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Exploring the middle ear function in patients with a cluster of symptoms including tinnitus, hyperacusis, ear fullness and/or pain

Philippe Fournier^{1,2}, Dany Paleressompoulle¹, Marie-José Esteve Fraysse³, Fabien Paolino⁴, Arnaud Devèze^{4,5}, Frédéric Venail⁶, Arnaud Noreña¹

¹- Centre national de la recherche scientifique (CNRS), Université d'Aix-Marseille, Centre St-Charles-Pôle 3C, Marseille, France

²- School of Rehabilitation, Faculty of Medicine, Université Laval, Québec, QC, Canada

³- Service d'Oto-Rhino-Laryngologie, d'Oto-Neurologie et d'ORL Pédiatrique, Centre Hospitalier Universitaire de Toulouse, Place du Dr Baylac

⁴- ORL and Skull Base Surgery, Clairval Hospital, Ramsay GDS Health Care, Marseille, France

⁵- Laboratory of Biomechanism, IFSTTAR UMR T24, Faculty of Medicine Nord, Aix Marseille University, Marseille, France

⁶- Centre Hospitalo-Universitaire de Montpellier, Montpellier, France

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Correspondence should be addressed to:

Dr. Arnaud Noreña

Aix-Marseille Université - Laboratoire Neurosciences Cognitives –
ST CHARLES - Case B - 3 Place Victor Hugo - 13003 Marseille

Tél: +33(0)4 13 55 08 65

Email: arnaud.norena@univ-amu.fr

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Philippe Fournier ^{1,2}

Dany Paleressompouille ¹

Marie-José Esteve Fraysse³

Fabien Paolino ⁴

Arnaud Devèze ^{4,5}

Frédéric Venail ⁶

Arnaud Noreña ¹

¹- Centre national de la recherche scientifique (CNRS), Université d'Aix-Marseille,
Centre St-Charles-Pôle 3C, Marseille, France

²- School of Rehabilitation, Faculty of Medicine, Université Laval, Québec, QC, Canada

³- Service d'Oto-Rhino-Laryngologie, d'Oto-Neurologie et d'ORL Pédiatrique, Centre
Hospitalier Universitaire de Toulouse, Place du Dr Baylac

⁴ ORL and Skull Base Surgery, Clairval Hospital, Ramsay GDS Health Care, Marseille,
France

⁵- Laboratory of Biomechanism, IFSTTAR UMR T24, Faculty of Medicine Nord, Aix
Marseille University, Marseille, France

⁶- Centre Hospitalo-Universitaire de Montpellier, Montpellier, France

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Correspondence should be addressed to:

Dr. Arnaud Noreña

Aix-Marseille Université - Laboratoire Neurosciences Cognitives –

ST CHARLES - Case B - 3 Place Victor Hugo - 13003 Marseille

Tél: +33(0)4 13 55 08 65

Email: arnaud.norena@univ-amu.fr

ABSTRACT

Middle ear muscle (MEM) abnormalities have been proposed to be involved in the development of ear-related symptoms such as tinnitus, hyperacusis, ear fullness, dizziness and/or otalgia. This cluster of symptoms have been called the Tonic Tensor Tympani Syndrome (TTTS) because of the supposed involvement of the tensor tympani muscle (TTM). However, the putative link between MEM dysfunction and the symptoms has not been proven yet and the detailed mechanisms (the causal chain) of TTTS are still elusive. It has been speculated that sudden loud sound (acoustic shock) may impair the functioning of the MEM, specifically the TTM, after an excessive contraction. This would result in inflammatory processes, activation of the trigeminal nerve and a change of the MEMs state into a hypersensitive one, that may be associated to the cluster of symptoms listed above. The goal of this study is to provide further insights into the mechanisms of TTTS. The middle ear function of 11 patients who reported TTTS symptoms has been investigated using either admittanceometry and/or measurement of air pressure in the sealed external auditory canal. While the former method measured the middle ear stiffness the latter provides an estimate of the tympanic membrane displacement. Most patients displayed results consistent with phasic contractions of the TTM (n=9) and/or Eustachian Tube (ET) dysfunction (n=6). The MEM contraction or ET dysfunction could be evoked by acoustic stimulation (n=3), somatic maneuvers (n=3), or pressure changes in the ear canal (n=3). Spontaneous TTM contraction (n=1) or ET opening (n=1) could also be observed. Finally, voluntary contraction of MEM was also reported (n=5). On the other hand, tonic contraction of the TTM could not be observed in any patient. The implications of these results for the mechanisms of TTTS are discussed.

Keywords: Tensor Tympani, Stapedius Muscle, Tensor Tympani Syndrome, Middle ear, Acoustic shock, Hyperacusis, Otalgia, Middle ear myoclonus

INTRODUCTION

The middle ear's main function is to improve the transmission of the sound to the cochlea by adapting the impedance difference between air and cochlear liquid, mainly through the surface difference between the tympanic membrane and the stapes (Møller, 1963). In brief, the middle ear is a cavity filled by air and containing the tympanic membrane and the ossicles (malleus, incus and stapes). The ossicles are maintained by ligaments and are connected to two skeletal muscles: the stapedius muscle (SM), of 6 mm in length, attached to the stapes and the tensor tympani muscle (TTM), of about 25 mm, attached to the neck of malleus (Mansour et al. 2013). The SM and the TTM are innervated by the facial nerve and the trigeminal nerve, respectively (Loeb 1964; Mansour et al. 2013). The SM contracts to sound and to vocalization (Møller 1984). The TTM is activated by face stroking, airpuffs against the eyes, electrical stimulation of the tongue, swallowing, head movements and cutaneous stimulation (Salomon and Starr 1963). While TTM does not usually contract in response to sound (Jones et al. 2008; Fournier et al., submitted), it can be triggered by a sound if it activates a startle response (Klockhoff, Ingmar and Anderson, Henry 1960). There is no consensus regarding the function of these muscles, but as they both reduce sound transmission from the middle ear to the cochlea, it can be speculated that they both play a role in the protection of the ear against loud noises (Bell 2011; Noreña et al. 2018; Tschiasny 1949).

Middle ear muscle (MEM) abnormalities have been hypothesized to be involved in the development of ear-related symptoms (Klockhoff, Ingmar 1979; Londero et al. 2017; Noreña et al. 2018; Pau et al. 2005; Westcott et al. 2013). More specifically, Klockhoff (1979) proposed that tonic contraction of the TTM can result in the so-called ‘‘tonic tensor tympani syndrome (TTTS)’’. The most common aural symptoms of TTTS are fullness in the ear which is sometimes painful (83%), tinnitus which is sometimes pulsating (62%) and dysacusis with various abnormal acoustic sensations including sound distortion (42%). Tension headaches and dizziness are also very prevalent symptoms ($\geq 80\%$) (Klockhoff, Ingmar 1979). Klockhoff (1979) proposed that tonic TTM contraction can be observed with admittanceometry: «...impedance in those patients is not constant over prolonged recording, which is ordinarily the case, but fluctuates appreciably, quite

irregularly and rather slowly.» Interestingly, it was noted that small changes in the air pressure such as 3 mm H₂O resulted in change of admittance that would require at least 25 mm H₂O pressure in a normal ear. This was again interpreted as a sign of TTM tonic state in those patients. It is important to mention, however, that TTTS is not clearly established and that part of the scientific community doubt its existence (Bance 2019).

Recently, a model has been proposed speculating further about the putative role of the TTM in generating the symptom cluster (Noreña et al. 2018). The authors suggested that TTM overuse (due to the acoustic shock, for example, but not only), TTM overload (due to muscle tension), and TTM injury (due to hypoxia and "energy crisis") could lead to inflammation, thereby activating the trigeminal nerve, the trigeminal cervical complex and ultimately the central nervous system, including the cortex (Noreña et al. 2018). The dysfunctional TTM may be in a hypersensitive and/or hyperactive state. In hypersensitive state, it may be hyper-reactive (with a reduced contraction threshold) to a broad range of stimulation such as sound stimulation, pressure change, somatic maneuvers and/or emotional shock. In the hyperactive state, the spontaneous tonus of the TTM is enhanced either tonically or sporadically (leading to phasic contraction or myoclonus).

Phasic middle ear muscle contractions (MEMCs) (or myoclonus) have been reported in many case reports including men and women of different ages such as children, teens, adults and the elderly (Abdul-Baqi 2004; Badia, Parikh, and Brookes 1994; Bance 2019; Brigo et al. 2013; Dang and Carol Liu 2019; Ellenstein, Yusuf, and Hallett 2013; Freund 1956; Hornibrook and Keast 2019; Howsam et al. 2005; Kim et al. 2013; Kwee and Struben 1972; Lee et al. 2012; Oliveira et al. 2003; Phillipps et al. 1989; Rajah 1992; Rock 1995; Salehi et al. 2019; Watanabe, Kumagami, and Tsuda 1974; Zipfel, Kaza, and Greene 2000). The most common comorbid symptom is ear fullness/pressure in the myoclonus ear (Abdul-Baqi 2004; Badia et al. 1994; Ellenstein et al. 2013; Kwee and Struben 1972; Zipfel et al. 2000). Comorbid hearing deterioration and pain in the myoclonus ear have also been reported (Hearing: Abdul-Baqi 2004; Watanabe et al. 1974, Pain: Badia et al. 1994; Ellenstein et al. 2013). These contractions are usually spontaneous and uncontrollable in nature but there have been reports of particular cases of MEMC only triggered by forceful eyelid closure, a phenomenon that has been called

Forceful Eyelid Closure Syndrome (FECS) (Kim et al. 2013; Lee et al. 2012; Rajah 1992; Rock 1995). A large variety of low and high-frequency sounds including dialing tones, fax machines, singing birds and particular pieces of music have been reported to trigger myoclonus episodes (Badia et al. 1994).

Phasic MEMCs can cause a movement of the eardrum that can be visually observed under otoscopy or microscopy (Abdul-Baqi 2004; Brigo et al. 2013; Hornibrook and Keast 2019; Howsam et al. 2005; Kim et al. 2013; Kwee and Struben 1972; Oliveira et al. 2003; Rajah 1992; Zipfel et al. 2000). Impedance modifications described as “admittance peaks” synchronous with the report of click symptoms can also be reported when the contractions are observed under microscopy/otoscopy (Dang and Carol Liu 2019; Howsam et al. 2005; Kwee and Struben 1972; Oliveira et al. 2003; Rajah 1992; Zipfel et al. 2000). Finally, phasic MEMC can be objectivated using a device measuring the pressure in the sealed external auditory canal (EAC). Indeed, assuming that the tympanic membrane displacement is the main factor changing the EAC volume, an inward or outward movement of the tympanic membrane increases or decreases the EAC volume and hereby decreases or increases the pressure in the EAC, respectively. Since the TTM is attached to the malleus, TTM contraction generates an eardrum retraction (inward displacement) and thus results in a negative pressure in the sealed EAC (Phillipps et al. 1989). This technique of recording pressure change in the sealed EAC was recently validated on 14 normal ears following auditory stimulation and 8 ears with voluntary MEMC control (vMEMC) (Fournier et al, submitted).

The objective of the present case series was to assess the presence of phasic and/or tonic MEMC in 11 patients reporting symptoms consistent with TTTS and/or MEM dysfunction. The current evaluation included either, admittanceometry, EAC air pressure measurement or both. The etiology, the triggers and modulators of the symptoms including somatic maneuvers and sounds were recorded from patients and were used to trigger the MEMC. The tests were personalized to each patient and depended on their symptoms, their time availability and the equipment at our disposal. We also assessed if the patients could voluntarily contract their MEM and the impact of those contractions on their symptoms.

METHODS

Patients:

The patients were referred to us by ENT doctors from very diverse regions of France (including Marseille where our laboratory is located) to assess the ME function in patients in whom ME was suspected to be the putative source of their symptom cluster (tinnitus, hyperacusis, ear fullness, pain etc.). In most cases, all the routine clinical tests came out negative and no satisfactory explanations could be provided about the source of the symptoms. This study focused on eleven patients (mean age: 35 y.o., M/F: 9/2): their sociodemographic characteristics, their primary concerns and the presumed etiology of their symptoms are presented in Table I. The most prevalent primary concerns were tinnitus, hyperacusis, otalgia and clicking-popping-spasms in the ear. Acoustic shock and/or trauma was the most reported etiology but stress, ear surgery, sudden single sided deafness (SSSD) in the contralateral ear and adverse reaction to medication were also mentioned. The characteristics of patients' ears including the static tympanometry results and hearing thresholds are presented in table II. Most patients reported symptoms in only one ear (n=5) or both ears but with one ear being more symptomatic (n=4) and only two patients reported similar symptoms in both ears.

Most ears tested with the static tympanometry test displayed results suggestive of a normal mobility of the tympano-ossicular chain (type A tympanogram) (Jerger 1970). Most patients displayed normal hearing: two patients displayed hearing loss across low, mid and high frequencies bilaterally (#2 & #5) and one patient had normal hearing in one ear and profound hearing loss in the other ear (#7). For all the patients, the frequency of occurrence of each symptom associated with TTTS is presented in Table III. The most reported symptoms are tinnitus, hyperacusis and ear fullness. Additionally, the modulation of tinnitus intensity by somatic maneuver is presented in Table IV. The most prevalent tinnitus modulation by somatic maneuvers is an increased in intensity upon jaw protrusion and contraction. For patient #9, all the somatic maneuvers increased tinnitus intensity.

Materials:

Audiometry

Hearing thresholds (HT) were assessed monaurally, for both ears, by presenting pure tones from 250 to 8 kHz by half-octave steps using the conventional clinical procedures using Sennheiser HDA-300 connected to an Astera audiometer (Natus Medical; formerly Otometrics, Denmark) (Harrell 2002). Loudness discomfort levels (LDLs) were assessed monaurally in some patients with the same equipment and earphones, for both ears, by first presenting a pure tone 5 dB above the threshold and then increasing the level by 5 dB steps until the patient judges the sound uncomfortable. Patients were specifically advised not to reach their pain threshold. Both the hearing thresholds and the loudness discomfort levels were performed in a soundproof room.

Tympanometry

All the tympanometry measurements were recorded in a soundproof room or a quiet office using the Madsen Zodiac (Natus Medical, formerly Otometrics, Denmark). For all tympanometry measurements, a probe was inserted in the external ear until a good airtight seal was achieved. For static tympanometry, the pressure scale was set from -400 to 200 daPa, and the sound probe was set at 226 Hz. The patient is asked not to move and swallow during the measure. The pressure is modified quickly (200 daPa per sec) from positive to negative pressure, and the admittance of the 226 Hz probe tone is recorded. Stapedius reflex thresholds are tested using tonal stimuli of 0.5, 1, 2 kHz of 2.4 seconds' duration in ipsilateral conditions for both ears (5.5 ms fall/rise time). The presentation level started at 60 dB HL and increased by 5 dB steps until a .02 ml change in admittance was automatically detected twice at the same level.

The Madsen Zodiac's Y-recorder option was used for continuous recordings of admittance change with the frequency probe set at 226 Hz or 1 kHz in some case. This feature allows for continuous recording of admittance for 30s. The Y-recorder feature allows modification of the air pressure inside the EAC by an amount of +/- 50 daPa. Recordings were made under two different EAC pressure conditions: 0 and -50 daPa. This modification in EAC pressure had been made available to improve the acoustic stapedius reflex threshold measurements in ears with high static acoustic admittance: in

those cases, stapedius reflex thresholds are detected at lower stimulation level with -50 daPa EAC pressure compared to normal EAC pressure (0 daPa) (Atcherson and Stoody 2011; DiGiovanni and Ries 2007). Some patients were asked to produce vMEMC every 5s during the recording.

Air pressure sensor

A device to measure the air pressure inside the EAC when it is airtight sealed has been developed and validated (Fournier et al, submitted). The pressure sensor is fully calibrated and temperature compensated for sensor offset, sensitivity and temperature effects. The pressure range measured by the sensor is ± 498.16 Pa and the noise floor is below 5 Pa. The use of the device is briefly reported here. The EAC was airtight sealed using an admittance ear tip connected to a pressure sensor by a plastic tube of 10 cm in length. The sensor was connected to an Arduino that was connected to a computer. The MegunoLink software (Number Eight Innovation Limited, New Zealand) allowed visualization and data recording. The contralateral stimulation was presented through Sennheiser HD-600 supra-auricular headphones connected to a Sound Blaster X-fi HD model SB1240 sound card. It was previously shown that TTM and SM contractions have opposite effects on the tympanic membrane, i.e., retraction and extrusion, respectively. These modifications are observable by negative and null/positive air pressure, respectively (Fournier et al. submitted). The pressure recording offers several advantages over the admittance recording particularly important for testing hyperacusis patients: 1) it does not require the presentation of a sound and 2) it can be obtained simultaneously in both ears.

Evaluation of somatic modulation of tinnitus

The modulation of tinnitus intensity by different somatic maneuvers was systematically performed for all the patients except two (#3, #6). At the beginning of the evaluation, the patient was asked to rate on a scale from 0 to 10 the current intensity of their tinnitus (0 = no tinnitus to 10 = maximum tinnitus intensity). The experimenter then demonstrated the first maneuver to the patient, and he was asked to reproduce it. The

image representing the different maneuver is provided in Supplementary Figure 1. The movement mainly consisted of the head, jaw and eye movements (see Table III). If the tinnitus intensity was modified during the maneuver, the patient was asked to rate the modification using the same numerical scale as the baseline measurement.

Hyperacusis Diagnostic Test

Hyperacusis was diagnosed using a newly validated test developed at the lab and described in a previous study (Enzler, Fournier, and Noreña 2021). In brief, the patient sat in front of a computer screen and wore Sennheiser HD-600 supra-auricular headphones connected to a Sound Blaster X-fi HD model SB1240 sound card. In this test, natural and artificial sounds (n=69) are presented incrementally at four different levels (i.e., 60, 70, 80 and 90 dB SPL). After each sound presentation, the patient is asked to rate the sound heard on a pleasant to unpleasant visual analog scale using the computer mouse. The response could be given at any position on the scale by a click of the mouse. Once the sound was rated, the patient decided when to start the next trial by pressing the space bar. The system was calibrated with a Type 4230 sound level calibrator (Bruel & Kjaer), Type 2804 microphone power supply (Bruel & Kjaer), Type 4191 free-field ½-inch microphone (Bruel & Kjaer) and a custom-made artificial ear (designed from the specifications of the Type 4152 artificial ear and the DB 0913 6cc coupler of Bruel & Kjaer). Patients' ratings for each sound were compared to normative values obtained in Enzler et al. (2021). More so, by using the rating on seven very specific sounds called the Core discriminant Sounds (CDS), it was possible to diagnose hyperacusis. Based on the overall rating of these seven sounds for each intensity, a global score called the CDS Score is used to determine if a patient score is higher than the normative value for each sound intensity. If so, the patient is considered suffering from loudness hyperacusis.

Procedure

The patients first completed a questionnaire regarding their symptomatology followed by a hearing test, including hearing thresholds and loudness discomfort levels.

Some patients who reported "loudness hyperacusis" as part of their symptoms were also tested with the "hyperacusis diagnostic test" developed at the lab (Enzler et al. 2021). Finally, the middle ear tests were adapted to each patient's condition and symptoms, including the continuous admittance recording and the air pressure sensor. For example, MEMCs were assessed following somatic maneuvers for the patient reporting a high level of tinnitus intensity modulation by these maneuvers. The "Comité de Protection des Personnes Nord Ouest IV" review board approved this research. Reference number: 2018 A01183 52.

RESULTS

All patients are first described individually in details in the text below. We chose to group the patients as a function of the characteristics of the symptoms. The results collected in patients with symptoms that are triggered spontaneously are shown in Figure 1-2 (patients #1 and #2, respectively). The results obtained in patients with symptoms triggered by sound stimulation are shown in Figure 3-4 (patients #3 and #4, respectively) and Figure 6 (patient #5). The results obtained in patients with symptoms triggered by pressing trigger points on the face or neck are shown in Figure 5 (patients #3 and #6). The results obtained in patients with symptoms triggered by somatic maneuvers are shown in Figure 6 (patients #5, #7 and #8) and Figure 7 (patient #9). Figure 8 shows the static admittance, vMEMC and MEMC evoked by eye blinking in patient #10. Figure 9 shows the results obtained in patient #11 who underwent a surgery of the TTM. A summary of this symptom classification per patient is provided in Table V.

1. Spontaneous changes in the middle ear

- *Patient #1*

This patient reported MEM spasms only in his LE that started a year and half ago during a stressful period. He reported that he could feel the muscle contraction in his ear that he described as a spasm. This sensation came along with a noise. These contractions were spontaneous, and no triggers were identified: movements of the head, neck, jaw, eyes didn't have any triggering effect, nor sounds. The duration of the symptom was also random: it could last a few days or a few minutes in a day. In addition, he reported a tinnitus most audible at night and ear fullness in the RE. He had passed many clinical exams: CT angiography of the neck vessels, magnetic resonance imaging, cervical spine x-ray, high resolution CT scan of the temporal bone, cerebral angiography, hearing tests and an eustachian tube test (tubanometry). None of these tests revealed significant abnormalities. On the day of his visit at the lab, he had spasm symptoms in the LE. Both middle ears displayed normal mobility of the tympano-ossicular chain (Table I) and the stapedial reflex thresholds measured in both ears were normal (≤ 95 dB HL for 0.5, 1 & 2 kHz). The air pressure sensor was used to assess the spontaneous spasms in this patient:

he was asked to sit quietly without moving and only raise his left finger every time he had an episode of spasm. The top and bottom panel of Figure 1 display two different episodes of the spasm. In the first episode, he described the beginning of the symptom as a hail of machine gun and a few sparser gun shots thereafter only in his LE. The description of this episode completely fits with the very quick and successive negative pressure deflections seen at the beginning of the air pressure recording and the sparser few peaks thereafter. In the second episode, he only reported quick and successive spasms. These results suggest that the TTM is involved in the spontaneous phasic MEMC in this patient (see discussion).

- Patient #2

This patient had spontaneous audible clicks coming out of his RE, and this new phenomenon appeared right after the RE surgery for otosclerosis. The surgery for otosclerosis (called “stapedectomy”) involves cutting the stapedius muscle and removing the stapes bone. The clicks were audible by the experimenter at one meter distance. There was no sound coming out of his LE. This disabling symptom was accompanied by ear fullness, pain around the ear, heat pain and needle pain in the ear (Table III). He also reported constant tonic contraction of the right masseter and tension in his RE. He had a mild hearing loss in his LE and a mild to moderate hearing loss from 2 to 8 kHz in the RE (Table I). The admittance recordings showed very sharp positive and negative peaks of admittance (<100 msec) in his RE and a much more stable signal on his LE (Figure 2, left panel). These peaks were time-locked with the audible clicks produced by the patient even with the probe inserted in his ear. Interestingly, the occurrence of these peaks was enhanced by adding a negative pressure inside the auditory ear canal (-50daPa) and by jaw contraction. The contraction of the jaw also produced a long decline of admittance that develops over time. The pressure sensor recordings showed sharp and very small pressure changes (positive or negative) that may correspond to the peaks observed with admittance (Figure 2, right panel).

2. Changes in the middle ear evoked by sound

- Patient #3

The symptoms of hyperacusis and spasm in the RE started three years ago after an adverse reaction to an antibiotic, fluoroquinolone. The adverse reaction included visual floating body, skin problems, neuromuscular disorder, ear fullness, hyperacusis and spasms in the RE. The neuromuscular problems became so severe that it led to difficulties in walking and to a loss of sensibility of his limb suggestive of neuropathy. The most painful sounds reported by the patient were the noise of dishes that bangs against each other. The spasm is reported to be triggered by talking, by impact sounds (like pen drops), by pressing the temples (see Figure 5) and by introducing a finger in the ear. The symptoms are only affecting the RE, the LE is considered normal. The EAC air pressure assessment revealed negative peaks of pressure in the RE triggered by pen dropping on a table (LE was opened) (Figure 3). This result suggests that TTM contraction is triggered by sound stimulation. Interestingly, TTM contraction is likely triggered through LE stimulation since the RE is blocked by the plug of the sensor pressure. This patient was also able to produce vMEMC. One notes that the amplitude of vMEMC is much larger than the one evoked by sound stimulation.

- Patient #4

The cluster symptoms started at the age of 18-19 years-old following attendance to a loud concert. The cluster of symptoms include a sensation of vibration of the eardrum, popping of the ear, ear fullness, a low frequency tinnitus, hyperacusis and pain that mostly affect the RE. These symptoms are triggered mostly by sound and by talking and is not instantaneous, it requires a few seconds (10-15 seconds) before it appears. In addition, the perception of sound is reported as completely distorted upon the symptoms. The symptoms usually stop 4 to 5 seconds following the offset of the trigger. The most irritating sound are metallic sounds and noise of dishes. The patient was worried because of recent exacerbation of the symptoms. At the laboratory, admittance and EAC air pressure recordings with different sounds were tested. The sound of a baby crying at three different intensities (70, 75 and 80 dB SPL) was used to trigger the symptoms

(since it was reported as a sound trigger) (Figure 4). No symptoms were triggered during the reflex decay test and near-normal reflex decay was observed when a 500 Hz tone at 101 dB SPL was presented (Figure 4, left panel). At 70 dB SPL, a clear negative admittance deflection was seen during the presentation of the baby crying sound. The patient reported an uncomfortable sensation around 12 seconds of recording, which corresponded to sharp changes in admittance. The sound of 2 sec duration was played in a loop with a few hundred msec of silence. At 75 dB SPL all the symptoms of vibration, ear fullness, low frequency tinnitus and pain appeared at around 18 sec of the recording. The occurrence of the symptom cluster was coincidental with “instability” in the admittance recording. A similar phenomenon appeared earlier at 80 dB SPL (around 10 sec), with even more intense instability than the one seen at 75 dB SPL. Moreover, at 75 and 80 dB SPL, the reduction of admittance persists even after the sound is turned off.

The same stimulation, i.e. baby crying sound, was used (at 75 dB SPL) with the pressure sensor (Figure 4, right panel). Positive pressure was observed during the stimulation, suggesting that the SM was contracted for this type of stimulation and was producing an extrusion of the eardrum (Fournier et al., submitted). In addition, a negative deflection was seen for both recordings, one during the presentation of the sound and one after the presentation of the sound suggesting TTM contraction. These results suggest that both the TTM and SM are involved in the sound distortion phenomenon.

3. Changes in the middle ear evoked by pressing trigger points

Figure 5 shows the two patients (#3 and #6) in whom pressing trigger points on the head-neck complex triggered sharp decrease in EAC pressure. Patient #3 has been described above (symptoms result from an adverse reaction to an antibiotic). This patient reported spasms in the ear when he pressed the left or right temple. Interestingly, each time the patient was pressing the left or right temple, a sharp decrease of the EAC pressure was observed, suggesting that a sharp contraction of the TTM was triggered. One also notes on patient #3, slow fluctuations of the EAC pressure that may be related to breathing, suggesting that the ET is opened.

Patient #6 was referred to the laboratory for popping and pain sensation in his LE following an acoustic shock: he was driving his car while a loud sound produced a startle reflex response. Two days following the shock he reported tremors in his LE, pain in the external auditory canal including spontaneous needle pain sensation. This tremor is triggered by object falling on the floor. He has bilateral tinnitus: it was low frequency pitch in the RE and a high pitch in the LE. He reports pressure within the ear and the head. He reports loudness hyperacusis bilaterally of either very low or very high frequencies. He was able to produce the tremor in his left ear by voluntary contraction and by pressuring a specific region of his neck as well as his left temporomandibular joint (TMJ). This was attested by negative air pressure peaks during vMEMC and upon pressure of trigger points located in the neck and the TMJ (Figure 5). The negative pressure peaks suggest the involvement of TTM contraction in both vMEMC and MEMC by pressure on trigger points. To note, there was no pressure peaks and tremor symptom when the pressure was applied in a zone adjacent to the trigger point of the neck. The air pressure measured in the right ear presents a sawtooth aspect: it reflects the tympanic membrane movement due to heart beats at around 1Hz.

4. Changes in the middle ear evoked by somatic maneuvers

Figure 6 shows three patients (#5, #7 and #8) in whom symptoms are modulated by somatic maneuvers. They all reported loudness hyperacusis, defined as a reduced tolerance to loud sound (Table III) and they all scored highly on the Khalfa hyperacusis questionnaire with a total score of 32, 35 and 37, for patients #5, #7 & #8 respectively. These scores were consistent with loudness hyperacusis (Fackrell et al. 2015; Khalfa et al. 2002).

- Patient 5

Patient #5 suffered from tinnitus, hyperacusis and otalgia in both ears after being exposed to a sound blast during a music concert. At the time of the experiment, he still had tinnitus bilaterally and suffered from loudness hyperacusis and sound-induced pain. He reported that the symptoms were more important in his RE. He had mild hearing loss

bilaterally with normal loudness discomfort levels in the LE but reduced LDL in the RE mainly for the high frequencies (6 & 8 kHz). The ratings on the hyperacusis test confirmed its presence (Enzler et al., 2021) (Supplementary Figure 2).

We observed that admittance was unstable over time (increased slowly) when the patient contracted his jaw (Figure 6, left panels). Moreover, the patient reported a burning sensation in his RE after performing the hyperacusis test. With his approval, we measured the continuous admittance in both of his ears while the burning sensation symptom was present and observed middle ear instability in the RE (Figure 6). This MEM instability was reduced at the second measurement when the burning sensation was lowered and completely disappeared after the burning sensation had ceased.

For patient #7, the symptoms occurred following a sudden single sided deafness (SSSD) in her contralateral ear. She reported that a pre-existent hyperacusis in her RE was exacerbated by the SSSD in the LE. She had reported multiple symptoms with pain in the ear and hyperacusis being the most severe symptoms. The hyperacusis test has been performed at 60 dB SPL but had to be stopped because of the severeness of the hyperacusis.

For patient #8, the etiology of the symptoms is exposure to loud sound. This patient suffered from tinnitus, hyperacusis and ear fullness after several days of exposure to loud power tools noises during renovations. At the time of the experiment, she still reported constant tinnitus, hyperacusis and sensation of vibration in her ear triggered by some specific sounds such as the wind. Both ears were equally affected. She had completely normal hearing thresholds bilaterally, and the binaural LDLs measured at 4, 6, and 8 kHz were within normal values. The rating scores on the hyperacusis test (Enzler et al., 2021) are shown in Supplementary Figure 2.

The continuous admittance recording was first assessed for each ear at rest. Then, the same measurement was performed during (and after) jaw contraction: the patient was asked to contract masseter muscle just before the beginning of the measurement and to keep them contracted for the time of the measurement (30s) (Figure 6). For patients #5 and #7, this maneuver resulted in admittance instability (increased admittance) for their

most symptomatic ear, their RE. During the rest period just after the jaw contraction, patient #7 showed admittance fluctuations that is consistent with the respiration rate: this result suggests that the jaw contraction led to an opening of the Eustachian tube only in her symptomatic ear. On closer examination, slow fluctuations compatible with respiration can also be observed in patients #5 and #7 during jaw contraction. Static admittance obtained in patient #7 showed sharp positive and negative peaks.

For patient #8, both the LE and the RE showed signs of middle ear instability during jaw contraction, decreased and increased admittance, respectively. In this patient, sharp variations of admittance were superimposed on slower variations. The fast and slow changes in admittance are likely resulting from different processes (see discussion). Patient #8 was also able to contract her MEM voluntarily in both ears: she reported that the sensation of vibration in her ears felt spontaneously was like the kinesthetic sensation triggered by vMEMC. Interestingly, vMEMC was associated with an increase in admittance (Figure 6). Patients #5 and #7 were not able to voluntarily contract their MEM.

Figure 7 shows the results obtained in patient #9. This patient has bilateral tinnitus but louder in the RE. Increase in tinnitus intensity in that ear was reported to be sometimes associated with a vibration in his ear. This patient had normal hearing thresholds bilaterally from 0.25 to 8 kHz and a mild hearing loss for the higher frequencies (> 8 kHz) in both ears. His LDLs were abnormally low in both ears but even more for the RE. The LDLs were measured at 70 dB HL for 1, 2 & 4 kHz and 65 dB HL for 8 & 12 kHz for the RE and 85, 75, 70, 75, 70 dB HL on the LE for the same frequencies, respectively. However, he did not complain of loudness hyperacusis. One of the interesting particularities in this patient is the important modulation of tinnitus intensity by somatic maneuvers. Compared to the other cases, the intensity of his tinnitus increased by almost all somatic maneuvers. Jaw and mouth maneuvers were particularly efficient, generating the highest increase (+4 on a 0-10 numerical tinnitus intensity scale) (Table IV). We thus decided to assess middle ear function during these maneuvers in the most symptomatic ear (RE). Middle ear function was assessed using continuous admittance and EAC air pressure sensor recordings during head front, left head turn

(Figure 7). For the head front maneuver, the patient's forehead was placed against a foam cushion glued to the extremity of a pole fixed to the soundproof wall. The patient was asked to firmly press his forehead against the pole to generate neck muscle contraction while admittance and/or air pressure were/was recorded in the RE. The same measurements were performed on the RE of a control participant in a similar fashion to ensure that these maneuvers are not associated with artefacts (data not shown). At rest, both the admittance continuous recordings and the pressure sensor recordings are relatively stable in the RE. The air pressure measured in the right ear has a sawtooth aspect at a rate of 1 Hz, which reflects the tympanic membrane movement due to heart beats. When the head front movement was performed, negative admittance peaks could be observed. Similar results were obtained on other similar maneuvers such as rotation of the head to the left.

5. Changes in the middle ear evoked by eyelid closure

Patient #10 first experienced pain in his ears following an acoustic trauma at a concert: he spent hours in front of a subwoofer. After the concert, he experienced high peaks of intense pain in his RE only: he was treated with corticosteroid for four months, and his condition improved. He then exposed himself again to loud sounds in a concert, and the symptoms of pain reappeared in his RE and did not improve since then. He never experienced any symptoms in his LE. He now reports that impulsive, low frequency and high frequency sounds, not necessarily loud, trigger symptoms in his RE usually in the same temporal order: he first feels discomfort in his ear, followed by ear pain described as burning and is usually followed by ear fullness. He tried sound therapy, muscle relaxants, acupuncture, and osteopathy without any real success. The only treatment that may have improved minimally his condition is clonazepam (Rivotril): his tolerance thresholds increased following the treatment. He also reports intermittent tinnitus in his RE that is usually faint but is modulated by the presence of pain in the same ear. His hearing thresholds were normal bilaterally, and the static tympanometry results suggested normal mobility of the tympano-ossicular chain bilaterally. However, in his RE, at around -60 daPa, a sudden increase in admittance was observable and repeatable on

multiple occasions (Figure 8, upper left panel). He reported that he felt a backlash in his ears (but no pain) concomitant with the sudden rise in admittance. The same sensation and admittance peak were repeatable.

Patient #10 was also able to produce vMEMC simultaneously in both of his ears and his RE only. His ability to produce vMEMC was assessed with continuous admittance. The results suggested that he could contract his TTM in his RE and his stapedius muscle in his LE (Figure 8, middle panels). Finally, he reported that his eyes' contraction was triggering a click in both of his ears but more pronounced in his RE: this was assessed by the pressure sensor in two conditions, strong (first three events) and medium (last three events) eyes contraction recordings (Figure 8, bottom panels). In his RE, the contractions always yielded positive peaks suggesting that SM was the muscle involved with higher positive pressure peaks for strong vs. medium contractions. Interestingly for the LE, the contractions generated bi-phasic peaks for the strong contractions (with higher amplitude for the negative component) and positive peaks only for the medium contractions. These results suggest that both MEMs are contracting following the contractions of the eyes. Each muscle's contribution to the measured peaks depends on each of the MEM's relative contraction levels. Of importance for the patient symptomatology and primary concerns (pain in the ear), the voluntary contraction of the MEM did not generate pain (outside the periods of symptoms where the pain is present). This observation suggests that the MEM contraction is not sufficient to cause pain. The patient recently received a treatment consisting of a botulinum toxin injection in the tensor and levator veli palatini muscles. One month later the patient reports that the intervention was a complete success: he doesn't experience pain in the ear after exposition to impulsive sound anymore. Following the intervention, he is not able to voluntarily contract his MEM. These results suggest that some muscle activity in the oro-facial area was responsible for the pain and was deactivated by the toxin.

6. Psychoacoustic and admittance measurements before and after TTM section

Patient #11 had constant high-pitched tinnitus in his RE for more than a year. A few months before his visit at the lab, he experienced new symptoms in his LE: a disturbing bell sounds described as "small bell sounds" was triggered by yawning, burping, car vibration, exposure to some low-frequency sounds and provoked when he was producing a voluntary tremor of his eyes. This triggered tinnitus type in his LE first started after yelling after someone. It was judged so disturbing that the patient was willing to undergo surgery to section the TTM in his LE. He also reported that at some intensity level, low-frequency sounds were distorted. A few days before the surgery, patient #11 came to the lab to undergo a series of tests. The results are summarized in Figure 9. In the LE audiogram, the frequency and sound level of the low frequencies causing this distortion are shown: 250 and 300 Hz sounds were triggering these distortions at the lowest intensity level (around 60 dB SPL). Static tympanometry results using a 226 Hz were normal bilaterally, suggesting a normal mobility of the tympano-ossicular chain in both ears (Figure 9).

During simultaneous bilateral pressure sensor measurements, the patient was asked to perform voluntary eyes tremor in order to trigger the tinnitus ("small bell sounds") in his LE. As shown for the LE, clear negative biphasic spike-like pressure peaks were seen every time the eye tremor was produced and only when it was associated with the tinnitus perception: the negative and positive peaks suggest TTM and SM involvement, respectively (Fournier et al., submitted). The high amplitude of the negative peaks suggested an important contribution of the TTM. Right after the section of the TTM, burping, yawning, and eye tremor did not trigger the tinnitus anymore. However, two months after the surgery, he reported that the tinnitus was still triggered by low-frequency sounds and by car vibration but at 80% of the intensity prior to the surgery. These results suggest that the TTM was involved in generating the transient tinnitus in his LE, at least for some triggers (yawning, burping, tremors of the eyes) and that the pressure sensor can be used to objectively measure TTM contractions in these cases. However, as the symptoms did not completely disappear, we suspect that the SM may also be involved in the patient symptoms. Four months later, the patient report that the occurrence of the sound distortion is rare and that the intensity has dramatically dropped.

On an interesting note, the TTM resection didn't affect the hearing thresholds and the mobility of the tympano-ossicular chain as assessed by static tympanometry (Figure 9). The stapedial reflex thresholds measured before and after the resection were also very similar with reflex thresholds of 85, 90 and 90 dB HL for 0.5, 1 and 2 kHz before the intervention and 80, 85 and 90 dB HL for the same frequencies two months post-intervention. On this case, it seems that TTM resection has no impact on hearing detection abilities, on the mobility of the tympano-ossicular chain and on the stapedius reflex.

DISCUSSION

It has been postulated that MEM dysfunction could lead or be associated with a cluster of symptoms, including but not restricted to, tinnitus, hyperacusis, ear fullness, sound distortion and/or otalgia (Klockhoff, Ingmar 1979; Londero et al. 2017; Noreña et al. 2018; Westcott 2016). The mechanisms of this clinical condition, i.e. the putative relationship between middle ear and the cluster of symptoms, are largely speculative and remain elusive. The main objective of the present project was to evaluate middle ear function in patients reporting these symptoms. A total of 11 patients were evaluated by medical specialists and in most cases, all the clinical tests came out normal. The most reported symptoms from this cohort of patients were tinnitus, hyperacusis, ear fullness and pain in or around the ear. Even though many patients (n=8) displayed normal hearing bilaterally, all of them reported disturbances in their perception of sound. These disturbances included a distorted perception of sound, increased loudness, sound induced pain and sound triggering spasms. Out of the 11 patients tested here, six would have reaction to loud sounds consistent with loudness hyperacusis and four with pain hyperacusis (Tyler et al. 2014). The description of the pain varied from very acute pain such as stabbing type pain to more diffuse pain such as heating pain. Sound induced pain was always located in the ears. In addition, sound induced spasms were reported by three patients: they reported feeling a spasm in their ear following specific sound stimulation such as impulsive and dishes sounds. To note, some reported that both spasm and pain was triggered by impulsive, and kitchen sounds. Kitchen sounds are frequently reported as uncomfortable and even painful in first time hearing aids users (Tedder 2014). Why these sounds are considered so uncomfortable for patients with TTTS symptoms and for first time hearing aid users should be investigated further.

Assessing the middle ear function using admittance and EAC air pressure sensor

In the present study, the MEM function was investigated using either admittance and/or an EAC air pressure sensor. Admittance is the reciprocal of the

impedance, i.e. it is related to the rigidity of the middle ear or to how much energy is transferred to the inner ear. The measure of the ME admittance is used routinely in clinics to diagnose middle ear dysfunctions, such as otitis media, myoclonus, patulous eustachian tube, otosclerosis etc. More specifically, measuring the middle ear admittance can objectify the contraction of TTM and SM. Indeed, the contraction of one of these two muscles is accompanied by a stiffening of the tympano-ossicular chain, which results in a decrease in admittance (Fournier et al., submitted).

The ME function can also be assessed using a pressure sensor in the sealed EAC. This simple and complementary measure detects very small displacements of the tympanic membrane. This method is sensitive enough to detect the periodic fluctuations in meatus volume associated to heartbeats (Marchbanks 1984). They can be seen in most subjects (patient #1, #3, #5, #6, #9, #10, #11). These “pressure waves” are thought to result from the pulsations of the intracranial fluid and arteries. Interestingly, it has been proposed that abnormally large pressure changes in the EAC can reflect pathology such as otitis media or glomus tumors (Andréasson, Harris, and Ivarsson 1978).

Moreover, this method is particularly useful to differentiate between TTM and SM contraction. In a recent study carried out in control and in subjects who were able to contract their MEMs at will, we have been able to show that TTM contraction is associated to a relatively large decrease in pressure in the EAC (Fournier et al., submitted). Consistent with earlier literature (Phillipps et al. 1989), this result suggests that TTM contraction is accompanied by an inward displacement of the tympanic membrane. On the other hand, the SM contraction was associated to a small positive deflection in 30% of patients. This suggests that SM contraction, when causing a tympanic membrane displacement, is accompanied by an outward movement of the tympanic membrane. This method is also able to detect patulous eustachian tube (slow variation in EAC pressure synchronized with respiration) (Figure 5, patient #3). Finally, this method is particularly suited in patients with hyperacusis since it does not require any sound stimulation.

Spontaneous changes in the middle ear

In the present study, two patients (#1 and #2) reported symptoms originating from “the ears” and occurring spontaneously. Symptoms such as ear fullness, sound distortion and otalgia have been reported in cases of MEM phasic contractions (myoclonus), defined as repeated fast contractions resulting in clicks or other sounds (Abdul-Baqi 2004; Ellenstein et al. 2013). In patient #1, the EAC pressure recordings suggest that the symptom (bursts of machine gun) is triggered by TTM contraction (repeated negative peaks) in the left ear. This result is in line with previous reports of visible retraction of the eardrum under otoscopy/microscopy upon MEM myoclonus (Abdul-Baqi 2004; Brigo et al. 2013; Hornibrook and Keast 2019; Howsam et al. 2005; Kim et al. 2013; Kwee and Struben 1972; Oliveira et al. 2003; Rajah 1992; Zipfel et al. 2000). The advantage of the EAC air pressure assessment is that it can measure small tympanic displacement related to MEMC that may get unnoticed under microscopy/otoscopy. It also provides the possibility to store the pressure data and used them as an outcome measure. To note, Phillipps et al. (1989) observed negative pressure peaks in the EAC in a patient hearing clicks.

Interestingly, during the second symptom episode reported by patient #1, large negative peaks started in the left ear, but smaller peaks were also present in the right ear which started a few seconds after the beginning of the symptom episode. Moreover, the contraction saccades in the two ears are antagonistic: a positive peak in one ear corresponds to a negative peak in the contralateral ear (see the zoom in Figure 1). This result is reminiscent of what we found earlier in one symptomatic patient: when symptom severity was high in one ear, it was low in the contralateral ear (Londero et al. 2017). This suggests that TTM contraction in patient #1 may be, at least partially, under the control of some central process which is responsible for the antagonistic behavior between the two ears. As mentioned above, a positive and negative pressure peaks are indicative of SM and TTM contraction, respectively. It is then possible, at least in this subject, that when one muscle is contracting the other is not, and reversely.

Patient #2 is another case of objective tinnitus. Clear positive and negative peaks could be observed from admittanceometry. Similar results during static tympanometry was

previously reported in a middle-ear myoclonus case (Abdul-Baqi 2004). On the other hand, very small peaks could be observed from the pressure sensor. Altogether, these results suggest that the admittance peaks are “sound artefacts” corresponding to the very brief clicks emitted by the middle ear. The positive and negative peaks in admittance may result from the phase relationship between the stimulus used for the admittance and the sound artefacts. It is interesting to note that the “artefacts” are more numerous during jaw contraction or when a negative pressure is applied in the EAC. The sound artefacts may result from the opening/closing of the ET. The pressure change in the EAC and the jaw contraction may further impact the ET through the activation of both the tensor veli palatini and the TTM. Indeed, it has been proposed that these two muscles may constitute a functional unit: they are both innervated by the trigeminal nerve and they are connected by a tendinous connection (Kierner, Mayer, and v Kirschhofer 2002; Ramirez, Ballesteros, and Sandoval 2008). The contraction of one (TTM, when the subject is contracting his jaws) may trigger the contraction of the other (tensor veli palatini muscle) (see also the section below on the changes in the middle ear evoked by somatic manoeuvres).

MEMC evoked by sound stimulation or pressing trigger points

Patients #3 and #4 reported symptoms in their ears triggered by sound stimulation. Since patient #3 informally reported that pen dropping on a table was triggering symptoms, this sound was used to explore the middle ear function (a pen was dropped over a table). The pressure was monitored in the EAC of the right ear while the left ear was unplugged. Each time the pen was making a sound by a collision with the table, the pressure was transiently decreased. This result indicates that the TTM was contracting. It is worthwhile mentioning that, in this case, the TTM contracts upon auditory stimulation of the contralateral ear. This patient could also contract his TTM voluntarily as shown in Figure 3. One notes that the size of the vMEMC is much larger than the MEMC triggered by sound (by a ratio of 4). Patient #4 reported a “saturation-like” perception when hearing specific sounds above a certain level. Since this patient reported that baby crying sound was triggering this symptom, we used that sound monaurally while measuring

admittance or EAC air pressure in the contralateral ear. The baby crying sound was able to trigger clear SM contraction as assessed by both admittanceometry and pressure measurement. Interestingly, the baby crying sound produced “instability” in both admittance and pressure measurements, and long-lasting MEM contraction beyond the sound stimulation. Since the pressure changes are positive and negative, the instability is likely resulting from the contraction of both SM and TTM. The contraction of both muscles is likely accounting for the “saturation-like” percept reported by the patient. It is possible that prolonged contraction of TTM and/or SM can account for the persistence of admittance decrease after sound stimulation. The results obtained in patients #3 and #4 indicate that the sound level is not the only acoustic feature triggering MEM contraction. Indeed, the overall spectro-temporal acoustic characteristics also play role.

Patients #3 and #6 reported symptoms when they pressed trigger points on their face or neck. Pressing the trigger points was associated to large and transient decrease of pressure (Figure 5). This result is consistent with TTM contraction. One notes that the SM may contract as well but it may be “hidden” by the larger TTM contraction. One also observes “slow waves” (5-sec period fluctuation) in patient #3 suggesting that ET is opened in this patient. The mechanisms accounting for MEM contraction when trigger points are stimulated are unclear. The temples (trigger points in patient #3) are innervated by the mandibular branch of the trigeminal nerve. In patient #6, the temporomandibular joint area and the neck (trigger points in patient #6) are innervated by the mandibular branch of the trigeminal nerve and the greater occipital nerve, respectively. Our results suggest that the activation of the trigeminal nerve or the occipital nerve when pressing trigger points can activate the motor branch of the trigeminal nerve. This may result from the fact that the head and neck form a highly interconnected complex, where most elements, both sensitive and motor, can communicate bilaterally between each other. This high level of interconnection between the sensory inputs (auditory, somatosensory and visual) and muscles of the head-neck complex may be a specific adaptation to the startle reflex. In abnormal state (TTTS), the existing but usually “masked” connections between remote elements of the complex may be unmasked. It is also possible that the activation threshold of MEM contraction is reduced. In any case, the crossroads structure that can route the sensory activation from a given area of the head-neck complex to the MEM

may be the trigeminal cervical complex (Noreña et al. 2018). Hence, a sensory input (auditory or somatosensory - trigger points) can trigger a given output (TTM contraction). Why a given input is associated to a given output remains largely unknown.

Changes in the middle ear evoked by somatic manoeuvres

Patients #5, #7 and #8 report that they can modulate their symptoms by doing somatic maneuvers (jaw contraction). They all show a similar pattern of admittance change when contracting the jaws: a slow increase or decrease over time (Figure 6) in the symptomatic ears only. In patient #5, the slow fluctuation is triggered during jaw contraction or after acoustic stimulation. It is remarkable to observe that the time course of admittance changes is very similar between the two recordings (until 15 sec). In patient #7, the jaw contraction is associated to a slow periodic modulation during the contraction and this fluctuation did not disappear after jaw contraction, it is even more pronounced. In patient #8, the slow fluctuation of admittance change is accompanied by faster changes. We suggest that the jaw contractions in these three patients open the eustachian tubes. The resulting slow fluctuations of admittance would be the result of the opening of the eustachian tube. We speculate that the jaw contraction or acoustic stimulation may activate the TTM, which can in turn activate the tensor veli palatini muscle (Kierner et al. 2002; Ramirez et al. 2008). As mentioned above, the two muscles may constitute a functional unit (Ramirez et al. 2008). In patient #7, there is no indication that the TTM is contracting during the somatic maneuver. On the other hand, fast changes in admittance can be observed in patient #5 (at 26 sec) and #8 (at 16 sec and 26 sec) after acoustic stimulation and during jaw contraction, respectively, that may be indicative of phasic TTM contraction. To note, patient #8 reported sound distortion during an episode of symptoms. Interestingly, this patient was also able to trigger putative MEMC at will associated to an increase of admittance. We hypothesize that each transient increase in admittance is caused by TTM contraction and not by SM contraction or ET opening. Indeed, the size of the admittance change seems too large to be evoked by SM contraction, and much too fast to be evoked by ET opening. Moreover, the temporal pattern of the admittance change is similar to the one obtained by vMEMC and reported

in Fournier et al. (submitted): fast initial change and a slower return to baseline. While these results argue in favour of TTM contraction, it is however surprising that TTM contraction could result in admittance increase (TTM contraction is known to increase the tympanic membrane stiffness). To account for an admittance increase triggered by TTM contraction we speculate that the pressure in the middle ear is positive (due to eustachian tube opening) and that the tympanic membrane position is moved outward. In this context, TTM contraction may then restore the tympanic membrane in its default position, hereby increasing the admittance (Aron, Floyd, and Bance 2015; Fournier et al. submitted). Finally, in patient #9, the somatic maneuvers are accompanied by strong and transient changes of admittance and pressure. These results are also consistent with TTM contraction triggered by somatic maneuvers. Indeed, it has been reported earlier that TTM contraction can be associated to head movements (neck muscle contraction) (Salomon and Starr 1963). Moreover, the positive and negative pressure changes suggest that the ET may be opened.

In the proceedings of an international conference, Klockhoff stated (Klockhoff, Ingmar 1979): “In several of the roughly 250 tonic tensor cases behind this presentation, this extreme impedance lability was the only abnormality immediately observed and the spontaneous tensor activity was not recorded until the position of the tympanic membrane had been smoothly adjusted by a slight air pressure change in the auditory canal, until a suitable position of the ear drum was found – usually close to the impedance minimum of the ear.” We speculate that the “extreme impedance lability” reported by Klockhoff is not caused by tonic TTM contraction but instead by ET dysfunction (i.e. ET opening). Consistent with this hypothesis, Figure 3 of the proceedings paper (Klockhoff, Ingmar 1979) shows slow variations in impedance (cycles of 5-6 seconds) that may reflect the effect of breathing on admittance.

Clinical management

Clonazepam and botulinum toxin

Patient #10 reported symptom of sound-evoked pain in the ear and could contract his MEM voluntarily. The vMEMC was not associated with pain, except in the periods of crisis, suggesting that pain was caused by muscle contraction plus an additional factor. We speculate that the additional factor may be inflammation, that can activate the trigeminal nerve (Noreña et al. 2018). The static admittance in the RE showed a sharp increase at around -60 daPa. This sudden admittance increase may result from TTM contraction. Indeed, the hypersensitive TTM may be activated by the negative pressure through stretch reflex contraction. It is also possible that this sudden increase in admittance was the result of ET opening.

The patient was treated with clonazepam (Rivotril) treatment: the clinical condition improved somewhat (the tolerance thresholds increased) after the beginning of the treatment. However, the treatment was stopped after habituation started. Later, this patient received botulinum toxin injection in the tensor and levator veli palatini muscles (Olthoff, Laskawi, and Kruse 2007). One month after, the patient did not experience pain in the ear after exposition to impulsive sound anymore. Moreover, he was not able to voluntarily contract his MEM. These results suggest that some muscle activity in the oro-facial area was responsible for the pain and was deactivated by the toxin. It further suggests that the ET could be involved in the patient's symptoms.

TTM tenotomy

The first tenotomy of the tensor tympani muscle was performed around 1868 by a doctor named Hytrl Weber-Liel in patients complaining of ear symptoms and tinnitus believed to be caused by abnormally strong contraction of the TTM (Tange 2017). This technique has gained new interests more recently for treating patients with MEM myoclonus (Hidaka et al. 2013), and for the treatment of Menières disease (Reichmayr et al. 2019). We assessed a patient with phasic MEMC triggered by eyes tremor just before he underwent specific tenotomy of the TTM and two months after (patient #11). This patient described sound distortion as « the sound that a loudspeaker would make when it is saturated » but did not report pain or loudness hyperacusis. The evaluation revealed

that the spasms triggered by eye tremor were linked to TTM contractions. After TTM section, the patient reported significant improvement of his symptoms a few days following the operation although he complained of postoperative symptoms including a new tinnitus described as a noise, pain in the ear and ear fullness. However, one month after the surgery, most of the postoperative symptoms had disappeared and the phasic MEMC reported as spasms triggered by eye tremor, yawning, burping and car vibration were gone. On the other hand, the intensity of the sound distortion was lowered but did not disappear, suggesting that the SM played a role in the distorted perception. Interestingly, the intervention had no effect on his middle ear function and his hearing thresholds as measured by the standard clinical procedure. Indeed, the hearing thresholds, the static tympanometry and the stapedial reflex thresholds were all similar two months after the intervention.

Conclusion

The present study was aimed at investigating the ME function in patients reporting a cluster of symptoms using admittanceometry and measuring the pressure in the EAC. More specifically, we wanted to test the hypothesis suggesting that tonic contraction of TTM can be involved in the generation of these symptoms (Klockhoff, Ingmar 1979; Westcott et al. 2013). This study reports the etiology, symptoms and ME measurements in eleven patients grouped into 4 categories: symptoms occurring spontaneously, symptoms evoked by sound, symptoms evoked by pressing trigger points and symptoms evoked by somatic maneuvers. Interestingly, while acoustic shock is the main cause of the symptom cluster, it can also be triggered by adverse reaction to antibiotic (patient #3) and strong emotional reaction (stress and anger, patient #1 and #11, respectively).

Overall, our results are not consistent with tonic contraction of the TTM. Instead, they argue in favor of a hyper-reactive TTM with reduced contraction threshold. It was possible to show phasic TTM contraction in 8 patients over 11 (73%). The term Tonic Tensor Tympani Syndrome should be abolished and replaced by a more neutral term, such as Hyper-Reactive Middle Ear Muscle Syndrome, for instance. Our study also

suggests that the ET may play a role which may have been underestimated until now. Assuming that the TTM and the tensor veli palatini may constitute a functional unit (Kierner et al. 2002; Ramirez et al. 2008), it is possible that the TTM dysfunction impact the tensor veli palatini muscle, which may in turn affect the ET. The symptoms such as ear fullness and vestibular disorders could result from ET dysfunction and the resulting pressure variation in the middle ear. In addition, the functional connection between TTM, tensor veli palatini and the eustachian tube provides a plausible explanation for the frequent association between temporo-mandibular joint disorder and eustachian tube dysfunction (Ramirez et al. 2008).

Finally, the pressure sensor we have developed is easy to use, it can collect data from both ears simultaneously, it is sensitive to MEMC, ET dysfunction and can differentiate between TTM and SM contractions.

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FIGURE Legends

FIGURE 1. Bilateral EAC pressure recordings (Pa) of two spontaneous episodes of spasm in the patient #1 LE (top and middle panel, (red line: right ear, blue line: left ear). The grey area indicates the time period of the spasm symptom as reported by the patient. The bottom panel is a zoom on the second symptom episode.

FIGURE 2. Left panels: Admittance recordings (ml) with a 1 kHz probe tone at 0 daPa of patient #2 ears (red line: right ear, blue line: left ear) measured at rest (top panel) and during symptom modulation (bottom panel). The modulations are - 50 daPa EAC pressure (pink line) and jaw contraction (red line). The right panels are the EAC pressure recordings (Pa) of patient #2 ears measured at rest (top panel) and during symptoms modulation by jaw contraction only (bottom panel). The middle panel is a zoom of both admittance and EAC pressure recordings at rest for both, admittance and pressure. Patients #2 had audible objective clicks coming out from his RE.

FIGURE 3. EAC air pressure (Pa) recordings in the most symptomatic ear, the RE (red), upon sound stimulation (pen drops) (top panel) and vMEMC (top panel), in patient #3. The grey area indicates when the event occurred either, voluntary contraction or sound stimulation.

FIGURE 4. Admittance with a 226 Hz probe tone (0 daPa) (left panels) in the most symptomatic ear of patient #4, the RE (red), upon different sound stimulation: a 500 Hz tone set at 101 dB SPL and a baby crying sound at 70-, 75- and 80-dB SPL. EAC air pressure (Pa) for the baby crying sound at 75 dB-SPL are presented in the right panels. The grey area indicates the presence of auditory stimulation.

FIGURE 5. Left panels: EAC air pressure (Pa) recordings of the RE (red) upon manual pressure of trigger points located on the right and left temples of patient #3. Right panels: EAC air pressure (Pa) recordings of the LE (blue) and RE (red) upon pressure of trigger points located on the neck and the temporomandibular joint (TMJ) of patient #6. The grey area indicates the occurrence of the action of pressuring the trigger point.

FIGURE 6. Admittance with a 226 Hz probe tone (0 daPa) continuous recording for the patients #5, #7 and #8, right (red) and left (blue) are presented. The recordings are presented for three conditions at rest (top panels), during jaw contraction (second row) and just after the contraction (third row). In addition, for patient #5 admittance recording when the patient reported a burning sensation after an acoustic stimulation is also shown on the second row (pink line). Finally, patient #7 static tympanometry results and patient #8 voluntary middle ear muscle contractions are presented on the fourth row.

FIGURE 7. Admittance (ml) with a 226 Hz probe tone at 0 daPa and EAC air pressure (Pa) recordings of the RE at rest for patient #9 (top panel). Admittance recordings for somatic maneuvers including head front and left rotation of the head are presented in middle and bottom panels respectively. The grey area represents the approximate time of the beginning and the end of the movement. Levels of tinnitus modulation are in brackets.

FIGURE 8. Top panels: Static tympanometry results for the RE (red line) and LE (blue line) of patient#10. The grey vertical dotted line indicates a positive admittance peak at around -60 daPa. This peak was reproducible on multiple recordings in the same ear. The middle panels: Admittance recording (ml) in the RE (red) and LE (blue) for EAC pressure of 0 daPa (dark) and -50 daPa (light) upon MEMVC. Bottom panels: Pressure recordings for the RE (red line) and LE (blue line) after three strong and three medium eye blinks.

FIGURE 9. Top panels: The hearing thresholds for the RE (red circle) and LE (blue cross) before (dark blue) and after (light blue) the section of the TTM of patient #11. The stars on the LE audiogram represent the frequency and sound level producing a subjective distortion in his LE before (black) and after (grey) the section of the TTM. Middle panels: Static tympanometry results for the LE (blue line) and RE (red line) before (dark) and after (light) the section of the TTM. The grey dotted line represents the area of normative values for pressure and admittance. Bottom panels: EAC pressure (Pa) recordings for the RE (red line) and LE (blue line) after the patient triggered a bell-type tinnitus in his LE by voluntarily producing a tremor in his eyes.

Patients	Age	Sexe	Primary concerns	Symptoms etiology
1	34	M	Spontaneous popping/clicking of the LE with pulsatile tinnitus	Confinement & stress
2	53	M	Continuous high-pitch tinnitus and audible clics in the RE	After ear surgery
3	33	M	Bilateral hyperacusis, popping/clicking of the RE following impulsive sound	Adverse reaction to medication including multiple neuropathies
4	36	M	Sound distorsion in the RE only, feel spasm/vibration in his ear, hyperacusis bilaterally but more in the RE	Acoustic trauma, following a loud concert
5	32	M	Tinnitus & hyperacusis, pain, bilaterally, RE more symptomatic	Acoustic shock: blast during a concert
6	32	M	Otalgia and popping/clicking in the LE, with bilateral tinnitus (LE: High pitch, RE: low pitch)	Acoustic shock with startle reflex
7	36	F	Tinnitus, Hyperacusis, Earfullness and otalgia mostly in the RE	Following a Sudden Hearing loss in the LE
8	26	F	Tinnitus and hyperacusis bilaterally, spasm in the ear	Acoustic trauma: Power tools used for several days
9	45	M	Tinnitus bilaterally, high intensity RE	Acoustic shock? After ME injectin, a bubble expoded in the ear
10	25	M	Pain hyperacusis and intermittent tinnitus in the RE	Acoustic trauma: several loud concert exposure
11	35	M	RE: continuous tinnitus, LE: tinnitus triggered by eye blinking, sound & vibrations	Acoustic shock? After yelling at someone

Table I: Demographic characteristics of the patients.

Table II: Characteristics of the patients' ears.

Patients#	Laterality	Symptomatic or not	Static Tympanometry			Hearing thresholds (dB HL)			
			TPP (daPa)	ECV (ml)	SA (mmho)	Type	PTA low	PTA mid	PTA high
1	LE	Symptomatic(++)	-1	1.4	1.4	A	5	5	
1	RE	Symptomatic	-8	1.4	1.4	A	5	7	
2	LE	Normal	-39	1.6	1	A	35	37	
2	RE	Symptomatic	-56	1.6	1.6	AD	13	33	
3	LE	Normal	-14	1.3	0.5	A	0	-2.5	
3	RE	Symptomatic	-6	1.3	0.6	A	0	-5	
4	LE	Normal	-10	1.1	0.5	A	3	-2	
4	RE	Symptomatic	-10	1.5	0.5	A	3	5	
5	LE	Symptomatic	NT	NT	NT	NT	28	34	
5	RE	Symptomatic(++)	NT	NT	NT	NT	32	33	
6	LE	Symptomatic(++)	NT	NT	NT	NT	10	8	
6	RE	Symptomatic	NT	NT	NT	NT	10	5	
7	LE	Anacousic	NT	NT	NT	NT	70	95	
7	RE	Symptomatic	-13	1	0.2	AS	8	5	
8	LE	Symptomatic	NT	NT	NT	NT	5	8	
8	RE	Symptomatic	NT	NT	NT	NT	8	10	
9	LE	Symptomatic	-8	1.6	1.5	A	5	2	
9	RE	Symptomatic(++)	-5	1.5	1	A	8	8	
10	LE	Normal	-5	1.6	0.7	A	7	-5	
10	RE	Symptomatic	-11	1.4	0.6	A	6	-3	
11	LE	Symptomatic	-3	1.5	0.7	A	4	7	
11	RE	Normal	-7	1.6	0.6	A	3	7	

NT = not tested, (++) = most symptomatic ear

TPP: Tympanometric Peak Pressure, ECV: Ear Canal Volume, SA: Static Admittance, PTA: Pure Tone Average hearing thresholds

Table III: Frequency of occurrence of the different symptoms for each patient.

Patients	Tinnitus	Hyperacusis	Ear fullness	Hearing impairments	Sensation of floating eardrum	Pain around the ear	Heat pain in the ear	Needle pain in the ear	Neck Pain	Postural instability/Dizziness	Headaches
1	Always	Never	Always	Never	Never	Never	Never	Never	Never	Never	Never
2	Almost Always	Rarely	Almost Always	Almost Always	Never	Always	Always	Almost Always	Never	Never	Never
3	Always	Always	Always	Always	Sometimes	Always	Never	Never	Never	Sometimes	Sometimes
4	Sometimes	Always	Always	Sometimes	Often	Never	Never	Never	Almost Always	Never	Sometimes
5	Always	Always	Sometimes	Rarely	Sometimes	Almost Always	Almost Always	Never	Sometimes	Rarely	Never
6	Always	Always	Always	Never	Often	Often	Often	Often	Always	Never	Never
7	Always	Almost Always	Often	Sometimes	Sometimes	Almost Always	Almost Always	Never	Always	Sometimes	Sometimes
8	Always	Almost Always	Never	Never	Often	Never	Never	Never	Never	Never	Often
9	Always	Never	Never	Sometimes	Never	Never	Never	Never	Never	Never	Never
10	Sometimes	Often	Sometimes	Never	Rarely	Rarely	Sometimes	Sometimes	Almost Always	Never	Never
11	Always	Never	Never	Almost Always	Never	Never	Never	Never	Never	Never	Never

Table IV. The baseline tinnitus intensity on a numerical scale (0-10) is first presented for each patient. The amount of increase (+) or decrease (-) of tinnitus intensity compared to the baseline tinnitus intensity is presented for each somatic maneuver for each patient.

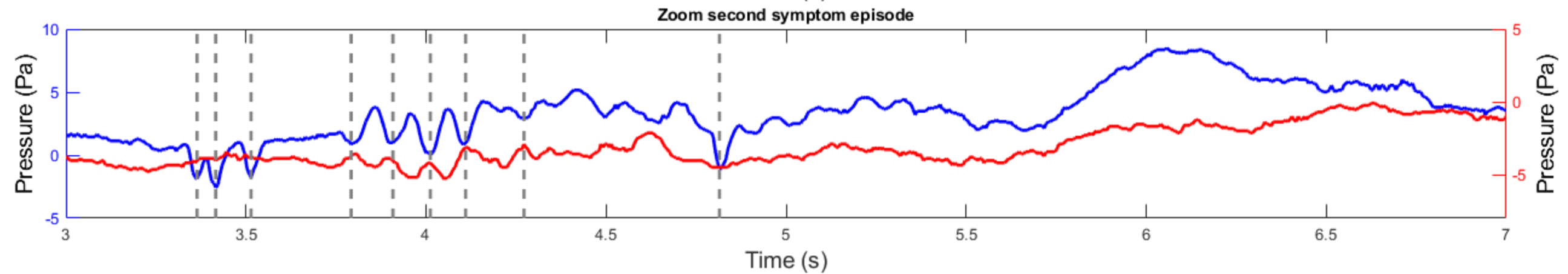
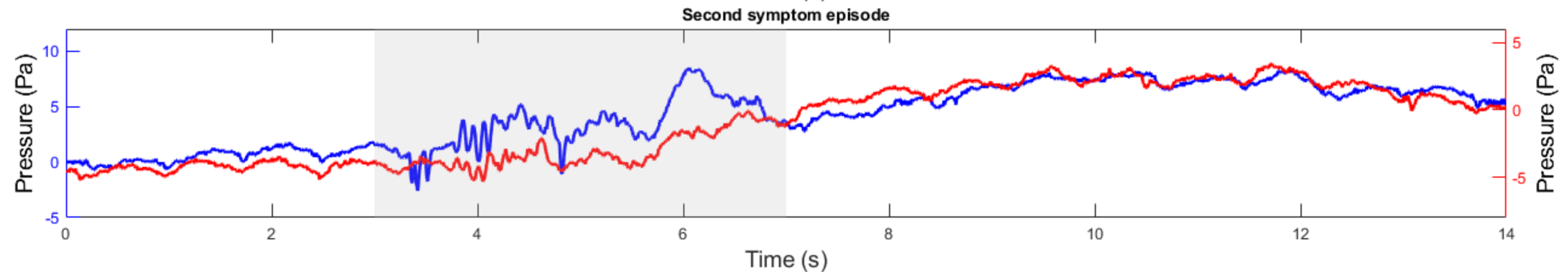
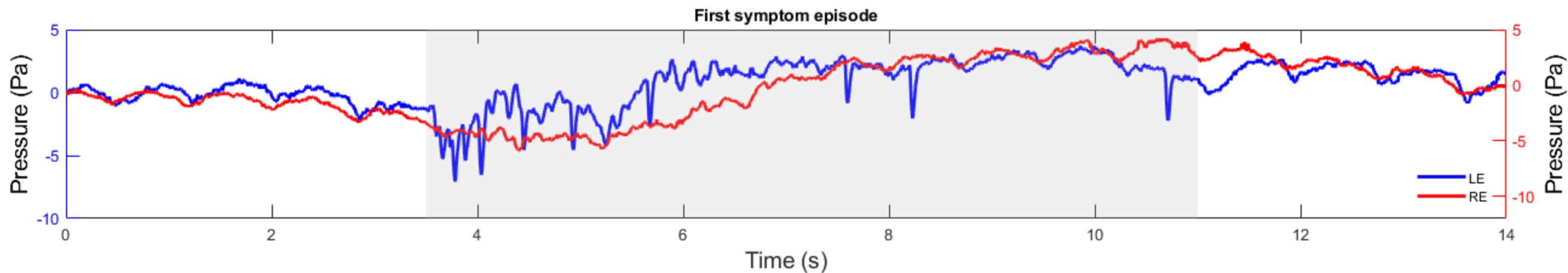
Patients	Baseline	Head back	Head front	Head left	Head right	Right rotation	Left rotation	Jaw right	Jaw left	Mouth opening	Jaw contraction	Jaw protrusion	Movement of the eyes
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	8	0	-3	-3	-3	0	0	0	0	0	0	+1	0
3#	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
4	0	0	0	0	0	0	0	0	0	0	0	0	0
5	3.5	0	0	0	0	0	0	0	0	0	0	0	0
6#	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
7	2.5	+0.5	0	0	0	0	0	0	0	0	0	+0.5	0
8	4	0	+0.5	0	0	0	0	0	0	+0.5	+1.5	+1	+0.5
9	4	+2	+2	+1	+1	+2	+2	+3	+3	+3	+4	+4	0
10	0	0	0	0	0	0	0	+1	0	0	+5	+4	0
11*	0	0	0	0	0	0	0	0	0	0	0	0	0

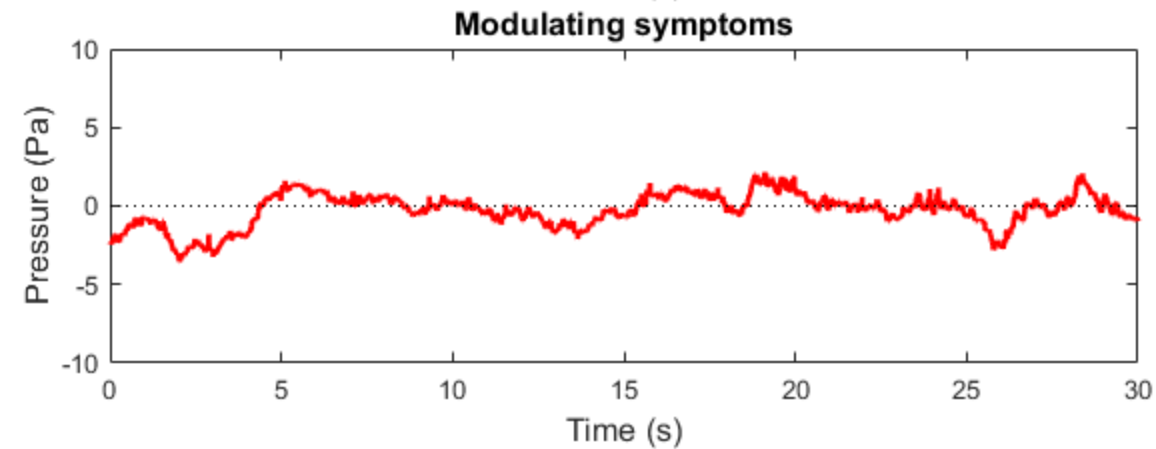
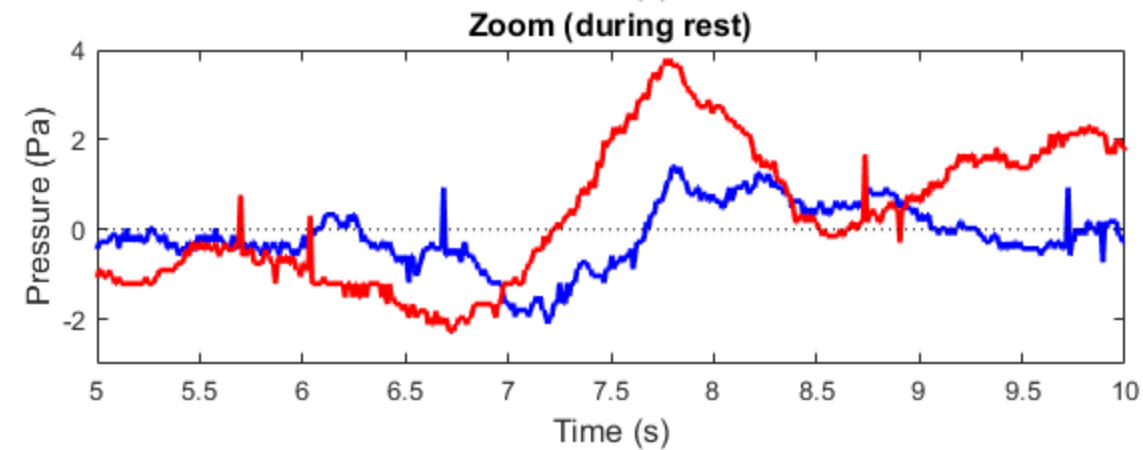
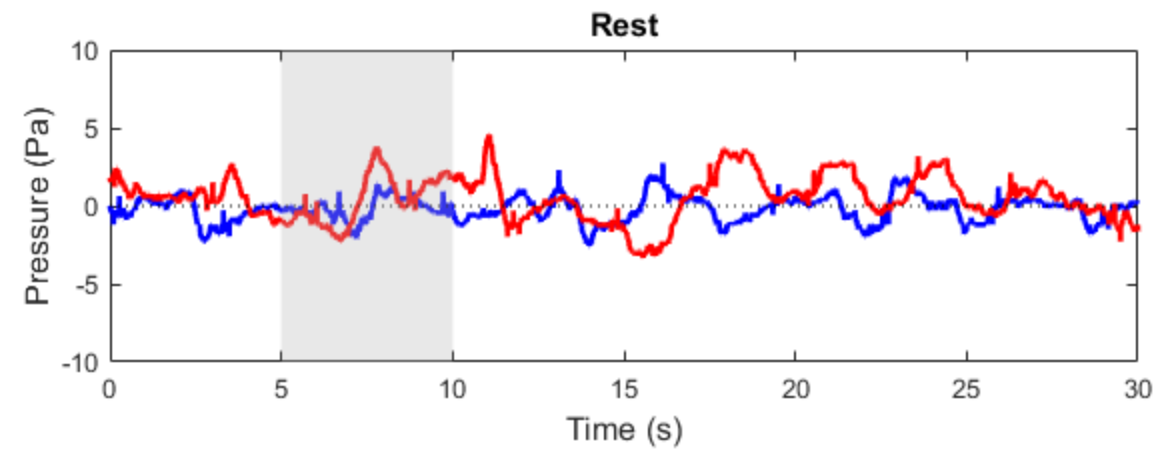
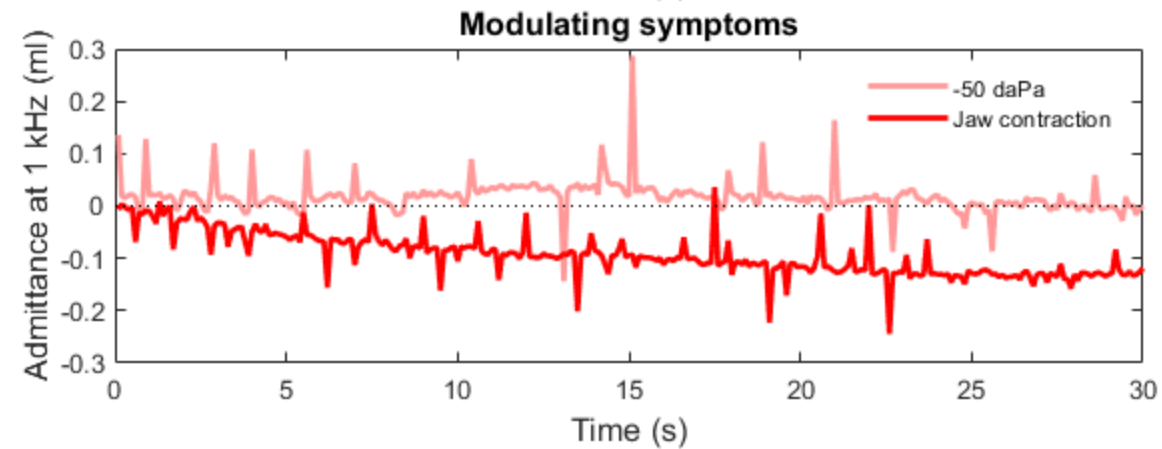
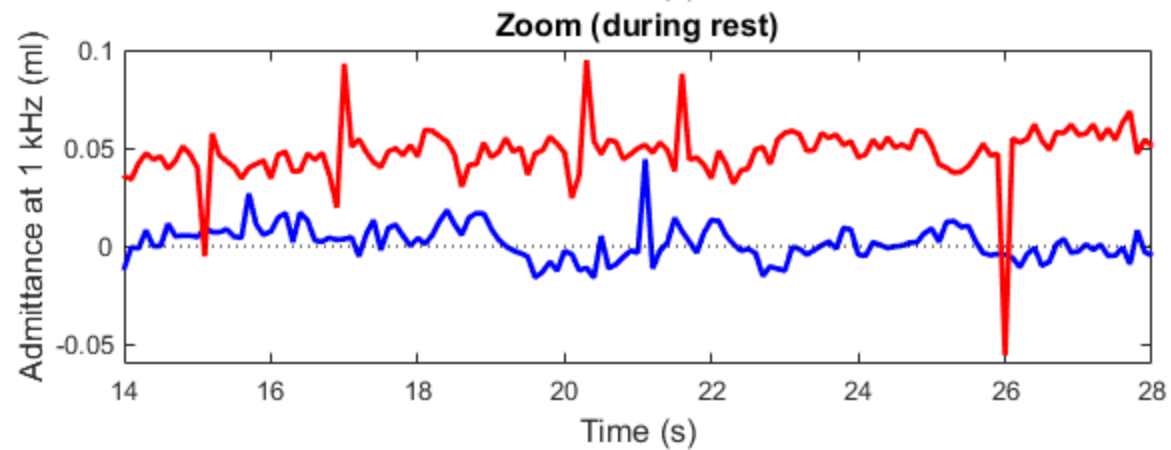
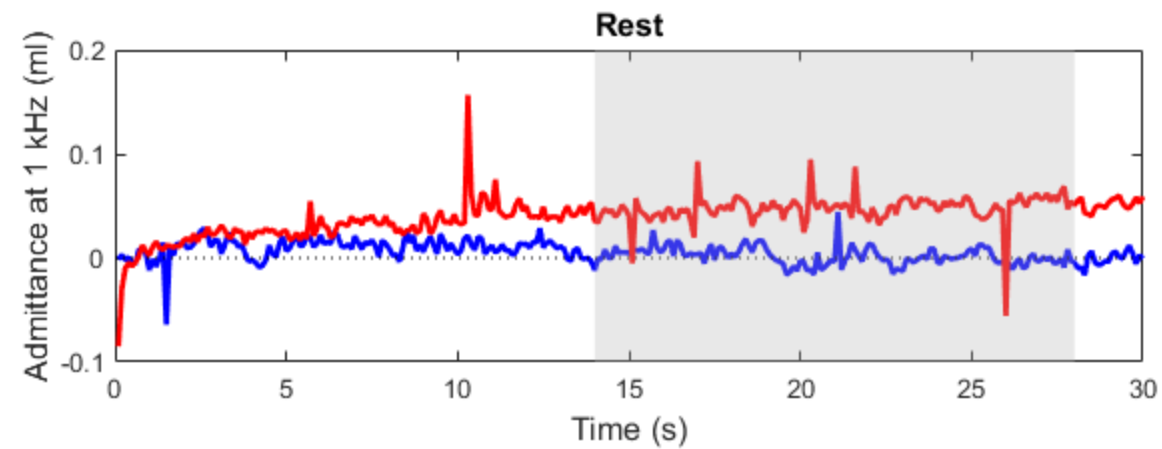
* Clicking in the ear by producing a voluntary eye blinking or tremor of the eyes

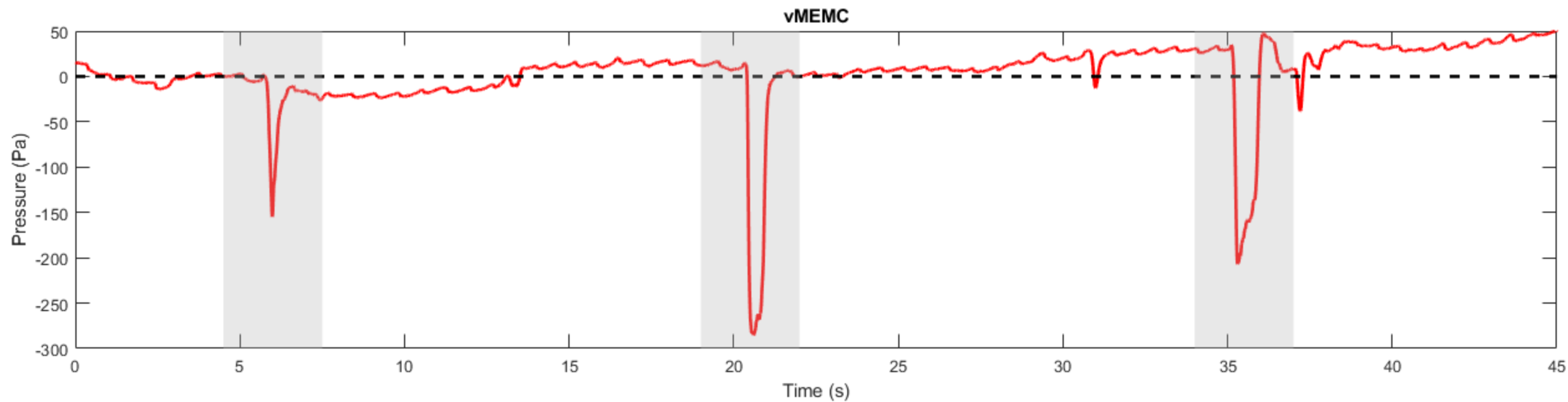
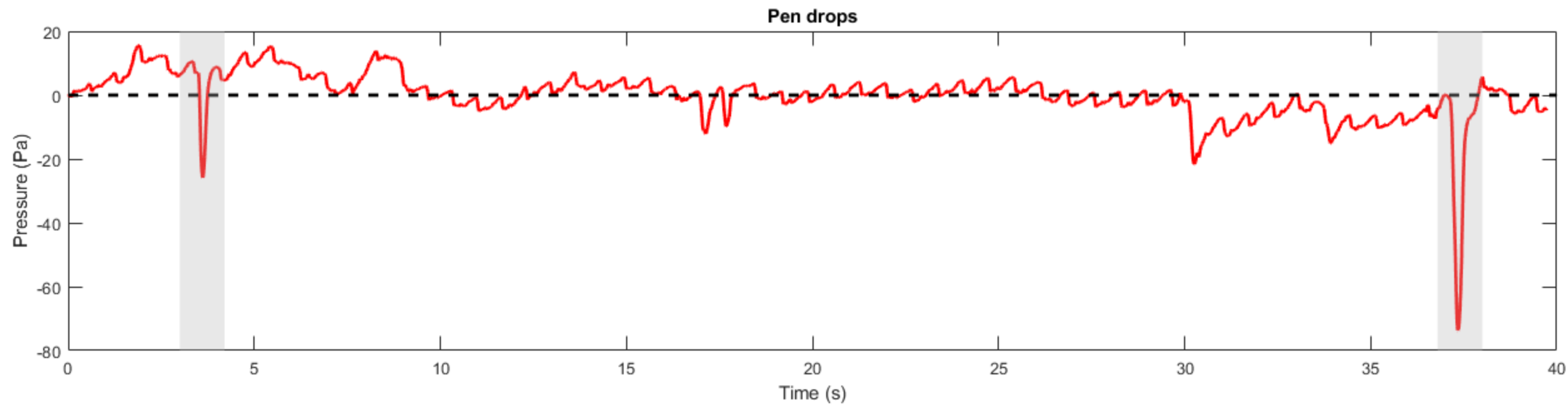
Clicking in the ear by pressure on trigger point

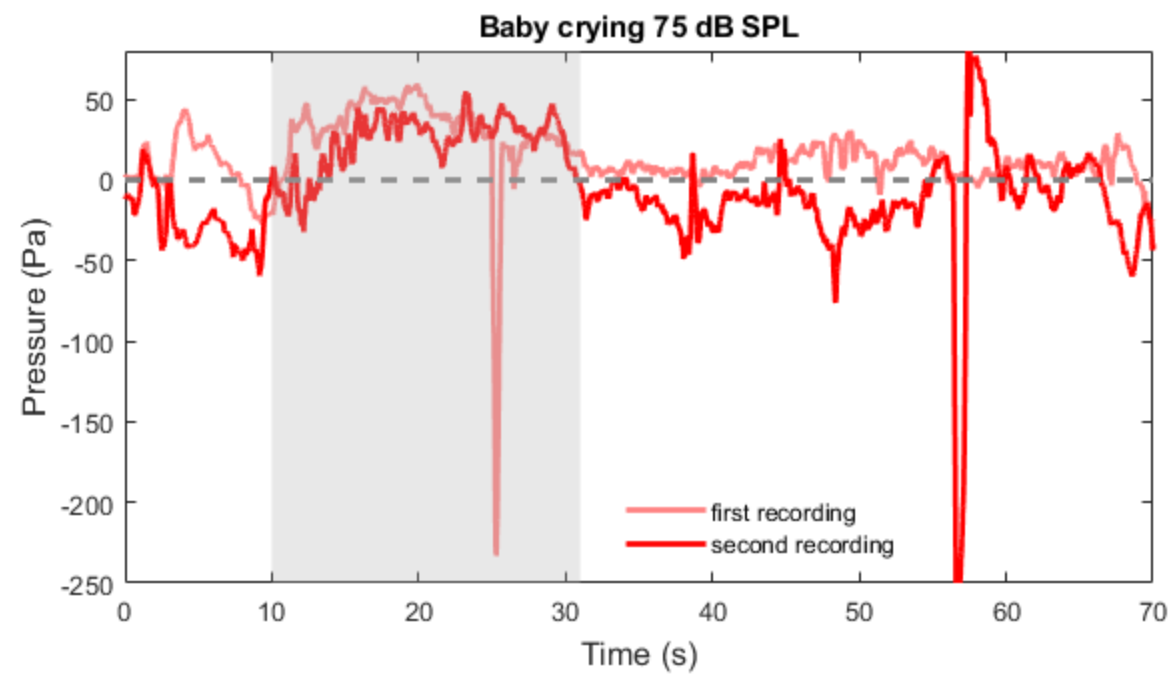
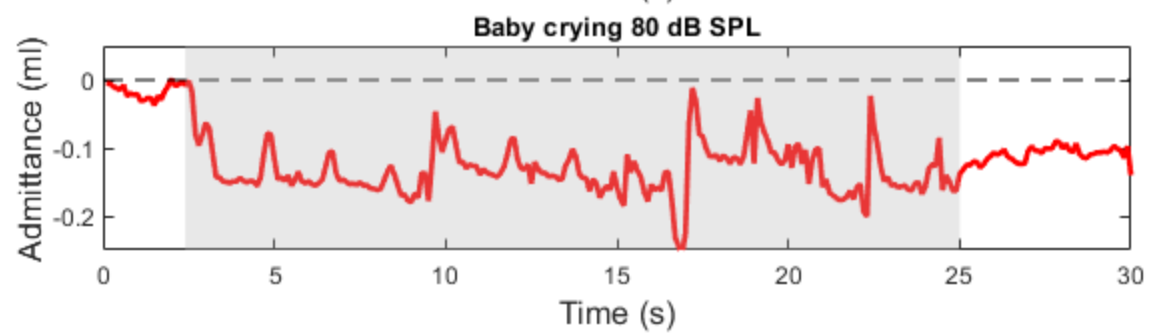
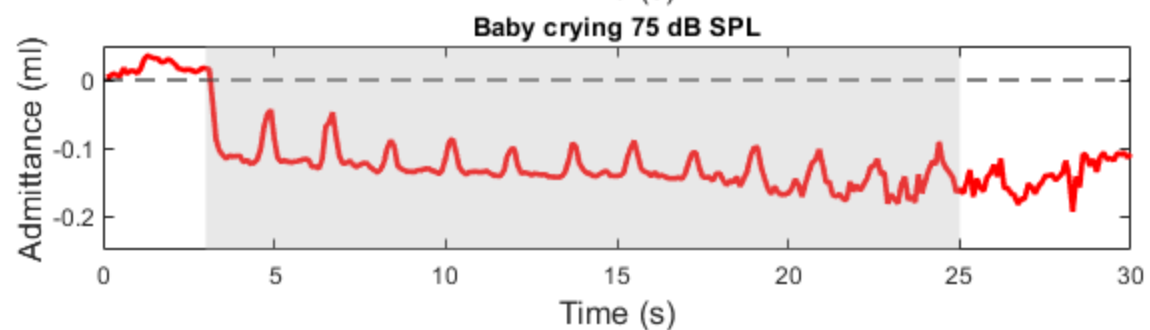
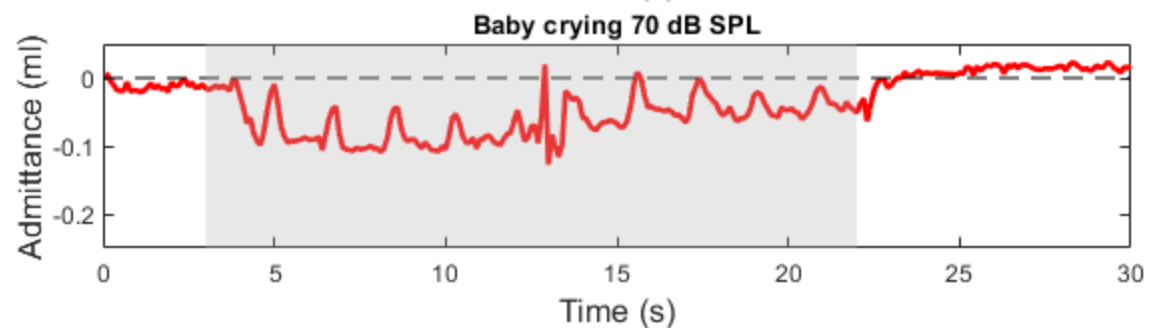
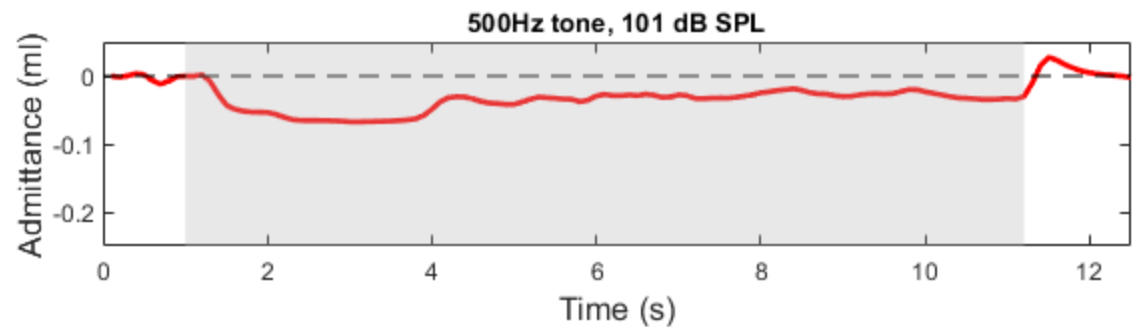
Table V. Classification of patients' symptoms. The classification considers spontaneous, triggered and voluntary induced symptoms. The triggers include sound, trigger point, somatic maneuver and air pressure.

Patient #	Spontaneous	Sound	Trigger point	Somatic maneuver	Air pressure	Voluntary
1	X					
2	X			X	X	
3		X	X			X
4		X				
5		X		X		
6			X			X
7				X	X	
8				X		X
9				X		X
10				X	X	X
11				X		

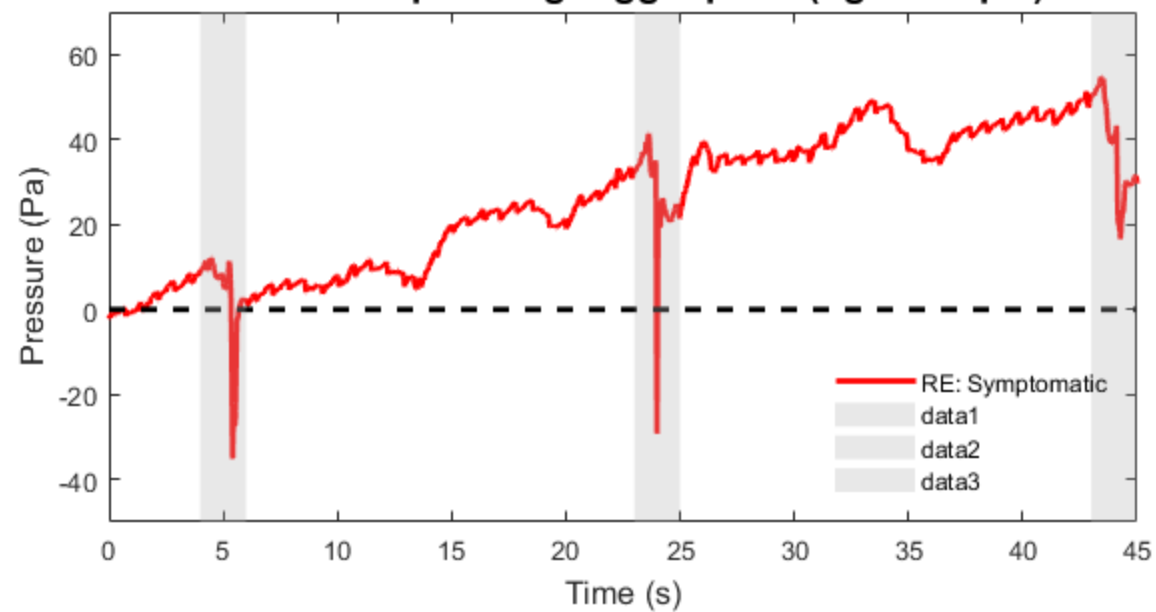




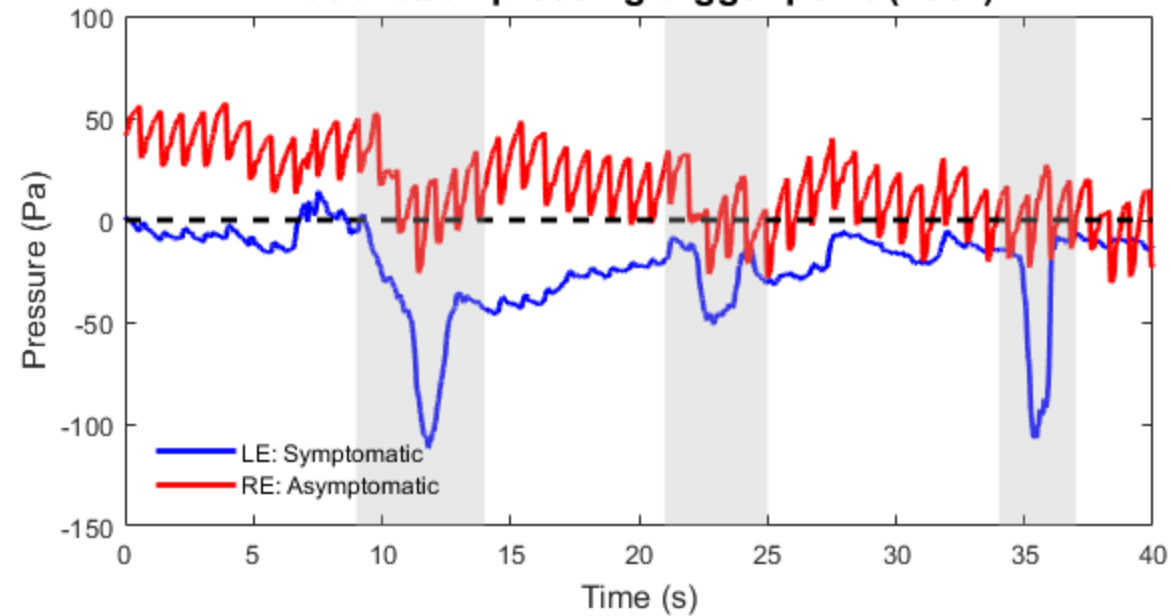




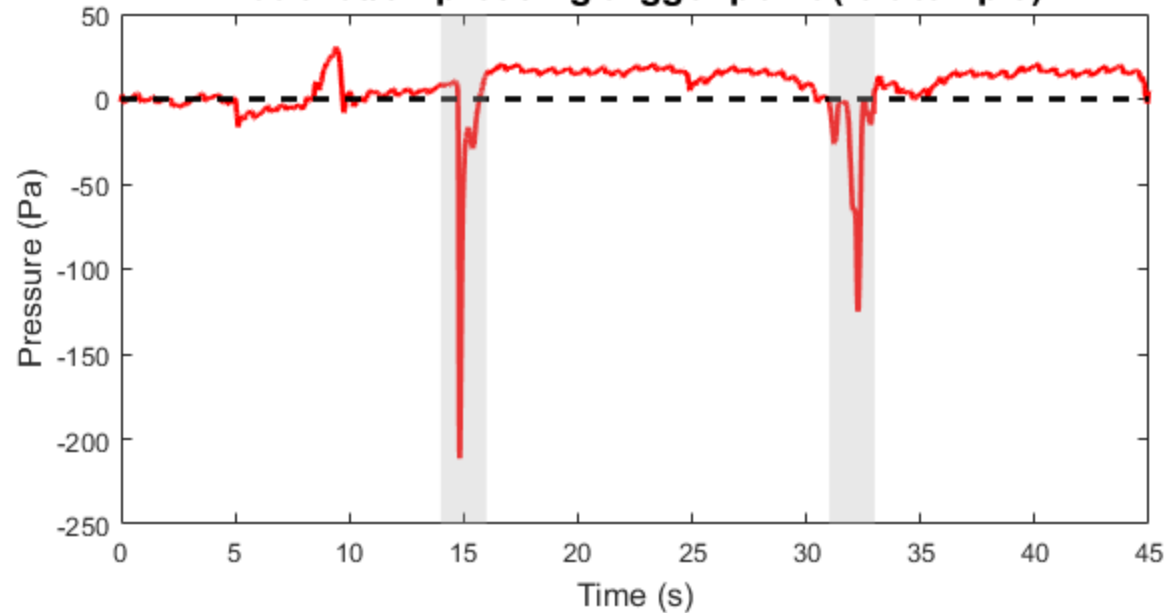
Patient #3 - pressing trigger point (right temple)



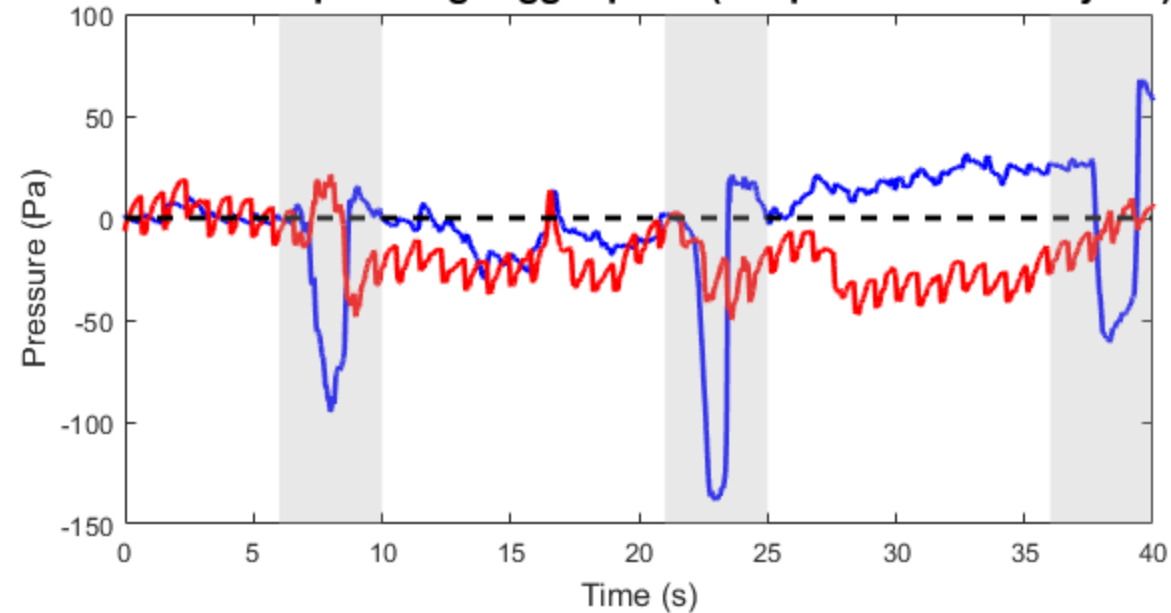
Patient #6 - pressing trigger point (neck)

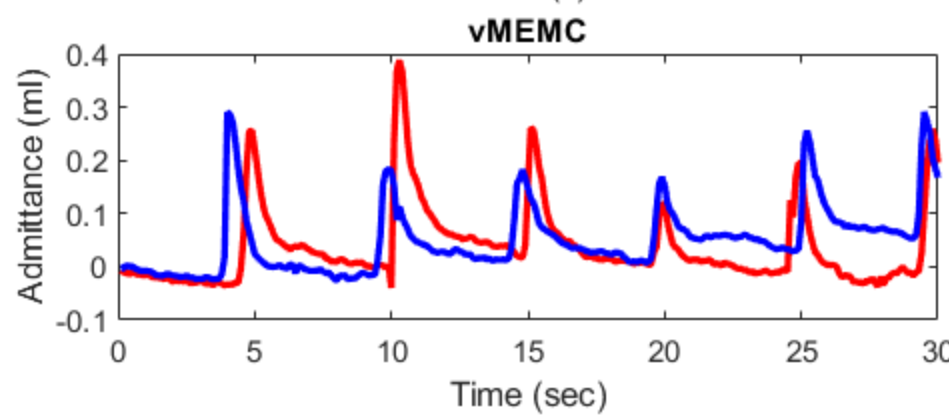
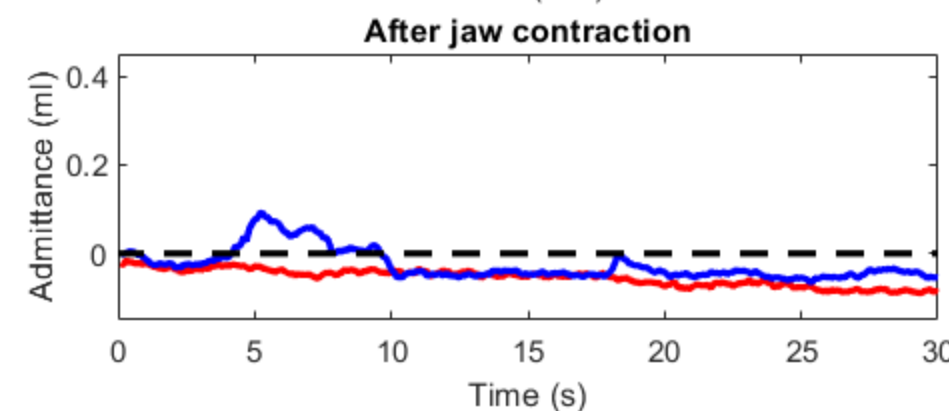
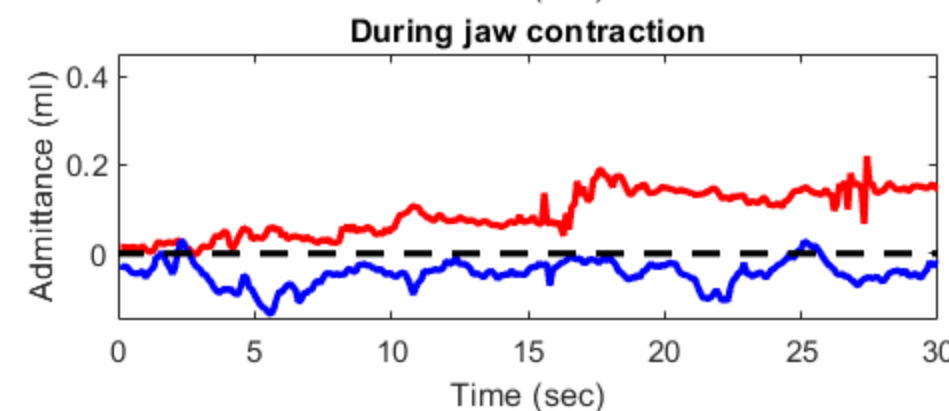
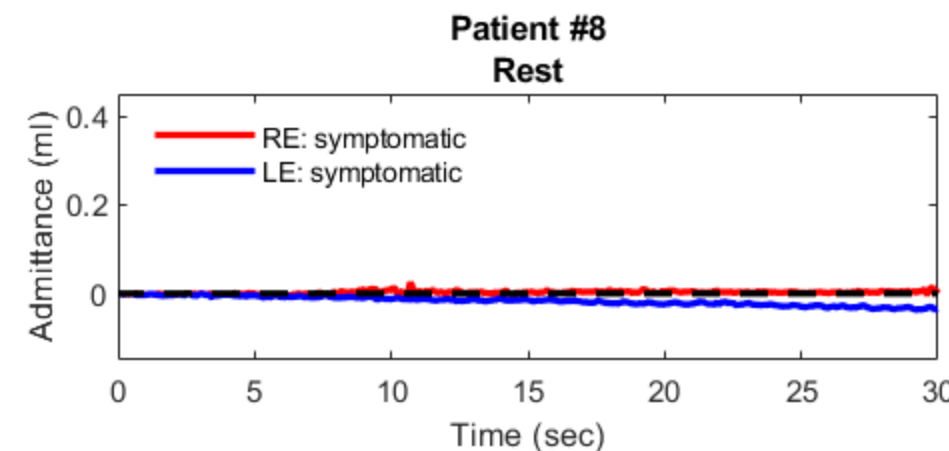
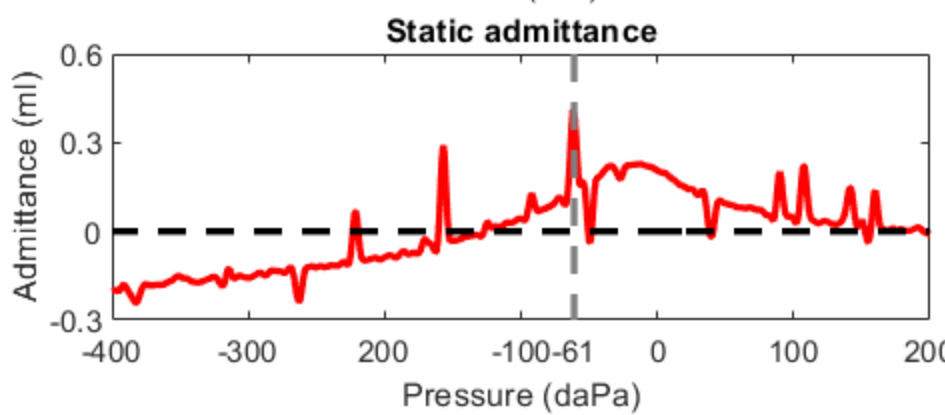
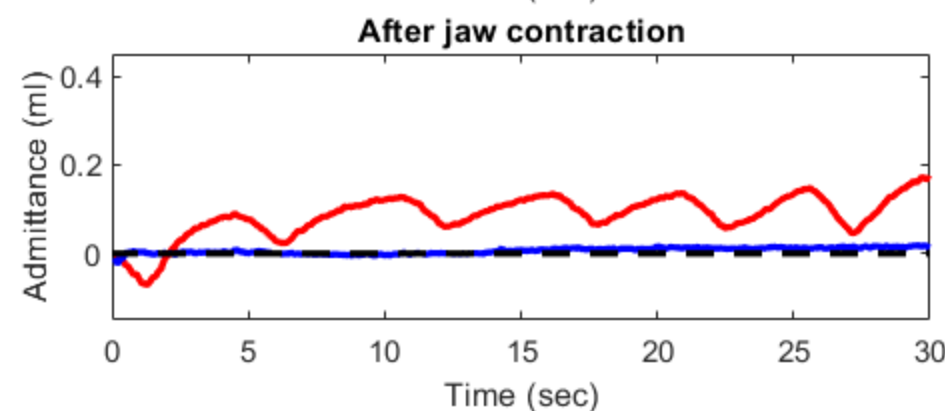
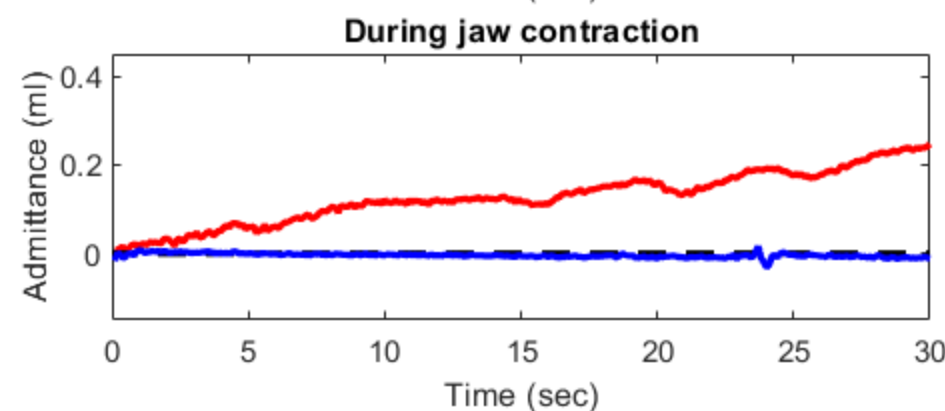
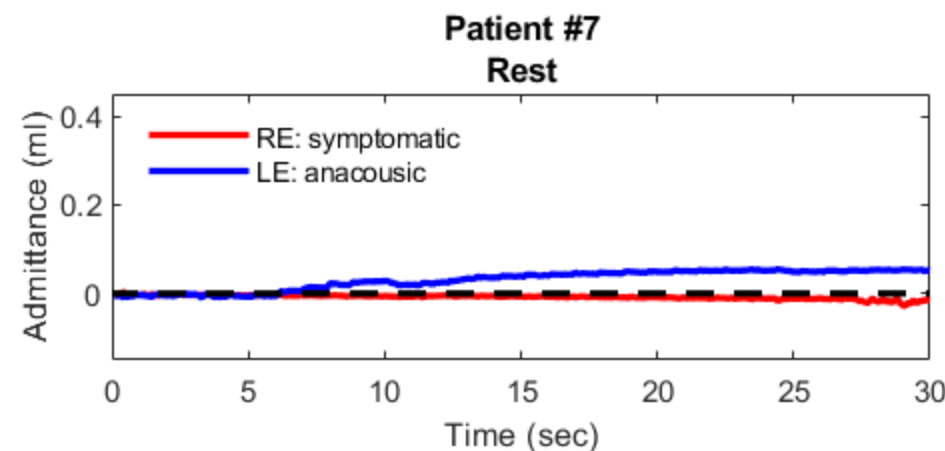
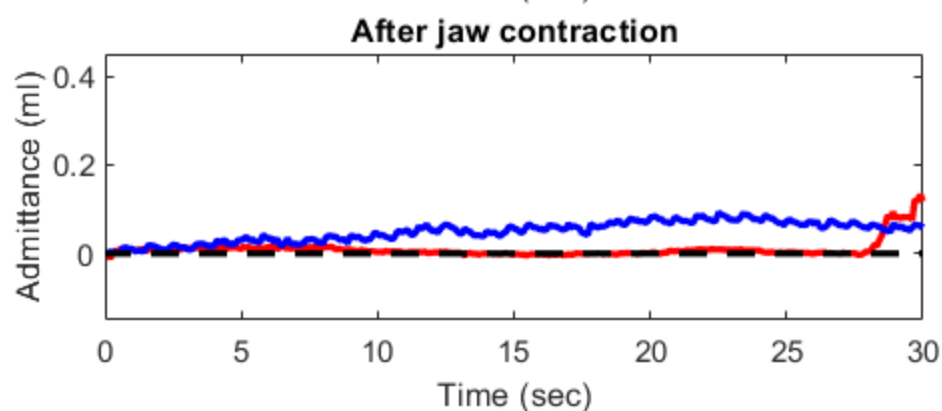
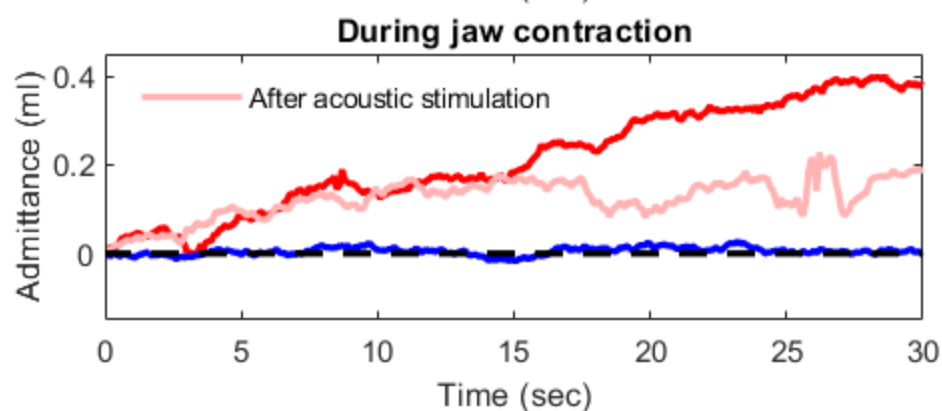
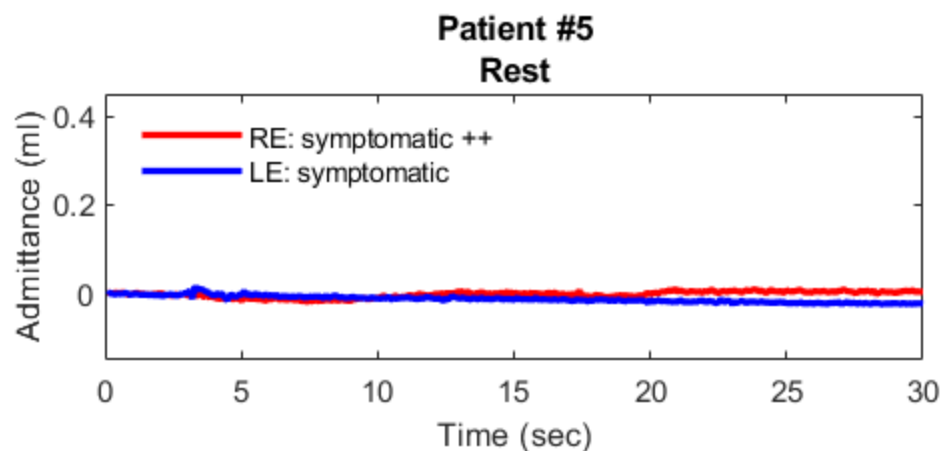


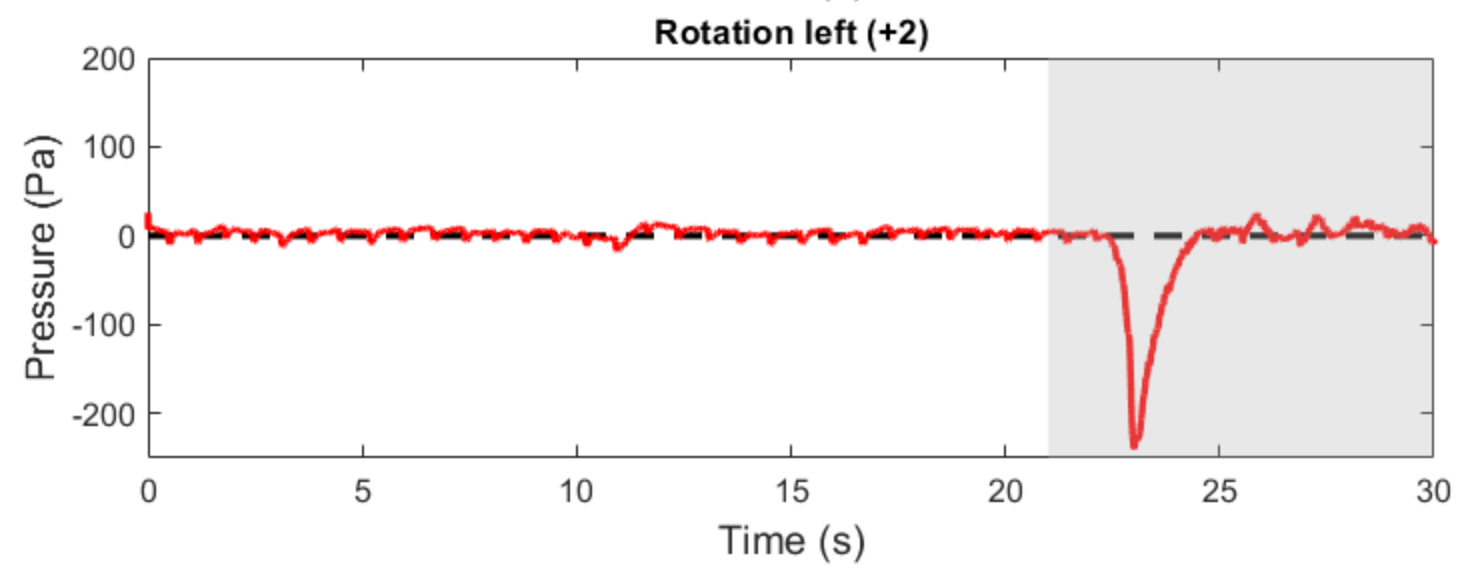
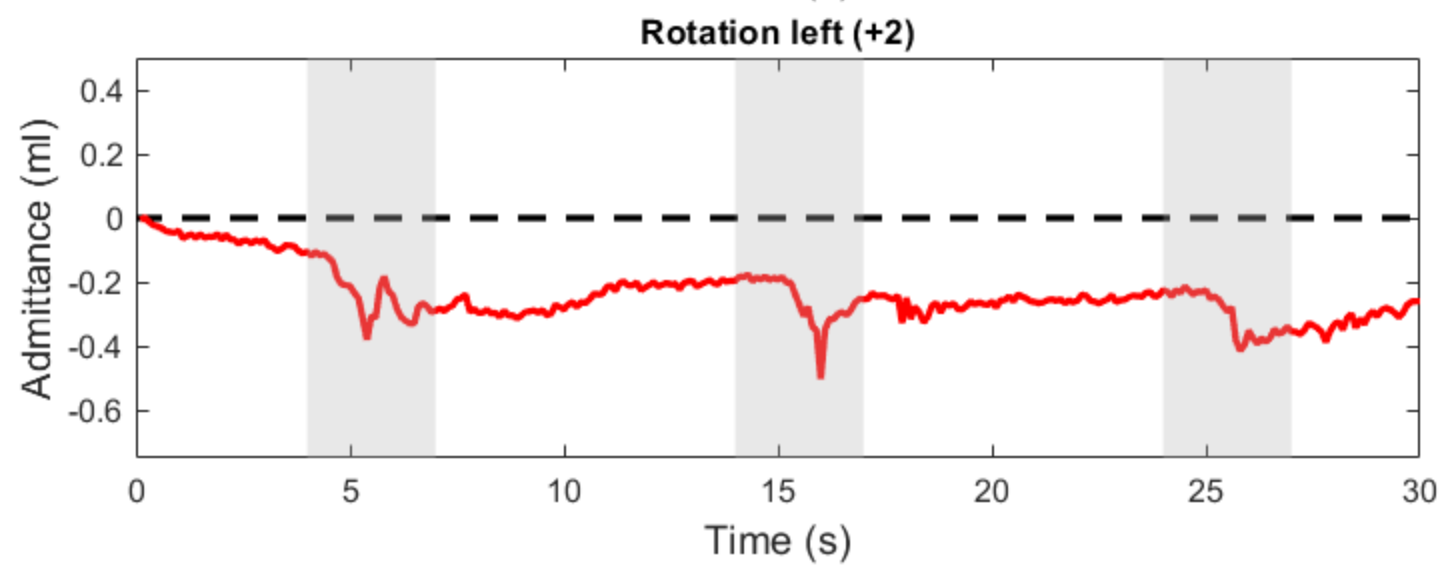
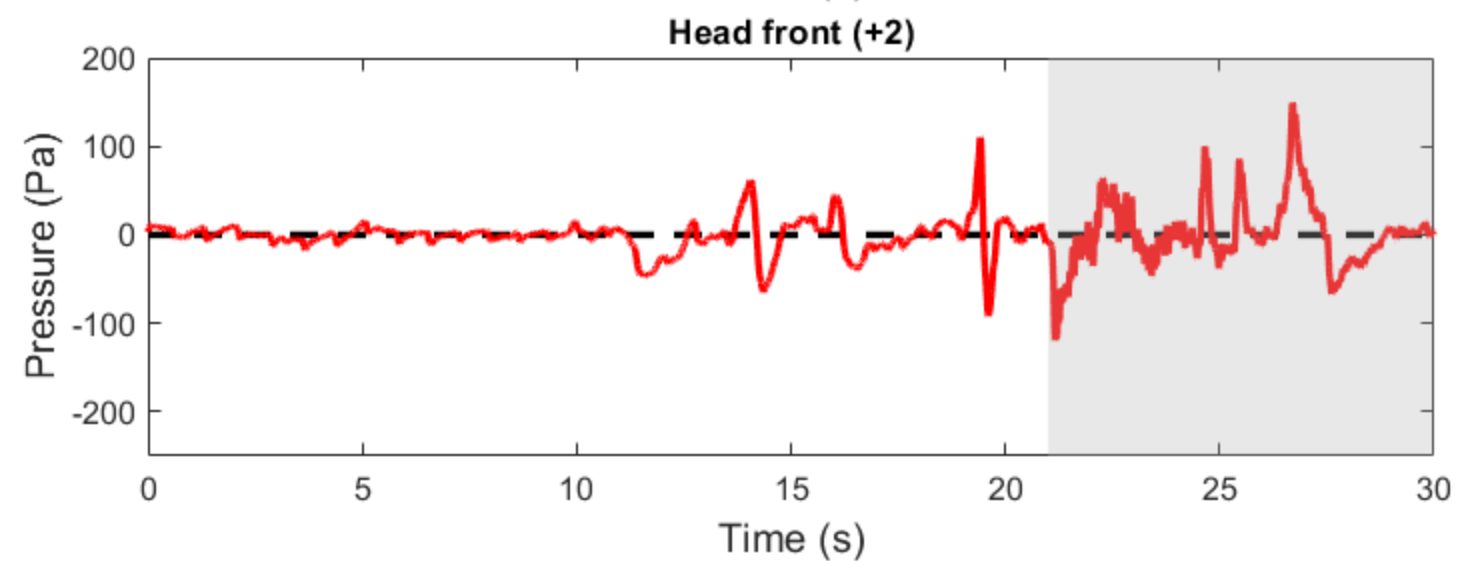
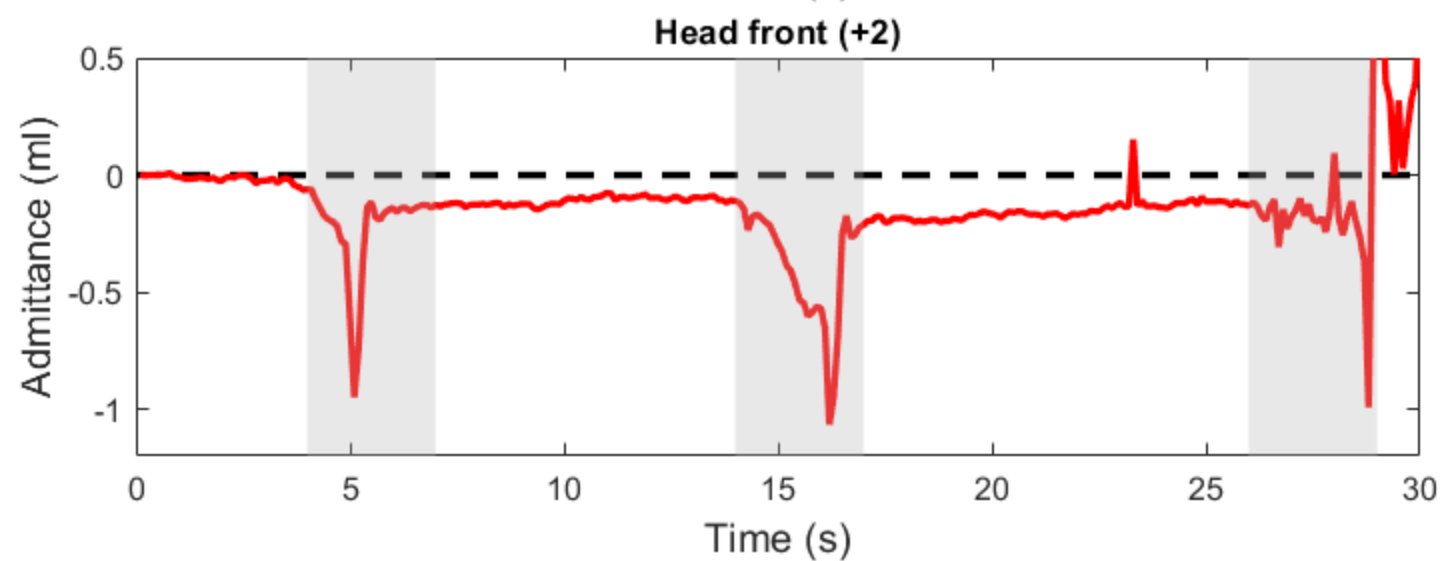
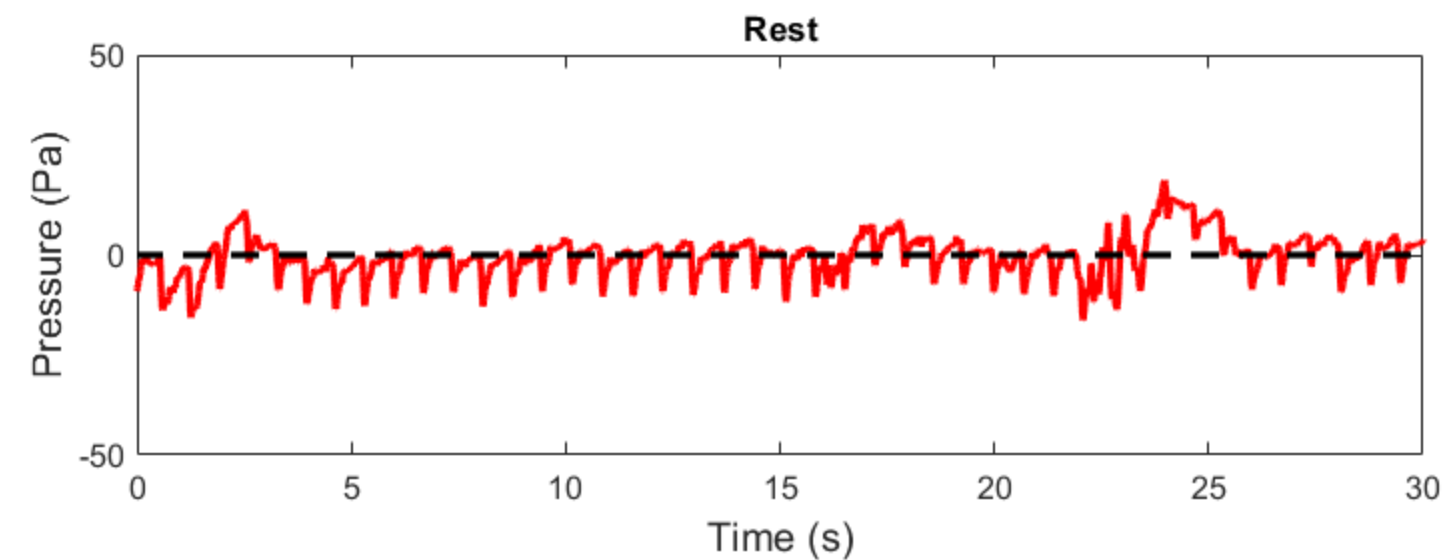
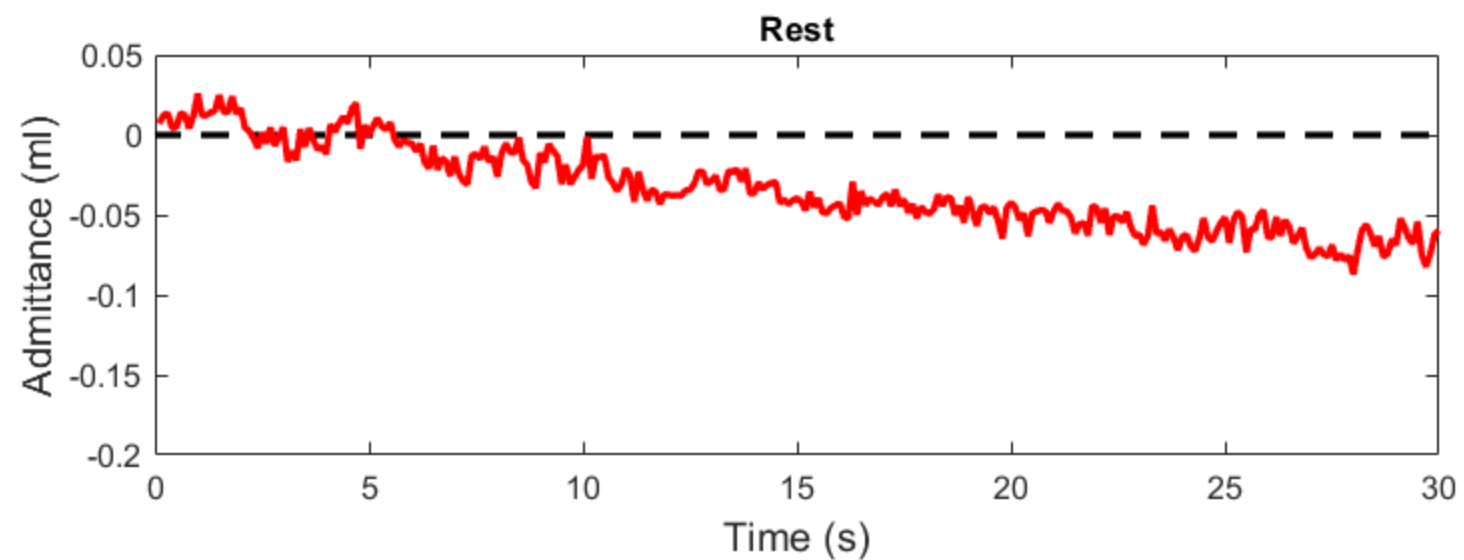
Patient #3 - pressing trigger point (left temple)

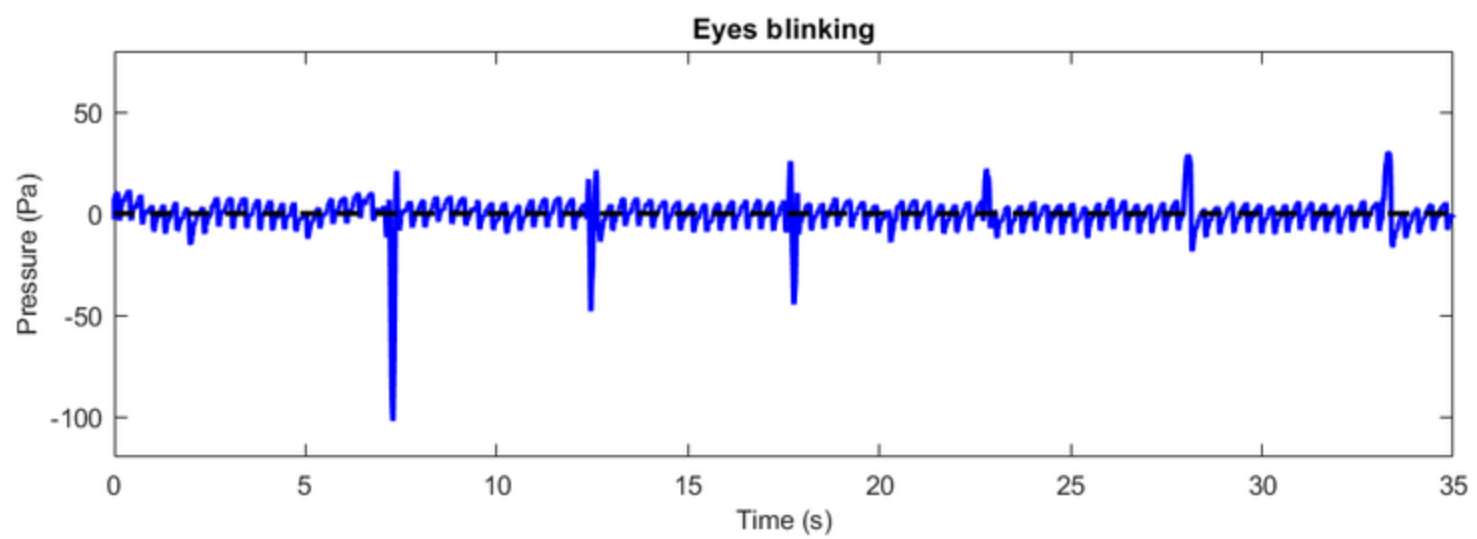
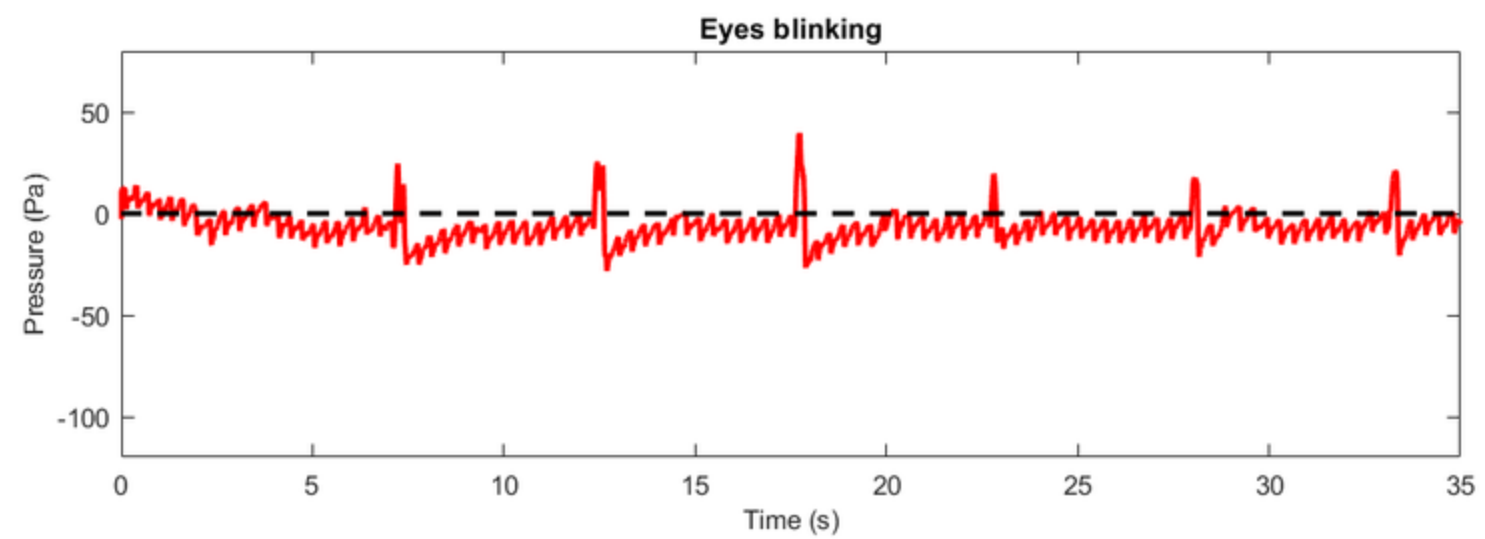
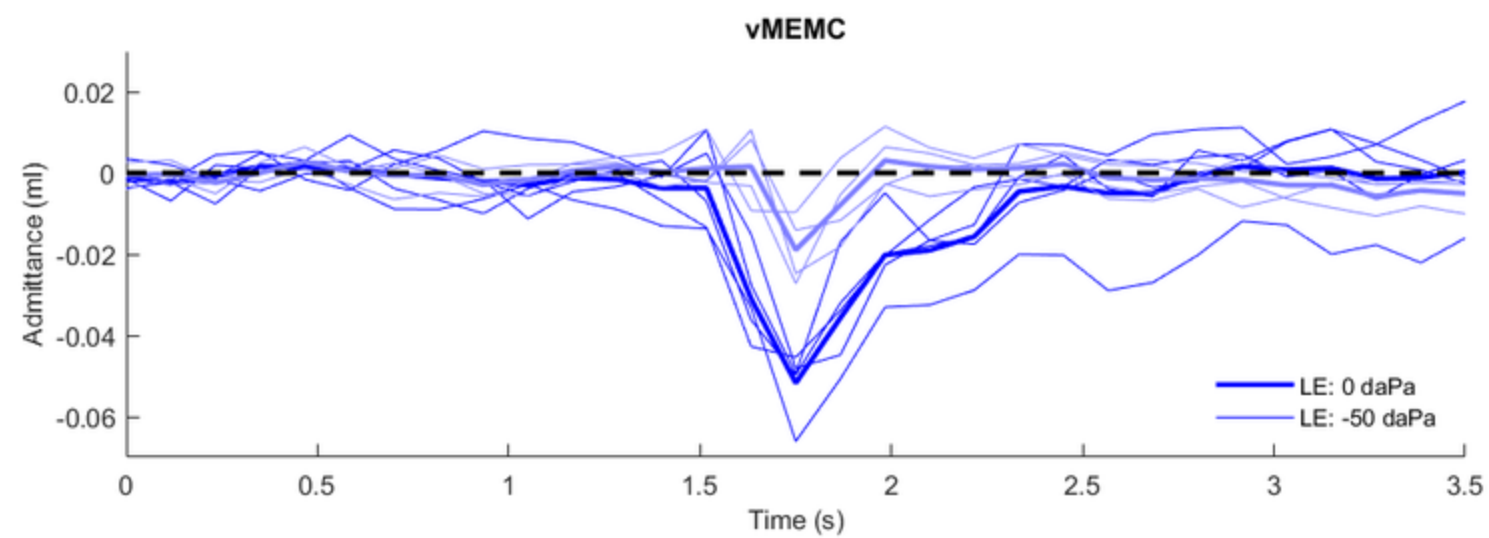
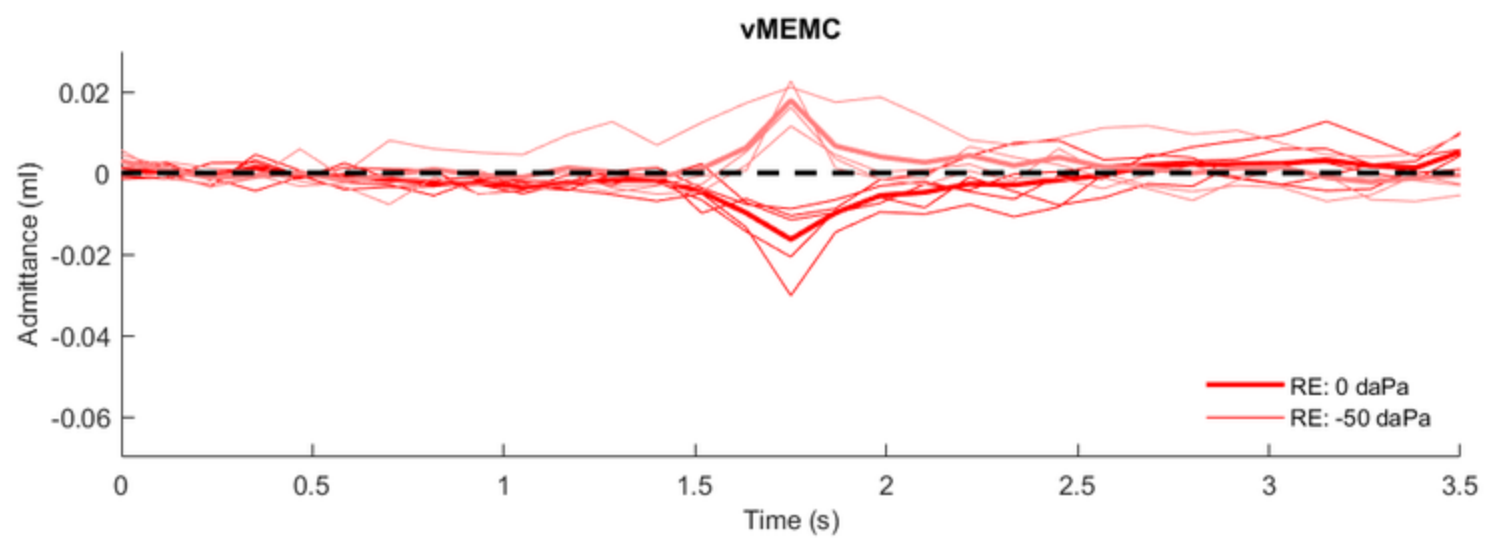
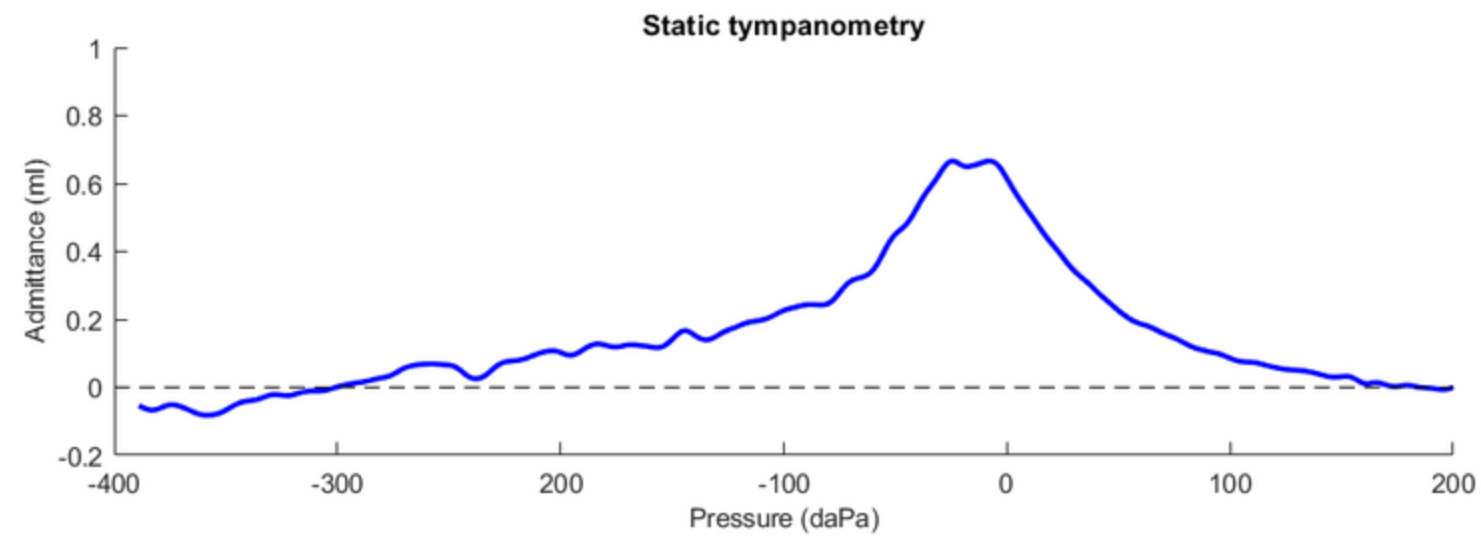
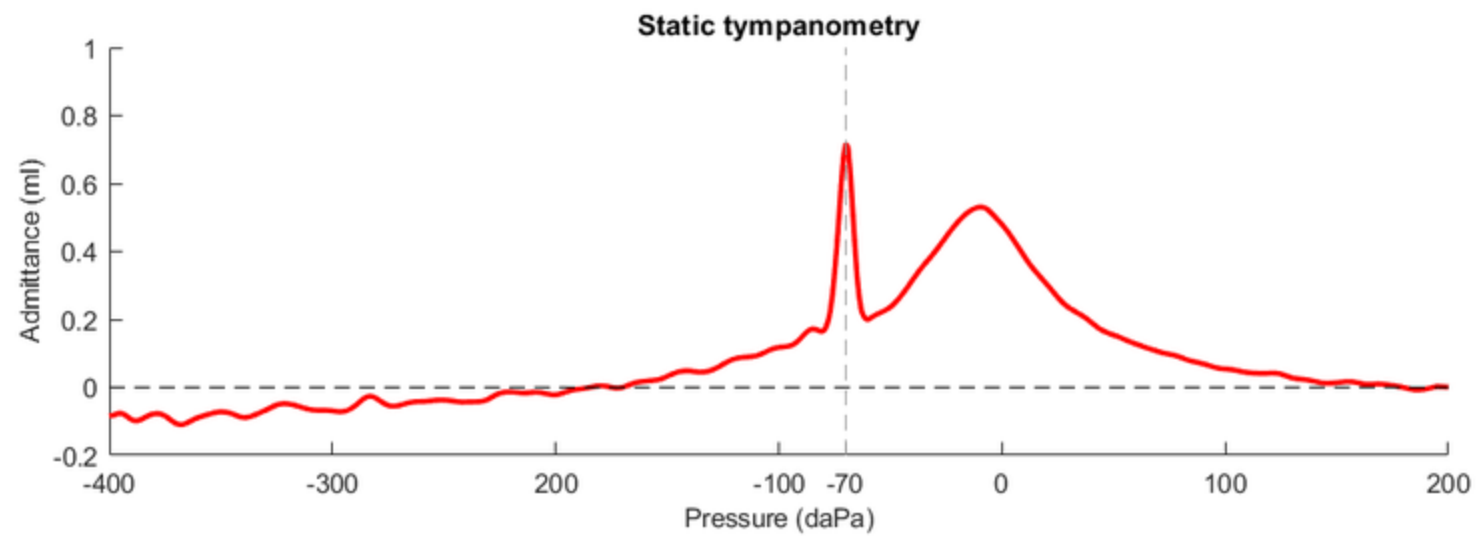


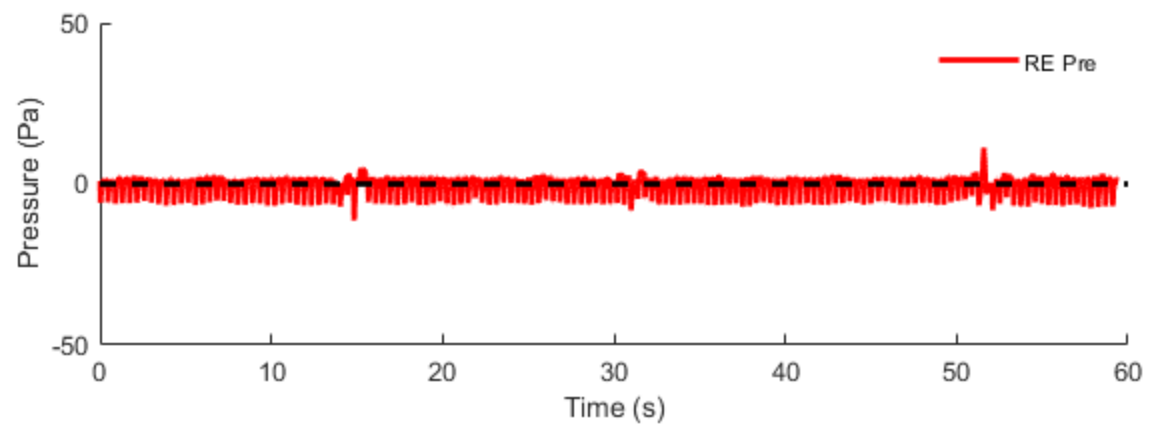
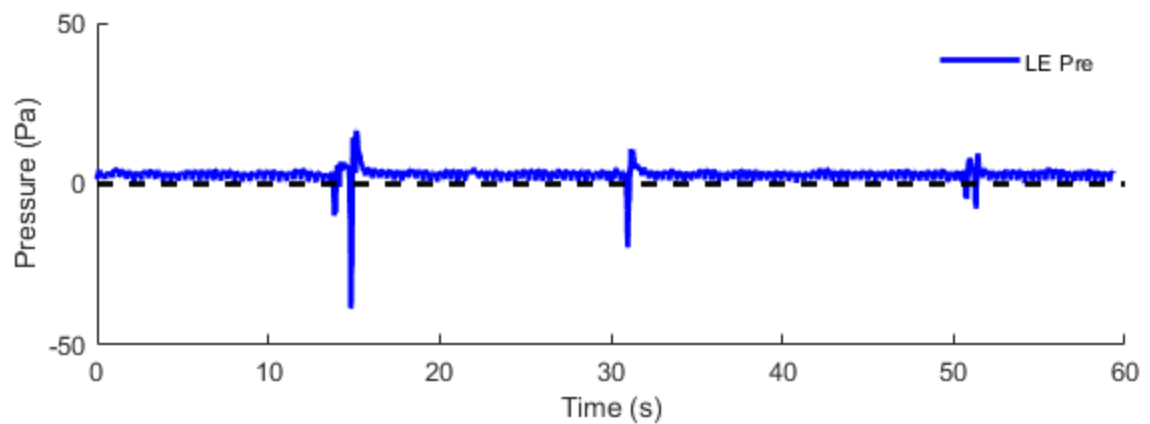
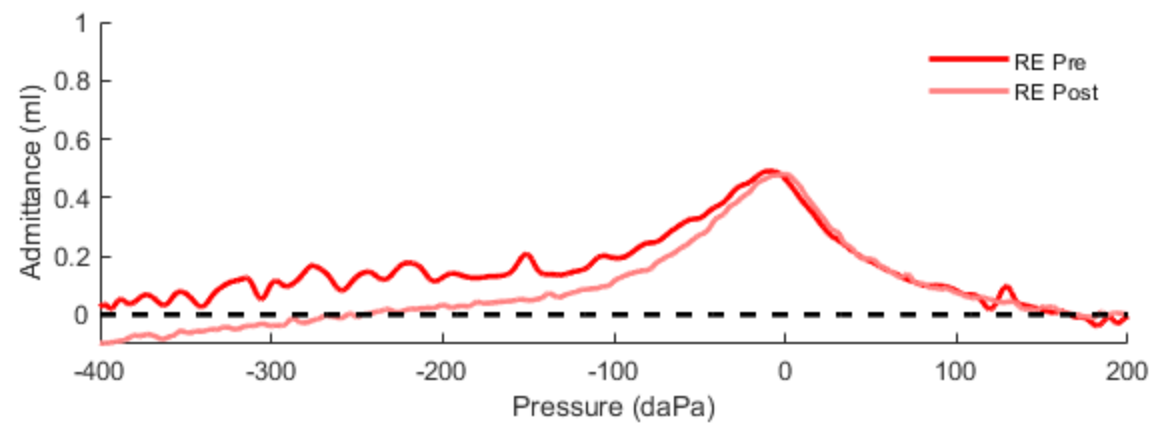
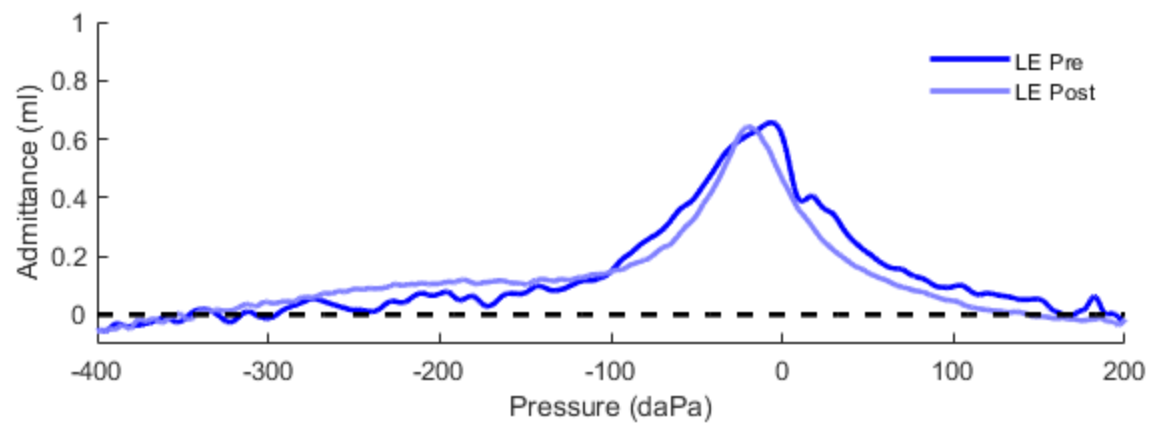
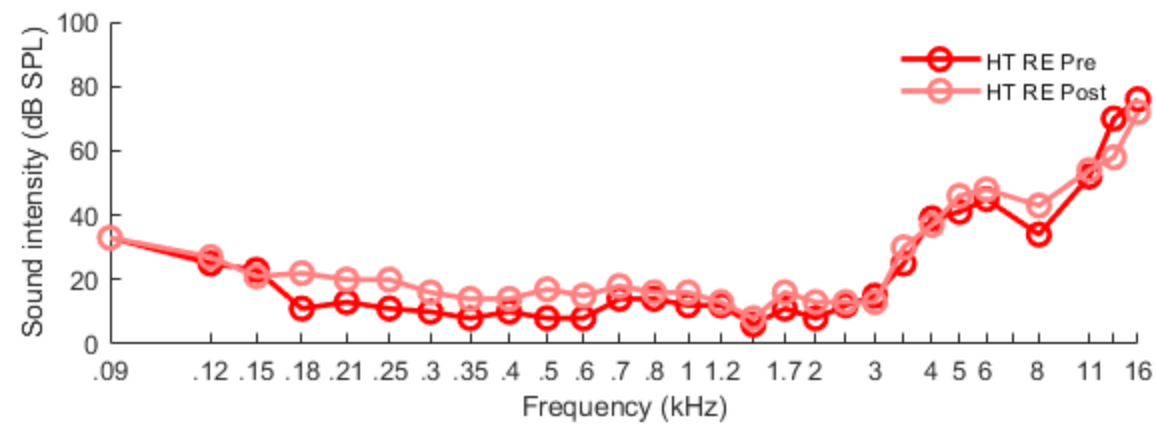
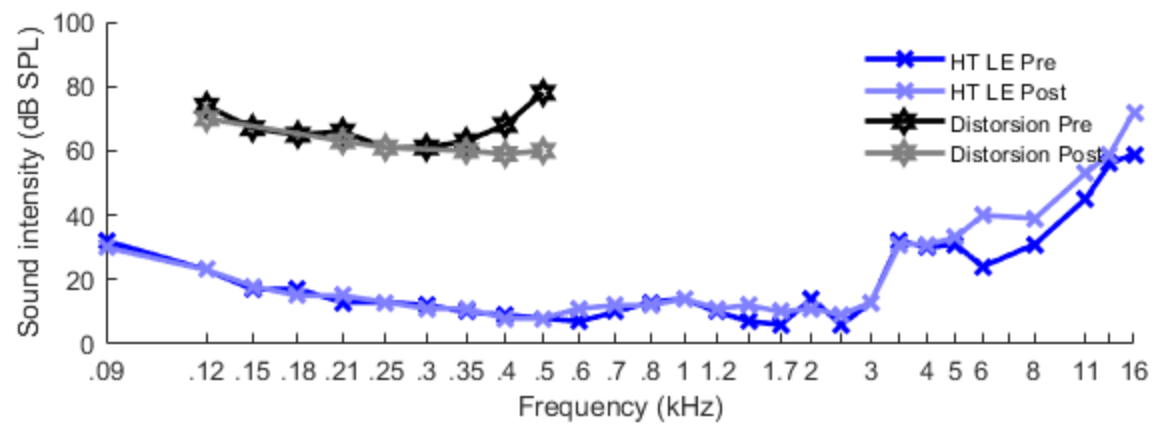
Patient #6 - pressing trigger point (temporomandibular joint)











Patients	Age	Sex	Primary concerns	Symptoms etiology
1	34	M	Spontaneous popping/clicking of the LE with pulsatile tinnitus	Confinement & stress
2	53	M	Continuous high-pitch tinnitus and audible clicks in the RE	After ear surgery
3	33	M	Bilateral hyperacusis, popping/clicking of the RE following impulsive sound	Adverse reaction to medication including multiple neuropathies
4	36	M	Sound distortion in the RE only, feel spasm/vibration in his ear, hyperacusis bilaterally but more in the RE	Acoustic trauma, following a loud concert
5	32	M	Tinnitus & hyperacusis, pain, bilaterally, RE more symptomatic	Acoustic shock: blast during a concert
6	32	M	Otalgia and popping/clicking in the LE, with bilateral tinnitus (LE: High pitch, RE: low pitch)	Acoustic shock with startle reflex
7	36	F	Tinnitus, Hyperacusis, Earfullness and otalgia mostly in the RE	Following a Sudden Hearing loss in the LE
8	26	F	Tinnitus and hyperacusis bilaterally, spasm in the ear	Acoustic trauma: Power tools used for several days
9	45	M	Tinnitus bilaterally, high intensity RE	Acoustic shock? After ME injection, a bubble exploded in the ear
10	25	M	Pain hyperacusis and intermittent tinnitus in the RE	Acoustic trauma: several loud concert exposure
11	35	M	RE: continuous tinnitus, LE: tinnitus triggered by eye blinking, sound &	Acoustic shock? After yelling at someone

vibrations

Patients#	Laterality	Symptomatic or not	Static Tympanometry			Type	Hearing thresholds (dB HL)		
			TPP (daPa)	ECV (ml)	SA (mmho)		PTA low	PTA mid	PTA high
1	LE	Symptomatic (++)	-1	1.4	1.4	A	5	5	8
1	RE	Symptomatic	-8	1.4	1.4	A	5	7	10
2	LE	Normal	-39	1.6	1	A	35	37	45
2	RE	Symptomatic	-56	1.6	1.6	AD	13	33	62
3	LE	Normal	-14	1.3	0.5	A	0	-2.5	-3
3	RE	Symptomatic	-6	1.3	0.6	A	0	-5	3
4	LE	Normal	-10	1.1	0.5	A	3	-2	2
4	RE	Symptomatic	-10	1.5	0.5	A	3	5	7
5	LE	Symptomatic	NT	NT	NT	NT	28	34	40
5	RE	Symptomatic (++)	NT	NT	NT	NT	32	33	27
6	LE	Symptomatic (++)	NT	NT	NT	NT	10	8	13
6	RE	Symptomatic	NT	NT	NT	NT	10	5	8
7	LE	Anacousic	NT	NT	NT	NT	70	95	120
7	RE	Symptomatic	-13	1	0.2	AS	8	5	5
8	LE	Symptomatic	NT	NT	NT	NT	5	8	8
8	RE	Symptomatic	NT	NT	NT	NT	8	10	8
9	LE	Symptomatic	-8	1.6	1.5	A	5	2	15
9	RE	Symptomatic (++)	-5	1.5	1	A	8	8	18
10	LE	Normal	-5	1.6	0.7	A	7	-5	-1
10	RE	Symptomatic	-11	1.4	0.6	A	6	-3	-1
11	LE	Symptomatic	-3	1.5	0.7	A	4	7	18
11	RE	Normal	-7	1.6	0.6	A	3	7	28

NT = not tested, (++) = most symptomatic ear

TPP: Tympanometric Peak Pressure, ECV: Ear Canal Volume, SA: Static Admittance, PTA: Pure Tone Average hearing thresholds

Patients	Baseline	Head back	Head front	Head left	Head right	Right rotation	Left rotation	Jaw right	Jaw left	Mouth opening	Jaw contraction	Jaw protrusion	Movement of the eyes
1	0	0	0	0	0	0	0	0	0	0	0	0	0
2	8	0	-3	-3	-3	0	0	0	0	0	0	+1	0
3#	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
4	0	0	0	0	0	0	0	0	0	0	0	0	0
5	3.5	0	0	0	0	0	0	0	0	0	0	0	0
6#	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT	NT
7	2.5	+0.5	0	0	0	0	0	0	0	0	0	+0.5	0
8	4	0	+0.5	0	0	0	0	0	0	+0.5	+1.5	+1	+0.5
9	4	+2	+2	+1	+1	+2	+2	+3	+3	+3	+4	+4	0
10	0	0	0	0	0	0	0	+1	0	0	+5	+4	0
11*	0	0	0	0	0	0	0	0	0	0	0	0	0

* Clicking in the ear by producing a voluntary eye blinking or tremor of the eyes

Clicking in the ear by pressure on trigger point

Patient #	Spontaneous	Sound	Trigger point	Somatic maneuver	Air pressure	Voluntary
1	X					
2	X			X	X	
3		X	X			X
4		X				
5		X		X		
6			X			X
7				X	X	
8				X		X
9				X		X
10				X	X	X
11				X		