0.01$) [71]. In another cross-sectional study performed on 69 PD patients who were evaluated more objectively for dysphagia that is FEES, more severe swallowing difficulties were directly correlated with the anxiety ($r = 0.472$, $p < 0.0001$) and depression scores ($r = 0.357$, $p < 0.003$) on TAI and BDI, respectively [72]. In fact, *Hans and colleagues* reported similar results in their cross-sectional study conducted on 127 patients with PD. The patients were segregated into four categories based on their BDI scores (total cohort depression, mild depression, moderate depression, and severe depression) and compared in accordance to their SDQ scores, either with scores ≥ 11 or with scores < 11 . Patients with mild depression were 3 times more likely to have dysphagia, and patients with moderate depression were 13 times more likely to have depression, whereas patients with severe depression were 30 times more likely to have dysphagia compared to the non-depressed patients [70]. Another logistic regression preliminary analysis from the French COPARK cohort of 419 patients with PD showed that severe dysphagia was

linked to higher depression symptom scores ($p = 0.001$) [78].

Further, in the elderly population severe dysphagia showed a strong relationship with higher depression scores. Two large studies performed on elderly patients reported a significant correlation between depression and varying grades of dysphagia. The first study, a prospective population-based one, conducted on 415 elderly individuals showed an odds ratio of 3.0 ($p = 0.02$) of major depression diagnosed according to DSM-IV criteria on dysphagia assessed by standardized swallowing examination [53]. The second study, a larger cross-sectional study, conducted on 13,361 elderly individuals, in which the clinical data for both depression and dysphagia were drawn from their medical records [88], showed an odds ratio of 1.7.

Psychological disease as a predictor for dysphagia

To add more information to the complex association between dysphagia and the psychological state, some researchers evaluated the predictive value of psychological diseases in determining the dysphagia outcomes. In fact, Kang et al. in a prospective study of 72 patients, explored the association between the psychiatric factors and development of chronic dysphagia, immediately post-anterior cervical spine surgery. They reported that the presence of psychological disorders prior to surgery was the only significant predictor of chronic dysphagia ($p = 0.005$) [81].

Similarly, Cnossen et al. in their prospective study of patients with head and neck cancer, reported that depression showed significant association with dysphagia, at baseline, as well as on follow-up ($r = 0.46$; $p = 0.001$), suggesting that the depression raises the risk of the chronicity of dysphagia among these patients [76]. Therefore, that depression might be considered a risk factor for poor recovery from dysphagia needs to be considered during the initial evaluation of patients with dysphagia, to optimize the outcome and enhance or speed up the recovery of dysphagia.

Dysphagia as a predictor of psychological disease

Just as depression may increase the chronicity of dysphagia, dysphagia may also increase the risk of depression. In a cross-sectional study conducted on 220 PD patients from a PD registry in Germany, patients with dysphagia were found to have three times greater likelihood of developing depressive symptoms (OR 3.06). Therefore, dysphagia was a significant predictor for depressive symptoms ($R^2 = 0.289$, $p = 0.006$). Concurring with this finding, Kang et al. in their non-randomized clinical trial,

evaluated the effect of a bedside exercise program on 50 stroke patients with dysphagia [75]. In their report, they stated that patients who had responded to the swallowing program and had less severe dysphagia on VFSS, showed lower depressive symptoms and higher QoL [75]. The results of both these studies suggest that suitable treatment of dysphagia reduces the risk of depression, and vice versa. Thus, the optimized management of dysphagia in its initial stages will definitely improve the well-being and quality of life on a long-term basis.

Limitations and future research

Major limitation of the literature assessment of dysphagia that is associated with psychological disorders is lack of objective assessment and variability in relation to the magnitude of severity of anxiety and depression and its impact for the precise assessment of dysphagia in this patient group. More deep assessment is needed to investigate the impact of anxiety and depression on the underlying neurological pathologies using spectral, brain waves in conjunction with the classical methods of subjective and objective assessment.

Conclusion

Dysphagia is associated with and positively correlated to depression and anxiety scores observed in PD, MS and stroke. Similarly, dysphagia does correlate with oral, tongue cancer. A bidirectional positive correlation exists with a vicious circle that loops between dysphagia and psychological disease. Moreover, the severity of dysphagia shows correlation with depression and/or anxiety scores. A critical understanding of this correlation between dysphagia and the neuropsychological pathologies would ultimately improve patient outcomes, quality of life, compliance, and adherence to management plan.

Abbreviations

CNS	Central nervous system
PNS	Peripheral nervous system
PD	Parkinson disease
GERD	Gastroesophageal reflux disease
O.R	Odds ratio
QoL	Quality of Life
MS	Multiple sclerosis
ENT	Ears, nose and throat
MBS	Modified barium swallow
SLP	Speech, language pathologist
MDADI	MD Anderson Dysphagia Inventory
SDQ	Swallowing disturbance questionnaire
VAS	Visual Analog Scale
HADS	Hospital Anxiety Depression Scale
FEES	Fiberoptic endoscopic evaluation of swallowing
VFSS	Video fluoroscopic swallow study
EORTC QLQ H andN35	European Organization of Research and Treatment of Cancer Quality of Life Core Questionnaire for head and neck cancer, version 35

GDS	Geriatric Depression Scale
BDI	Beck Depression Inventory
DASS	Depression Anxiety and Stress Scale
MARDS	Montgomery Asberg Depression Rating Scale
CES-D	Center for Epidemiological Studies-Depression
TAI	Trait Anxiety Inventory
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders criteria, version IV
UW QoL	University of Washington Quality of Life Scale
WHOQoL-Bref	World Health Organization Quality of Life-Bref

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None exists.

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