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Listening and Learning: Cognitive Contributions to the Rehabilitation of Older Adults With and Without Audiometrically Defined Hearing Loss

Kelly L. Tremblay and Kristina C. Backer

Department of Speech and Hearing Sciences, University of Washington, Seattle, Washington, USA

Abstract

Here, we describe some of the ways in which aging negatively affects the way sensory input is transduced and processed within the aging brain and how cognitive work is involved when listening to a less-than-perfect signal. We also describe how audiologic rehabilitation, including hearing aid amplification and listening training, is used to reduce the amount of cognitive resources required for effective auditory communication and conclude with an example of how listening effort is being studied in research laboratories for the purpose(s) of informing clinical practice.

Keywords

Aging; Cognition; Hearing loss; Listening effort

INTRODUCTION

This special issue is on the topic of cognitive energy as it relates to successful listening in challenging environments. It is part of the concerted endeavor of the Fifth Eriksholm Workshop on “Hearing Impairment and Cognitive Energy” to describe what is known on the topic, to work toward a consensus in the use of terminology, and to identify priorities for future research and implications for practice in audiology (Pichora-Fuller et al., this issue, pp. XXXX). In this article, we approach the topic as it relates to older adults with and without audiometrically defined hearing loss. Older adults frequently describe listening to be tiring and stressful, even when speech sounds are audible and words are recognized accurately (CHABA 1988). Our contribution is to describe some of the underlying neural mechanisms that may be contributing to the problem. More specifically, we describe how aging negatively affects the way sensory input is transduced and processed within the aging brain and how cognitive work is involved when listening to a less-than-perfect signal. Cognitive work refers to a series of cognitive processes engaged for the purpose of completing a task, and consumes cognitive resources. We also describe how audiologic

Address for correspondence: Kelly L. Tremblay, Department of Speech and Hearing Sciences, University of Washington, 1417 NE 42nd Street, Seattle, WA 98105, USA. tremblay@uw.edu.

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rehabilitation, including hearing aid (HA) amplification and listening training, is used to reduce the amount of cognitive resources required for effective auditory communication. HA amplification, for example, increases sound level, making it more audible to the listener. HAs have therefore been described in the literature as reducing the cognitive resources needed to process speech (Downs 1982; Gatehouse & Gordon 1990; Hällgren et al. 2005; Picou et al. 2011; Hornsby 2013). Listening training is used to improve an individual's use of residual hearing through goal-directed listening exercises designed to engage cognitive resources and promote auditory learning (for review, see Bamford 1981). We conclude by highlighting a few examples of how listening effort is being studied in research laboratories for the purpose(s) of informing clinical practice, as well as improving communication outcomes for people with hearing loss.

The core of this special issue is the Framework for Understanding Effortful Listening (FUEL). It helps to describe how the listening demands and the listener's motivation interact to determine the amount of listening effort that is exerted in a given situation (Pichora-Fuller et al., this issue, pp. XXXX). For example, more demanding listening situations (e.g., multiple concurrent sounds or dealing with a degraded sensory signal because of hearing loss) require additional cognitive resources (e.g., Zekveld et al. 2006; Pichora-Fuller 2007; Ronnberg et al. 2008). This type of mental exertion involved is sometimes referred to in the literature as listening effort (for a review see, McGarrigle et al. 2014), but here we use the term *listening effort* to specifically refer to the deliberate allocation of cognitive resources to overcome obstacles in goal pursuit when carrying out a listening task. The task we refer to throughout this article is the ultimate ability to communicate in complex listening environments, but it is important to keep in mind that the proposed framework is intended to extend beyond the scope we present here. It is meant to include listening to any auditory source, including music and environmental sounds.

THE AGING EAR–BRAIN SYSTEM: REDUCED CAPACITY AND INCREASED EFFORT?

Successful listening involves efficacious interactions involving the ear–brain system. To achieve a given goal when engaging in a task, the demand on cognitive resources will vary depending on top-down cognitive factors, such as the availability of contextual support or expectancies, as well as on the quality of bottom-up sensory inputs (Edwards, this issue, pp. XXXX; Pichora-Fuller et al., this issue, pp. XXXX). However, in addition to hearing loss, the typical older adult experiences multiple types of sensory and cognitive decline (see Humes et al. 2012; Albers et al. 2015 for reviews), and these too can make listening more demanding for the individual. It is therefore important to understand how sensory input is transduced from the ear to the brain, and how age-related changes in sensory (ear) and cognitive (brain) processing may interact and hinder successful auditory communication. With this information, it becomes possible to identify sources of the problem as well as target opportunities for intervention. Therefore, in the sections that follow, we will review key points about age-related changes in the ear–brain system that affect sensory and cognitive processing, and impede successful listening for the typical older adult.

The topic of listening effort is especially pertinent to older adults because the prevalence of audiometrically defined hearing loss, most often a sensorineural hearing loss (SNHL), can be as much as 46% in adults older than 40 years of age (Cruickshanks et al. 1998). Audiometrically defined hearing loss is associated with decreased speech understanding (CHABA 1988) and mental fatigue (Hornsby et al., this issue, pp. XXXX). What is more, individuals with hearing loss report fatigue and stress more frequently than individuals without an audiometrically defined hearing loss (Hétu et al. 1988; Kramer et al. 2006).

Hearing loss can also increase stress and strain relationships involving family, friends, and work colleagues. For instance, challenging listening conditions can include difficulty hearing clearly while on the phone or conversing at a restaurant with friends or family members. At work, it could be hearing an opposing attorney's comments in a courtroom or speaking with customers on the phone. These listening situations vary in the complexity of the input, as well as in the complexity of task demands, thus requiring varying amounts of listening effort. At some point, the cost-benefit ratio of participating in challenging communication situations will weigh into a person's decision to either withdraw from such activities or find ways to work through and around such listening situations. As pointed out by Richter (this issue, pp. XXXX), the proportional relationship between task difficulty and effort is limited by individual ability (Kukla 1972). If it is impossible to succeed at a task, an individual will disengage and no longer exert effort, and in many everyday situations, the typical older listener with hearing loss may choose to no longer participate in work or social events. Indeed, social withdrawal (Mick et al. 2014) and loneliness (Pronk et al. 2013) are reported in subgroups of older adults with hearing loss. Therefore, the goals of auditory rehabilitation (AR) are not only to address the problem of decreased sound audibility but also to minimize the hearing-loss-induced deficits affecting function, activity, and participation. AR should also enhance quality of life through sensory management, instruction, perceptual training, and counseling (for review, see Boothroyd 2007).

Age-Related Changes Affect the Sensory Auditory Pathway

One step in the rehabilitation process is to recognize how a person's sensory capacity can become compromised by the cumulative effect of intrinsic (e.g., Gamma-aminobutyric acid) and extrinsic factors (e.g., noise exposure). Two consequences are discussed here: (1) the degradation of signal quality being transmitted from the cochlea to the central auditory system and (2) the loss of audibility, marked by audiometric threshold shifts at higher frequencies.

With advancing age, the physical and functional integrity of the cochlea and neural pathways to the brain become compromised. Traditionally, age- and noise-related hearing loss have been thought to result primarily from hair cell damage/loss in the cochlea. However, Kujawa and Liberman (2009) recently found (in mice) that age and noise exposure can result in a loss of communication (synapses) between sensory inner hair cells and cochlear neurons, and that this damage does not necessarily reveal itself as a loss of audibility according to audiometric thresholds. Acoustic information is carried from the hair cells to the brainstem via the bipolar sensory neurons of the auditory nerve. Once the synapse has degenerated, the affected neuron can be said to be functionally disengaged from the hair cell and thus carry

little or no information to the central auditory system. This means, even when there is no evidence of audiometrically defined hearing loss, the capacity of the peripheral system to conduct sound can become compromised with advancing age, resulting in a degraded sensory signal being transmitted upstream.

It has been hypothesized that the loss of auditory nerve fibers disrupts the ability to encode temporal features of sounds through synchronized firing, or phase locking, in the central auditory system (Bharadwaj et al. 2014). This assumption would help to explain why older adults frequently describe conversational speech as being loud enough to hear, but not clear enough to understand because temporal coding is a fundamental process involved in the processing of speech in noise (Moore 2008; for a review, see Plack et al. 2014). What is more, impaired speech understanding, among older adults, has long been attributed to impaired frequency resolution as well as temporal processing (Billings et al. 2012; Clinard & Tremblay 2013; see Humes & Young, this issue, pp. XXXX;).

In addition to signal degradation, age-related SNHL often results in a loss of audibility at higher frequencies. The upstream effects of this partial auditory deprivation can be seen in the structure and function of central mechanisms. In mouse models of SNHL, deprivation-related alterations in the neural encoding of sound, from the cochlear nucleus to the auditory cortex, are well documented in the literature and described as the central effects of peripheral pathology (Willott et al. 1993; Willott & Bross 1996). In humans, the consequences of SNHL on central mechanisms are less clear. However, results thus far reveal a reduction in gray matter volume in auditory cortices (Peelle et al. 2011; Eckert et al. 2012), as well as functional changes in cingulo-opercular activity, important for adaptive control (i.e., adaptively adjusting behavior to optimize performance) (Vaden et al. 2013, 2015). Given these changes involving the ear-to-brain auditory pathways, one can recognize how older adults have a reduced physiologic capacity to encode the acoustics of sound, as well as attend to multiple concurrent sound sources.

Age-Related Changes in Brain Structure and Function

Even in the absence of reported hearing loss, the typical aging brain can be said to include modifications of both gray and white matter, as well as atrophy of brain volume (for reviews, see Fjell et al. 2010; Lockhart & DeCarli 2014). Sometimes referred to as the central effects of biological aging in the animal literature (see Willott 1996 for review), age-related changes can begin fairly early in the human life course. Cross-sectional data have shown whole-brain volume reductions beginning around 30 years of age (Fotenos et al. 2005). Frontal brain regions and, to a lesser extent, the temporal lobe (Jernigan & Stout 2001; DeCarli et al. 2005; Raz et al. 2005) are thought to be most affected, although some parietal regions have also been shown to atrophy with age (Resnick et al. 2003), as can the cerebellum and hippocampus (Raz et al. 2005). Fjell and Walhovd (2010) postulate that neuronal shrinkage and the loss of synapses and dendritic spines mediate gray matter atrophy, with a small contribution from loss of neurons; furthermore, the length of myelinated axons are substantially reduced with age, leading to white matter atrophy.

How do such structural alterations relate to listening effort? Age-related atrophy of frontal and temporal regions of the brain is relevant to the discussion of listening effort because

these areas are known to be actively involved in attending to speech, while suppressing competing signals such as background noise (Zekveld et al. 2006). As described by Eckert in this special issue (p. XXXX), frontoparietal activity is consistently observed during tasks that require directing attention to relevant information (Nee et al. 2013) and has been implicated in executive function, allowing suppression of irrelevant information and selection of a task-appropriate response (Durstun et al. 2003; Kerns et al. 2004; Wager et al. 2005; Kerns 2006; Luks et al. 2007). In addition, behavioral studies have demonstrated that older adults with weaker inhibitory control abilities (i.e., worse Stroop task performance) have worse speech recognition in noise than those with stronger inhibitory control, especially for words with many phonological competitors (Taler et al. 2010; Janse 2012). Collectively, these types of structural and functional changes are thought to put the older adult at a disadvantage when trying to selectively attend to a speaker when multiple talkers are present, thus increasing the cognitive load.

Grady (2012) further illustrates how structural and functional aspects of the aging brain can relate to one another and affect cognitive processing (Fig. 1). Age-related cognitive declines can include decreased executive function (e.g., the ability to ignore task-irrelevant stimuli, Hasher & Zacks 1988) or task-switching (Kramer et al. 1999; Cepeda et al. 2001). Also affected are slowed processing speed (Wingfield et al. 1985; Salthouse 1996; Fitzgibbons & Gordon-Salant 1998) and reduced memory abilities, including working memory capacity (Kausler 1994; Humes & Floyd 2005; see also Wingfield, this issue, pp. XXXX) and episodic memory (Spencer & Raz 1995; Shing et al. 2010), which is the ability to remember events or information and the context in which they were experienced (Tulving 1983). All of these aspects of cognition are essential to real-time cognitive processing during communication because a person must be able to focus attention, ignore irrelevant stimulus input, and process and remember rapid amounts of auditory and visual (e.g., lip movement) information to comprehend what another person is saying.

To summarize, older adults can be said to be at a double disadvantage, compared with younger adults, for successful communication in challenging situations; because, in addition to an increased probability of having sensory impairment, resulting in less audible and distorted signals reaching a previously deprived central auditory system, they are likely to also be experiencing age-related changes in cognition. Such age-related changes in ear–brain structure and function might help to explain the excessive perceived effort older adults describe when trying to listen to someone speak in an adverse listening environment. Moreover, it also helps to explain how improving the fidelity of the incoming signal (e.g., increase audibility) could reduce the consumption of resources needed to achieve success on some listening tasks (Downs 1982; Gatehouse & Gordon 1990; Hällgren et al. 2005; Picou et al. 2013).

AR: IMPLICATIONS FOR LISTENING AND LEARNING

Listening

The previously mentioned studies describe the many changes in the ear–brain system that are negatively affected by age and limit the capacity to effortlessly process ongoing communication. Not all cognitive abilities decline with age though. As cognitive processing

capacity generally declines with age, there are potentially compensating gains in knowledge (Horn & Cattell 1967; for reviews, see Bialystok & Craik 2010; Phillips, this issue, pp. XXXX; Grady 2012). Some cognitive capabilities, particularly semantic memory (i.e., knowledge of facts and events that are not based on personal experience, Squire et al. 1992) and emotional processing/regulation, remain stable or even strengthen throughout the lifespan (Grady & Craik 2000; Scheibe & Carstensen 2010; Carstensen et al. 2011). Therefore, some older adults can capitalize on intact cognitive abilities by utilizing prior knowledge and semantic memory to compensate for declines in other aspects of cognitive processing (Grady 2012; Ofen & Shing 2013). There is even physiological evidence to explain how this happens. During cognitive tasks, especially those involving working memory and long-term memory, older adults have more extensive activity in prefrontal regions and reduced activity in sensory (i.e., visual) processing cortical regions—a phenomenon known as the Posterior–Anterior Shift with Aging (Davis et al. 2008). When the degree of prefrontal activity is correlated with behavioral performance, this observation is commonly interpreted as a compensatory mechanism (Grady 2012). One important caveat is that at higher levels of memory load, older adults tend to show *decreased* activity in prefrontal regions relative to young adults (e.g., Mattay et al. 2006; Schneider-Garces et al. 2010). The Compensation-Related Utilization of Neural Circuits Hypothesis (Reuter-Lorenz & Cappell 2008) has been proposed to explain this caveat; such that the compensatory mechanism mediated by prefrontal activity loses its efficacy once memory load exceeds a certain level (Cappell et al. 2010). However, the Scaffolding Theory of Aging and Cognition suggests that it is possible to enhance compensation strategies through training (for a review, see Lustig et al. 2009), and this possibility is giving rise to new cognitive-based rehabilitative interventions for older people with hearing loss (for a review, see Pichora-Fuller 2013). In other words, people with hearing loss may be able to use cognition to support speech perception as a means of compensating for the degraded auditory input. For example, interventions targeting problem areas (e.g., audibility, memory, and selective attention) may be more effective in enhancing listening, comprehension, and communication when combined with strategies that capitalize on intact cognitive abilities (for a review, see Lustig et al. 2009; Pichora-Fuller 2013). Indeed, a recent study involving working memory training resulted in improvements in cognition, speech perception, and self-reported hearing abilities for adult HA users with mild-to-moderate hearing loss (Henshaw & Ferguson 2013).

As previously mentioned, the goals of AR are to minimize hearing-loss-induced deficits affecting function, activity and participation, and enhance quality of life through sensory management, instruction, perceptual training, and counseling (for review, see Boothroyd 2007). Sensory management is typically directed at the audibility problem through the provision of hearing assistive technologies such as HAs. When compared with unaided performance, listening with HAs has been shown to improve performance and reduce response times, suggesting that HA use lessens the cognitive demands associated with processing unaided speech, thus mitigating effort (Downs 1982; Gatehouse & Gordon 1990; Hällgren et al. 2005; Hornsby 2013; Picou et al. 2013). In spite of these perceptual gains, HAs fall short of fully resolving the listening needs of people with hearing loss. According to consumer surveys MarkeTrak V (2000) and MarkeTrak VIII (2009), a quarter (25.3%) of

the consumers reported that they did not wear their HAs because they did not help in difficult listening situations. This is particularly true in background noise, where only approximately 60% of HA users report being satisfied with their performance in noisy environments (Kochkin 2005). What is more, nearly three in 10 (29.6%) customers who are not using their HAs reported that they received minimal or no benefit from their HAs, and some consumers indicated that their HAs amplified sound, making it more audible, but they still could not understand words. In other words, for these people, improved audibility might have reduced a person's consumption of resources, but the demands needed to discriminate speech in complex listening situations likely exceeded their capacity.

Many approaches have been taken to enhance speech intelligibility. Some have taken an engineering approach whereby signal processing strategies designed to improve signal to noise ratios have been implemented into HA models (see also Edwards, this issue, pp. XXXX; Lunner et al., this issue, pp. XXXX), but these advances in technology have not resulted in considerable increases in HA use over time (Kochkin 2000, 2009). Also, advanced technology does not necessarily result in better clinical outcomes (Cox et al. 2014), perhaps because clearer audible signals still need to be transmitted through the impaired biological systems described earlier (for reviews, see Tremblay & Miller 2014; Tremblay et al. 2014b). Moreover, HAs deliver a modified amplified signal to an impaired, reorganized auditory system, and this can pose a problem for HA users. It has been suggested that HA users who have difficulties comprehending speech in noise may have more difficulty *learning* how to associate the new patterns of neural activity, evoked by the new and modified signals, to existing sound templates or memory (Robinson & Summerfield 1996). One might expect people would learn or acclimatize to these new amplified sounds over time; however, there is little evidence to support this idea. When Humes & Wilson (2003) tracked changes in HA performance and benefit among elderly HA users over a 3-year period after their HA fitting, there was little evidence of improvement over time.

Learning

One way to promote auditory learning is through the use of auditory training exercises. Loosely defined, auditory training can be described as a process that involves teaching the brain to listen through active engagement with sound. Simply put, as a person partakes in goal-oriented listening tasks to acquire new skills, they compile knowledge into efficient chunks so less effort is required to reach a maximum level of performance (Anderson & Fincham 1994; Yeo & Neal 2004). In the case of training experiments, successful acquisition is often quantified as a change in performance scores and/or reaction times. Improved performance is often accompanied by faster reaction times, and when a person becomes fatigued, reaction times can become slower (Welford 1968, 1980).

Historically defined, listening training is said to “encourage an allocation of cognitive resources to the residual hearing in such a way as to improve the coding and decoding processes basic to auditory learning” (Bamford 1981, p. 75). While there is evidence to show that repeated practice and sound exposure indeed alters the way sound is coded in the brain (Ross & Tremblay 2009; Tremblay et al. 2010, 2014) and various approaches to auditory training can promote learning (for reviews, see Carhart 1960; Bamford 1981; Boothroyd

2010; Pichora-Fuller & Levitt 2012; Dubno 2013; Sweetow & Henderson-Sabes 2013), there is currently insufficient evidence to conclude that auditory training enhances listening skills in a way that generalizes to improved everyday communication for older adults with hearing loss (see systematic reviews by Chisolm et al. 2013; Ferguson & Henshaw 2013). That is, although significant generalization of learning has been shown for untrained measures of speech intelligibility, cognition and self-reported hearing abilities can be found in the literature, the amount of improvement is small and the results are not robust.

Such conclusions about auditory training may not be definitive, however, because the contribution of motivation, compliance, and effort are often overlooked.

Compliance, for example, can be low among participants who enroll in training programs. In a study conducted by Sweetow and Henderson-Sabes (2010), compliance for a cohort of home-based auditory therapy trainees was less than 30%. One method of improving compliance is to make the training process pleasurable so as to maintain motivation. As described in the proposed FUEL and consensus paper (Pichora-Fuller et al., this issue, pp. XXXX), motivation is assumed to affect participation and performance because it influences the way that individuals allocate effort to tasks (Blau 1993; Katzell & Thompson 1990). When discussed within the context of an individual partaking in training exercises, or attempting to listen in challenging communication situations, a person's level of motivation might determine the amount of processing resources they wish to allocate to the task. Their level of motivation also influences the point in the cost-benefit ratio at which the individual will decide to withdraw or overcome the obstacles in pursuit of their goal (see Matthen, this issue, pp. XXXX).

To better understand what motivates computer-based auditory training (CBAT) adherence so that these types of interventions have high rates of success, Henshaw et al. (2015) examined a group of participants who partook in a CBAT program. These participants demonstrated post-training benefits such as improved concentration and attention leading to improved listening. When the role of motivation was queried, both intrinsic (e.g., a desire to achieve higher scores) and extrinsic (e.g., wanting to help others with hearing loss) motivations affected engagement and compliance with CBAT. With this information in mind, training programs might prove to be more beneficial than previously realized if made to be more entertaining (Pichora-Fuller & Levitt 2012).

Another issue often overlooked in training studies is the relationship between effort and outcome measures. It is possible that similar changes in speech intelligibility measures, obtained under different listening conditions, could demand different levels of effort or involve different types of processing strategies (Broadbent 1958; Rabbitt 1966 1968). If so, there may be benefits to listening training that are not being realized when using typical outcome measures such as percent correct scores. To test this possibility, Kuchinsky et al. (2014) examined if speech perception training would improve word identification ability, and listening effort, in older adults with hearing loss. After training, they observed improved word recognition in noise performance as well as changes in the pupillary response. The authors concluded that objective measures, such as pupillometry, are sensitive to the changes in amount of effort involved in a given task and might therefore be useful as an intervention

outcome measure (see also, Lunner et al., this issue, pp. XXXX; Pichora-Fuller et al., this issue, pp. XXXX; Rudner, this issue, pp. XXXX).

QUANTIFYING EFFORTFUL LISTENING: CLINICAL RELEVANCE

Even though there is interest among scientists and clinicians in determining the factors that underlie effortful listening, a challenge in this quest has been reaching a consensus about what is meant by listening effort and how to measure it (McGarrigle et al. 2014; Johnson et al. 2015). As summarized in the consensus paper (Pichora-Fuller et al., this issue, pp. XXXX), different tools (e.g., pupillometry, EEG alpha oscillations, word recall, self-report, etc.) have been used to measure similar concepts, even though these measures may not reflect the same neural mechanisms or processes. It is also important to acknowledge that measuring cognition is not the same as measuring effort. Two individuals may have equal performance on a cognitive task, but one person may exert more effort than the other to achieve the same performance.

Take, for example, the study by Winn et al. (2015). They systematically degraded the spectral resolution of speech stimuli using vocoder techniques often used to simulate cochlear implant speech processing algorithms and found that pupil dilation grew with each successive degradation in spectral resolution. Importantly, pupillary responses were sensitive to changes in stimulus degradation even when performance scores approximated 100%. Therefore, the authors concluded that pupillary responses are a sensitive and highly granular measurement that presumably reflects listening effort in a way that is not captured by clinically obtained word recognition scores on their own. What is more, the authors suggest that the measurement of pupil dilation could be applied to situations in which different processing strategies for CIs are compared to determine which method provides better spectral resolution. But could this really be done?

There is little doubt that the use of measures, sensitive to the changes in amount of effort involved in a given task, can inform theory and clinical practice. However, the likelihood of clinicians using pupillometry for this purpose is highly doubtful at this time. The infrastructure needed to record pupillometry exceeds what is practical and affordable in most clinical settings. Take, for example, the use of probe microphone measures in clinical practice. According to audiology best practice guidelines, probe microphone verification measures should be done to ensure adequate HA gain and audibility for the individual (Valente et al. 2006). Despite these practice guidelines, when audiologists and hearing instrument specialists were surveyed, Mueller and Picou (2010) found that respondents used real-ear verification only about 40% of the time. In another study, Bamford (2001) reported that only about 20% of individuals fitting pediatric patients used real-ear measures. The reasons most often cited for skipping probe microphone measures were based on financial, time, or space constraints. Therefore, even if universal definitions of effort can be agreed upon and our proposed FUEL successfully differentiates among the candidate measures, the next challenge will be to identify a measurement that is sensitive and specific to the agreed upon definition; one that can be implemented in an expedient and cost-effective way.

CONCLUSION

The topic of listening effort is relevant to the rehabilitation of older people with hearing loss because they often report a need for increased attention, concentration, and listening effort when compared with persons without hearing loss. Interventions like HA amplification and listening training can be used to lessen the amount of cognitive resources required for effective auditory communication, but they do not compensate for the biological limitations imposed by aging and hearing loss. This means, older adults are left with the extra burden on processing resources when trying to make use of sound in noisy environments and the resultant complaint is often listener fatigue.

Rehabilitation is described within the context of FUEL because it takes into consideration how listening effort varies with difficulty hearing and/or task demands, and how the listener's motivation to expend mental effort can change in challenging situations. The ability to quantify such changes in effort, using time-and cost-efficient tools, is a much-needed priority because it could assist clinicians with the identification and rehabilitation of mental fatigue.

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Fig. 1.

A hypothetical model of the various dimensions that can interact with aging. The model is intended to show the interplay among a wide array of physical and behavioral aspects and the aging process. The arrows are bidirectional to indicate that the influence can potentially arise from these factors on the aging process, or vice versa. For example, genetic factors could influence how an individual ages, and aging can enhance the effects of genes on specific behaviors. There are other factors that could be included here, such as risk factors for vascular disease or dementia, but this incomplete list gives a sense of how complex the study of aging is and how difficult it would be to comprehensively assess these variables in a single experiment. [Reprinted with permission from Grady, *Nat Rev Neurosci*, 2012, 13,491–505.]