

Exploiting Experience-Dependent Plasticity in Dysphagia Rehabilitation: Current Evidence and Future Directions

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Abstract Experience-dependent plasticity (EDP) is a general term used to describe neural and associated behavioral adaptations resulting from experience. Because the objective of dysphagia rehabilitation is to induce long-term permanent change in swallowing physiology, understanding EDP processes is crucial for documenting the efficacy of treatments. There is little information about natural processes of EDP related to swallowing (i.e., changes associated with aging and impairment). Therefore, the “baseline” on which we apply dysphagia treatments remains unclear. Because EDP is characterized by peripheral and central adaptations of physiologic and functional measures over time, effectively documenting EDP requires multiple outcome measures at multiple time points. This review will discuss mechanisms of endogenously induced EDP, including aging and impairment. A review of current dysphagia rehabilitation literature will be provided to indicate the state of evidence for exogenously induced EDP. Future considerations for the study of EDP related to dysphagia will also be offered.

Keywords Swallowing · Dysphagia · Deglutition · Plasticity · Rehabilitation

Introduction: What is Experience-Dependent Plasticity?

Experience-dependent plasticity (EDP), sometimes used interchangeably with experience-dependent learning, is a

broad term referring to changes of neural and behavior networks in response to experience. “Experience” can be characterized by physiological mechanisms, including impairment, and environmental influences [1••]. These changes can be short-term (i.e. adapting to a temporary oral appliance) or long-term (i.e. adapting to a partial glossectomy). Our understanding of the impact of environmental effects on plasticity has deepened with manifold evidence that neuroplasticity occurs over the lifespan of normally developing humans, long after critical developmental periods of infancy and childhood [1••]. EDP is particularly interesting in adults, because it can be manipulated through research to understand the underlying mechanisms in multiple sensorimotor systems. In some medical disciplines, EDP is regarded as an essential part of clinical intervention and research, for providing insight into the course of recovery from impairment. Specifically, the field of rehabilitation is coming to terms with the magnitude of EDP, both in terms of *naturally occurring*, or *endogenous EDP*, and *externally induced*, or *exogenous EDP*. Endogenously induced EDP can include phenomena such as normal aging (i.e. gradually adapting to weakening muscles or weight changes) and impairment (i.e. stroke or neurodegeneration). Exogenously induced EDP involves the manipulation of experiences and environments to induce learning and plasticity processes. The most complex hurdle in characterizing EDP is understanding how multiple, co-occurring forms of EDP interact and affect functional outcomes [2••]. The importance of considering plasticity in the arena of swallowing research and clinical rehabilitation of dysphagia has been introduced in recent publications [3, 4]. The purpose of this review is to provide an update on how studies to date have addressed this area of EDP associated with healthy and disordered swallowing, and dysphagia rehabilitation.

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Even for the most common and well-studied etiologies of dysphagia, we lack a sound understanding of the naturally occurring changes that result from the experience of impaired swallowing. This is largely because treating patients identified with dysphagia is rightfully a far greater priority than studying natural EDP processes. However, “the need to treat” has been determined without convincing evidence that exogenously induced EDP is superior to endogenously induced EDP. Determining the benefit of treatment over no treatment is restricted by a number of factors. First, the shortage of information on endogenously induced EDP associated with dysphagia means we cannot adequately characterize “normal response”, or ascertain a true “baseline” of EDP. Second, the cross-effects of different EDP phenomena on swallowing behavior are not understood. For example, how one’s experience of endogenously induced EDP (i.e., aging and impairment) influences their response to exogenously induced EDP (i.e., treatment). One is reminded to remain cognizant of the limited knowledge we have of natural aging and impairment as we discuss the processes of exogenously induced EDP, which are frequently overlaid on to endogenous experiences. Finally, we do not have sound evidence demonstrating how EDP is affected by dysphagia treatments [4]. The section on exogenously induced EDP will show that a large number of studies investigate components of this process. These components include when treatment effects are measured (during treatment versus post-treatment changes), and what outcome measures are utilized (physiological versus functional outcome measures). However, our understanding remains limited because many studies do not link these components to obtain a full picture of EDP processes. This review will provide an overview of how EDP is measured. The mechanisms of endogenously induced EDP will be discussed, including aging and impairment. A review of dysphagia rehabilitation literature will be provided to indicate the evidence available for characterizing EDP associated with current treatments. Future considerations for the study of EDP related to dysphagia will also be offered.

Measuring Experience-Dependent Plasticity (EDP)

One key component for examining EDP is time. In many studies that investigate the effect of experiences on plasticity or learning, a structure or function is examined over time to document the process of change. The duration of examination depends on the outcome variable that is being tested (i.e. hand movement versus neuronal growth) [2•]. Another important concept is that EDP manifests through central and peripheral nervous system (PNS) changes [1•], meaning simple observations of behavior may provide insight into plasticity mechanisms. It must be remembered

that such observations only *infer* plasticity of neural processes considered necessary for lasting behavioral change. It is well known that behavioral changes may manifest in the absence of neural changes, i.e., through changes in muscle composition [5–8], or refined movement control resulting from repetitive practice [8]. Throughout this review, the distinction between physiological and functional measures of EDP is made. Swallowing-specific functional measures are defined as any of the following: measures of penetration or aspiration, estimates of residue, and quality of life indicators. This is based on the fact that changes in these measures in isolation can be definitively categorized as beneficial or detrimental to patient well-being. Peripheral physiologic measures are defined as temporal or spatial measures of various physiologic or kinematic events, for example tongue pressures and laryngeal vestibule closure duration, respectively. Changes in these measures alone cannot be deemed beneficial or detrimental to effective nutritional deglutition; thus, concurrent assessment of functional measures is needed. In other words, longer duration of laryngeal vestibule closure that is not accompanied by reduced aspiration does not necessarily reflect positive treatment outcomes. The principles of EDP propose that behavioral changes (i.e., functional and peripheral physiologic measures) associated with learning are accompanied by plasticity of the neural networks responsible for that behavior [2•]. We define such neural changes as central physiologic measures, involving the brain and corticobulbar projections, but not the peripheral structures. In the case of injury to the PNS, it is known that axons are capable of regeneration (i.e., plasticity). However, PNS plasticity in the absence of CNS plasticity is unlikely to result in functional recovery [9]. Peripheral nerves have been studied in swallowing only as a vehicle for inducing CNS plasticity [10, 11], rather than for documenting the process of PNS plasticity. Because the PNS is most frequently discussed as the means by which central adaptations are communicated, plasticity specific to the PNS is not included in this discussion of neural plasticity.

When studies attempt to link changes in physiologic outcomes to functional outcome measures, this provides a unique opportunity to evaluate the effect of physiological change on meaningful swallowing measures. Thus, when studies document changes in physiologic measures but find no concurrent changes in functional measures, this relationship must be called into question. A lack of change in functional measures suggests one or more of the following:

- 1 the measure of function is not sensitive to changes in relevant physiology;
- 2 the physiologic measures chosen are not crucial to the functional outcome being tested; or
- 3 more than one physiologic process gives rise to the functional outcome of interest, i.e., detecting a 1:1

change requires measurement of multiple physiologic processes.

Peripheral EDP is defined as change in peripheral structure or function, for example muscle physiology or kinematics. As mentioned above, PNS plasticity is not included in this definition. Central EDP involves adaptations of the central nervous system. Despite the interdependence of central and peripheral adaptations in EDP, these processes are frequently investigated in isolation. As mentioned above, simple observations of behavior are often used to infer the presence of responsible central EDP mechanisms. Therefore, the dichotomy between central and peripheral EDP is made for facilitating the review of studies that aim to investigate only one of these components. Peripheral EDP associated with swallowing has been measured with a number of tools, including videofluoroscopy (VFS), fibreoptic endoscopic evaluation of swallowing (FEES), pharyngeal manometry, oral pressure sensors, surface electromyography (sEMG), magnetic resonance imaging (MRI), and ultrasound. Central EDP has been documented using measures of neural activation and cortical excitability, made with techniques such as functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), and motor evoked potentials (MEPs) induced with transcranial magnetic stimulation (TMS).

Aging and Endogenously Induced Experience-Dependent Plasticity

Development clearly plays a critical role in EDP. The most widely understood developmental stage is the critical period of plasticity in early development [12–15]. However, there is evidence that central and peripheral EDP processes occur well into adulthood [1•, 16]. Aging as a form of EDP has been examined through cognitive, sensory, and motor task training [17, 18]. Compensatory mechanisms as a means of adapting to senescence have also been reported for various sensorimotor systems [19, 20]. Inherent in the process of aging is exposure to a countless number of experiences. Experiences such as stress, diet, and task-learning all have the ability to produce durable changes in neural networks [2••]. A combination of these experiences is known to affect spontaneous recovery, and response to intervention [2••]. Therefore, the simple occurrence of life experience throughout the aging process predisposes the geriatric population to greater variability in their response to injury and recovery. Additional factors that may induce EDP over protracted periods of time during the aging process include reduced strength and endurance, as well as cognitive, social, and emotional experiences [19, 21–23]. Understanding these processes and how they relate to

dysphagia recovery may provide insight into optimal treatment conditions for elderly patients.

In swallowing, aging has been examined in many research studies. Presbyphagia is a term used to refer to normal, age-related changes in the swallowing mechanism of otherwise healthy older adults [24]. Some age-related anatomical differences in structures involved in swallowing include smaller cross-sectional area of the tongue and atrophy of the thyroarytenoid muscles [25–27]. Sensory function of the oral cavity is also affected, with reduced spatial tactile perception of the lips and tongue, and deficiencies in stereognosis, taste, and viscosity in the oral cavity [28–32]. These anatomical and functional variations probably underlie kinematic changes that are characteristic of presbyphagia, including delayed initiation and slower kinematics of the pharyngeal swallow [24, 33–36]. Healthy older adults also report dysphagia symptoms more frequently than healthy young adults, including coughing and food sticking in the throat [37]. fMRI studies of the brain have reported both decreased and increased blood-oxygen-level-dependent (BOLD) signals in healthy older adults compared to young adults for swallowing tasks, indicating that age-related neurophysiologic changes in swallowing are also evident [38–42].

Despite these established age-related changes in swallowing function, few studies have investigated how the factors associated with age affect the presence and recovery of dysphagia. Studies of overall motor function suggest that while outcomes at discharge may be worse for older patients after stroke [43, 44], the amount of improvement from admission to discharge does not differ with regards to age [44, 45]. Similarly, studies have documented increased age as a predictor of poorer outcomes related to persistence of dysphagia [46, 47], but improvements from admission to discharge are not determined by age [48, 49]. Functional abilities on admission are lower in the geriatric population because of factors associated with age [45], suggesting that age in and of itself should not be considered prognostic of poor functional outcomes. Further research is needed to identify the factors *associated* with age that are more likely to result in poor outcomes for dysphagia recovery. Research is also required to determine which of those factors are more (or less) amenable to therapy.

Dysphagia and Endogenously Induced Experience-Dependent Plasticity

Dysphagia itself is a symptom of an array of disorders, affecting individuals across the lifespan. Because of the multitude of medical diagnoses associated with dysphagia, it is an immense task to document the changes typical of each disorder, let alone the natural response of individuals

to such changes. There are well-documented degenerative and regenerative processes that occur implicitly with injury, for example edema, cell death, and regeneration [2••]. The term “natural response” denotes adaptations or learning associated with the experience of disorder, and therefore incorporates processes that both facilitate and hinder recovery. It is known that these adaptations, in the absence of intervention, occur in both peripheral and central systems [50, 51].

Peripheral response to injury manifests as compensatory behavioral changes that develop from learning to facilitate function in the face of impairment [51, 52]. Animal research suggests that restoration of functional movement is largely a result of these compensatory movements, with motor training (or exogenously induced EDP) having a minimal effect [50, 52]; in other words, motor training may only provide a forum in which self-taught compensatory behaviors can develop. The findings that these natural behavioral responses are tightly linked to neural plastic adaptations [53] and functional recovery [50, 52] reveal the importance of characterizing this natural compensatory behavior. Evidence of self-taught compensatory behaviors in dysphagic patients has previously been reported by Kahrilas et al. [54], and is certainly frequent in clinical anecdote. Endogenous learning during impairment can also induce maladaptive behavior [50], further reinforcing the importance of understanding natural response. It is known that in the field of speech production, self-taught articulation patterns that develop during cleft palate can be persistent after corrective surgery [55]. Increased time spent using these compensatory patterns before surgery increases the chance they will persist [56]. Therefore, spontaneous recovery not only provides a window of opportunity for beneficial compensatory strategies to develop, but may also render maladaptive behavior resistant to therapy. While clinical anecdote suggests maladaptive self-taught swallowing behaviors can develop in the absence of intervention, as far as we are aware, research describing such behaviors does not exist.

Two studies have investigated central adaptations that occur in association with acquired dysphagia [57, 58]. These studies documented neural correlates of behavioral changes associated with natural recovery from dysphagia. Observed increases in somatosensory cortex activation [58] and increased cortical representation of target muscles [57] were associated with improved functional outcomes, measured using VFS [57] and FEES [58]. These functional assessments are an important aspect of EDP studies, as neurophysiologic measures alone do not reflect peripheral physiology or functional outcomes, and therefore do not provide a direct measure of swallowing per se. Understanding the relationship between physiological and functional measures is crucial for interpretation of either. For example, it is tempting to view reduced cortical excitability

(central physiology) as detrimental to swallowing function. However, if accompanied by an increase in oral intake, or reduced aspiration (functional outcome), reduced cortical excitability may be viewed as beneficial. Alternatively, such an outcome could also suggest that the central and peripheral measures do not have a direct relationship and perhaps some other neural measure is changing alongside the functional improvements.

As already stated, knowledge of endogenously induced EDP is important because it can affect therapeutic endeavor. An example of this is the tongue-hold maneuver. The maneuver was developed after the observation that some patients with presumed reduction in base of tongue retraction due to anterior tongue resection had a natural compensatory adaptation of posterior pharyngeal wall bulging during the swallow [59, 60]. Therefore the technique was devised to mimic impairment, and replicate the effects of endogenous learning seen as a result. It should be noted, however, that simply replicating a natural EDP process as an intervention does not preclude the behavior from being maladaptive. Confirmation of positive functional gains alongside observations of increased posterior pharyngeal wall bulging is required to determine the benefit of such change. Furthermore, without confirmation of central adaptations associated with the technique, it remains unknown whether the peripheral modifications are reflective of lasting changes or merely represent altered muscle physiology or kinematics.

Dysphagia Treatments and Exogenously Induced EDP

The objective of dysphagia rehabilitation is to induce long-term permanent change in swallowing physiology. The relationship between environmental experience and EDP is well documented [1••, 2••, 51, 53, 61, 62], but how these phenomena can be positively affected by dysphagia intervention is not clearly understood [4]. Allred argues “It is not enough to know that experience matters” [50]. Because a multitude of experiences interact to affect EDP and functional outcomes [2••], we need to understand the relationships among the various processes before attributing benefit to intervention. This section focuses on factors that swallowing treatment studies should consider to maximize their observations of EDP.

Measuring Treatment Effects at Multiple Time Points is Required to Characterize EDP

To document relatively permanent changes in swallowing neurophysiology resulting from treatments, investigation of changes during and after extended duration of treatment is required. Much research effort in dysphagia management

has been focused on documenting changes that occur during execution of treatment techniques, with fewer studies providing evidence of more permanent changes, i.e., pre and post-treatment designs. The terms “standard” and “traditional therapy” are frequently used in swallowing literature to refer to a combination of therapies, including effortful swallowing, Mendelsohn maneuver, tongue-hold technique, and Shaker exercise. Emerging treatments are those that are frequently compared to traditional treatment in the literature, including neuromuscular electrical stimulation (NMES), expiratory muscle strength training (EMST), lingual strengthening, and McNeill dysphagia therapy program (MDTP). Treatments are therefore dichotomized for this review according to these categorizations used frequently in the swallowing literature. When reviewing the literature, one will note that the traditional techniques have very few pre and post-treatment studies dedicated to documenting long-term learning and plasticity (Table 1). Studies that have investigated long-term treatment effects of these traditional treatments have typically combined multiple exercises into their treatment protocols [63–71], and therefore, positive (or negative) outcomes cannot be attributed to any one exercise.

This lack of long-term evidence for traditional therapy poses a problem for two reasons. First, traditional techniques are commonly prescribed for dysphagic patients, with very little understanding of their long-term effects. Second, the terms “traditional therapy” or “standard therapy” are repeatedly used in the scientific literature to describe control groups against which emerging therapies are evaluated, often to avoid the ethical limitation of not providing treatment. Furthermore, many studies combine traditional techniques with other treatments in their investigations. As the long-term

effects of these traditional treatments on EDP are not well studied or understood, the condition used as a control for many emerging treatments is equally obscure. The last two years has seen the re-emergence of investigations into the effect of traditional therapies in isolation [72–74]. The increasing number of available treatments and the multiple etiologies and physiologic abnormalities associated with dysphagia make it an immense task to document the long-term effects of all treatments. However, methodically filling these gaps in the literature is required to ensure that we not only provide adequate evidence to support robust treatments but also equip ourselves with sufficient evidence to exclude treatments that hold no promise of enhancing recovery from dysphagia.

In addition to pre and post-treatment measures, Humbert et al. [75, 76] highlight the important role of during-treatment measures in understanding the process of learning, or EDP resulting from swallowing treatment. Changes measured during treatment reflect *performance* of a task [77]. However, measures of performance cannot be presumed to reflect *learning* [77]. Learning is defined as “a relatively permanent change resulting from practice or experience” [78]. There is evidence to suggest that the conditions which induce the most desirable performance effects can be least effective in inducing desirable learning effects, and vice versa [78]. Therefore, measures obtained both during and following treatments are required to establish this relationship. Table 1 shows that although emerging therapies have improved on the number of pre and post-treatment studies compared with traditional therapies, there are still few investigations documenting performance effects. An additional important consideration is that both during-treatment and post-treatment behaviors can gradually adapt over time, because of learning and recalibration of

Table 1 Common treatments used in dysphagia management

	During treatment effects (A)				Pre and post-treatment effects (B)			
	NMES	EMST	Lingual strengthening	MDTP	NMES	EMST	Lingual strengthening	MDTP
Emerging treatments								
Physiologic outcomes	[91–95]	[96–98]	[89, 90, 99–102]		[92, 103–113]	[96, 114, 115]	[89, 90, 99, 100, 116]	[104, 117, 118]
Functional outcomes	[95]		[89, 90]		[103–107, 109, 111, 112, 119–130]	[114, 115]	[89, 90, 99, 100]	[104, 117, 118, 131]
Traditional treatments	Effortful swallowing	Mendelsohn	Tongue-hold	Shaker	Effortful swallowing	Mendelsohn	Tongue-hold	Shaker
Physiologic outcomes	[98, 132–150]	[98, 139, 147, 151–157]	[60, 142, 158–160]	[102, 161–165]	[110]	[72, 73]	[74]	[165–170]
Functional outcomes	[133, 135]	[155]				[72, 73]		[168, 169]

Treatments are separated into emerging (above) and traditional (below). Studies have been categorized according to whether they provide “during-treatment” effects (A), or “post-treatment” effects (B) based on pre and post-treatment design. Studies have further been categorized according to whether they utilize peripheral physiologic outcome measures, or functional outcome measures

movements [75, 76]. Many studies obtain only a small number of swallows at any given time point. Furthermore, these swallows are often averaged to reduce variance. It is therefore possible that gradual change associated with learning goes undetected. Some studies make assessments at multiple time points after completion of treatment to define the timeframe of treatment effects [79–88]. To characterize learning effects within each time point, observation of multiple, consecutive trials is required.

Table 1 shows there is a small number of studies for any given treatment, traditional or emerging, investigating both physiologic *and* functional outcome measures. A total of two studies in Table 1 document both physiological and functional outcomes during and after treatment [89, 90]. Although there is more physiologic and functional evidence for emerging treatments compared with traditional, examining the two in tandem is a process that remains uncommon. More studies making these connections are crucial if we are to understand how to promote EDP processes that result in meaningful change for patients with dysphagia.

Although investigations of rehabilitative strategies on peripheral physiology are emerging, research must expand to determine the neurophysiologic foundations of peripheral adaptations [171]. Most studies investigating central EDP associated with dysphagia treatments have utilized pre and post-treatment designs to assess long-term adaptations. Very few of these studies incorporate during-treatment observations of central EDP processes. Similarly, studies looking at during-treatment effects have not extended their observations to post-treatment assessment. One study expanded their during-treatment observations to include multiple repetitions of each task, to investigate gradual changes in treatment response [172]. This fMRI study found the BOLD response increased with repeated exposure to heightened sensory experiences (visual bio-feedback and sour bolus), while it decreased with repeated water swallows [172]. As highlighted by the authors, investigations of peripheral physiology and functional outcomes are required to determine the clinical relevance of these central EDP observations. There are few demonstrations of how peripheral physiology and functional outcomes relate to central EDP associated with treatments. Two studies have combined neurophysiologic measures with functional outcome measures to draw functional conclusions about central changes [109, 171]. Oh and colleagues report functional improvements in stroke patients after NMES. Despite the authors' claim that increased cortical maps accompanied these functional improvements, their measures of central physiology did not reach statistical significance [109]. Malandraki et al. report a case study of a stroke patient who underwent eight weeks of lingual exercise [171]. They observed increased

activations in the primary motor and primary sensory cortex, and in the premotor area and the insula. Improved penetration and aspiration, reduced residue, and increased lingual pressures accompanied these central physiologic adaptations. Although the authors acknowledge the limitations of a single-subject design, it is interesting to note that aspects of their findings are similar to those reported for natural recovery [58]. The paucity of literature in this area highlights the need for more studies incorporating physiology and function, both during and after treatment periods. Only then can we gain a full picture of EDP processes associated with dysphagia treatments.

Studying Healthy Participants to Document EDP

Many would question the possibility of seeing EDP processes in healthy participants as a response to treatment. Numerous investigations of swallowing treatments show that healthy subjects are capable of demonstrating central [10, 11, 80, 82–88, 172–177] and peripheral [89–92, 99, 100, 103, 104, 108–116, 126, 176] adaptations. The limitations in investigating endogenously induced EDP (discussed above) require researchers to develop innovative ways to glean this information. Investigating EDP that occurs as the healthy system learns, or compensates and corrects for errors, offers an alternative [178]. Perturbing the swallowing process of healthy participants or creating “pseudo-impairment”, and observing the resulting change in physiologic and functional measures may provide useful information about the effect of, and response to, impairment. Healthy adults (young and old) are capable of safely responding to novel and unexpected circumstances [75, 76, 179]. The question of whether healthy participants are capable of demonstrating functional change depends on the criteria of “improvement” or “decline”. An alternative approach is to document the magnitude of change without qualitative assumption of such adaptations. Findings should then be replicated in patient populations, from whom qualitative conclusions can be made alongside meaningful measures of functional change.

Conclusions

An increasing number of treatments is available for dysphagia management. Treatments have been developed with the purpose of inducing long-lasting change in swallowing neurophysiology, by promoting peripheral and central plasticity through experience. Our understanding of natural processes of EDP, such as age and injury, are limited. To provide a thorough evidence-base for dysphagia treatments, we require more information about these natural processes, and about how overlying exogenous EDP

processes affect functional outcomes. The aging process, experience of injury, and the presence or absence of adaptive compensation may all be underlying factors contributing to variability among patients with a seemingly similar clinical history. Although natural EDP processes remain difficult to elucidate, focusing on the plasticity and learning capability of healthy subjects through studies that perturb swallowing will elucidate EDP processes related to “pseudo impairment”. Many basic questions regarding many treatments still require attention before the more complex process of documenting efficacy in patients is justified. More thorough investigation of the long-term effects of traditional therapies is required if we are to continue to use these therapies as control conditions. Observations should be made during treatment periods, and on completion of treatment protocols to adequately characterize the process of EDP. Outcome measures must address both physiological and functional adaptations if clinical conclusions are to be drawn from such research. Only when we begin to adequately characterize these processes of EDP can we begin to deduce the functional superiority of dysphagia treatments over spontaneous recovery.

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Compliance with Ethics Guidelines

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