Pupil dynamics in response to light and effortful listening

Wang, Y.

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General Introduction

Chapter 1

CHAPTER 1 GENERAL INTRODUCTION

1.1 HEARING IMPAIRMENT AND ITS PSYCHOPHYSIOLOGICAL IMPACT ON DAILY LIFE

... ... It's really stressful and exhausting after a single day of work or a long meeting with lots of people talking at the same time. I felt completely destroyed after such a day and did not have any energy left to do anything else…

– a comment from one of the hearing-impaired participants

Hearing impairment is one of the most prevalent chronic conditions. According to the World Health Organization, it is ranked highest among the chronic conditions accounting for moderate to severe disability burden worldwide. Around 5.3% of the global population (360 million people) suffer from moderate to severe hearing loss (WHO 2012).

There is mounting evidence showing that hearing impairment may have negative impacts on daily-life functioning. Many studies found that hearing impairment is related to psychosocial problems like depression, loneliness or anxiety (Strawbridge et al. 2000; Nachtegaal et al. 2009a; Saito et al. 2010; Pronk et al. 2011a). For listeners with hearing impairment, listening is more effortful than for normally-hearing listeners (Dwyer et al. 2014). Associations between hearing impairment and increased levels of stress are also frequently reported (Hasson et al. 2009; Nachtegaal et al. 2009a). Repeated exposure to stressful situations may lead to illness (Salleh 2008) and psychological conditions like fatigue (DeLongis et al. 1988). Long term stress and fatigue may – in turn – lead to participation restriction. There are indeed several studies showing associations between hearing loss and reduced ability to participate in work (Stam et al. 2013). Also, sick leave due to stress among hearing impaired workers has been reported as well as withdrawal from major social activities (Kramer et al. 2006; Nachtegaal et al. 2009a). Thus, stress, effort and fatigue add significantly to the burden of hearing impairment. It is therefore of great importance to understand the mechanisms underlying the associations between stress, listening effort, fatigue and hearing impairment (McGarrigle et al. 2014). Obtaining a better understanding of these mechanisms is the main overall goal of this thesis. Before describing potential mechanisms, it is important to provide definitions of the different terms.

1.2 DEFINITIONS

Listening effort

There is mounting evidence showing that for listeners with hearing impairment, listening is more effortful than for listeners with normal hearing (Ohlenforst et al. 2017a). This is particularly the case in challenging listening situations, for example in background noise. In these circumstances, people with hearing impairment have to concentrate to hear and understand the speaker and ignore the background noise (Petersen et al. 2017).

According to the Framework for Understanding Effortful Listening (FUEL) (Pichora-Fuller et al. 2016), listening effort is "The deliberate allocation of mental resources to overcome obstacles in goal pursuit when carrying out a task that involves listening". In short, FUEL proposes that listening effort is modulated independently by task demands, someone's cognitive capacity and the motivation of the listener to exploit effort (Pichora-Fuller et al. 2016).

Fatigue

Feeling fatigued is a common complaint that almost half of the adult population has experienced (Pawlikowska et al. 1994). The definition of fatigue varies depending on the research field and there is no standardized definition of fatigue available yet. An attempt had been made during The Fifth Eriksholm Workshop (Hornsby et al. 2016; Pichora-Fuller et al. 2016) on the topic of "Hearing Impairment and Cognitive Energy", Hornsby and colleagues described fatigue as *A complex construct that must be explicitly defined based on the discipline of the person describing the construct and the focus of their study (e.g., physical fatigue in athletes, cognitive fatigue in people with multiple sclerosis, general fatigue, or vigor deficits in people with hearing loss). It is commonly described as a feeling or mood state or in terms of a decrement in physical or cognitive performance.*

Within audiological research, fatigue is mostly investigated as a subjective outcome. Hornsby and colleagues described this as *A subjective experience or mood state, encompassing feelings of weariness, tiredness, lack of vigor or energy, or decreased motivation to continue a task*.

Need for Recovery

The early symptoms of fatigue can be assessed by measuring an individual's need for recovery (van Veldhoven & Broersen 2003). The concept of need for recovery reflects the ability to cope and recover from fatigue and distress (van Veldhoven & Broersen 2003). Insufficient recovery from stress after work is an intermediate stage between exposure to highly demanding working situations and the development of long-term health issues, like burnout (Sluiter et al. 2003; van Veldhoven & Broersen 2003; Nachtegaal et al. 2009a).

1.3 HOW TO MEASURE FATIGUE AND LISTENING EFFORT

Given the definition, the most intuitive way to assess fatigue would be via self-report questionnaires (Beurskens et al. 2000; van Veldhoven & Broersen 2003). *The Profile of Mood States,* for instance, is a questionnaire that can be used to measure fatigue and vigor (Lorr et al. 1971). Hornsby & Kipp (2016) administered this questionnaire to 149 adults with hearing impairment and compared the results with the scores of age-matched normally hearing controls. Results indicated that hearing-impaired adults were more fatigued than their normally-hearing peers. Another example of a self-report fatigue measure is *The Checklist Individual Strength (CIS)*. The CIS is a multidimensional questionnaire intended to measure chronic fatigue (Vercoulen et al. 1994), and it has been validated in various groups of workers like teachers and police officers (Beurskens et al. 2000; Shimizu et al. 2011; Lammers-van der Holst & Kerkhof 2015).

Another instrument is the *Need for Recovery (NfR)* scale. It is an 11-item scale to assess the short-term effects of stress at work (Sluiter et al. 2003). Previous studies using NfR showed a significant association between hearing status and need for recovery, such that with every 1 dB decrease in hearing status, the level of need for recovery increased with about 1.4 points (Nachtegaal et al. 2009a). However, the underlying mechanism responsible for hearing-related fatigue is not yet clear (Hornsby et al. 2016).

The consensus document produced as a result of the Eriksholm Workshop on "Hearing Impairment and Cognitive Energy" (Pichora-Fuller et al. 2016), the white paper on listening effort and fatigue by McGarrigle et al. (2014) and the systematic review by Ohlenforst and colleagues (2017) each provide thorough overviews of the existing methods to measure listening effort. These methods include subjective assessments via questionnaires (Gatehouse & Noble 2004; McAuliffe et al. 2012; Dawes et al. 2014), cognitive-behavioral measures using a dual-task paradigm (Anderson Gosselin & Gagne 2011; Hornsby 2013; Wu et al. 2016), and physiological measurements like functional magnetic resonance imaging (Vaden et al. 2015), alpha power in electroencephalography (Obleser et al. 2012; Petersen et al. 2015) and pupillometry.

Pupillometry is the continuous recording of the pupil diameter. The pupil dilation response evoked by a task is often used as an index of effort required to complete the task. It has been successfully used as an index of effortful listening during speech comprehension (Kramer et al. 1997; Zekveld et al. 2010, 2011; Kuchinsky et al. 2013; Koelewijn et al. 2014a; Koelewijn et al. 2014b; Winn et al. 2015). The pupil response is reflecting activity of the autonomic nervous system (ANS), which will be further described in the paragraph below.

1.4 AUTONOMIC NERVOUS SYSTEM

When the body is stressed, the autonomic nervous system (ANS) immediately becomes activated. The ANS is the involuntary nervous system that regulates both the internal environment and the sequence of basic physiological events allowing an organism to optimally adjust to environmental changes. The ANS is constantly active and it regulates basic functioning of the human body, such as the heart beat and metabolic processes (Janig & Habler 2000; Robertson 2004). There are two main branches of the ANS: the sympathetic nervous system (SNS) and the parasympathetic nervous system (PNS).

The SNS is known to control the 'fight or flight' response, and it functions as a gas pedal of a car. When facing a stressful situation, the SNS activation triggers the release of noradernaline from the adrenal glands so that the body is ready to respond to the stressors.

In contrast to the SNS's 'excitatory' role, PNS governs the so called 'rest and digest' response, and it acts as a brake of a car. PNS helps the body to restore energy and recover from stress and it is associated with constriction of the gut and salivary glands, and a slowing heart rate. The main neurotransmitter of PNS activity is acetylcholine (Robertson 2004; Clark 2005).

Given the important role of PNS at the recovery phase after stress, investigation of PNS activity may help to gain a more comprehensive understanding of the mechanisms and consequences of listening effort and its relation with hearing-related fatigue. To date, there are only a few studies available investigating the relationships between PNS activity and hearing impairment. Chapter 2 of this thesis presents a systematic review to seek the possible connections between PNS activity and hearing impairment.

1.5 AUTONOMIC NERVOUS SYSTEM REFLECTED IN THE PUPIL RESPONSE

There are several methods available to measure the ANS activity, and the relative contributions of the SNS and PNS to the overall ANS activity. For instance, measuring heart-rate variability (HRV) and skin conductance provide information about the relative contribution of the SNS and PNS branches into the total ANS activity (Malik 1996; Mackersie & Calderon-Moultrie 2016). The pupil response, the physiological response that is reflected in the change of the size of the pupils of the eye, has been extensively used as a measure of ANS activity.

The first research about the pupil response may date back to the early tenth century (Al-Razi 903), in which the Arabic physician Al-Razi described his observations about the change of the pupil in response to light. Otto Lowenstein and his collaborator Irene Loewenfeld laid the foundation of knowledge to understand the pupil, and the mechanisms underlying the pupil response. According to Loewenfeld & Lowenstein (1999), both PNS and SNS activity are reflected in the diameter of the pupil. In fact, the pupil diameter is a reflection of the ratio of SNS and PNS activity. Thus, measurement of the pupil diameter provides a way to assess SNS and the PNS activity. Activation of the SNS results in pupil dilation, via innervation of the dilator muscles. PNS activation results in pupil constriction, via innervation of the sphincter (constrictor) muscles of the eye (Loewenfeld &

Lowenstein 1999).

1.6 PUPIL DILATION RESPONSE DURING SPEECH UNDERSTANDING IN NOISE

The pupil diameter enlarges or dilates during cognitive processing. The task-evoked pupil dilation was first observed more than hundred years ago (Schiff 1875). Later studies by Hess & Polt (1964) and Kahneman & Beatty (1966) demonstrated that the pupil dilates in response to mental arithmetic and digit span tasks. This work laid the foundation to develop the concepts of cognitive psychology. Since then, the task-induced pupil dilation has become a popular measurement in many research fields within psychology (Beatty & Lucero-Wagoner 2000).

Kramer et al. (1997) showed that task-induced pupil dilation can be used to assess the cognitive load required for speech recognition in noise. In the last decades, many more researchers started to measure the task-induced pupil response as an index of effort required during speech comprehension (Zekveld et al. 2011; Kuchinsky et al. 2013; Koelewijn et al. 2014b; Winn et al. 2015; Kramer et al. 2016; Ohlenforst et al. 2017b). Up until now, research has demonstrated that the pupil dilation response is a sensitive measure of listening effort. The pupil dilation response has been shown to be related to speech intelligibility (Zekveld et al. 2010, 2011; Zekveld & Kramer 2014), type of masking noise (Koelewijn et al. 2014b), syntactic complexity (Piquado et al. 2010) and divided attention (Koelewijn et al. 2014a). A higher level of listening effort is usually accompanied by a larger pupil dilation. Multiple parameters can be extracted from the pupil signal. The Peak Pupil Dilation (PPD) is one of the parameters, and has proven to be an effective index to reflect the changes of cognitive processing load (Ahern & Beatty 1979; Siegle et al. 2001; Zekveld et al. 2011).

While measuring speech understanding across a wide range of signal-to-noise ratios (SNR), a recent study found that the relationship between speech intelligibility (range from 0% to 100% correct response) and PPD followed an inverted-U shaped curve. The largest pupil dilation occurred when the intelligibility was around 50% correct performance, and this pattern was observed in both normally-hearing and hearing-impaired listeners (Ohlenforst et al. 2017b). When assessing the PPD during the speech in noise task around this 50% correct level, one may intuitively assume that the listeners with hearing-impairment would show a larger pupil dilation compared to normally-hearing listeners, as they would experience more listening effort due to their hearing problem. However, previous studies have repeatedly reported the opposite findings in challenging listening conditions (50% intelligibility level), namely that the PPDs were smaller in hearing-impaired participants than in their normally-hearing controls (Zekveld et al. 2011; Kramer et al. 2016), whereas this pattern was reversed at higher intelligibility levels.

1.7 PUPIL LIGHT REFLEX AS A MEASURE OF PARASYMPATHETIC ACTIVITY

Whereas the pupil dilates in response to cognitive processing, the pupil constricts when exposed to bright light. The pupil light reflex (PLR) is the rapid change in the pupil diameter in response to an increase of light intensity falling on the retina (Beatty & Lucero-Wagoner 2000). Light falling on the retina leads to increased neural activity in the pretectal regions of midbrain and stimulates the Edinger-Westphal nucleus. This results in the activation of preganglionic parasympathetic neurons which innervate the ciliary ganglion. This sequence of neural activity ultimately commands the constrictor muscles of the pupil to tighten, resulting in pupil constriction (you may refer to FIGURE 2-1 in Chapter 2 for a detailed illustration of the PLR pathway). Both the ciliary ganglion and constrictor muscles contain acetylcholine receptors. Acetylcholine is the main neurotransmitter of the PNS (Loewenfeld & Lowenstein 1999).

A typical PLR involves three phases: a fast constriction phase shortly (about 200 ms) after exposure to the light stimulus, and the constriction is dominated by PNS activation; this is followed by a fast re-dilation phase which reflects both a reduction in PNS activation and an increase in SNS activation; then a slow re-dilation phase follows mainly influenced by SNS activation (Loewenfeld & Lowenstein 1999). Thus, the constriction part of the PLR provides an index of PNS activity uncontaminated by SNS activity.

The PLR has been used as a standard clinical diagnostic tool to examine the functional integrity of the subcortical afferent and efferent pathways of the visual system (Fenichel 2009). Studies using the PLR to evaluate PNS activity are also well established. For instance, the PLR has been shown to be a useful method to test PNS dysfunction in patients with Alzheimer's Disease (Fotiou et al. 2009), Parkinson's Disease (Giza et al. 2011), diabetes (Lanting et al. 1988), and psychiatric conditions like anxiety disorder (Bakes et al. 1990). A drawback of the research so far however is that results between studies cannot be easily compared, because different methods to generate a PLR have been used. The review study in Chapter 2 of this thesis therefore also addresses the effectiveness of the different methods using the PLR to test the PNS dysfunction. Equipment used to generate light stimuli for the PLR measurements can be expensive or technically demanding. A computer screen, a generally available display device, can be a potential solution to elicit the flash light. The development and validation of a method using a computer screen to elicit light stimuli, is the focus of Chapter 3 of this thesis.

1.8 UNRAVELLING THE SYMPATHETIC AND PARASYMPATHETIC COMPONENTS IN THE PUPIL SIGNAL

Traditionally, pupil dilation in response to cognitive processing is considered mainly driven by SNS activation (Kahneman 1973). However, Steinhauer and colleagues (2004) demonstrated that the inhibitory effect of the PNS pathway via the Edinger-Westphal nucleus, the motor center of the PNS pathway, also plays an important role in the task-induced pupil dilation. In Steinhauer et al. (2004), mental arithmetic tasks were performed in dark and light conditions. In darkness, the PNS activation is minimized and the "inhibitory effect via the PNS pathway" has the least residual effect on the pupil dilation due to the relaxation of pupil constrictor muscles (Loewenfeld & Lowenstein 1999; Steinhauer et al. 2004). With increasing ambient light intensity, the inhibitory effect via the PNS pathway acts as an additional component to dilate the pupil during task. The results from Steinhauer et al. (2004) showed that only in light conditions there was a larger pupil dilation in the more difficult task than in the easier task. This finding not only demonstrates the important role of PNS to task-induced pupil dilation, but also provides a possible way to quantify the contribution of the PNS to the pupil dilation (by subtracting the task-induced pupil dilation performed in the dark from the dilation evoked by the same task performed in light). FIGURE 1-1 shows the innervations of PNS and SNS during the pupil light reflex and task-induced pupil dilation.

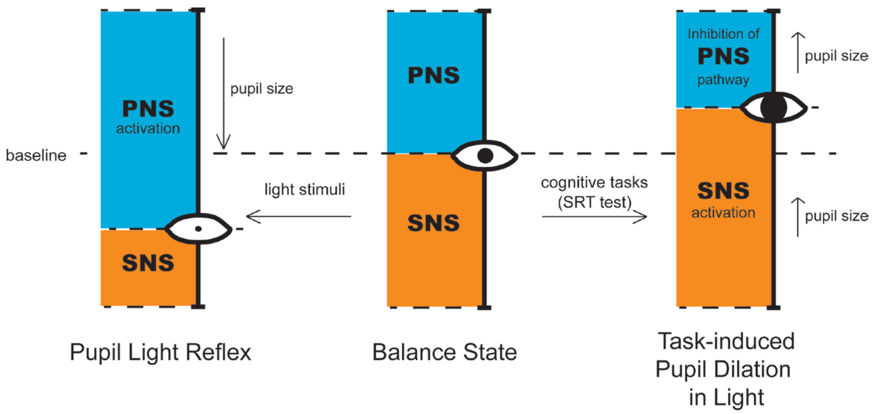

FIGURE 1-1 The contribution of the PNS and SNS during pupil light reflex and task-induced pupil dilation in light. PNS, parasympathetic nervous system; SNS, sympathetic nervous system

Therefore, the counter-intuitive findings that hearing-impaired participants showed smaller PPD than their normally-hearing peers during the speech comprehension in noise task in challenging conditions may be explained by the variations in PNS activity. One of the major focuses of this thesis is to investigate the role of the PNS in the task-induced pupil dilation response during effortful listening by performing the test in light (Chapter 4) and comparing its result with the pupil dilation when performing the test in darkness (Chapter 5).

1.9 OUTLINE OF THE THESIS

Chapter 2 presents a systematic review aiming to seek the possible connections between PNS functioning and hearing impairment. In addition, the effectiveness using the PLR to evaluate parasympathetic dysfunction is reviewed based on the existing literature. A theoretical framework for the possible usage of the PLR as a research method to evaluate the PNS activity in the audiological field is proposed.

Chapter 3 addresses the methodological aspects associated with the PLR measurement. A system using a computer screen instead of LED to generate and record the PLR is developed and validated. The association between PNS, as indicated by different PLR parameters, and need for recovery is reported.

Chapter 4 presents an experiment that examined the contribution of hearing acuity and fatigue to the pupil dilation response during a speech comprehension in noise task while targeting 50% correct performance. This chapter provides insight in the possible mechanisms explaining why in previous studies it has been repeatedly found that people with hearing impairment show smaller pupil dilations during a speech-in-noise task targeting 50% correct performance than their normally-hearing peers in this condition.

Chapter 5 further extends the findings from Chapter 4 by adding the task-induced pupil dilation data recorded in darkness. Combining the pupil dilation data from dark and light conditions unravels the possible role of the parasympathetic nervous system in the task-induced pupil dilation response, and shows how this role might vary in response to hearing problems or to high-level of need for recovery.

Chapter 6 provides a general discussion of the findings from the studies presented in this thesis.