# NOISE SENSITIVITY IN THE FUNCTION AND STRUCTURE OF THE BRAIN

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# Table of contents

# Abstract

Exposure to noise has a negative influence on human health, including an increased occurrence of cardiovascular diseases. Susceptibility to the harmful effects of noise can be further moderated by a personal trait called noise sensitivity (NS). It is not understood what makes some individuals more sensitive to noise than others. So far, the research on this topic has been largely limited to perceptual and population studies. The aim of this thesis was to broaden the understanding of NS by addressing its biological mechanisms. Thus, this thesis investigated the neuroanatomical correlates of NS and its effects on auditory processing.

The thesis consists of three studies. The first study examines whether NS can be developed as the result of musical training (Study I). The other two studies investigate whether NS is reflected in the functioning of the central auditory system (Study II) and whether it is related to the morphology of cortical and subcortical brain structures (Study III).

The research was conducted using questionnaires, combined magneto- and electroencephalography (MEG/EEG) and magnetic resonance imaging (MRI). The findings of this thesis suggest that NS moderates how and why individuals listen to music. However, NS is not associated with musical training and thus does not seem to relate to fine perceptual skills (Study I). An investigation of the central auditory processing in Study II, however, revealed compromised sound feature encoding and automatic discrimination skills in noise-sensitive individuals. Study III showed that NS is also associated with the structural organization of the brain. Noise-sensitive individuals were found to have enlarged volumes of the auditory cortical areas and hippocampus as well as thicker right anterior insular cortex. These results suggest that NS is related to the structures involved with auditory perceptual, emotional, and interoceptive processing. Overall, this thesis proposes that NS is not merely an attitudinal phenomenon but instead has underlying neuronal mechanisms.

# Tiivistelmä

Altistuminen melulle vaikuttaa negatiivisesti ihmisten terveyteen, muun muassa kohonneena riskinä sydän- ja verisuonitaudeille. Meluherkkyys on persoonallisuuden piirre, joka voi vaikuttaa alttiuteen melusta koituville haitoille. Syytä sille, mikä tekee toisista herkempiä melulle, ei tiedetä. Tähän mennessä asiaa on selvitetty lähinnä melun havaintokykyä ja sen esiintymistä väestössä kartoittavien tutkimusten avulla. Tämän väitöskirjan tavoitteena oli lisätä tietoa meluherkkyyden biologisista mekanismeista. Väitöskirjassa tutkittiin meluherkkyyteen liittyviä aivojen rakenteita sekä meluherkkyyden vaikutusta kuulotiedon käsittelyyn.

Väitöskirja koostuu kolmesta osatutkimuksesta. Ensimmäisessä tutkimuksessa selvitettiin, voiko meluherkkyys kehittyä musiikin harjoittelun seurauksena (Tutkimus I). Kahdessa muussa osatutkimuksessa selvitettiin, heijastuuko meluherkkyys aivojen kuulojärjestelmän toimintaan (Tutkimus II), ja liittyykö se aivokuoren ja sen alaisiin rakenteisiin (Tutkimus III).

Tutkimukset suoritettiin käyttämällä kyselytutkimuksia, yhdistettyä aivosähkökäyrää ja sen magneettista vastinetta, eli elektro- ja magnetoenkefalografiaa (EEG/MEG), sekä aivojen magneettikuvausta (MRI). Tämän väitöskirjan tulosten mukaan meluherkkyys vaikuttaa siihen, miten ja miksi ihmiset kuuntelevat musiikkia. Meluherkkyys ei kuitenkaan liity musiikin harjoitteluun eikä täten liene yhteydessä hienovaraiseen kuulohavaintokykyyn (Tutkimus I). Tutkimus II kuitenkin paljasti, että äänten erottelukyky ja äänipiirteiden koodaus aivoissa on heikentynyttä meluherkillä yksilöillä. Tutkimuksessa III osoitettiin, että meluherkkyys on myös yhteydessä aivorakenteiden järjestäytymiseen. Meluherkillä löydettiin suurentunut kuuloaivokuoren ja hippokampuksen tilavuus sekä paksumpi oikean etuaivopuoliskon aivosaari. Näiden tulosten mukaan meluherkkyys on yhteydessä rakenteisiin, jotka osallistuvat äänten havaitsemiseen sekä niiden tunneperäistä ja elimellistä tietoa välittävään tiedonkäsittelyyn. Kaiken kaikkiaan tässä väitöskirjassa esitetään, että meluherkkyydellä on hermostollista taustaa eikä se ole pelkästään negatiivinen asenne melua kohtaan.

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Мама и папа, спасибо за вашу бесконечную любовь, ваше доверие, и безусловную поддержку на каждом отрезке моего пути. Я безгранично вас люблю.

This has been a great journey.

Sincerely,
Marina Kliuchko

## List of original publications

This thesis is based on the following publications:

I Kliuchko, M., Heinonen-Guzejev, M., Monacis, L., Gold, B. P., Heikkilä, K. V., Spinosa, V., Tervaniemi, M. & Brattico, E. (2015). The association of noise sensitivity with music listening, training, and aptitude. *Noise & Health*, *17*(78), 350-357.

II Kliuchko, M., Heinonen-Guzejev, M., Vuust, P., Tervaniemi, M., & Brattico, E. (2016). A window into the brain mechanisms associated with noise sensitivity. *Scientific Reports*, *6*, 39236.

III Kliuchko, M., Puoliväli, T., Heinonen-Guzejev, M., Tervaniemi, M., Toiviainen, P., Sams, M., & Brattico, E. Neuroanatomical substrate for individual noise sensitivity, in revision.

The publications are referred to in the text by their roman numerals.
The thesis also includes unpublished material.

## Author contribution

I Kliuchko partially collected the data, scored the variables, analysed the results, and wrote the manuscript.

II Kliuchko conducted the measurements, pre-processed and analysed the data, and wrote the manuscript.

III Kliuchko designed the study, analysed the data, and wrote the manuscript.

# Abbreviations

| | |
|---|---|
| ANCOVA | analysis of covariance |
| dB | decibel |
| EEG | electroencephalography |
| ER | evoked response |
| ERF | event-related field |
| ERP | event-related potential |
| fMRI | functional magnetic resonance imaging |
| GLM | general linear model |
| ISI | inter-stimulus interval |
| LSD | least significant difference |
| MEG | magnetoencephalography |
| MMN | mismatch negativity |
| MMNm | mismatch negativity, magnetically recorded |
| MRI | magnetic resonance imaging |
| ms | millisecond |
| NS | noise sensitivity |
| ROI | region of interest |
| SD | standard deviation |

# 1. Introduction

In the modern world, noise permeates throughout our living, working and public environments. There is evidence showing that exposure to noise causes not only auditory problems, e.g., hearing loss, but also non-auditory health effects, such as annoyance, sleep disturbance, and cardiovascular diseases (Basner et al., 2014). Importantly, the risks of developing negative outcomes of noise exposure are higher among noise-sensitive people. Noise-sensitive individuals are more likely to attend to sounds, evaluate them negatively and feel strong displeasure because of them. Psychoacoustic and public health research takes noise sensitivity (NS) into account as a construct that describes individual differences in reactions to noise. However, the aetiology and underlying mechanisms of NS have not been adequately investigated – currently there is no consensus about the neural basis of NS.

This thesis aims at determining whether and how the mechanisms of NS lay in the function and anatomy of the brain.

## 1.1. Noise

Noise is one of the most common environmental stressors and pollutants, which can influence human health directly (e.g., loud noise damaging the inner ear) and indirectly (e.g., annoyance leading to stress) (Basner et al., 2014; Stansfeld & Matheson, 2003). However, the distinction between sound and noise is not straightforward. In the psychoacoustic domain, noise is any undesired and unpredictable acoustic signal, which masks any desirable sound. In physiology, the word noise is used to describe sound that is unwanted by the listener, presumably because it is unpleasant or bothersome, as it interferes with the perception of wanted sounds, or it is physiologically harmful (Kryter, 2013). Noise, as undesired sound, does not necessarily have physical characteristics that distinguish it from a wanted sound. Thus, whether a sound is a noise or not depends on a listener and the context. As an example, while background music in public places, such as shops, does not irritate some people, others may at the same time perceive it as a source of disturbance, and be largely discomforted by it.

## 1.2. Noise sensitivity

Job (1999) described NS as a personal trait encompassing internal factors (e.g., physiological, psychology, attitudinal) that increase an individual's susceptibility to the effects of noise. People vary in NS on a continuum between low and high. Different studies estimate the prevalence of highly noise-sensitive individuals from 20 to 40% of the healthy population (Heinonen-Guzejev, 2008; Matsumura & Rylander, 1991; Olsen Widén & Erlandsson, 2004). A remarkable body of population-based research showed that people with high NS are more prone to negative noise-related health outcomes, such as sleep problems, cardiovascular diseases, lower subjective health status and mental health (Booi & van den Berg, 2012; Heinonen-Guzejev, Vuorinen, Mussalo-Rauhamaa, Koskenvuo, & Kaprio, 2004; Kishikawa et al., 2009; Marks & Griefahn, 2007; Nivison, 1992). Despite the general agreement that NS indicates vulnerability to environmental stressors (Stansfeld, 1992), and may negatively affect one's health and well-being, there have not been many advancements towards understanding the mechanism underlying NS.

Conceptually, NS is viewed as a stable trait distinguishable from noise annoyance, which, unlike NS, is dependent on an attitude towards the noise source, physical characteristics of noise and noise exposure (Ellermeier, Eigenstetter, & Zimmer, 2001; Zimmer & Ellermeier, 1999). On the contrary, it is suggested that NS could be affected by musical activities, such as playing and listening to music, as well as by the exposure to background noise in the childhood (Franek, 2009).

An open question is whether the nature of the NS phenomenon is attitudinal (how noise is evaluated) or perceptual (how noise is perceived). The attitudinal hypothesis stands out from the notion that NS, as a self-report measure, reflects an evaluative predisposition towards sounds rather than aspects of auditory processing *per se* and thus can be potentially explained by other personality traits. There were findings suggesting a relation of NS to introversion

(Campbell, 1992; Dornic & Ekehammar, 1990) and neuroticism (Öhrström et al. 1988; Iwata 1984; Belojević & Jakovljević, 2001) but these findings appear to be controversial (Belojević, Jakovljević, & Aleksić, 1997; Dornic & Ekehammar, 1990). Recently, it was proposed that NS has a complex relationship with other personality traits, such that it is independent of emotional stability but can be predicted from extraversion and conscientiousness (Lindborg & Friberg, 2016; Shepherd, Heinonen-Guzejev, Hautus, & Heikkilä, 2015).

Some studies (Persson, Björk, Ardö, Albin, & Jakobsson, 2007; Weinstein, 1978) attributed NS to negative affectivity, which is an inclination to experience negative emotions towards events, sensations and self, even without a presence of an obvious stressor (Watson & Clarck, 1984). From this point of view, NS is only a part of more general sensitivity to environmental stimuli, irrespective to their modality. However, this explanation of NS is challenged by negative findings on association of NS with sensitivities in other sensory domains, such as olfaction (Heinonen-Guzejev et al., 2012; Shepherd, Heinonen-Guzejev, Heikkilä, et al., 2015).

The attitudinal explanation of NS also rose from psychoacoustic research because it was unsuccessful in explaining NS with peripheral hearing functions, such as intensity discrimination, absolute hearing threshold or auditory reaction time (Ellermeier et al., 2001; Heinonen-Guzejev et al., 2011; Moreira & Bryan, 1972; Stansfeld, Clarck, Turpin, Jenkins, & Tarnopolsky, 1985). However, despite the normal hearing threshold in noise-sensitive individuals, NS was shown to be associated with a self-reported hearing disability (Heinonen-Guzejev et al., 2011).

There have been only few investigations that placed their focus on biological mechanisms that may underlie NS. Heinonen-Guzejev et al. (2005) used twin-study design to estimate whether genetic differences may account for NS trait. In this study, NS was assessed with a one-item questionnaire in the Finnish Twin Cohort. According to the results, monozygotic twins reported more similar NS than dizygotic twins and a heritability of NS was estimated to be 36%. Furthermore, when hearing-impaired participants were excluded from the analyses, the estimate of heritability increased to 40% (Heinonen-Guzejev et al., 2005). As suggested from these findings, there is a genetic component to NS.

There have been few attempts to record electrophysiological responses in NS. One study used cardiovascular measures and found an increased blood pressure with increasing NS under exposure to loud traffic noise (Ising, Dienel, Günther, & Markert, 1980). In another study conducted on female psychiatric patients (Stansfeld, 1992), higher NS was associated with higher skin conductance and heart rate under presentation of continuous noise and tones, suggesting higher levels of physiological arousal in noise-sensitive subjects. Highly noise-sensitive individuals also showed slower habituation to threatening sounds (Stansfeld, 1992). A recent study by Shepherd at al. (2016) utilized heart rate and electroencephalography (EEG) measurements on healthy subjects. Three experiments were conducted within this study. Two of them indicated a relation between NS and activity of the autonomic nervous system. The first of these experiments showed that NS was not related to a heart rate response when negatively valenced stimuli were presented. However, heart rate reactivity increased to positive stimuli in subjects with low NS. In the second experiment, NS correlated with several indices of resting state heart rate variability, thus suggesting in NS, there is decreased parasympathetic and increased sympathetic autonomic nervous system regulation. In their third experiment, Shepherd and colleagues employed EEG to examine the sensory gating process in NS. Sensory gating refers to automatic mechanisms of filtering out irrelevant sensory input. It is observed as response suppression to a repetitive stimulus and response enhancement to a novel stimulus. Shepherd et al. (2016) measured response suppression to the second click in a paired click paradigm and found that the noise-sensitive group showed significantly less sensory gating in a condition when subjects' attention was directed to the clicks. The same group of researchers had previously reported a stronger decrease in the brain alpha activity in noise-sensitive participants as compared to noise-resistant ones when annoying sounds were presented (Shepherd, Hautus, Lee, & Mulgrave, 2014). This potentially reflects a higher arousal state or undesired attention towards annoying sounds in sensitive subjects. Observations from this study are also in line with findings reported in Lee et al. (2012). Taken together, these electrophysiological investigations advocate for the involvement of physiological mechanisms in NS.

## 1.3. Tools for investigating neurophysiological and neuroanatomical correlates of noise sensitivity

In the current thesis, the neural basis of NS is investigated using both functional and structural brain imaging methods, which will be briefly introduced below.

### 1.3.1. Electroencephalography and magnetoencephalography

The electrical activity of neurons generates electromagnetic fields, which can be measured non-invasively with electro- and magnetoencephalography (EEG/MEG). EEG is a technique in which the electrical activity of synchronously firing cortical neurons is recorded with electrodes placed on the scalp. In turn, MEG measures the magnetic fields generated by neuronal activity with radio-frequency superconducting quantum interference devices (SQUIDs, Zimmerman et al. 1970) located in proximity to the head's surface. The SQUID sensors contain three signal pickup coils, one being a magnetometer, measuring planar magnetic vector, and two gradiometers, measuring difference in magnetic field gradient in axial and planar directions. SQUIDs allow for measuring very weak magnetic fields generated by the brain, which, however, is only possible in a magnetically shielded room.

EEG and MEG provide complementary information about the synchronized activity of cortical neurons. Nevertheless, along with similarities, EEG and MEG have a number of differences (Neil Cuffin & Cohen, 1979). The signal registered by both EEG and MEG, represents summated postsynaptic potentials that are mainly generated in pyramidal cortical neurons. These cells are oriented perpendicularly to the cortical surface. Their orientation towards the scalp, in turn, depends on the geometry of cortical organization, such that pyramidal neurons located on top of a gyrus are oriented radially, while the sulcus neurons are positioned tangentially. EEG and MEG have different sensitivities to signals generated by radial and tangential sources due to their physical properties (Nunez & Srinivasan, 2006). As such, EEG is most sensitive to radial sources, whereas MEG is more sensitive to sources oriented tangentially.

Furthermore, MEG and EEG differ on source localization accuracy. MEG allows for a better separation of signals, for instance, from the left and the right hemispheres, and provides better signal-to-noise ratio, as the magnetic signal is less distorted by head tissues and does not spread over the scalp as compared to electrical signals (Hämäläinen, Hari, Ilmoniemi, Knuutila, & Lounasmaa, 1993). EEG signal, in turn, is dependent on volume conduction and is distorted by head tissues, such as scalp, skull and cerebrospinal fluid.

Overall, EEG and MEG offer the highest temporal resolution available in non-invasive brain imaging, performing on the scale of milliseconds. That makes these methods the most suitable for studying fast brain processes, such as auditory processing. However, their accuracy in determining the exact foci of the activity is limited.

### 1.3.2. Event-related potentials and mismatch negativity

Neurocognitive functions can be measured with the event-related potential (ERP) and its magnetic equivalent, an event-related field (ERF). They are evoked responses (ERs) that follow a stimulus presentation. In this thesis summary, I will be referring to ER as to an auditory ER, which is elicited for an auditory signal.

ER is obtained by a summation of EEG/MEG signal across tens of presentations of experimental stimuli (Luck, 2014). This procedure eliminates brain activity that is not time locked to a stimulus presentation. A sequence of ER components, which are positive and negative peaks following the stimulus onset, echoes the temporal dynamics of consequent transmission and processing of auditory information in the central auditory system. For instance, obligatory components, such as P1, N1, and P2, are thought to reflect the initial stages of cortical processing of sensory information (Crowley & Colrain, 2004; Näätänen & Picton, 1987). ERs have been a useful tool for studying auditory processing enhancements, e.g., learning processes (Brattico, Näätänen, & Tervaniemi, 2001; Fujioka, Trainor, Ross, Kakigi, & Pantev, 2004; Kujala & Näätänen, 2010; Tremblay, Kraus, & McGee, 1998), and atypical sound processing in various auditory conditions such as William's syndrome (Zarchi et al., 2015), misophonia (Schröder et al., 2014) and tinnitus (Hoke, Feldmann, Pantev, Liitkenhiiner, & Lehnertz, 1989; Weisz, Voss, Berg, & Elbert, 2004). In

NS research, ERs helped to identify a deficient response suppression to repetitive sound in noise-sensitive individuals as compared to less sensitive ones (Shepherd, Hautus, Lee, & Mulgrew, 2016).

A well-known neural correlate of behavioural sound discrimination ability is the mismatch negativity (MMN). MMN and its magnetic equivalent MMNm are elicited when a regularity of auditory input is violated by a perceptible event. MMN appears as a negative deflection on a difference waveform resulted from subtracting a standard ERP from a deviant ERP. Amplitude and latency of MMN are reliable indices for the estimation of accuracy in discriminating sound changes (Näätänen, Paavilainen, Rinne, & Alho, 2007). MMN has proven to be an effective tool for investigating pre-attentive sound discrimination in different healthy populations, including musicians (Fujioka, Trainor, Ross, Kakigi, & Pantev, 2004; Koelsch, Schröger, & Tervaniemi, 1999; Tervaniemi et al., 2009; Vuust et al., 2012), children (Lovio et al., 2009; Partanen, Torppa, Pykäläinen, Kujala, & Huotilainen, 2013), infants (Partanen, Pakarinen, Kujala, & Huotilainen, 2013; Virtala, Huotilainen, Partanen, Fellman, & Tervaniemi, 2013) as well as clinical groups such as schizophrenics (Hirayasu et al., 1998; Todd et al., 2008), autistic (Kasai et al., 2005) and tinnitus patients (Mahmoudian et al., 2013). Näätänen et al. (2012) provided an extensive review of research where MMN was successfully implicated for delineating disturbed auditory processing in various conditions. For instance, by means of MMN, it was shown that exposure to occupational noise has detrimental effects on the central language processing in healthy individuals with unaffected peripheral hearing (Brattico et al., 2005; Kujala et al., 2004).

According to the memory trace hypothesis, MMN reflects a process of an automatic comparison of incoming sounds with a memory trace formed by regularities of the preceding auditory context (Näätänen et al., 2007). That includes short-term sensory memory level as well as existing long-term memory representations such as ones formed for phonemes of a native language (Näätänen et al., 1997). Recently, MMN has been discussed within a predictive coding framework in which it is considered an index of an error that occurs when incoming sensory information does not match a prediction made by the brain (e.g., Friston, 2005, 2012; Vuust, Ostergaard, Pallesen, Bailey, &

Roepstorff, 2009; Vuust & Witek, 2014; Winkler & Czigler, 2012; Ylinen et al., 2016).

The MMN is sensitive to deviations of simple acoustic features, such as frequency, location of the sound source, intensity and duration (Jacobsen, Horenkamp, & Schröger, 2003; Paavilainen, Jiang, Lavikainen, & Näätänen, 1993; Paavilainen, Tiitinen, Alho, & Näätänen, 1993; Salo, Lang, Aaltonen, Lertola, & Kärki, 1999; Schröger, 1996) or violation of the regularity rule, for instance, a sound repetition in an otherwise descending pitch sequence (Tervaniemi, Maury, & Näätänen, 1994) or omission of a sound (Yabe et al., 1997). The MMN is elicited even in multifeature paradigms when several types of deviations are included in the same sequence (Näätänen, Pakarinen, Rinne, & Takegata, 2004). As compared to classic "oddball" settings, when only one type of deviant irregularly occurs among standard sounds, multifeature paradigms have a number of advantages. First of all, adding several deviations to the sequence allows for the simultaneous recording of MMNs to different features thus creating a comprehensive profile of one's discrimination abilities in a shorter time than in a classical oddball paradigm (Pakarinen et al., 2009). Second, multifeature paradigms have higher complexity as compared to the standard oddball paradigm, which can be important when looking for processing alterations in healthy subjects. Third, the complexity of multifeature paradigms increases the ecological validity of experimental settings. An example of a realistic-sounding paradigm is a musical multifeature paradigm created by Vuust and colleagues (2011). This paradigm consisted of piano tones organized in a musical arrangement commonly presented in Western music, and included six different sound feature deviations. This paradigm was successfully used for examining variations in automatic discrimination skills between musicians performing in different genres (Vuust, Brattico, Seppänen, Näätänen, & Tervaniemi, 2012), investigating deviant discrimination skills by cochlear implant users (Petersen et al., 2015; Timm et al., 2014) and identifying a dysfunction of pre-attentive processing in major depression patients (Mu et al., 2016). The musical multifeature paradigm was utilized in the current thesis work to probe automatic sound feature discrimination skills in NS.

### 1.3.3. Magnetic resonance imaging

An imaging method allowing the studying of anatomy rather than the physiology of the brain is magnetic resonance imaging (MRI). MRI provides high spatial resolution images that can be used for investigating a detailed morphology of the brain.

The essential parts of an MRI scanner are a static magnetic field, a gradient coil, and radiofrequency coils, consisting of a transmitter and a receiver. In most cases, MRI relies on the magnetic properties of hydrogen to produce images. Hydrogen is the simplest atom, which in its bound-state represents, in essence, a proton. In a normal magnetic field, protons spin around their magnetic pole and are randomly oriented producing no magnetic field overall. When placed in the static magnetic field of the MRI machine, protons line up along the long axes of its magnetic field. Then, a radiofrequency transmitter produces a pulse that causes a disturbance in proton alignment. After the pulse ends, the protons return to their equilibrium state, emitting energy that is captured by a receiver. The relaxation of protons happens at a different rate depending on tissue type, which allows for distinguishing between, for instance, white and grey matter of the brain. Gradient coils generate gradual changes in the magnetic field along three spatial dimensions causing each point of the measured volume to resonate at a different frequency and localize the origin of the MRI signal within its volume.

Structural MRI studies have revealed differences in the volume of particular brain structures in several conditions associated with sound intolerance such as schizophrenia (Palaniyappan & Liddle, 2012; Thoma et al., 2008), tinnitus (Leaver et al., 2012; Schneider et al., 2009; Vanneste et al., 2010), misophonia (Kumar et al., 2017), autism (Rojas, Bawn, Benkers, Reite, & Rogers, 2002) and William's syndrome (Reiss et al., 2000). It has also been helpful for investigating anatomical enhancements resulting from training, for instance, in musicians (Gaser & Schlaug, 2003; Hutchinson, Lee, Gaab, & Schlaug, 2003; Schneider et al., 2002; Schneider, Sluming, Roberts, Scherg, et al., 2005; Vaquero et al., 2016). Until recently, manual segmentation of brain structures has been accepted as standard. However, this approach is time- and costintensive since it requires many hours of manual work from an expert in neuroanatomy. For these reasons, automated procedures for brain segmentation have been developed and are increasingly used in research (Desikan et al., 2006, 2009; Ranta et al., 2014; Takayanagi et al., 2011).

One of the most commonly reliable tools for automated brain parcellation is provided by FreeSurfer software (Dale, Fischl, & Sereno, 1999; Fischl, Sereno, & Dale, 1999). The cortex has a great geometric complexity with which only limited cortical areas are visible on the top of gyri, while the rest is hidden in deep sulci. FreeSurfer uses a surface based morphometric (SBM) approach with which it computationally reconstructs the cortical surface based on anatomical boundaries. Then, it automatically parcellates cortical structures, and extracts several distinct morphological measures, such as grey matter volume, cortical thickness, cortical area and cortical folding. Detailed investigation of cortical morphology allows for the understanding of which aspects contribute to anatomical changes at a given structure. For instance, cortical thickness and cortical area, constituting a structure’s volume, are not necessarily correlated (Panizzon et al., 2009) and thus any change in grey matter volume could be confounded by these measures independently. Cortical area and cortical thickness show different left-right asymmetry patterns in the auditory-related cortex (Meyer, Liem, Hirsiger, Jäncke, & Hänggi, 2014). Moreover, different morphological characteristics of cortical anatomy seem to have a separate genetic origin (Winkler et al., 2010), follow different patterns of maturation (Winkler et al., 2010), and asynchronous age-related reduction (Lemaitre et al., 2012). Thus, a complex investigation of cortical morphology may become advantageous for acquiring insights into the nature of the phenomena of interest.

# 2. Aims of the thesis

The present thesis investigated brain mechanisms and substrates underlying NS using questionnaires, combined EEG/MEG measurements, as well as structural MRI scanning.

**Study I** aimed to investigate whether auditory advantages gained from musical practice increases sensitivity to sounds in general, resulting in altered NS in musicians compared to non-musicians. Based on information obtained from questionnaires, individual NS was analysed for associations with musicianship, musical aptitude, weekly hours of listening to music, and music importance.

**Study II** aimed to investigate whether central sound feature processing and discrimination are altered in NS. Information about the central auditory processing in individuals with low to high NS was assessed with combined MEG/EEG, providing data with fine temporal resolution. Neuronal abilities for sound processing were estimated by means of the P1 obligatory ERP component and MMN, extracted from EEG and MEG data.

**Study III** aimed to identify which cortical and subcortical auditory-limbic structures are involved with NS as reflected in their structural morphology. Neuroanatomical correlates of NS were studied with MRI, providing high spatial accuracy, allowing for the detailed investigation of the brain's anatomy. The surface-based analysis, provided with FreeSurfer, was used to measure grey matter volume as well as cortical thickness, folding, and surface area of selected cortical structures to identify a potential relationship to NS.

# 3. Methods

A part of the data for Study I was collected in University of Foggia, Italy. The rest of the data for Study I, as well as the entire datasets for **Studies II** and **III** were collected in Finland.

**Studies I** (Finnish part), **II** and **III** were included in the broad research protocol “Tunteet”, which was approved by the Coordinating Ethics Committee of the Hospital District of Helsinki and Uusimaa (the approval number 315/13/03/00/11, obtained on March the 11th, 2012). All experiments were conducted in agreement with the ethical principles of the Declaration of Helsinki. All participants had given their written consent to participate in the study prior to the measurements. In Finland, subjects were compensated for their traveling to the lab and committed time in the form of vouchers used for cultural activities. In Italy, subjects were psychology students for whom filling in the questionnaire was a part of a psychology course’s curriculum.

## 3.1. Participants

There were no inclusion criteria for subject recruitment in Italy since the study consisted of a questionnaire alone and was administered only to university students. In Finland, subjects were recruited for MRI and EEG/MEG measurements. Hence, they had to comply with MRI safety considerations and did not have hearing, neurological nor psychiatric problems. Subsets of participants in **Studies I, II** and **III** overlapped.

Details of participants in each study are summarized in Table 1.

**Table 1.** Subjects included in **Studies I-III**.

| Study | N | Finland/Italy | Male/Female | Mean age in years (range) | NSS* (mean ± SD) |
|---|---|---|---|---|---|
| I | 197 | 94/103 | 54/143 | 26.6 (19 − 56) | 81.1 ± 17.6 |
| II | 71 | 71/0 | 34/37 | 28.5 (19 − 51) | 80.5 ± 17.4 |
| III | 76 | 76/0 | 36/40 | 28.6 (19 − 50) | 81.8 ± 17.4 |

* Noise Sensitivity Score assessed with Weinstein’s Noise Sensitivity Scale

In **Study I**, the subjects were divided into three groups according to their musical background: non-musicians (N = 103), amateur musicians (N = 44) and musicians (N = 50). In **Study II**, the sample was tertiary split based on NS, forming high NS (N = 23), medium NS (N = 23) and low NS (N =25) groups.

## 3.2. Questionnaires

In **Studies I-III**, subjects were asked to fill the Helsinki Inventory of Music and Affective Behaviors (HIMAB; Gold et al., 2013; Burunat et al., 2015), which is an internet-based test battery (see Appendix 1). It included the Weinstein's Noise Sensitivity Scale used for assessment of NS in **Studies I-III**. The scale consists of 21 statements that subjects were asked to agree or disagree with, using a six-point Likert scale. Two-thirds of the scale items were reversed scored. The higher the sum of the statements ratings, the higher is NS.

Musical background questions of the HIMAB were used to determine a subject's musicianship and profile their musical behavior in **Study I**. Reports of active listening to music (hours per week), and passive listening to music (hours per week) were used for the analysis. Furthermore, subjects evaluated the importance of music in their life on a six-point scale ranging from "not at all important" to "very important". In **Study II**, years of musical training and playing were used to control for effects of musical training on auditory evoked responses.

In **Study I** subjects' musical aptitude was tested with Seashore Tests for Pitch and Time (Seashore et al., 1960), and an online test for the evaluation of amusia (Peretz et al., 2008) with three subscales (Beat, Scale, Out-of-Key), all of which are incorporated in HIMAB.

The Use of Music questionnaire (Chamorro-Premuzic & Furnham, 2007) was used to describe why individuals listen to music. The questionnaire evaluates three uses of music: cognitive, e.g. focusing on performance quality; emotional, e.g., inducing a mood; background, e.g., listening to music while performing other tasks or socializing. This questionnaire was included only in the Finnish version of HIMAB, thus these data were not available for Italian subjects in

**Study I** and not included into the paper reporting the findings of **Study I**. However, as the information provided with the Use of Music questionnaire is relevant to the discussion of findings of **Study I**, the analysis was performed and reported here.

In **Study II** subjects completed Hospital Anxiety and Depression Scale (HADS-A; Zigmond & Snaith, 1983). The questionnaire was administrated at Biomag Laboratory of the Helsinki University Central Hospital prior to an EEG/MEG measurement. Depression symptoms were evaluated and participants with high depression scores were excluded from the analysis as functional and structural abnormalities can be present in the brain of a depressed person (Bonetti, Haumann, Vuust, Kliuchko, & Brattico, 2017; Grieve, Korgaonkar, Koslow, Gordon, & Williams, 2013).

## 3.3. Paradigm and experimental procedure (Study II)

Subjects were presented with a musical multifeature MMN paradigm, which is illustrated in Figure 1. Stimuli were synthesized piano tones arranged in patterns of four to represent a common accompaniment figure of Western music (‘Alberti bass’). The third tone of each pattern deviated from the standard tones by one of the following features: noise, pitch, location, intensity, pitch slide, and rhythm. The presentation of deviants was randomized. The musical key of the sequence changed regularly.

All sound feature deviations presented with the musical multifeature paradigm evoked a reliable MMN response. The deviant-minus-standard difference waveforms obtained for each deviant are presented in Figure 1 (bottom).

## 3.4. EEG/MEG data acquisition and analysis (Study II)

The recording was done in an electrically and magnetically shielded room at the Biomag Laboratory of the Helsinki University Central Hospital. The data were recorded with a 306-channel Vectorview™ whole head MEG device (ElektaNeuromag®, Elekta Oy, Helsinki, Finland) and a compatible EEG system. The MEG device had 102 sensor elements with two planar gradiometers and one magnetometer. The EEG cap had 64 channels. The reference electrode was attached to the nose. Four electrodes were used to record blinks as well as vertical and horizontal eye movements. Four head position coils were placed over the EEG cap and located by a digitizer. Stimuli were presented with inserted earphones with foam tips. Before the EEG/MEG recordings each subject chose a movie, which they watched silenced and with subtitles. Subjects were instructed to concentrate on the movie, remain still and to not pay attention to the presented sounds.

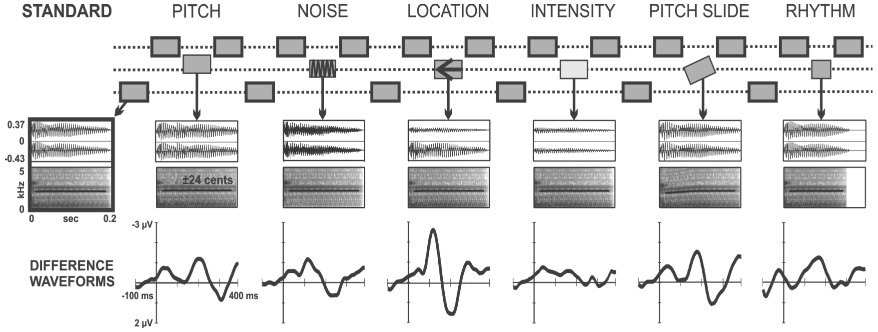

**Figure 1.** No-standard musical multifeature MMN paradigm. Top row: a piano tone sequence. Blocks with thicker outline represents standard tones, the ones with thinner outline are deviant tones. Tones were 200 ms long with interstimulus interval of 5 ms. PITCH: tone mistuning; NOISE: 'old-time radio' effect; LOCATION: sound source shift; INTENSITY: decreased sound intensity; PITCH SLIDE: gradual frequency change from one note below; RHYTHM: shortening by 40 ms. Sound waveforms and spectrograms of a standard tone and each type of deviant are illustrated (second and third rows). The thick lines on the spectrograms are the base frequency. The bottom row of the figure depicts grand-averaged difference waveforms obtained by subtracting the standard ERP from a deviant ERP (channel Fz).

The data were preprocessed with BESA Research 6.0 Software (BESA GmbH, Munich, Germany). EEG recordings were visually inspected. Channels with noisy signals were interpolated. Segments of the recording containing eye-blink artifacts were automatically corrected. For other artifacts, rejection thresholds of ±100 μV for EEG and 1200 fT/cm for MEG data were applied. Further, the data were divided into epochs and time-locked to the stimulus onset. The epoch length was 500 ms, including 100 ms of pre-stimulus time used for baseline correction. The data were averaged according to the stimulus type. For the MEG data, vector sums of each gradiometer pair were then computed in MATLAB by squaring the signals and taking the square root of their sum. After that, individual areal mean curves were averaged over four areas above the left and right temporal areas where the response appeared the most prominent.

The grand averaged ERP for the standard stimuli was inspected to determine the P1 component. Based on visual inspection, the latency of P1 was automatically searched in the time-window between 40 and 90 ms. The mean amplitude value was calculated as a 40 ms period centered around the peak.

For obtaining the MMN, the ERP of the standard stimulus was subtracted from each deviant ERP. The difference waveforms (Figure 1) were visually inspected and the time-windows for automatic searching of the peak MMN amplitudes were identified for each deviant. The mean amplitudes were extracted from the Fz electrode as a mean voltage over 40 ms around the peak. The polarity reversal of MMN was evaluated at the TP9 and TP10 channels.

An identical procedure was performed for extracting mean MMNm amplitudes and latencies recorded with MEG.

## 3.5. MRI data acquisition and image processing (Study III)

The measurements were carried out in the Advanced Magnetic Imaging (AMI) Center at Aalto University, Espoo, Finland. Scanning was performed using a 3-T MAGNETOM Skyra whole body scanner and a standard 20-channel head-neck coil (Siemens Healthcare, Erlangen, Germany). High-resolution anatomical T1-weighted MR images (176 slices, field of view ¼ 256 mm; 256×256 matrix; voxel size ¼ 1×1×1 mm; spacing ¼ 0 mm) were collected.

Surface-based morphometry was performed with FreeSurfer (Dale et al. 1999; Fischl et al. 1999) using an automated procedure. The parcellation was based on sulco-gyral cortical anatomy as described in Destrieux et al., (2010). Subcortical nuclei were parcellated as well. Eight bilateral cortical structures related to perception and appraisal of auditory information were chosen for the analysis (Figure 2). Six of these structures are located in the temporal lobe: Heschl’s sulcus and gyrus, lateral part of the superior temporal gyrus, planum polare, planum temporale and temporal pole. The two other areas belonged to the insular cortex, namely, anterior insula, anatomically represented by short insular gyrus, and posterior insula, comprised of the combination of the long insular gyrus and central sulcus of the insula. The extracted morphological measures of the selected cortical structures were grey matter volume, cortical thickness, cortical area and cortical folding. Grey matter volume of subcortical amygdala and hippocampus were also included in the investigation.

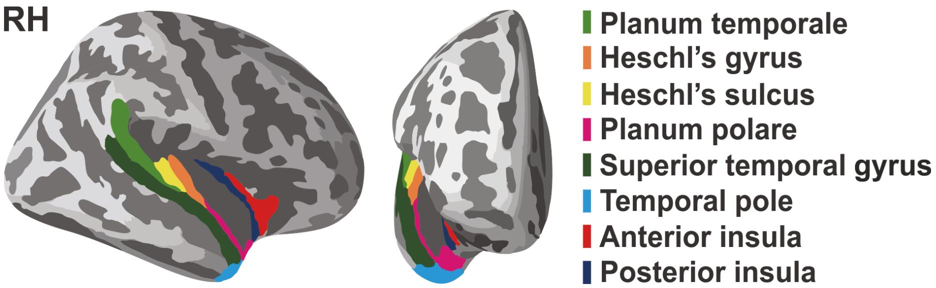

**Figure 2.** Lateral and rostral views of the right hemisphere (RH) showing a parcellation scheme of eight selected regions of interest (ROIs) projected onto an inflated standard brain.

The brain's morphology is known to undergo changes related to aging (Lemaitre et al., 2012; Pereira et al., 2014). As such, cortical thickness and grey matter volume decrease with age and the loss of grey matter is happening at a different speed depending on a structure (Lemaitre et al., 2012). To remove a potential confounding effect of aging, all morphological measures were adjusted for age. Additionally, grey matter volume of cortical and subcortical structures were controlled for intracranial volume. Cortical thickness of each structure was controlled for mean cortical thickness.

## 3.6. Statistical analyses

In **Study I**, one-way ANOVAs were used for testing the difference in NS between countries (Italy, Finland), gender (males, females) and musicianship groups (musicians, amateurs, non-musicians). Spearman's rho coefficient was used to test the correlations between NS and musical variables (passive/active listening to music, music importance, musical aptitude).

In **Study II**, t-tests were used to determine whether MMN responses were different from zero. Subjects were split into three equally sized groups according to their NS (high, medium, low). Group differences in the amplitudes of P1 response, as well as the amplitudes and latencies of MMN to each of the deviant were analyzed with ANCOVA. The amplitudes of MMNm responses were tested for group differences using ANCOVA for repeated measures with Group as a between-subject factor and Region of Interest (ROI) and Hemisphere as within-subject factors. In all ANCOVAs in **Study II**, subjects' age and years of musical training were used as covariates.

**In Study III**, a general linear model (GLM) was applied to grey matter volumes of cortical structures with Hemisphere (two levels) and ROI (eight levels) as within-subjects factors and NS score as a regressor of interest. Hippocampal and amygdalar volumes were tested using a similar but separate GLM model. Cortical thickness, surface area, and cortical folding were tested for a relationship with a NS score using one-tailed Pearson's correlations.

All described in the results section are significant with p-values below 0.05. When applicable, Bonferroni correction for multiple comparisons was used. Post-hoc comparisons are done with the LSD method.

# 4. Results and Discussion

## 4.1. Relationship between noise sensitivity and musical behaviour (Study I)

**Study I** aimed to investigate whether NS is related to musical expertise and musical behaviour. Musically trained individuals are known to have improved auditory abilities, which are manifested but not limited to an enhanced processing of musical sound (Kraus & Chandrasekaran, 2010). For instance, demonstrate an efficiency of language processing (Dick, Lee, Nusbaum, & Price, 2011) and retrieving information masked with background noise (Coffey, Mogilever, & Zatorre, 2017; Parbery-Clark, Skoe, & Kraus, 2009). Thus, the main question addressed in **Study I** was whether the general advantage of musicians in sound processing could result in higher sensitivity to noise.

**Table 2.** Statistical results obtained in **Study I**. *Upper panel*: ANOVA results of comparison of NS between countries, genders and musicianship groups. *Bottom panel*: Correlation analysis (Spearman rho) results for several listening tests vs. NS and for musical variables vs. NS.

| | **ANOVA results** | | |
|---|---|---|---|
| **Main effects** | **F** | **df** | **p** |
| Country | 0.070 | 1, 196 | 0.79 |
| Gender | 3.128 | 1, 196 | 0.08 |
| Music group | 0.036 | 2, 196 | 0.96 |

| | **Correlation analysis results** | |
|---|---|---|
| **Listening tests** | **rho** | **p** |
| Seashore Pitch | -0.147 | 0.06 |
| Seashore Time | -0.015 | 0.85 |
| Amusia test: Scale | 0.008 | 0.92 |
| Amusia test: Beat | -0.044 | 0.57 |
| Amusia test: Out-of-Key | -0.019 | 0.81 |
| **Musical variables** | | |
| Active listening to music | -0.081 | 0.26 |
| Passive listening to music | -0.243 | 0.001 |
| Importance of music | -0.175 | 0.016 |

The analysis was performed on the whole set of subjects irrespective of the country of data collection, as NS did not vary between Finnish and Italian samples. The details of statistical results obtained in **Study I** are reported in Table 2.

NS was not related to the musical aptitude that was measured with Seashore test and On-line tests for the evaluation of amusia, containing five subscales in total. Judging from that, trained or pre-existent skills for behavioural recognition of pitch and beat cannot account for sensitivity to noise. Also, these findings add to the previous observations that NS does not affect performance on behavioural auditory tasks such as intensity discrimination and reaction time to sound stimuli (Ellermeier et al., 2001). It is worth noting, however, that because the listening tests used in **Study I** were created for evaluating basic musical skills and diagnosing amusia (tone deafness), they were probably not demanding enough to reveal an influence of NS, especially considering that more than half of the participants in **Study I** were professional and amateur musicians.

Group-level comparison of NS in musicians, musical amateurs, and non-musicians did not reveal any differences. In the next step, NS was analysed for association with specific aspects of musical behaviour, such as listening to music. The correlation plots for NS vs. active and passive music listening are illustrated in Figure 3 (left plot). The correlation between NS and active listening to music was found to be non-significant. However, NS negatively correlated with passive listening to music, which is non-attentive background listening, and music importance. NS is considered a stable trait meaning that it does not significantly change over time (Stansfeld, 1992; Weinstein, 1978; Zimmer & Ellermeier, 1999). The findings of **Study I** contribute to this notion, although it is not possible, retrospectively, to assess NS at the beginning of musical training. However, non-differing mean NS among musicians, amateurs and non-musicians may indicate the fine auditory abilities that musicians gain through musical training does not make them either more nor less sensitive to noise compared to non-musicians. Moreover, together with the observation of NS being non-related to active listening of music, which includes such activities as attending concerts and playing music, these findings indicate that individuals still dedicate their time to musical activities irrespective to their sensitivity to noise.

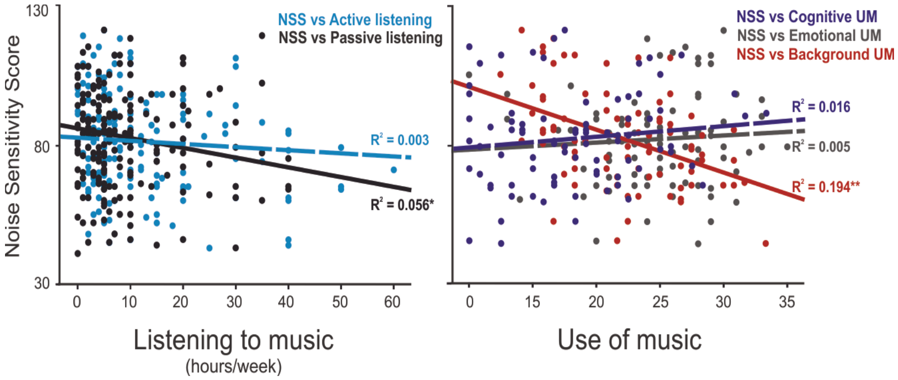

**Figure 3.** Relationship between NS and (left) passive and active listening to music, (right) cognitive, emotional and background use of music. The trend lines for the significant correlations are shown with bold lines and the non-significant ones are dashed lines.

However, noise-sensitive individuals reported music as less important to their lives than noise-resistant ones, which contradicts the conclusion made above. Probably this could be explained by the amount of background music that noise-sensitive individuals listen to in a day. The negative correlation between NS and weekly hours spent listening to background music was observed in **Study I** but the attempt to use this observation for explaining the findings on lower music importance in noise-sensitive individuals was not made. To test this, a partial correlation analysis was performed for this thesis (thus, this analysis is not included in original **Study I**). A correlation between NS and importance of music turned non-significant when controlling for weekly hours of passive listening to music ($r = -0.096$, $p = 0.21$). Yet, while controlling for the importance of music, a correlation between NS and passive listening to music remained significant ($r = -0.202$, $p = 0.007$). This means that the observed relationship between NS and the importance of music is confounded by the amount of passive listening and if this effect is eliminated, NS does not seem to affect the value of music in one's life.

Further support for this explanation is gained from the use of music questionnaire (unpublished results; Figure 3: right plot). Because this data was available for only 83 subjects of the Finnish sample, the analysis was not included in original **Study I**. The analysis performed for the purposes of the thesis summary showed that NS does not correlate with emotional and cognitive use of music (rho = 0.086, p = 0.44; rho = 0.114, p = 0.30; Figure 3). However, it is negatively correlated with the background use of music (rho = -0.422, p < 0.001; Figure 3, page 26). Thus, while noise-sensitive individuals seem to be able to enjoy the sound of music, use it for mood regulation, and they attentively (actively) listen to music like non-sensitive individuals, they prefer not having it in the background.

Taken together, the findings of **Study I** and of the additional analyses of the uses of music in NS go in line with the understanding of NS as intolerance to unwanted sounds and not to the sound *per se*. However, as these findings were made in respect to music, the conclusions should be generalized with caution.

## 4.2. Noise sensitivity in electrophysiological response (Study II)

The **Study II** was conducted to investigate whether NS is related to the mechanisms of central auditory processing. The hypothesis of the study was that the efficiency of the central sensory processing could be affected in NS, based on previous findings where an effect of NS (Shepherd et al., 2016) and noise annoyance (Pripfl, Robinson, Leodolter, Moser, & Bauer, 2006) was found to be reflected in early cortical ERP components. The second hypothesis was that NS could relate to the ability of automatic discrimination of certain sound features, such as its noisiness. Thus, in **Study II** P1 and MMN responses recorded in the musical multifeature paradigm were tested in three groups of subjects with NS from low to high.

Table 3 depicts the descriptive information about P1 and MMN responses. The grand averaged difference waveform (the deviant ERP minus the standard ERP) obtained from the Fz channel is presented in Figure 1 (page 20). MMN responses to all deviants were significantly different from the zero baseline. The positive reversal of the response at the mastoid electrodes, distinguished it from other components occurring at the same latency (e.g., N2b, see Kujala et al. 2007). In general, the observed MMNs were comparable to those obtained in other studies using the musical multifeature MMN paradigm based on the "Alberti bass" pattern (Petersen et al., 2015; Vuust et al., 2011, 2012; Vuust, Liikala, Näätänen, Brattico, & Brattico, 2016).

The obligatory P1 component of an ERP to standard stimuli is displayed in Figure 4 (page 30). P1 was the smallest in the high NS group, which was significantly different from the P1 observed in the low NS group. P1 is thought to reflect early cortical processing of auditory information and is associated with mechanisms of sensory gating and inhibition (Boutros et al., 1995). Diminished P1 amplitude in noise-sensitive individuals suggests that these processes are possibly affected in NS. Interestingly, deficits in sensory gating can be manifested in self-evaluation of sound processing. With this, I am referring to the findings by Kisley et al. (2004) who showed that lower P1 suppression to the second click in a paired-click paradigm was correlated with a feeling of being "flooded by sounds" and "hearing everything at once" assessed with Sensory Gating Inventory. Because the abilities of sensory filtering can be reflected in the behavioural evaluation of sound experience (Hetrick, Erickson, & Smith, 2012; Kisley, Noecker, & Guinther, 2004), it is possible to assume that negative evaluation of background noise in NS is related to pre-attentive filtering processes. However, this conclusion is speculative because it is not possible to delineate what processes contributed to a reduction of P1 in the high NS group.

Both MMN and MMNm were generally attenuated in the high NS group. Figure 5 illustrates difference waveforms and group-averaged MMN amplitudes for all deviants. The details of the statistical analysis are presented in Table 4. Analogous information for MMNm is presented in Figure 6 and Table 5. The separate analysis of MMN for each type of deviation confirmed the primary predictions on altered discrimination of noise in noise-sensitive individuals. Accordingly, the group differences in MMN responses were the most apparent for the noise deviant, which were observed as significantly smaller MMN amplitudes in the high as compared to the low NS groups in both the EEG and MEG data. However, as the main effect of NS on MMN was observed, it is possible that sound feature discrimination in noise-sensitive individuals is affected at a more general level.

**Table 3.** MMN amplitudes and latencies at Fz and inferior temporal (TP9, TP10) electrodes.

| | Mean Amplitude | *SD* | *t* | Mean Latency | *SD* |
|---|---|---|---|---|---|
| **Pitch-MMN** | | | | | |
| Fz | -1.4 | 1.1 | -12.8 | 199 | 21 |
| TP9 | 0.5 | 1.0 | 4.9 | | |
| TP10 | 0.7 | 1.0 | 7.6 | | |
| **Noise-MMN** | | | | | |
| Fz | -1.3 | 1.1 | -11.4 | 140 | 27 |
| TP9 | 0.2 | 0.8 | 2.8 | | |
| TP10 | 0.5 | 0.9 | 5.3 | | |
| **Location-MMN** | | | | | |
| Fz | -2.5 | 1.5 | -17.2 | 120 | 12 |
| TP9 | 0.7 | 1.0 | 6.8 | | |
| TP10 | 0.9 | 1.1 | 8.5 | | |
| **Intensity-MMN** | | | | | |
| Fz | -1.1 | 1.0 | -10.4 | 157 | 32 |
| TP9 | 0.1 | 0.7 | 1.7 | | |
| TP10 | 0.3 | 0.7 | 4.2 | | |
| **Slide-MMN** | | | | | |
| Fz | -1.7 | 1.2 | -14.2 | 186 | 22 |
| TP9 | 0.7 | 1.2 | 5.2 | | |
| TP10 | 0.9 | 1.2 | 7.4 | | |
| **Rhythm-MMN** | | | | | |
| Fz | -1.38 | 1.0 | -14.2 | 153 | 25 |
| TP9 | 0.79 | 0.8 | 9.5 | | |
| TP10 | 0.78 | 0.9 | 8.4 | | |

Several speculations on the interpretation of attenuated MMN can be made. First, MMN is shown to reflect the accuracy in perceiving the acoustic difference between standard and a deviant sound on the behavioural level (Näätänen et al., 2007). From this perspective, attenuated MMN in NS may be related to perceptual deficits of noise-sensitive individuals, especially concerning sound noisiness. Second, it may be related to an altered ability in forming a bottom-up prediction of changes in the auditory stream due to insufficient sound feature encoding at earlier processing stages, as indicated by the amplitude of P1. Third, a decrease in MMN response may be due to a maladaptive inhibition of response to auditory sensory input that is developed in the central nervous system because of high sensitivity to environmental noises.

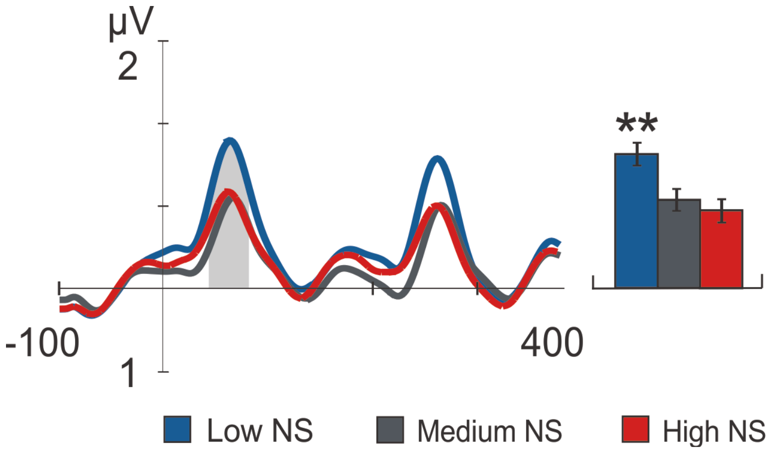

**Figure 4.** Group-averaged ERPs to standard stimuli measured at Fz in low, medium and high NS groups. Bars represent mean amplitude of P1 component averaged over a 40 ms time-window (grey area) and adjusted for age and years of musical training. Asterisks represent a statistically significant difference in amplitude at the p level below 0.01.

**Table 4.** Results of separate ANCOVAs in **Study II** testing MMN amplitude differences between NS groups

| | **Main effect of Group** | | | **Covariate effects** | |
|---|---|---|---|---|---|
| **Deviation** | **F** | **$P_{(uncorr)}$** | **ηp2** | **P (Years of Musical Training)** | **P (Age)** |
| **Pitch** | 1.76 | 0.180 | 0.055 | 0.004 | 0.262 |
| **Noise** | 6.14 | 0.004* | 0.168 | 0.418 | 0.059 |
| **Location** | 3.83 | 0.027• | 0.111 | 0.199 | 0.233 |
| **Intensity** | 2.56 | 0.086 | 0.077 | 0.071 | 0.041 |
| **Slide** | 2.12 | 0.128 | 0.065 | 0.044 | 0.272 |
| **Rhythm** | 0.50 | 0.611 | 0.016 | 0.081 | 0.095 |

• The P-value does not survive Bonferroni correction

**Table 5.** Results of separate ANCOVAs in **Study II** testing MMNm amplitude differences between NS groups

| | **Main effect of Group** | | | **Covariate effects** | |
|---|---|---|---|---|---|
| **Deviation** | **F** | **P** | **ηp2** | **P (Years of Musical Training)** | **P (Age)** |
| **Pitch** | 3.04 | 0.055 | 0.084 | 0.012 | 0.991 |
| **Noise** | 3.82 | 0.027* | 0.104 | 0.237 | 0.058 |
| **Location** | 1.65 | 0.201 | 0.047 | 0.383 | 0.002 |
| **Intensity** | 2.02 | 0.140 | 0.058 | 0.259 | 0.048 |
| **Slide** | 2.99 | 0.057 | 0.083 | 0.000 | 0.013 |
| **Rhythm** | 0.004 | 0.996 | >0.0001 | 0.015 | 0.534 |

Throughout the analyses performed, the effect of subject's age was not affecting the brain responses in relation to NS (for covariate effects see Tables 4 and 5). However, the amplitude of MMN and MMNm were generally enhanced by musical experience. The effect of musical expertise on neuronal sound discrimination has been repeatedly shown in studies with adult subjects as an enhanced MMN amplitude (Schneider, Sluming, Roberts, Bleeck, & Rupp, 2005; Tervaniemi, Just, Koelsch, Widmann, & Schröger, 2005; Vuust et al., 2005). Moreover, the observations of an increasing MMN with years of musical training is consistent with enhanced responses recorded in musicians in other studies that used similar versions of the musical multifeature paradigm (Vuust et al. 2012, 2016).

Therefore, the results of **Study II** suggest that individuals with high NS display adjusted auditory processing. This was indexed by a smaller P1, which is an obligatory auditory ERP component, reflecting pre-attentive processes of information encoding and filtering, and followed by a generally diminished MMN response. The most apparent deficit in automatic feature discrimination was observed for a noisy deviant. As evidenced by these findings, there are several stages of the central auditory processing that are affected by NS.

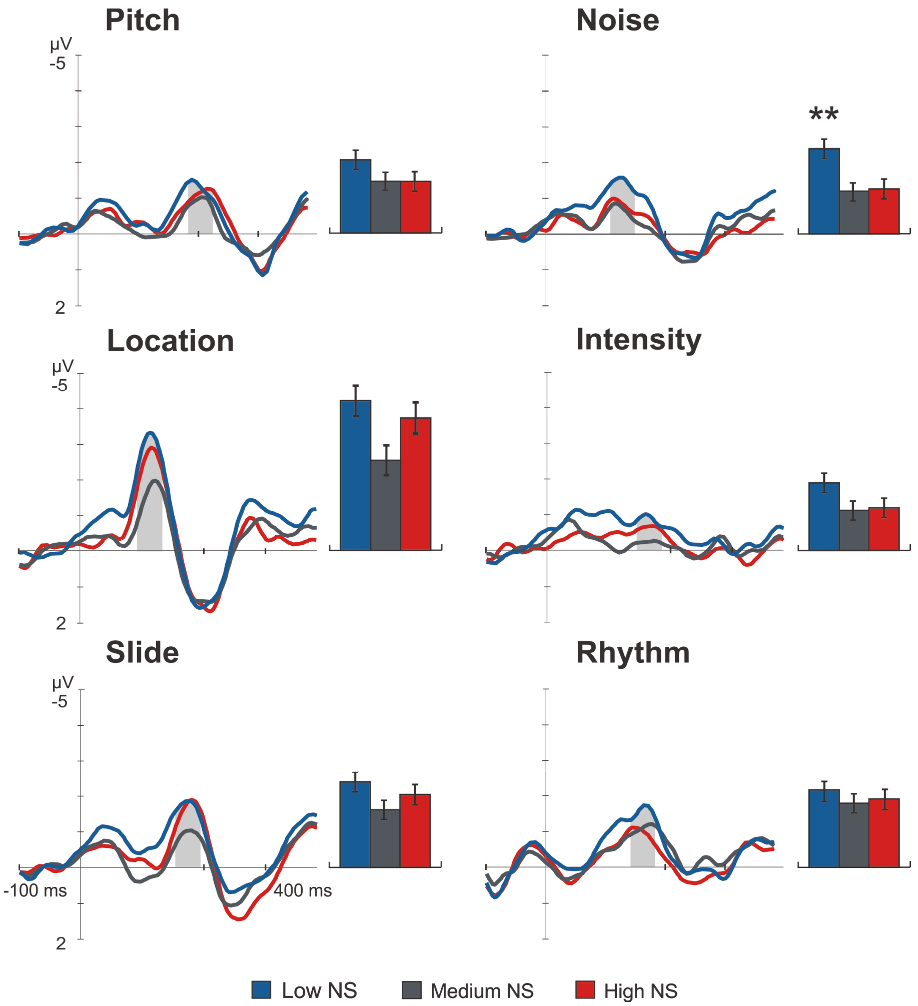

**Figure 5.** MMN responses to six types of deviations measured at Fz in low, medium and high NS groups. Bars represent mean amplitudes of MMN averaged over a 40 ms time-window (grey area) and adjusted for age and years of musical training. Asterisks represent a statistically significant difference in amplitude with $p < 0.01$.

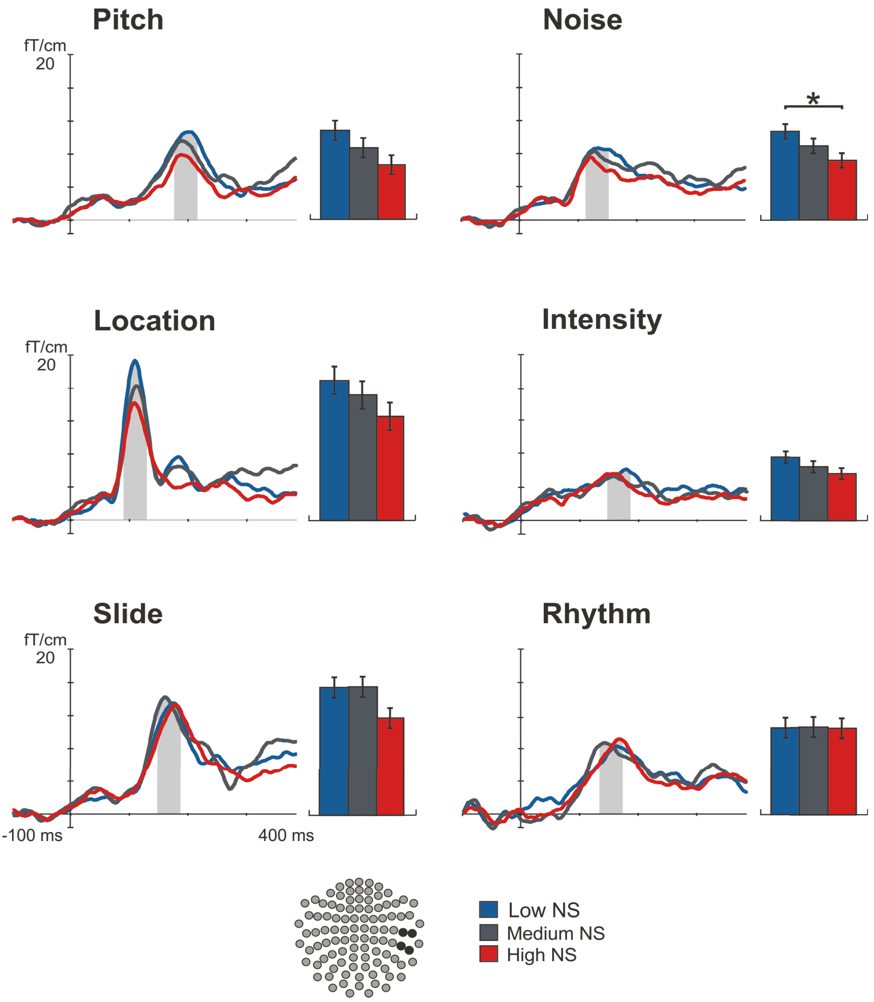

**Figure 6.** Right hemisphere MMNm responses to six types of deviations in low, medium and high NS groups. Bars represent mean amplitudes of MMNm averaged over a 40 ms time-window (grey area) and adjusted for age and years of musical training. Asterisk represents a statistically significant difference in amplitude with $p < 0.05$.

## 4.3. Noise sensitivity in the brain morphology (Study III)

In **Study III**, anatomical MRIs were used to identify neuroanatomical correlates of NS in the auditory and insular cortices, as well as subcortical structures, involved with sound processing and evaluation. The first hypothesis of this study was that NS is related to the structure of the auditory cortex according to the electrophysiological findings of an alteration in the central auditory processing in noise-sensitive as compared to noise-resistant individuals made in **Study II**. The second hypothesis was that NS could be associated with the morphology of the insular cortex, amygdala, and hippocampus, as they are involved with the prediction of aversive stimuli, evaluation of emotional salience and control of autonomic stress reaction in response to auditory stimuli.

As illustrated in Table 6 and Figure 7, NS was associated with grey matter volume of several cortical and subcortical structures. The association was found in the left Heschl's sulcus and bilaterally in the temporal pole. These changes were not explained by cortical thickness, cortical surface area, and cortical folding index probably because none of these aspects of the cortical organization solely contributed to the grey matter volume increase. Heschl's sulcus separates Heschl's gyrus and planum temporale (Destrieux, Fischl, Dale, & Halgen, 2010). Heschl's gyrus contains the primary auditory cortex, where the initial stages of cortical sound processing are taking place (Hickok & Poeppel 2007). Planum temporale is a key structure for spectro-temporal processing of auditory information (Griffiths & Warren, 2002). The observation of relationship of NS to the volume of Heschl's sulcus only in the left hemisphere is interesting from the perspective of functional asymmetry of the human auditory cortex. The left hemisphere is thought to be involved with analysing fast-rate auditory information thus being largely involved with processing temporal regularities of auditory information (Poeppel, 2003; Warrier et al., 2009; Zatorre & Belin, 2001). The right hemisphere, in turn, analyses acoustical information that changes at a slower rate (Poeppel, 2003) and thus is responsible for processing complex spectral aspects of a sound (Zatorre & Belin, 2001). The findings of increased grey matter of the left Heschl's sulcus suggest that NS may be related to an altered processing of rapid temporal aspect of auditory information.

**Table 6.** Statistically significant effects and interactions of GLMs performed in **Study III**.

| Effects | F | df | p |
|---|---|---|---|
| **General: cortical effects** | | | |
| NSS* | 4.70 | 1,74 | 0.031 |
| **Heschl's sulcus** | | | |
| NSS | 7.56 | 1,74 | 0.007 |
| Hemisphere | 4.37 | 1,74 | 0.040 |
| **Temporal pole** | | | |
| NSS | 7.31 | 1,74 | 0.009 |
| **General: subcortical effects** | | | |
| NSS | 5.49 | 1,74 | 0.022 |
| ROI | 5.34 | 1,74 | 0.024 |
| ROI x NSS | 5.69 | 1,74 | 0.020 |
| **Hippocampus** | | | |
| NSS | 5.85 | 1,74 | 0.018 |

* Noise Sensitivity Score assessed with Weinstein's Noise Sensitivity Scale

The temporal pole was bilaterally enlarged in NS (Figure 7). The temporal pole is a multifunctional area that receives sensory input from sensory associative areas and via other structures, such as the amygdala (Olson, Plotzker, & Ezzyat, 2007; Pascual et al., 2015). One of the proposed functions of the temporal pole is the integration of complex modality-specific perceptual inputs with bodily emotional responses (Olson et al., 2007). The temporal pole is connected with the insula and hippocampus, as shown by functional connectivity analysis (Pascual et al., 2015). These connections are interesting, since the hippocampus, too, was bilaterally enlarged in NS, and the right anterior insula was thickened.

The hippocampus takes part in processing and storing of meaningful information (Zheng et al., 2017). Moreover, it demonstrates sensory gating-like activity in response to repetitive stimuli (Liberman, Velluti, & Pedemonte, 2009; Thoma et al., 2004). Together with the amygdala, the hippocampus is important for aversive learning in which the role of the hippocampus is contextual processing and modulation of emotions and emotional memory (Phelps, 2004). The amygdala, in turn, is critical for saliency detection, emotion evaluation and regulating autonomic response to it (Cacciaglia, Pohlack, Flor, & Nees, 2014; Zheng et al., 2017). In **Study III**, changes in volume of the amygdala in respect to NS were not found. A speculation based on these observations is that NS, perhaps, does not relate to the affective evaluation of noise but to the contextual processing of elicited emotions.

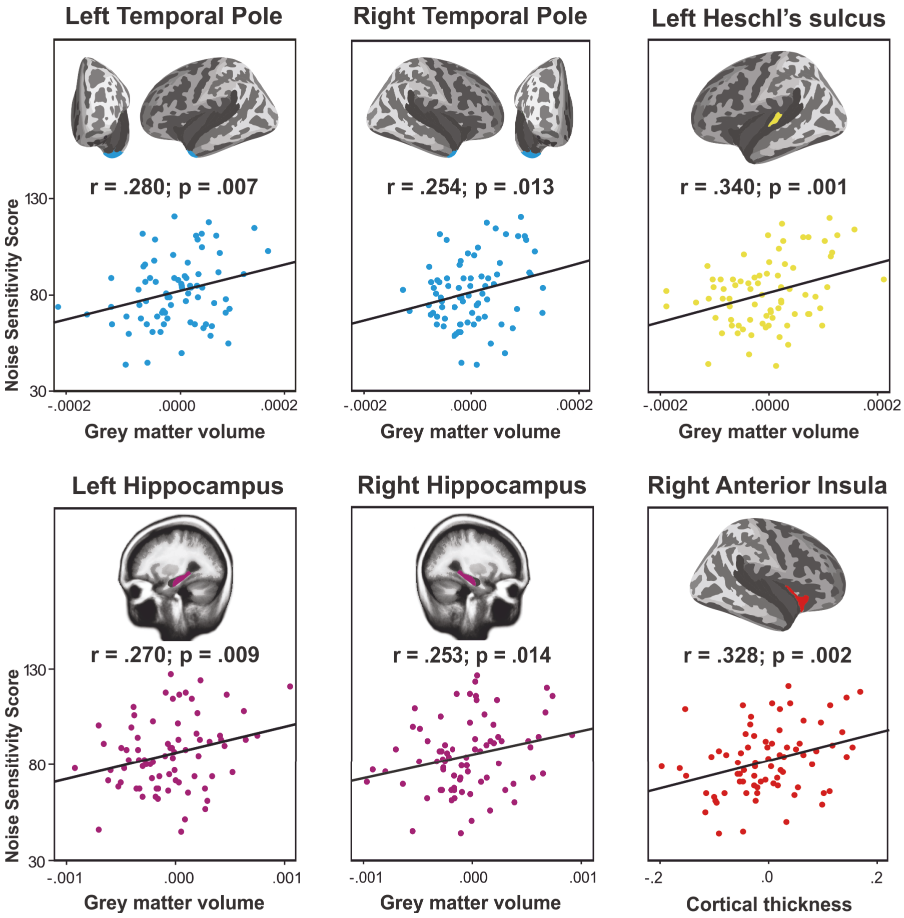

**Figure 7.** Noise-sensitivity-related changes in the brain morphology. The morphological measures are adjusted for age.

As it was expected, NS was related to the structure of the anterior insula, so that the cortical thickness of the anterior insula in the right hemisphere increased with higher NS. It has been suggested that the right anterior insula supports representations of visceral information and makes it available for explicit awareness of one's inner state (Critchley, Wiens, Rotshtein, Öhman, & Dolan, 2004). Moreover, the anterior insula contributes to salience processing and the integration of exteroceptive, interoceptive and emotional awareness (Simmons et al., 2013). For instance, experience-dependent modulation of sensorimotor feedback integration in the right anterior insula was found in professional singers, for whom connecting external and internal sensations is important for accurate pitch producing (Kleber, Friberg, Zeitouni, & Zatorre, 2017; Kleber, Zeitouni, Friberg, & Zatorre, 2013). An increased attention to bodily functions can induce neuroplastic changes in the right anterior insula. For example, a thicker right anterior insula is found in yoga practitioners whose practice style is concentrated on body cues, such as breathing (Lazar et al., 2005). An enlargement of this area can also result from involuntary attention placed on the bodily state such as due to distress caused by tinnitus (Leaver et al., 2012) and in chronic pain (Blankstein, Chen, Diamant, & Davis, 2010). Increased awareness of inner state evolves into stronger emotional experiences (Barrett, Quigley, Bliss-Moreau, & Aronson, 2004; Pollatos, Gramann, & Schandry, 2007) and thus it may be speculated that the negative attitudes that noise-sensitive individuals report towards background noise might be related to their enhanced awareness of inner emotional and visceral state induced by sounds.

The findings of **Study III** suggest that NS is related to the structural organization of brain areas playing a role in auditory perception, interoception, as well as processing of emotion and salience.

# 5. General discussion

The most commonly used definition of NS, proposed by Job (1999), highlights that there are several factors, namely, psychological, physiological, and attitudinal, that may be contributing to individual NS. A large body of public health research has considered NS as a factor describing individual reactivity to noise and has persuasively linked it to increased susceptibility to non-auditory health effects of noise. However, the attempts in explaining NS have been methodologically limited to psychometrics and psychoacoustic approaches. This thesis provides strong evidence that NS has neurophysiological and neuroanatomical underpinnings and highlights the potential of using objective brain imaging methods for understanding NS.

## 5.1. Contribution of the present thesis

The combination of the electrophysiological and anatomical findings in **Studies II** and **III** suggest that NS is related to the central auditory system. In **Study II**, P1 and MMN responses were diminished in highly noise sensitive individuals as compared to those of low NS individuals. Both of these components index cortical stages of the pre-attentive auditory processing. P1 originates and is distributed over the primary auditory cortical areas close to the boundaries of the secondary areas (Liégeois-Chauvel, Musolino, Badier, Marquis, & Chauvel, 1994). The location of MMN source is mainly in the auditory cortices and may depend on a sound feature it is elicited by (Picton, Alain, Otten, Ritter, & Achim, 2000). A NS-related change in structural organization of the auditory cortical areas was observed in **Study III**: higher NS corresponds to the larger left Heschl's sulcus which is adjusted to primary and secondary auditory areas. The anatomical findings complement the functional results and together indicate that NS is related to the mechanisms of the central auditory processing. However, further investigations are necessary to disclose how the anatomy of auditory cortical areas is related to its functional activity in NS.

An adjusted sound feature processing may be a potential explanation for the negative experience of noisy environments and background noises that noise-sensitive individuals express. Processing fluency is thought to have an influence on affective evaluation of stimuli (Reber, Schwarz, & Winkielman, 2004). The poorer ability of noise-sensitive individuals for sound feature discrimination, indexed by MMN, and the lower abilities for sound feature encoding, indexed by P1, may require them to put an extra effort into sound processing and thus lead to more negative judgments of noise. Moreover, difficulties with processing auditory information in NS are suggested by previous findings on altered gating mechanisms in noise-sensitive individuals (Shepherd et al., 2016). Sensory gating is considered to be a protective mechanism that prevents irrelevant sensory information reaching higher-order structures (Boutros et al., 1995; Todorovic, van Ede, Maris, & de Lange, 2011). Hence, an impairment of this sensory gating process could lead to cognitive outcomes (Lijffijt et al., 2009). Furthermore, diminished sensory gating can relate to self-reported perceptual phenomena (Kisley et al., 2004). As such, a higher ratio of P1 to the first click vs. the P1 to the second click in the paired click paradigm corresponded with higher self-rating of perceptual modulation (feeling over-flooded with sounds). Specifically, insufficient P1 suppression was correlated with the reports of filtering difficulties but not loudness sensitivity (Kisley et al., 2004). Thus, it is possible that negative evaluation of noise in sensitive individuals relates to difficulties in sound feature processing that take place already on pre-attentive stages of auditory perception.

The findings of **Study III** further suggest that NS is not only related to the auditory sensory system. Participants with higher NS had larger hippocampus and temporal poles in both hemispheres and their right anterior insula was thickened. The hippocampus is related to contextual processing and memory of emotion and plays an important role in aversive learning (Zheng et al., 2017). It is functionally connected with the temporal pole, which is involved with high-order sensory processing and attribution of emotions to a meaningful percept (Olson et al., 2007). The anterior insula, in turn, is crucial for interoceptive processing and integration of external and internal awareness (Craig, 2009). Consequently, the findings of **Study III** on morphological changes in the right anterior insula, bilateral hippocampus and bilateral temporal pole indicate that mechanisms of NS go beyond auditory perceptual system and may also be potentially related to affective learning, evaluation of salience in external sensory information and integrating it with interoceptive sensations.

**Study I** addressed the relationship between NS and musical behaviour. Musicians have enhanced auditory abilities that are not tied to only musical sound, but have a degree of transfer to other auditory skills (Coffey et al., 2017; Kraus & Chandrasekaran, 2010), and that could potentially have an influence on NS. One study has previously reported that NS is higher among people who practice music (Franek, 2009). In this study the participants were asked whether they played a musical instrument currently or in the past, and whether they liked listening to music or not. With this approach, it would be not possible to estimate whether people who played a musical instrument were professional musicians or occasional players, how many years they have spent practicing an instrument and when the practice began. However, details of musical training, such as the age of training onset, are important for development of experience-dependent brain adaptations (Schlaug, Jäncke, Huang, Staiger, & Steinmetz, 1995). Thus, **Study I** used a more careful description of musicianship than that in the study by Franek (2009). According to the findings of **Study I**, there was no effect of musicianship on NS as the average NS scores were not different between groups of musicians, amateur musicians, and non-musicians. **Study I** adds to the view on NS as being a stable trait of an individual. Moreover, it describes that NS has an effect on daily musical behaviour. **Study I** shows that noise-sensitive individuals listen to music in the background less often than less sensitive individuals. However, how much time individuals spent listened to music actively, e.g., at a concert or during music practice, does not seem to be affected by NS trait.

Furthermore, **Study I** showed no relation between NS and performing on the listening tests, contributing to the body of literature on the normal performance of noise-sensitive individuals on auditory tasks (Ellermeier et al., 2001; Heinonen-Guzejev et al., 2011; Moreira & Bryan, 1972; Stansfeld et al., 1985). Together with that, **Study II** showed a compromised auditory processing in NS that takes place on a pre-attentive level of the central auditory processing.

## 5.2. Future perspectives

The present thesis opens directions for future research and applications.

First of all, several incoming investigations of NS might be motivated by the findings of **Studies II** and **III**. For instance, **Study III** found a unilateral relationship between NS and grey matter volume of Heschl's sulcus in the left hemisphere. Considering the functional asymmetry of the auditory cortex in terms of processing spectral and temporal auditory information (Poeppel, 2003; Warrier et al., 2009; Zatorre, Belin, & Penhune, 2002), it could be assumed that NS is differentially related to the processing of these two sound aspects and needs to be functionally tested.

A second potential direction in an investigation of mechanisms of NS arises from **Study II** that revealed an attenuation of P1 and MMN responses in noise-sensitive individuals. These results suggest that there are at least two stages of pre-attentive cortical sound processing that are affected in NS. Further studies on NS could test whether alterations in neural sound encoding can be detected already at the subcortical level, e.g., by measuring auditory brainstem responses. Furthermore, later stages of central auditory processing could be targeted for investigating as well. Noise-sensitive individuals report that noise is distractive to them and they have difficulties to concentrate in the presence of background sounds (Belojević, Jakovljevic, & Slepcevic, 2003). That may suggest attention-related deficits associated with NS. Thus, addressing the top-down and bottom-up mechanisms of auditory attention could be beneficial for understanding NS.

Third, NS-related enlargements in several brain areas, which are involved with auditory processing, affective learning, sensory awareness, and interoception, were revealed in **Study III**. These findings, however, do not answer whether the structural change is related to increased or decreased functionality of these brain regions (Meyer et al., 2014). Also, based entirely on structural observations, it is not possible to reveal which functions in particular and how they are affected in NS. That calls for functional studies to be conducted.

Moreover, in future work brain research methods can help understanding whether NS shares common mechanisms with other conditions in which negative reactions to sounds are described. Currently, especially in clinical literature, the term “noise sensitivity” is often misattributed to such sound intolerances as misophonia (intolerance to particular sounds, e.g., chewing), hyperacusis (loudness hypersensitivity) and phonophobia (sound-induced anxiety) (discussed in Job, 1999; Shepherd et al., 2015; Stansfeld, 1992). Thus, identifying a neural profile of NS can help to clarify the definition of NS and distinguish it from other sound sensitivities.

Nevertheless, in populations with certain conditions, such as tinnitus or impaired hearing, NS is more prevalent than in healthy populations (Heinonen-Guzejev et al., 2011, 2005). A relevant question for investigating is whether NS in healthy and clinical populations have shared mechanisms. For instance, a recent structural study by Leaver and colleagues (2012) showed that chronic tinnitus was related to a decreased volume of ventromedial prefrontal cortex. Moreover, this relationship was not explained by other factors, such as discomfort caused by the tinnitus sound. Instead, symptoms of tinnitus-induced distress in this study were related to the cortical thickness of the anterior insula. Perhaps, a thickened right anterior insula in NS, reported in **Study III**, could also be related to stress that noise-sensitive individuals experience from noise. This assumption could be put to investigation.

Last but not least, knowing mechanisms of NS can help the development of protective interventions against negative effects of noise on susceptible individuals, and particularly in occupational settings. Moreover, with the help of neurophysiological indices, it may be possible to create new objective ways of assessing individual NS in order to improve, complement or replace the questionnaires that are currently in use.

# 6. Conclusions

Noise sensitivity has received great attention in population-based research as a risk factor for noise-induced health problems but the attempts to study its physiological mechanisms have been surprisingly little. The present thesis used several brain imaging techniques as well as questionnaires to fill the gap in knowledge about the functional and structural neural underpinnings of NS.

**Study I** showed that NS is not increased in musicians as compared to non-musicians and music amateurs. However, NS moderates background listening to music as the higher NS corresponded to fewer hours spent by an individual having music in the background. **Study II** used EEG/MEG to investigate pre-attentive stages of the central auditory processing in NS. The findings showed that individuals with high NS, as compared to those with low NS, had compromised neural sound feature encoding, followed by smaller neurophysiological responses to sound feature deviations, especially in the case of the noise deviant. This conclusion is supported with the results of **Study III**, where structural MRI analysis was employed to learn about the neural substrate of NS. There it was found that NS is associated with enlarged core auditory cortical areas, such as the left Heschl's sulcus. Furthermore, the findings on the relationship of NS with brain morphology were not restricted to auditory-related cortex. NS was positively correlated with thickness of the right anterior insula as well as with grey matter volume of the hippocampus and temporal pole in both hemispheres. These areas have been previously linked to auditory processing, aversive learning and emotional evaluation as well as binding internal and external sensory information.

Taken together the results of this thesis indicate that NS does not relate only to attitudinal or psychological factors but has biological underpinnings. Moreover, this thesis makes it evident that brain imaging is a promising way of studying the mechanism by which individuals are noise-sensitive and how that leads to impaired health.

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Appendix 1

# Helsinki Inventory of Music and Affective Behaviors English Version

This questionnaire is private. Please answer questions carefully by selecting and/or writing the correct answers. Please answer each question you're instructed to answer, even if the question seems redundant. Thank you!

## **Identification** (Hollingshead, 1975; Ukkola-Vuoti et al., 2013)

**1. Age:**

**Gender:**

☐ Male ☐ Female

**2. What is the highest level of education you have completed?**

**3. Education years (from the beginning of elementary school)**

**4. What is your current occupation?**

**5. Which of the following describe(s) you best? You may choose one or two answers.**

☐ Musician ☐ Amateur musician ☐ Dancer ☐ Amateur dancer ☐ None of the above

**6. Mother's age:**

**7. What is the highest level of education your mother has completed?**

**8. Mother's education years (from the beginning of elementary school)**

**9. What is your mother's current occupation?**

**10. Father's age:**

**11. What is your father's current occupation?**

**12. What is the highest level of education your father has completed?**

**13. Father's education years (from the beginning of elementary school)**

## **A. Musical training** (Ukkola-Vuoti et al., 2013) **and identification of amusia** (**8:** Peretz et al., 2008)

**1. Please list all of the musical educational experiences you've had.**

If you have never played any instrument or sung in a choir, please continue to question 5 in this section.

How old were you when you started playing music or singing?

How old were you when you started taking music lessons (if applicable)?

What is your highest level of musical education (e.g. a degree, an exam, years of lessons, etc.)?

**2a. Have you ever received compensation (e.g. money, food, drinks, etc.) for playing music or singing?**

☐ Yes ☐ No

**2b. How frequently do you perform (i.e., play, sing, or dance) for an audience?**

I perform music for an audience...

☐ Never
☐ Once a year
☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More often
☐ Professional

**3a. How many hours do you play/sing/practice music a day?** Average hours/day:

Nowadays:
Earlier (e.g. as a student):

**3b. If you play/sing/practice music less than daily, approximately how frequently do you play/sing/practice music?**

| Nowadays: | Earlier (e.g. as a student): |
|---|---|
| ☐ Never | ☐ Never |
| ☐ Once a year | ☐ Once a year |
| ☐ Once a month | ☐ Once a month |
| ☐ 2-3 times per month | ☐ 2-3 times per month |
| ☐ Once per week | ☐ Once per week |
| ☐ 2-3 times per week | ☐ 2-3 times per week |
| ☐ More often | ☐ More often |

**4. Which of the following describe(s) you the best?**

☐ Musician
☐ Musical enthusiast/amateur musician
☐ Dancer
☐ Dance enthusiast/amateur dancer

**Please write one or more musical genres that describe(s) your musical and/or dance status here:**

**4b. Using the following scale, please indicate one or more musical genres that describe(s) your musical and/or dance status.**

Does not describe me at all 1 --- 2 --- 3 --- 4 --- 5 --- 6 --- 7 Describes me very well

☐ Classical
☐ Blues
☐ Country
☐ Electronic music, techno
☐ Folk music
☐ Rap/hip-hop
☐ Soul/R&B
☐ Latin-American music
☐ Religious (gospel, hymns)
☐ Alternative
☐ Jazz
☐ Rock
☐ Pop
☐ Iskelmä (Finnish pop tunes)
☐ Heavy metal
☐ Music from movies and TV-series
☐ Punk
☐ World music
☐ Funk
☐ Other/s

**If you answered "Other/s," please write the style or styles of music you had in mind along with ratings for each one.**

**5. Do you enjoy performing (i.e. singing, playing music, or dancing) for other people?**

☐ No, I avoid situations where I have to perform.
☐ No, but I have to perform now and then.
☐ Yes, I enjoy performing for other people.
☐ Yes, performing motivates me.
☐ I have other reasons to avoid performing/to perform.

**If you answered "I have other reasons to avoid performing/to perform," please describe them here:**

**6. Do you dance, do music gymnastics, or some other exercise in time with music?**

I dance, do music gymnastics, or some other exercise in time with music...

☐ Never
☐ Once a year
☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More often
☐ Professional

**7a. Does anyone else in your family (i.e. grandparents, parents, siblings, cousins, etc.) have any musical experience?**

☐ Yes ☐ No

**7b. If you answered 'Yes,' please write the following for each family member with musical experience: relation to you, age, approximate years of musical training, years since last musical playing (write "0" if still playing), how often**

**he/she plays or played, musical degrees and school/s has, and any other information that might be relevant.**

For example:

"Father, 60, 30, 5, 10 hours per week, Bachelor's in music from Sibelius Academy, semi-professional drummer for 15 years.

Sister, 21, 10, 0, 6 hours per week, no music degrees, 5 years of singing and 10 years of trumpet."

**8. Please copy and paste the following URL into a new window of your web browser and complete the music test there.**

www.brams.umontreal.ca/amusia-new/

## B. Listening to music (adapted from Rentfrow & Gosling, 2003; Ukkola-Vuoti et al., 2013), absolute pitch test (9: Zatorre, 2003) and Seashore test for pitch and time (15-18; Seashore, Lewis, & Saetveit, 1960)

**1a. How often do you actively listen to music (attentive listening to music, including attending concerts)?** Average hours/week

During childhood about:
From ages 12 - 20 about:
From ages 21 - 30 about:
From ages 31 - 40 about:
From ages 41 - 59 about:
From ages 60 about:

**1b. If you actively listen to music less than weekly, approximately how frequently do you actively listen to music?**
Nowadays:
☐ Never ☐ Once a year ☐ Once a month ☐ 2-3 times per month
Earlier (e.g. as a student):
☐ Never ☐ Once a year ☐ Once a month ☐ 2-3 times per month

**2a. How often do you passively listen to music (hearing or listening to music as background music)?** Average hours/week

During childhood about:
From ages 12 - 20 about:
From ages 21 - 30 about:
From ages 31 - 40 about:
From ages 41 - 59 about:
From ages 60 about:

**2b. If you passively listen to music less than weekly, approximately how frequently do you passively listen to music?**

| Nowadays: | Earlier (e.g. as a student): |
|---|---|
| ☐ Never | ☐ Never |
| ☐ Once a year | ☐ Once a year |

☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More often

☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More often

**3. Please evaluate how important music is in your daily life.**

To me, music is... Not at all important 1 --- 2 ---3 --- 4 --- 5 --- 6 --- 7 Very important

**4. Do you recognize familiar melodies (like folk songs) well without lyrics?**

I recognize familiar music without lyrics...

☐ Never ☐ Rarely ☐ Sometimes ☐ Often ☐ Very often

**5. Do you think you are missing a sense of music?**

☐ Yes ☐ No

**6. Do you think you are musical (e.g. compared with your siblings, friends, and parents)?** If "Yes," write the strongest feature of your musicality.

☐ No
☐ Yes, and I think the strongest feature of my musicality is:

**7. Do you notice when someone sings out of tune?**

☐ Yes ☐ No

**8. Do you notice when someone plays a wrong note?**

☐ Yes ☐ No

**9. Please, click each of the following links to listen to and identify each note one at a time.**

Do not use any musical instrument or check your answers until you've identified all ten notes.

For each note, write down the pitch chroma and octave number (e.g. C4, G#3) that you think you just heard. Do not check your answers.

**10. Other music activities (choose the appropriate alternatives)**

☐ I compose music
☐ I arrange music
☐ I improvise music
☐ Something else

If you answered "Something else," please describe it here:

**11. Are you involved in any other artistic activities (e.g. drawing, painting, writing, sculpting, etc.)?**

If so, please write which one(s) and how often in the box below.

**12. How often do you compose music?**

I compose music...
☐ Never
☐ Once a year
☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More

**13. How often do you arrange music?**

I arrange music...
☐ Never
☐ Once a year
☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More

**14. How often do you improvise musically?**

I improvise...
☐ Never
☐ Once a year
☐ Once a month
☐ 2-3 times per month
☐ Once per week
☐ 2-3 times per week
☐ More

**15. Please, click each of the following links to listen to them. Is the second note higher or lower than the first note?**

Do not use any musical instrument or check your answers.

**16. Please, click each of the following links to listen to them. You will hear a series of note pairs. In each pair, is the second note high or lower than the first note?**

Do notuse any musical instrument or check your answers. Do not worry about being consistent in your responses.

**17. Please, click each of the following links to listen to them. Is the second note longer or shorter than the first note?**

Do not use any musical instrument or check your answers.

**18. Please, click each of the following links to listen to them. You will hear a series of note pairs. In each pair, is the second note longer or shorter than the first note?**

Do not use any musical instrument or check your answers. Do not worry about being consistent in your responses.

## C. Musical preferences (adapted from Rentfrow & Gosling, 2003)

**1a. Using the following scale, please indicate how much you enjoy the following musical styles overall. Please write a number after each musical style.**

Do not like at all 1 ------- 2 -------- 3 -------- 4 --------- 5 -------- 6 ------- 7 Like very much

☐ Classical
☐ Blues
☐ Country
☐ Electronic music, techno
☐ Folk music
☐ Rap/hip-hop
☐ Soul/R&B
☐ Latin-American music
☐ Religious (gospel, hymns)
☐ Alternative
☐ Jazz
☐ Rock
☐ Pop
☐ Iskelmä (Finnish pop tunes)
☐ Heavy metal
☐ Music from movies and TV-series
☐ Punk
☐ World music
☐ Funk
☐ Other/s

**1b. If you answered "Other/s," please write the style or styles of music you had in mind along with ratings for each one.**

**2a. Using the following scale, please indicate how familiar you are with the following musical styles. Please write a number after each musical style.**

Not at all familiar 1 ------- 2 -------- 3 -------- 4 --------- 5 -------- 6 ------- 7 Very familiar

☐ Classical
☐ Blues
☐ Country
☐ Electronic music, techno
☐ Folk music
☐ Rap/hip-hop
☐ Soul/R&B
☐ Latin-American music
☐ Religious (gospel, hymns)
☐ Alternative
☐ Jazz
☐ Rock
☐ Pop
☐ Iskelmä (Finnish pop tunes)
☐ Heavy metal
☐ Music from movies and TV-series
☐ Punk
☐ World music
☐ Funk
☐ Other/s

**2b. If you answered "Other/s," please write the style or styles of music you had in mind along with ratings for each one.**

**3. Please, list your three favorite songs (name and artist) below.**

Favorite song #1:
Favorite song #2:
Favorite song #2:

**4. What is your favorite music (music genre or favorite band/artist)?**

## **D. Music consumption** (Chamorro-Premuzic, Swami, & Cermakova, 2012)

**Using the scale below, please indicate how frequently you engage in each of the following activities.**

Very rarely 1 -------- 2 -------- 3 -------- 4 --------- 5 -------- 6 ------- 7 Very often

☐ I purchase music from online music stores (iTunes, 7digital, etc.)...
☐ I download music (free downloads) from internet sites...
☐ I share music (exchange, record, borrow) with friends or colleagues...
☐ I read about musicians' biographies (online/books/magazines)...
☐ I update my mp3 player with new music...
☐ I watch television programs or films about musicians...
☐ I attend musical concerts or recitals...
☐ I visit music shops with the idea of buying music...
☐ I play a musical instrument (including vocals)...
☐ I imagine myself performing the song I am listening to...

## **E. Uses of music** (Chamorro-Premuzic & Furnham, 2007)

**Using the scale below, please indicate the extent to which you agree or disagree with each of the following activities.**

Strongly disagree 1 ------- 2 -------- 3 -------- 4 --------- 5 -------- 6 ------- 7 Strongly agree

☐ Listening to music really affects my mood.
☐ I am not very nostalgic when I listen to old songs I used to listen to.
☐ Whenever I want to feel happy I listen to a happy song.
☐ When I listen to sad songs I feel very emotional.
☐ Almost every memory I have is associated with a particular song.
☐ I often enjoy analyzing complex musical compositions.
☐ I seldom like a song unless I admire the technique of the musicians.
☐ I don’t enjoy listening to pop music because it’s very primitive.
☐ Rather than relaxing, when I listen to music I like to concentrate on it.
☐ Listening to music is an intellectual experience for me.
☐ I enjoy listening to music while I work.
☐ Music is very distracting so whenever I study I need to have silence.
☐ If I don’t listen to music while I’m doing something, I often get bored.
☐ I enjoy listening to music in social events.
☐ I often feel very lonely if I don’t listen to music.

**Why do you listen to music or go to concerts?**

☐ I listen to music in order to relax or to feel good.
☐ I choose different kinds of music for different emotional states.
☐ I listen to music in order to study new pieces of music.
☐ I listen to music to concentrate better while working or studying.
☐ I have other reasons for listening to music.

If you answered "I have other reasons for listening to music," please, elaborate here:

## F. Music-directed attention scale (from Kantor-Martynuska & Fajkowska, in preparation)

**These questions regard listening to music at a medium volume. For each sentence, choose the answer that is more relevant to your experience. Respond quickly, according to the first decision that comes to your mind.**

| Agree | Disagree | |
|---|---|---|
| ☐ | ☐ | 1. When I eat out, music playing in the background is of no importance to me. |
| ☐ | ☐ | 2. I turn off my music and go out only after the piece of music I'm listening to has finished. |
| ☐ | ☐ | 3. When I have a difficult mathematics task to do, music disturbs me. |
| ☐ | ☐ | 4. Background music diverts my attention from what another person is saying to me. |
| ☐ | ☐ | 5. I don't mind if I have to stop a piece of music halfway through. |
| ☐ | ☐ | 6. When I eat, inappropriate music disturbs me. |
| ☐ | ☐ | 7. When I hear someone else’s music playing through his/her earphones, I can detach myself from the music if I want. |
| ☐ | ☐ | 8. When I have to write an essay, I do it with the music on. |
| ☐ | ☐ | 9. Even when I am concentrating on something, I like to have the music on. |
| ☐ | ☐ | 10. In a conversation, I can be distracted by music playing in the background. |
| ☐ | ☐ | 11. When I study for an exam, music playing in another room distracts me. |
| ☐ | ☐ | 12. When I hear music, I find it hard not to listen to it attentively |
| ☐ | ☐ | 13. I am more effective when I study in silence than with the music on. |

## G. Interpersonal reactivity index (Davis, 1983)

**The following statements inquire about your thoughts and feelings in a variety of situations. Using the following scale, indicate how well each item describes you by writing the appropriate**.

Does not describe me well 1 --- 2 ---3 --- 4 --- 5 --- 6 --- 7 Describes me very well

☐ I daydream and fantasize, with some regularity, about things that might happen to me.
☐ I often have tender, concerned feelings for people less fortunate than me.
☐ I sometimes find it difficult to see things from the "other guy's" point of view.
☐ Sometimes I don't feel very sorry for other people when they are having problems.
☐ I really get involved with the feelings of the characters in a novel.
☐ In emergency situations, I feel apprehensive and ill-at-ease.
☐ I am usually objective when I watch a movie or play, and I don't often get completely caught up in it.
☐ I try to look at everybody's side of a disagreement before I make a decision.
☐ When I see someone being taken advantage of, I feel kind of protective towards them.
☐ I sometimes feel helpless when I am in the middle of a very emotional situation.

☐ I sometimes try to understand my friends better by imagining how things look from their perspective.
☐ Becoming extremely involved in a good book or movie is somewhat rare for me.
☐ When I see someone get hurt, I tend to remain calm.
☐ Other people's misfortunes do not usually disturb me a great deal.
☐ If I'm sure I'm right about something, I don't waste much time listening to other people's arguments.
☐ After seeing a play or movie, I have felt as though I were one of the characters.
☐ Being in a tense emotional situation scares me.
☐ When I see someone being treated unfairly, I sometimes don't feel very much pity for them.
☐ I am usually pretty effective in dealing with emergencies.
☐ I am often quite touched by things that I see happen.
☐ I believe that there are two sides to every question and try to look at them both.
☐ I would describe myself as a pretty soft-hearted person.
☐ When I watch a good movie, I can very easily put myself in the place of a leading character.
☐ I tend to lose control during emergencies.
☐ When I'm upset at someone, I usually try to "put myself in his shoes" for a while.
☐ When I am reading an interesting story or novel, I imagine how I would feel if the events in the story were happening to me.
☐ When I see someone who badly needs help in an emergency, I go to pieces.
☐ Before criticizing somebody, I try to imagine how I would feel if I were in their place.

## H. **Weinstein's noise sensitivity scale** (Weinstein, 1978)

**The following statements describe different attitudes towards noise. Using the scale below, please indicate the extent to which you agree or disagree with each one.**

I strongly agree 1 --- 2 ---3 --- 4 --- 5 --- 6 --- 7 I strongly disagree

☐ I wouldn't mind living on a noisy street if the apartment I had was nice.
☐ I am more aware of noise than I used to be.
☐ No one should mind much if someone turns up his stereo full blast once in a while.
☐ At movies, whispering and crinkling candy wrappers disturb me.
☐ I am easily awakened by noise.
☐ If it's noisy where I'm studying, I try to close the door or window or move somewhere else.
☐ I get annoyed when my neighbours are noisy.
☐ I get used to most noises without much difficulty.
☐ How much would it matter to you if an apartment you were interested in renting was located across from a fire station?
☐ Sometimes noises get on my nerves and get me irritated.
☐ Even music I normally like will bother me if I'm trying to concentrate.
☐ It wouldn't bother me to hear the sounds of everyday living from neighbours (footsteps, running water, etc.).
☐ When I want to be alone, it disturbs me to hear outside noises.
☐ I'm good at concentrating no matter what is going on around me.

☐ In a library, I don't mind if people carry on a conversation if they do it quietly.
☐ There are often times when I want complete silence.
☐ Motorcycles ought to be required to have bigger mufflers.
☐ I find it hard to relax in a place that's noisy.
☐ I get mad at people who make noise that keeps me from falling asleep or getting work done.
☐ I wouldn't mind living in an apartment with thin walls.
☐ I am sensitive to noise.

## I. Family psychiatric history

**Does anyone in your family (i.e. grandparents, parents, siblings, cousins, etc.) have any psychiatric or neurological diseases or disorders?**

☐ Yes ☐ No

If you answered 'Yes,' please write the following for each family member with a psychiatric or neurological disorder or disease: relation to you, age, name of the disorder/disease, approximate years of the disorder/disease, and any other information that might be relevant.

For example:
"Father, 58, clinical depression, 40 years, sometimes medicates with SSRIs."

## J. Screening

**1. Do you regularly use tobacco products?**

☐ Yes ☐ No

If so, how much do you use, and how often?

**2. Do you regularly drink coffee or other caffeinated beverages?**

☐ Yes ☐ No

If so, how much do you use, and how often?

**3. Are you currently taking any medication?**

☐ Yes ☐ No

If so, please provide the specific medications and doses:

Please list any medications and doses you have used in the past month:

**4. Have you ever experienced a head trauma resulting in a loss of consciousness or been diagnosed with a neurological impairment or illness?**

☐ Yes ☐ No

If so, describe here:

## K. Feedback

**Please answer the following questions about your experience in this study.**

Very bad 1 ------- 2 -------- 3 -------- 4 --------- 5 Very good

☐ How would you rate your experience in this study?
☐ Would you come back to BioMag for more MEG-EEG experiments?
☐ Would you come back to AMI for more fMRI experiments?
☐ How bothersome was the scanner noise during the fMRI experiment?

**Please answer the following questions about your experience in this study.**

Not serious/No concentration 0 ----- 100 Very serious/High concentration

☐ How seriously were you willing to participate in this questionnaire?
☐ What was your level of concentration during this questionnaire?

**Do you have any comments about this experiment? Please, write your feedback here:**

**Thank you for your participation!**

Approximately, how long did it take you to complete this inventory?

Thank you!