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Chapter 5

Swallowing impairment in Huntington's disease: videofluoroscopic findings

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Abstract

Objective

Dysphagia is a frequent finding in Huntington's disease (HD) and aspiration pneumonia is known to be a frequent cause of death. However, it is unknown what the specific dysphagia features in HD are, and if dysphagia is more severe in more advanced disease. The goal of our study was to identify the specific dysphagia features in HD, and to investigate the severity of dysphagia in the different stages of HD.

Methods

Forty-five HD patients (clinical stage I: n=13, stage II: n=18, stage III: n=14) participated and underwent videofluoroscopy using a variety of liquids and solid food. Oral, pharyngeal, and esophageal characteristics were analyzed per clinical stage.

Results

Dysphagia was found in 78% of the patients in all stages and was more severe for liquids (p=0.003) than solid food (p=0.035). Disturbances were found in especially the oral, and oropharyngeal phase of the swallow. Also disturbances in the duration times of the swallow were found in the oral and pharyngeal phase.

Conclusions

Swallowing abnormalities due to oral phase problems and oropharyngeal dysphagia are a frequent finding in HD patients. Dysphagia features are present in all three clinical stages of the disease. Given the high rate of dysphagia and the early onset of this problem in the course of HD potential swallowing disturbances deserve continuous attention from the earliest stages of the disease.

Introduction

The act of swallowing is a complex coordination of the sequence of activation and inhibition of muscles in the mouth, pharynx, larynx, and esophagus [1]. Swallowing is divided into four phases: the preparatory oral phase, oral phase, pharyngeal phase, and esophageal phase [2]. The preparatory oral phase includes transport from the bolus in the mouth, and mixing it with saliva. During the oral phase the bolus is propelled from the oral cavity to the pharynx. The pharyngeal phase refers to the passage through the pharynx and into the esophagus. During the esophageal phase the bolus is transported to the stomach by the peristaltic movements of the esophagus.

In Huntington's disease (HD) dysphagia is a frequent finding. HD is an autosomal, progressive, neurodegenerative disease, and is characterized by disturbed movements, behaviour, and cognition [3]. HD is caused by a CAG repeat expansion of the *HTT* gene on chromosome 4. The mean age at onset is in the third or fourth decade of life, and the disease duration is about 15 to 20 years [3-10]. Three clinical stages of the disease are described [11]. During stage I patients are independent and develop their first symptoms; in stage II patients start to be dependent and the symptoms are more generalized; during the last stage patients are completely dependent for all daily-life activities. Many patients with HD die of aspiration pneumonia, which has a close relation with dysphagia. In HD aspiration pneumonia is even the most frequently encountered primary cause of death [12]. It is therefore important to study the specific dysphagia features in HD, and their progress during the disease. It has been reported that patients with HD have dysphagia in all phases of ingestion [13-18]. However, it is not known when the dysphagia starts and how it progresses in the different stages of the disease. Further, specific dysphagia features, like aspiration, penetration, spilling, residue have not systematically been studied in HD. Also duration times, like oral transit time (OTT), pharyngeal transit time (PTT), oropharyngeal transit time (OPTT), pharyngeal delay time (PDT), pharyngeal passage time (PPT), and velopharyngeal closure time (VPCT) are unknown. The goal of our study was to identify these specific dysphagia features in HD at all three stages of the disease.

Methods

Subjects

Forty-five HD patients (23 men; mean ± SD age: 54 ± 12 years; mean ± SD disease duration: 10 ± 5 years) participated in the study (Table 1). Patients with a CAG repeat size ≥36 and without other diseases that could affect swallowing were included. Patients from all three clinical stages- in our study defined as stage I: patients living at home (n=13); stage II: patients living at home and having day care (n=18); and stage III: patients living in a nursinghome (n=14) - were enrolled. Patients in stage I were consecutively selected from April 2012 until June 2012 from the outpatient department of neurology of the Leiden University Medical Center (LUMC), while patients in stage II and III were consecutively selected in the same period from a Huntington Care center. The study was approved by the medical ethics committee of the LUMC. All patients gave informed consent.

Table 1 Clinical and demographic information of the Huntington's disease patients

Patients	
N (males/female) (n=45)	45 (23/22)
Age, y	53.7 (11.8)
Age at onset, y	43.8 (10.1)
Disease duration, y	9.8 (5.2)
CAG repeat length (n=37)	44.2 (3.2)
N Stages of HD (n=45)	
Clinical stage I	13
Clinical stage II	18
Clinical stage III	14

Unless otherwise stated, values are means (SD).
Abbreviations: SD, standard deviation; HD, Huntington's Disease; CAG, repeat length triplets number (≥36, pathological range)

Imaging acquisition and analysis

Each patient underwent videofluoroscopy (VFSS). The protocol for the VFSS involved presentation of two swallows each of 3cc and 10cc thin liquid, 5cc thick liquid, and a piece of bariumbread. For safety reasons water soluble liquids were used. Thick liquids were thickened with Nutilis Clear®. VFSS were recorded on a Toshiba Ultimax-i. The video recordings had 15 frames per second. Each video was analyzed in slow motion mode to identify any swallowing disorder. The videos were analyzed separately by two raters, one rater was experienced in HD

and dysphagia, and the second rater was experienced in dysphagia. The following features were analyzed: tongue protrusion, hyperextension of the head, adequate mastication; spilling before and during the swallow; penetration and aspiration; residue in the valleculae, and piriform sinus. The following duration times (in sec) were calculated: OTT, PTT, OPTT, PDT, PPT, and VPCT. For penetration and aspiration the Penetration-Aspiration-Scale (PAS) [19] was used; a score between 2 to 5 on this scale was defined as penetration, while a score of 6 to 8 was defined as aspiration [19]. The duration measures were defined as listed in Table 2. These measures all start with the first frame showing the first movement and end with the last frame on which the movement is detected. Investigating if dysphagia increased across the different stages of HD was performed for the following features: tongue protrusion, hyperextension of the head, inadequate mastication, and for PAS-score. Based on all analyzed features patients were also classified as dysphagic or not if they had disturbances in swallowing liquids or solid food. The examination was also recorded on video to assess the oral intake and oral preparatory phase.

Table 2 Definitions of the duration measures

Duration times	Applied definitions
Oral transit time (OTT) <1.5sec*	The first frame showing the first movement of the head of the bolus to the oropharynx until the first frame showing the bolus head reaching the point where the lower edge of the mandible crosses the tongue base
Pharyngeal transit time (PTT) <1sec*	The first frame showing the bolus head reaching the point where the lower edge of the mandible crosses the tongue base until the first frame showing the bolus leaves the cricopharyngeal area and the tail of the bolus is in the esophagus
Oropharyngeal transit time (OPTT) <2.5sec	The first frame showing the first movement of the head of the bolus to the oropharynx until the first frame showing the bolus leaves the cricopharyngeal area and the tail of the bolus is in the esophagus
Pharyngeal delay time (PDT) 0-0.2sec*	Time from the bolus head reaching the point where the lower edge of the mandible crosses the tongue base until the first laryngeal elevation in the swallow is seen
Pharyngeal passage time (PPT) <1sec*	The first frame where laryngeal elevation in the swallow is seen until the first frame showing the bolus leaves the cricopharyngeal area and the tail of the bolus is in the esophagus
Velopharyngeal closure time (VPCT) <1sec**	The first frame showing the first contact of the palatum to the pharyngeal wall until the last frame showing contact of the palatum to the pharyngeal wall.

normal value [2]
**Logemann described no specific number for the VPCT, but states that the velopharynx must be closed, just the few moments when the bolus is passing [2]. We therefore took <1sec.

Statistics

A 0ne-sample t test was used to compare the mean outcomes of the duration measures to the maximal normal values described by Logemann [2]. The Kruskal-Wallis test was used to investigate if the dysphagia is more severe in more advanced stages of the disease. For the statistical analyses SPSS 20 was used.

Results

All 45 HD patients underwent VFSS. Thirty-five of all participants (77.8%) were diagnosed as dysphagic, from which 32 (71.1%) had disturbances for solid food, and 30 (66.7%) had disturbances for liquids. The outcomes of the swallowing abnormalities and the duration times are shown in Table 3. The outcomes of the duration times compared to the maximal normal values are shown in Table 4. Significant shorter duration times were found in the OTT for all consistencies. The OPTT was shortened for liquids. Also a decreased VPCT was found for liquids (3cc and 5cc) and solid food. Significant longer duration times were seen in the PTT for solid food, and in the PPT for liquids. The findings of the analysis that examined if dysphagia is more severe in the more advanced stages of the disease are presented in Table 5. Results showed that tongue protrusion and inadequate mastication increased significantly (respectively p=.028, and p=.012). Hyperextension of the head does not increase significantly (p=.081). A score of ≥2 on the PAS showed a significant increase (p=0.018) across HD stages. The analyses further showed that dysphagia in patients was more severe for liquids (p=0.003) and solid food (p=0.035) across the various stages of HD.

Table 3 Videofluoroscopic findings of the preparatory oral phase, oral phase and pharyngeal phase of ingestion

	3cc thin liquid	10cc thin liquid	5cc thick liquid	Solid	Percentage
	%[1]	%[1]	%[1]	%[1]	%[1]
Tongue protrusion					12.2
Hyperextension					31.8
Mastication					
- moderate				29.3	
- inadequate				14.6	
Total				43.9	
Spilling					
- before	32,6	23.8	25.6	20.5	
- during	23.3	45,2	30,8	10,0	
Total	55.9	69.0	56.4	30.5	
PAS					
- penetration	15.9	14.0	4.8	0	
- aspiration	6.8	13.9	7.3		
Total	22.7	27.9	12.1		
Residue					
- valleculae					
mild	20.5	27.9	25.0	7.3	
severe	20.5	25.6	25.0	24.4	
Total	41.0	53.5	50.0	31.7	
- piriform sinus					
mild	27.3	30.2	22.5	2.4	
severe	4.5	20.9	22.5	7.3	
Total	31.8	51.1	45.0	9.7	
	sec	sec	sec	sec	
OTT (<1.5 sec)[2]	.585 (.606)	.367 (.292)	.502 (1.111)	.851 (1.066)	
PTT (<1 sec)[2]	.954 (.403)	.999 (.432)	1.199 (1.145)[1]	1.651 (1.552)[1]	
OPTT (<2.5 sec)[2]	1.558 (.724)	1.334 (.498)	1.699 (.879)	2.187 (1.882)	
PDT (0-0.2 sec)[2]	-.387 (.605)[1]	-.172 (.443)[1]	-.196 (1.372)[1]	.189 (1.179)	
PPT (<1 sec)[2]	1.319 (.567)[1]	1.165 (.475)[1]	1.413 (.544)[1]	1.336 (1.114)[1]	
VPCT (<1 sec)[3]	.705 (.320)	.850 (.659)	.788 (.405)	.781 (.521)	

[1] patients with abnormal values
[2] normal value [2]
[3] Logemann described no specific number for the VPCT, but state that the velopharynx must be closed, just the few moments when the bolus is passing [2]. We therefore took <1sec.
Abbreviations: PAS, Penetration Aspiration Scale; OTT, Oral Transit Time; PTT, Pharyngeal Transit Time; OPTT, Oral Pharyngeal Transit Time; PDT, Pharyngeal Delay Time; PPT, Pharyngeal Passage Time; VPCT, VeloPharyngeal Closure Time

Table 4 Duration measures in relation to the maximal normal values

Test variable	Max normal value	n	t	95% CI	p
OTT	1.5 sec				
3cc thin liquid		40	-9.548	-1.109_-.721	<0.001
10cc thin liquid		38	-23,917	-1.229_-1.037	<0.001
5cc thick liquid		38	-5.536	-1.363_-.633	<0.001
solid		33	-3.496	-1.027_-.271	.001
PTT	1 sec				
3cc thin liquid		40	-.725	-.175_ .083	.473
10cc thin liquid		41	-.017	-.137_ .135	.987
5cc thick liquid		39	1.085	-.172_ .570	.285
Solid		37	2.552	.134_ 1.169	.015
OPTT	2.5 sec				
3cc thin liquid		39	-8.129	-1.177_-.707	<0.001
10cc thin liquid		38	-14.443	-1.330_-1.002	<0.001
5cc thick liquid		38	-5.614	-1.090_-.512	<0.001
Solid		33	-.955	-,981_ .354	.347
PDT	0.2 sec				
3cc thin liquid		40	-6,135	-.780_-.393	<0.001
10cc thin liquid		41	-5.381	-.512_-.233	<0.001
5cc thick liquid		37	-1.758	-.854_ .061	.087
Solid		37	-.055	-.404_ .382	.956
PPT	1 sec				
3cc thin liquid		40	3.556	.138_ .500	.001
10cc thin liquid		41	2.220	.015_ .315	.032
5cc thick liquid		37	4.621	.232_ .595	.000048
Solid		37	1.883	-.036_ .707	.075
VPCT	1 sec**				
3cc thin liquid		40	-5.830	-.397_-.192	<0.001
10cc thin liquid		39	-1.422	-.364_ .064	.163
5cc thick liquid		38	-3.228	-.345_-.079	.003
Solid		37	-2.560	-.393_-.046	.015

One sample T Test with 95% Confidence Interval of the difference. Transit times as test variables. *, normal values in sec described by Logemann [2]. **Logemann described no specific number for the VPCT, but state that the velopharynx must be closed, just the few moments when the bolus is passing [2]. We therefore took 1sec.

Abbreviations: n, numbers of patients; SD, standard deviation; t, T Test: one sample; CI, Confidence Interval; OTT, Oral Transit Time; PTT, Pharyngeal Transit Time; OPTT, Oral Pharyngeal Transit Time; PDT, Pharyngeal Delay Time; PPT, Pharyngeal Passage Time; VPCT, VeloPharyngeal Closure Time; sec, seconds; p, p-value

Table 5 Dysphagia during the progression of Huntington's Disease

	n*	Mean rank	Chi-square	p	p**
Tongue protrusion					
- stage I	12	18.50[1]	7.129	0.028	.401[1]
- stage II	17	19.71[2]			.032[2]
- stage III	12	25.33[3]			.058[3]
Mastication					
- stage I	12	19.29[1]	8.282	0.016	.520[1]
- stage II	18	17.36[2]			.029[2]
- stage III	11	28.82[3]			.008[3]
Hyperextension of the head					
- stage I	13	17.19	5.018	0.081	
- stage II	18	24.06			
- stage III	13	25.65			
PAS					
- stage I	13	16.19[1]	8.041	0.018	.054[1]
- stage II	18	23.06[2]			.005[2]
- stage III	13	28.04[3]			.221[3]
Dysphagia for Liquids					
- stage I	13	14.92[1]	11.841	0.003	.024[1]
- stage II	18	24.25[2]			.001[2]
- stage III	14	28.89[3]			.144[3]
Dysphagia for solid					
- stage I	13	17.93[1]	6.680	0.035	.266[1]
- stage II	18	22.17[2]			.020[2]
- stage III	14	28.79[3]			.050[3]

Kruskal-Wallis test for measuring the severity of dysphagia in the three different stages. *some measurements have a number of patients <45. The missing patients could not be judge properly on that issue. **Asymp sig (2-tailed) for post-hoc differences using the Mann-Whitney U test: [1] stage I-II; [2] stage I-III; [3] stage II-III.
Abbreviations: n, numbers of patients; df, degrees of freedom; p, p-value; PAS, Penetration Aspiration Scale

Discussion

A videofluoroscopic study was done to evaluate the specific dysphagia problems in HD patients. Our results show that swallowing abnormalities due to problems in the oral phase as well as oropharyngeal dysphagia are frequent findings in patients with HD. Dysphagia features were present in all three clinical stages of the disease, and were more severe in the more advanced stages. In the preparatory oral phase some patients exhibited tongue protrusion during swallowing, and almost half of patients had difficulty with mastication of solid food. During

the oral phase many patients had spilling before and during the swallow. Further, patients had a significantly shorter OTT in comparison to the maximal normal value. This is in line with existing knowledge that HD patients have the habit to rapidly and impulsively consume food and beverage. The shorter duration time may reflect the inability to masticate properly. It is also possible that patients do not have the possibility to masticate properly due to poor lingual control or chorea. Irrespective of the precise mechanism it follows that insufficiently chewed food is swallowed. It is striking that patients in stage I seems to masticate poorer than patients in stage II. We do not have a clear explanation for this finding. Our results further show that more than a quarter of patients have residue of food in the valleculae during the pharyngeal phase. This bears the risk of suffocation when the residue falls into the trachea. An earlier study on aspiration pneumonia and death in HD showed that 4.1% of the patients died due to suffocation [12]. Complaints of patients about a lump in their throat when swallowing should therefore be taken very seriously and timely dysphagia management is warranted in such cases. Another finding in the pharyngeal phase was penetration and aspiration for all fluid consistencies. Also spilling before or during swallowing, and the presence of residue were seen for liquids and solid food. Spilling during swallowing, aspiration and residue were typically more pronounced with larger boluses of liquids (10cc versus 3cc). This may be related to the temporal coordination of swallowing; typical for the swallow of a small amount of beverage is that the swallow starts with the oral phase, followed by triggering the pharyngeal phase. For swallowing a large amount of beverage, in contrast, a simultaneous effectuation of the oral and pharyngeal phase is needed [2]. Based on our results smaller amounts of fluid intake seem therefore recommendable for HD patients. Another important issue is the bolus viscosity. When the viscosity of the bolus increased - in this study 5cc thick liquid was offered - there was less penetration and aspiration compared to small or large amounts of fluid. It is known that as the bolus viscosity increases to the thickness of pudding, the tongue base and the pharyngeal walls require more pressure to trigger a safe swallow [2]. In Parkinson's disease (PD) it was observed that when patients swallowed pudding-thickened liquids, they had residue in the valleculae and piriform sinus, and thus had the risk to aspirate after the swallow [2]. When the viscosity of liquids increased to the thickness of honey, Butler et al. [20] found that less pharyngeal pressure was needed. Honey-thick liquids seem the ideal viscosity to pass the pharynx without much pharyngeal driving force [20]. In our study we found less aspiration while swallowing honey-thick liquid, although piriform sinus and vallecular residue was present in 45-50% of the patients. Since considerably less penetration and aspiration in comparison to thin liquid was found, we think it would be best to recommend honey-thick liquids as soon as HD patients complain of dysphagia. Given the common finding of residue,

we also recommend to trigger a dry swallow after each swallow, to empty both valleculae and piriform sinuses and reduce the risk of aspiration after the swallow.

Pharyngeal duration times were particularly disturbed. An increased PTT was found for thick liquids and solid food. It is likely that thick liquid and solid food need more time to pass the esophagus because of their thick consistency. Yet, this was not associated with an increased frequency of residue. Further, an accelerated laryngeal elevation (PDT) was measured in all fluid swallows and a prolonged PPT in all consistencies. We hypothesize that the latter serves as a compensation strategy for the early initiation of the laryngeal elevation and prevents aspiration of hypopharyngeal residue.

In examining the clinical stages of HD we not only noted a significant increase of tongue protrusion as well as poor mastication, but also an increase of the PAS-score. The increased swallowing dysfunction with a higher incidence of penetration and aspiration in higher stages of the disease is consistent with the reported high number of patients that die of aspiration pneumonia in the end stage of HD. However, swallowing abnormalities in HD can already be found in clinical stage I. It is our experience that patients in stage I sometimes complain of swallowing abnormalities, but that they are seldom referred for a swallowing examination by a speech and language therapist, although there is general consensus that early detection and effective intervention can help to prevent choking [21]. In this respect it is helpful for patients to receive information and advice about the progression of dysphagia during the disease [21]. This information can now be offered more specific based on our findings.

To conclude, disturbances in oral intake and swallowing abnormalities due to oral phase problems and oropharyngeal dysphagia are a frequent finding in HD patients in all three clinical stages of the disease. Based on our findings the following recommendations for the treatment of swallowing disturbances are made: decreased volume and increased viscosity of liquid intake, and triggering a dry swallow after each swallow in all food consistencies.

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