Use Authorization

In presenting this thesis in partial fulfillment of the requirements for an advanced degree at Idaho State University, I agree that the Library shall make it freely available for inspection. I further state that permission to download and/or print my thesis for scholarly purposes may be granted by the Dean of the Graduate School, Dean of my academic division, or by the University Librarian. It is understood that any copying or publication of this thesis for financial gain shall not be allowed without my written permission.

Signature_____

Date_____

THE EFFECTS OF OPIOIDS ON HEARING, EXECUTIVE FUNCTIONING, AND LANGUAGE

by

Marissa N. Dey

A thesis

submitted in partial fulfillment

of the requirements for the degree of

Master of Science in the Department of Communication Disorders and Sciences

Idaho State University

Summer 2017

Committee Approval

To the Graduate Faculty:

The members of the committee appointed to examine the thesis of Marissa Dey find it satisfactory and recommend that it be accepted.

_____

Dr. Nicholas Altieri
Major Advisor

_____

Dr. Tony Seikel
Committee Member

_____

Dr. Curt Anderson
Graduate Faculty Representative

TABLE OF CONTENTS

LIST OF TABLES

THE EFFECTS OF OPIOIDS ON HEARING, EXECUTIVE FUNCTIONING, AND LANGUAGE

Thesis Abstract—Idaho State University (2017)

Due to the increased use of opioids for pain management in postoperative and disordered populations, healthcare professionals must become more educated on the effects of these medications. This study reviewed the data set provided by previous researchers and compiled evidence relating use of opiate analgesics to vital aspects of communication. Additionally, this study aimed to explore relationships between reported communication deficits and opiate type, duration of use, dosage, and recovery outcomes. Data from 28 previous studies was collated and presented for analysis in the present study. Case study analysis and effect size comparisons were utilized to analyze the collected data. A pattern of relationships regarding opiate pain medications and communication deficits emerged throughout the course of this study. The findings imply there is a potential for opioids to increase an individual's risk level for hearing loss and cognitive deficits.

Chapter 1: Review of Literature

Introduction

In recent years, the use of prescription opioids for pain management has significantly increased (Manchikanti et al., 2012). In fact, Manchikanti et al. (2012) reported a 149% increase in opioid retail sales from 1997 to 2007, with hydrocodone/acetaminophen being the most commonly prescribed medicine in the United States (U.S.) during 2011. Due to the increased use of opioids for pain management in postoperative and disordered populations, healthcare professionals must become more educated on the effects of these medications. The following review will examine the nature of opioids, the hearing mechanism, executive function, language processing, and the relationship between opiate use and communication outcomes.

Opioids

Opioid analgesics, commonly known as opiates or narcotics, are a class of medications used for the treatment of moderate to severe or chronic pain. In a study conducted by Palmer et al. (2014), the most common non-cancer pain related diagnosis associated with chronic opiate use include back and neck pain, mental health diagnosis, arthritis, migraine/tension headache, neuropathy, and fibromyalgia. These medications act on opiate receptors in the brain and nervous system to diminish the pain experienced by the individual. Opiates stimulate the mesolimbic reward system of the midbrain and cerebral cortex through activation of dopamine, a neurotransmitter (Kosten & George, 2002). Dopamine activation occurs when opioids attach to specialized proteins, called mu

opioid receptors, that are located on opiate-sensitive neurons (Kosten & George, 2002). The euphoria that is experienced as a result of the dopamine activation significantly increases the risk for dependence and addiction in patients taking opioids. Physical dependence, also called tolerance, is the body's response to long-term use of opioids and oftentimes results in a need for higher doses to achieve the same effects (Kosten & George, 2002). Most individuals who use narcotics chronically are attempting to manage long-term pain; however, the development of physical dependence can also contribute to chronic opioid use.

Common health-related side effects of opioid pain-medications include: constipation, nausea, euphoria, slowed breathing, low blood-pressure, drowsiness, confusion, and poor coordination (Mayo Foundation for Medical Education and Research, 2016). Although many health-related side effects of opioids have been identified, the majority of current research has neglected to consider the effects of opioids on aspects that relate to communication. To examine the effects of opiates on various aspects of communication, we must first identify the systems that interact to make communication possible.

The Speech Chain

The speech chain is a representation of the complex interaction between the linguistic, physiological, and acoustic levels of the communication system in humans. A widely-accepted model of the speech chain was described by Denes and Pinson (2012). They stated that a message begins at the linguistic level of the speaker and involves the

selection of appropriate words and sentences. Once a message has been selected, the physiological level is responsible for the required neural and muscular activity to produce the message. The speech event then reaches the physical level, which involves the generation and transmission of the sounds wave. At this point, the speaker's message has been delivered and the process then reverses during the listener's perception of the message. At the physical level, the listener's auditory mechanism is activated at the presentation of the sound wave. The event continues to neural activity in the hearing and perceptual mechanisms at the physiological level and is completed when the listener recognizes the words and sentences at the linguistic level (Denes & Pinson, 2012).

Opioid-Induced Hearing Loss

The hearing mechanism, also called the auditory system, is considered to be one of the primary components involved in speech perception. The auditory system is composed of the outer ear, the middle ear, the inner ear, the auditory nerve, and the auditory brainstem. The outer ear consists of the externally visible aspects of the ear, as well as the ear canal, and plays a relatively small role in the hearing process (Denes & Pinson, 2012). The middle ear forms the mechanical link between the ear drum and the inner ear and consists of three auditory ossicles: the malleus, the incus, and the stapes (Denes & Pinson, 2012). The auditory ossicles are suspended by several ligaments in the middle ear chamber, a cavity in the skull bones. According to Denes and Pinson (2012), the middle ear's two primary functions are to increase the amount of acoustic energy entering the fluid of the inner ear and to protect the inner ear from loud sounds.

The inner ear is an intricate system of small cavities in the skull bones. While it contains mechanisms vital to auditory perception, the inner ear is also home to the vestibular system, which monitors and manages the body's orientation with respect to gravity (Gray, 1997). The vestibular system primarily lies within the membranous labyrinth of the inner ear and consists three semicircular ducts and two otolithic organs. The semicircular ducts are pairs of sensory organs oriented approximately 90 degrees to each other that respond to angular acceleration of the head, ultimately working to detect head movements (Gray, 1997). Each semicircular duct contains hair cells that bend upon presentation of fluid traveling as the result of the head turning (Gray, 1997). The saccule and utricle are the otolithic organs of the vestibular systems and contain receptors, called maculae, formed by hair cells that respond to head tilts in any direction (Gray, 1997).

In terms of the auditory system, the inner ear also contains the cochlea, a cavity coiled similar to a snail's shell and the location where mechanical vibrations are transduced into electro-chemical nerve impulses (Denes & Pinson, 2012). The Organ of Corti is a collection of cells that lie on the basilar membrane in the cochlear duct; these cells convert the mechanical motion of the basilar membrane into signals that can be transmitted to the brain (Denes & Pinson, 2012). Hair cells serve as the sensory organs in the Organ of Corti and are rooted in the basilar membrane, which is mechanically responsible for how the cochlear partition responds to sine-wave stimuli. The Organ of Corti is structurally supported by Corti's Arch, which is formed by the joining of two rods into a "V-shape" (Denes & Pinson, 2012). These rods separate the inner and outer

hair cells, with the inner hair cells lying on the side closest to the central core around which the cochlea spirals (Denes & Pinson, 2012).

According to Denes and Pinson (2012), signals in the nervous system are transmitted as electrochemical pulses along nerve fibers from the auditory nerve. These nerve fibers extend into the Organ of Corti, with their endings in close proximity of the sensory hair cells (Denes & Pinson, 2012). As the basilar membrane vibrates in response to incoming sound waves, the hair cells are bent. This stimulates the auditory nerve fibers, which produces the electrochemical pulses that are sent to the brain (Denes & Pinson, 2012). When these pulses reach the auditory cortex in the temporal lobe of the brain, ultimate perception of the "heard" event occurs.

Each auditory nerve fiber is responds to a different narrow range of frequencies and are maximally responsive to one frequency, called the characteristic frequency (Gray, 1997). Neuronal tuning curves serve as the standard tool in characterizing contributions of individual neurons during the process of auditory perception (Butts & Goldman, 2006). Tuning curves plot the average firing rate of a neuron when provided a set of stimuli, with the stimulus that evokes the highest firing rate appearing at the peak of the curve (Butts & Goldman, 2006).

When examining the relationship between auditory input and an individual's perception of sounds, the event-related potential (ERP) technique can be used to measure brain activity through signal averaging (Woodman, 2010). Woodman (2010) explains that averaged ERPs measure the electrical potentials in the extracellular fluid that are created by ions flowing across cell membranes during the release of neurotransmitters. Unlike

many spatial imaging techniques, ERPs produce a temporal resolution of brain activity measured in milliseconds (Woodman, 2010). This makes ERPs a preferred method of measurement in regards to attention and perception, as many related aspects seem to occur at tens of milliseconds, according to Woodman (2010). Every ERP waveform is composed of many ERP component waves, each of which represents a different aspect of cognitive processing (Woodman, 2010). This study aims to examine the cognitive processes involved in auditory perception and will therefore utilize research using long latency auditory evoked potentials (LLAEPs), an ERP specific to auditory processing. Didone et al. (2016) describe LLAEPs as electrophysiological tests that assess central auditory nervous system dysfunction. By objectively measuring associated cognitive processes, LLAEPs assess auditory ability, which includes discrimination, memory, attention, and detection of stimuli (Didone et al., 2016).

For the purpose of this study, we will be examining the P300 component and its implications for auditory target processing in opiate users. According to Didone et al. (2016), the positive potential of the P300 component is produced by an individual's recognition of uncommon stimulus within a series of common stimuli, referred to as an oddball paradigm. Muller et al. (2007) examined auditory target processing, specifically P300 component amplitudes and latencies, in methadone substituted opiate addicts. When compared to controls, methadone-using participants demonstrated no reduction in attention dependent processing (Muller et al., 2007). These results indicate that opioids do not affect the neural processing of auditory stimuli.

Mechanisms Underlying Hearing Loss

According to Campbell (2007), two general mechanisms by which cells die have been classified: necrosis and programmed cell death (PCD). While PCD is the natural occurrence of genetic cell death, necrosis is described as "a passive cellular event that is characterized by formation of vacuoles in the cytoplasm, swelling of mitochondria, dilation of the endoplasmic reticulum, cellular debris, and disintegration or a loss of cell membrane intensity (Campbell, 2007, p. 71)." Necrosis is typically the result of severe cellular stress or damage induced by mechanical means, lack of nutritional supply, or exposure to toxic organisms (Campbell, 2007).

According to the American Speech-Language-Hearing Association (ASHA) (ASHA, 2015), sensorineural hearing loss (SNHL) occurs when there is damage to the inner ear or to the nerve pathways that travel from the inner ear to the brain. Typically, SNHL reduces an individual's ability to hear faint sounds and causes normal speech to sound muffled or unclear (ASHA, 2015). Traux (1999) describes the reduction in hearing ability as a threshold shift, in which the ear's sensitivity decreases as a protective mechanism against the damaging stimulus. When a threshold shift occurs, sounds must be produced at or above a certain intensity to be heard (Truax, 1999). According to Schow and Nerbonne (2013), hearing is considered to be within normal limits when pure tone thresholds are 25 dB or less between frequencies of 250 and 4,000 Hz. If pure tone thresholds are greater than 25 dB at these frequencies, a hearing impairment is present and amplification should be considered when a hearing loss affects a person's ability to

hear speech (Schow & Nerbonne, 2013). Candidacy for cochlear implantation is possible when pure tone thresholds are greater than 70 dB in the mid to high frequencies.

In recent years, a growing number of case studies have related chronic opioid abuse to sensorineural hearing loss. A comprehensive review of these case studies and the associated hearing losses has been provided in Appendix A. A possible explanation of opioid-induced SNHL has been related to research conducted by Jongkamonwiwat et al. (2006), who examined the relationship between the auditory mechanism and the opioid system in male albino guinea pigs. Upon death, the cochleas were removed from the guinea pigs and underwent DNA and immunohistochemical testing. Jongkamonwiwat et al. (2006) then used florescence double-labelling of the cochlear tissues to examine the relative distribution of opioid receptors. By examining the immunoreactivity of each type of opioid receptor, the researchers were able to localize the receptors within the cochlea. All three types of opioid receptors, which include mu opioid receptors (MOR), delta opioid receptors (DOR), and kappa opioid receptors (KOR), were found within the cochleas of the experimental group of guinea pigs (Jongkamonwiwat et al., 2006). Many of the opioid receptors were located directly beneath the inner hair cells, which strengthens the theory of hair cell involvement in opioid-induced hearing loss. With the auditory nerve fibers residing so closely to the hair cells, however, one must also consider the possible auditory nerve involvement. This study offered the first description of the expression and localization of opioid receptors in specific areas of the guinea pig cochlea. The results of this study provide evidence that opioids play a role in the auditory system, specifically in the cochlea.

Treatment of Sensorineural Hearing Loss

In the event of a sensorineural hearing loss, medical professionals may implement a course of treatment to either reverse or compensate for the damage. Audiologic rehabilitation for sensorineural hearing loss commonly consists of the use of hearing aids, hearing assistive technology systems (HATS), or cochlear implantation (Schow & Nerbonne, 2013). Hearing aids have been found to increase word understanding ability in individuals with a sensorineural loss through improving the signal-to-noise ratio (Schow & Nerbonne, 2013). Oftentimes used in addition to hearing aids, HATS assist in the maintenance of independent function for those with a hearing loss, according to Schow & Nerbonne (2013). HATS can either improve the ability to hear in background noise or utilize integration of other senses and consist of the following devices: hardware devices, FM sound systems, infrared systems, audio loop systems, telephone listening devices, television modifications, and alerts and alarms (Schow & Nerbonne, 2013). For individuals who do not benefit from traditional amplification methods, cochlear implantation may be considered. Cochlear implants are surgically inserted into the cochleas of individuals with severe to profound sensorineural hearing losses to provide stimulation of the auditory nerve (Schow & Nerbonne, 2013).

With specific regards to opioid-induced hearing loss, measures may be taken to reverse the auditory damage. Evidence suggesting complete recovery of auditory function as a result of opiate abstinence immediately following reported hearing loss has been presented by Van Gaalen, Compier, and Fogeloo (2009) and Christenson and Marjala (2010). The use of oral steroids, such as prednisone, to reverse the effects of idiopathic

SSNHL was explored by Chen et al. (2015). In a retrospective study of 215 participants who were administered steroids, approximately one-third of participants recovered full hearing function, one-third recovered partial hearing function, and one-third did not recover any hearing function (Chen et al., 2015). These results suggest steroid treatment may be a viable treatment option for some patients with sensorineural hearing losses; however, in cases reporting administration of steroids after an opioid-induced hearing loss, recovery of hearing function may instead be the result of opioid abstinence, or a combination of the two. Future studies should aim to examine the effects of steroid treatment on hearing loss in an abstinent group and a non-abstinent group.

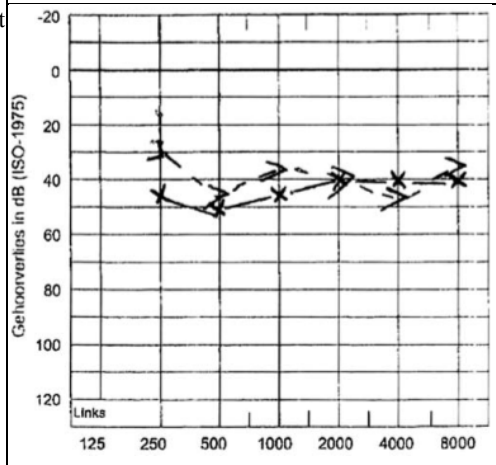
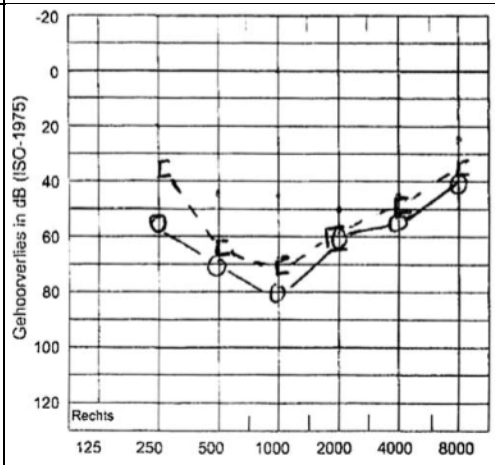
Methadone

Although the current literature is lacking controlled, longitudinal studies regarding opioid involvement in hearing loss, a significant amount of case-studies on the topic are emerging. When examining relevant case-studies, it is important to note the possible involvement of extraneous factors such as the simultaneous use of other medications or substances. Methadone, however, is produced by professional laboratories, legally distributed, and commonly prescribed to opioid addicts as part of recovery programs. Since methadone is manufactured and typically administered in a controlled environment, extraneous factors such as additional substances, dosage, and intake method are significantly minimized.

This allows these cases to begin exploring the potential relationship between opioid-use and hearing loss. Van Gaalen, Compier, and Fogeloo (2009) presented a case

study of a patient who showed signs of a sudden hearing loss after a methadone overdose, in which the subject's hearing function was completely recovered within 10 days of methadone abstinence. The audiometric details of this case study are shown in Table 1.

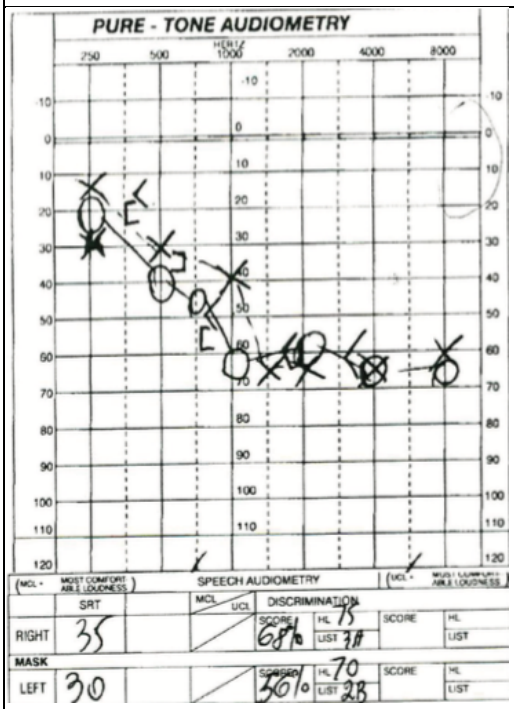
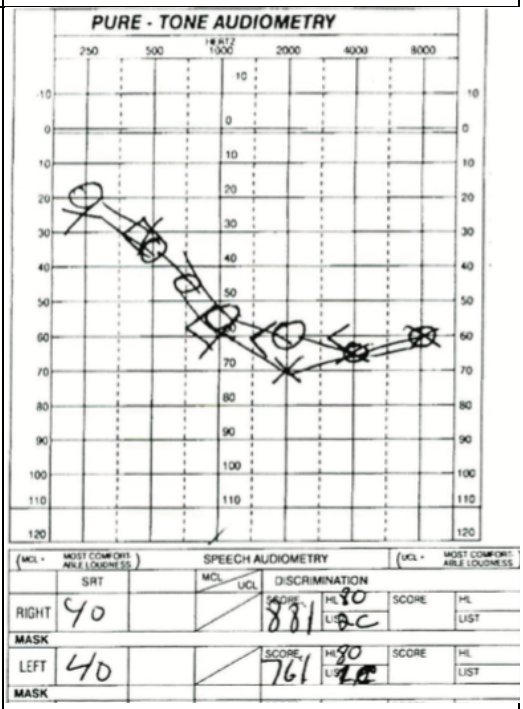
Table 1. Summary of case study presented by Van Gaalen, Compier, and Fogeloo (2009)

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Van Gaalen et al. (2009)	37	M	Methadone	Reported no previous use	Bilateral Sudden Sensorineural	Mild tinnitus	None	Normal audiometry 10 days later
	Audiogram 1 day after overdose: Left Ear					**Audiogram 1 day after overdose: Right Ear**		
								

Christenson and Marjala (2010) presented two cases of sudden SNHL after methadone overdose, in which one of the subject's hearing function completely recovered within 24 hours of methadone abstinence. Saifan, Glass, Barakat, and El-Sayegh (2013) also documented a patient who showed signs of hearing loss related to methadone overdose; however, this patient was reported to restart his use of methadone at his regular dose shortly after the onset of hearing loss symptoms. Upon follow-up audiometry

exams, the participant displayed persistent moderate to severe SNHL bilaterally and was prescribed binaural hearing aids. Table 2 shows the audiometric data of this case study. The permanent, severe hearing loss with continued opioid use is notable because other cases of methadone-induced hearing loss indicated full auditory recovery with opioid abstinence.

Table 2. Summary of case study presented by Saifan, Glass, Barakat, and El-Sayegh (2013)

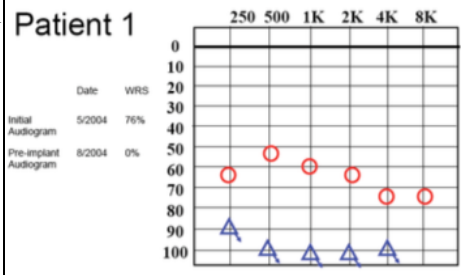
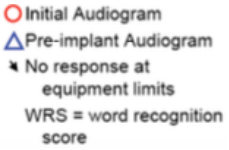
Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Saifan, et al. (2013)	31	M	Methadone	Unknown	Bilateral Sudden Sensorineural	None	None	Persistent profound hearing loss; prescribed binaural hearing aids
	Audiometry 1 month after discharge					**Audiometry 2 months after discharge**		
								

Not only do the findings of these case studies indicate that methadone overuse can cause sudden SNHL, they also indicate that the amount of hearing function recovered may be influenced by the continued versus discontinued use of methadone. Partial recovery of functioning is referred to as "semi-transient." The possibility of a semi-transient hearing loss, in contrast to a permanent loss, could significantly impact how opioid-induced hearing loss is clinically approached and treated.

Hydrocodone

Similar to methadone, hydrocodone is professionally manufactured and distributed, and is currently one of the most commonly prescribed opioids in the U.S. (Manchikanti et al., 2012). However, hydrocodone is typically combined with acetaminophen, also called Tylenol, which is lacking research in regards to possible ototoxic effects. Ho, Vrabec, and Burton (2007) reported five cases of bilateral, progressive sensorineural hearing loss. Oral steroids were initially administered to four of the patients, all of whom were nonresponsive to the treatment and ultimately underwent cochlear implantation. Audiometric data from one patient in this study is presented in Table 3. Friedman, Gherini, House, Luxford, and Mills (2000) documented twelve cases of sudden SNHL after hydrocodone/acetaminophen abuse, all of which were nonresponsive to steroid treatment. Although these results suggest opioid involvement in SNHL, they also present the issue regarding acetaminophen as a confounding factor that could contribute to hearing loss.

Table 3. Summary of case study presented by Ho, Vrabec, and Burton (2007)

Author (Year)	Case Study: Patient 1							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Ho, Vrabec, & Burton (2007)	28	F	Hydrocodone Acetaminophen	> 2 years	Bilateral Progressive Sensorineural	Tinnitus	Steroids, Abstinence unknown	No spontaneous recovery, cochlear implantation
	Audiogram Comparison					**Legend**		
								

In a study conducted by Curhan, Shargorodsky, Eavey, and Curhan (2012), self-report data from 62, 261 women between the ages of 31-48 was used to examine the relationship of analgesics and risk of hearing loss. The use of both ibuprofen and acetaminophen for 2 or more days per week was statistically associated with an increased risk of hearing loss in women; however, aspirin use was not found to increase the risk of hearing loss. In a similar study conducted on 26, 917 men between the ages of 40-74, the use of aspirin, non-steroidal anti-inflammatory drugs, and acetaminophen were all found to increase the risk of hearing loss in men (Curhan, Shargorodsky, Eavey, & Curhan, 2010). Although previous research provides evidence that Tylenol consumption can increase the risk of hearing loss, acetaminophen use oftentimes fails to be mentioned or asked about in initial evaluations. Future research should aim to look at the interaction between opioids and Tylenol by comparing individuals taking both and opioid and Tylenol to those on opioids alone.

Heroin

Heroin, a non-prescription opioid that is illegally manufactured and contaminated with numerous unknown substances, is a common "street" opioid. Multiple case studies regarding the relationship between heroin and hearing loss have been documented. Nair, Cienkowski, and Michaelides (2010) presented the case of a 29-year-old woman with sudden SNHL following a heroin overdose. The audiometric details of this case study are shown in Table 4. A similar case study of a sudden, bilateral SNHL after heroin injection was reported by Schrock, Jakob, Wirz, and Bootz (2008). The audiometric details of this case study are shown in Table 5. In these cases, it is difficult to attribute the hearing losses strictly to opioids, due to the numerous factors that can not be controlled for within heroin use. However, these cases do add to the growing evidence of opioid-overdose-induced hearing loss and the significant need for further research in this area.

Table 4. Summary of case study presented by Nair, Cienkowski, and Michaelides (2010)

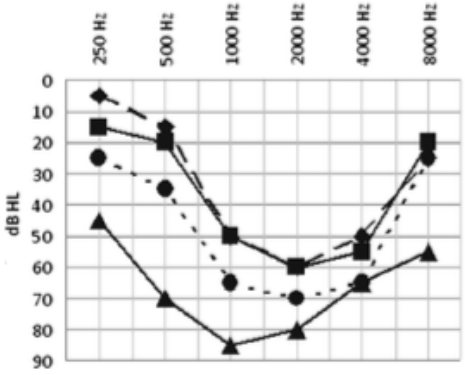
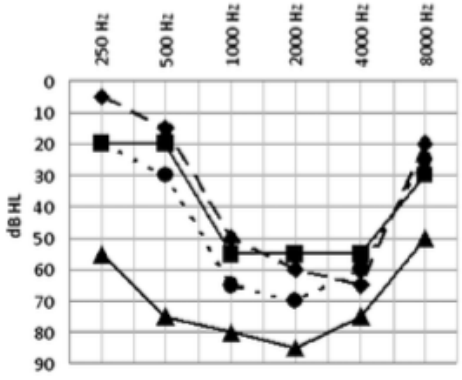
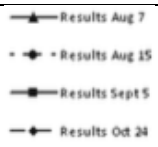
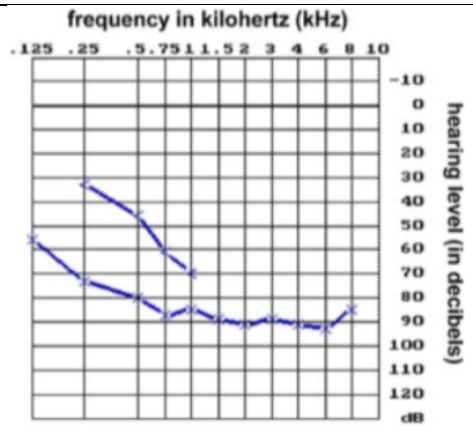
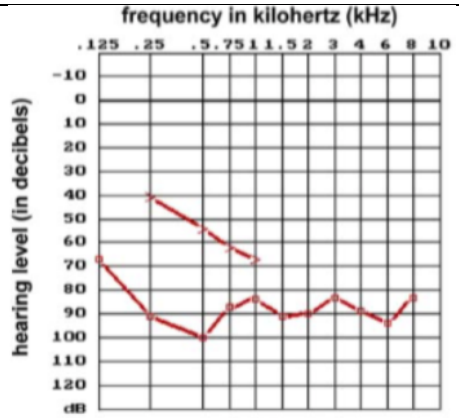
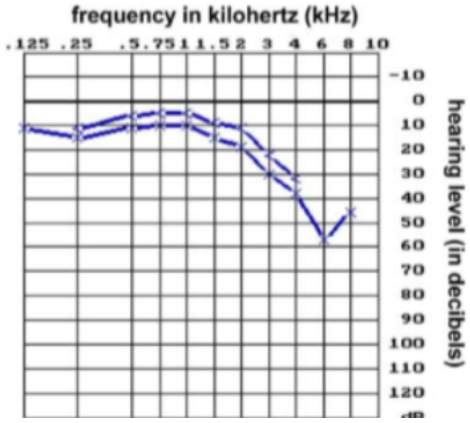
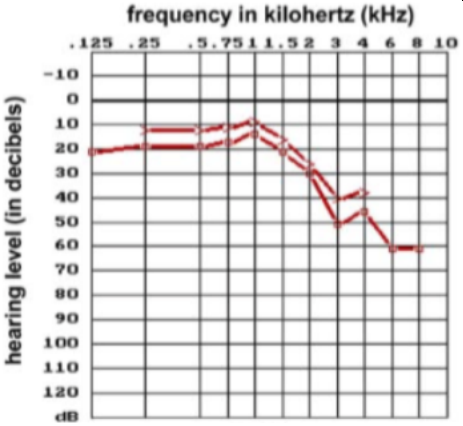
Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Nair, et al. (2010)	29	F	Heroin	Unknown	Bilateral Sudden Sensorineural	Tinnitus	Oral Steroids	Some improvement with initial treatment, ultimately fitted with binaural amplification
	Left Ear Thresholds					**Right Ear Thresholds**		
								
	Legend							
								

Table 5. Summary of case study presented by Schrock, Jakob, Wirz, and Bootz (2008)

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Schrock, et al. (2006)	23	M	Heroin	2 g/day 2 years	Bilateral Sudden Sensorineural	None	Corticoids, vasoactive substances	Persistent symmetric high frequency hearing loss 3 days later
	Initial Audiogram and TEOAE: Left Ear					**Initial Audiogram and TEOAE: Right Ear**		
								
	Audiogram and TEOAE after 3 days treatment: Left Ear					**Audiogram and TEOAE after 3 days treatment: Right Ear**		
								

Implications

The documentation of sudden SNHL as a result of various opiates suggests a strong relationship between chronic opioid use and loss of auditory function. The growing number of documented cases suggests that preventative measures need to be taken by consumers. Education regarding the possible risks and risk-factors, including dosage and dependence, should be readily provided to clients throughout the treatment process. As a primary contributor to successful communication, the auditory system should be taken into consideration with any opioid use. The maintenance of a healthy hearing mechanism allows for successful integration of auditory input, which can then be cognitively processed with the assistance of executive functioning.

Effects of Opioids on Executive Functioning

Executive functioning is a cognitive domain primarily controlled by multimodal association areas located in the prefrontal cortex of the brain (Baehr & Frotscher, 2012). Working memory, mental flexibility, and self-control are all considered to be aspects of executive functioning (Baehr & Frotscher, 2012). Executive functioning skills assist individuals in being successful in the areas of occupation, health, and positive relationships.

Patients with lesions to the prefrontal cortex have historically demonstrated deficits in executive functioning (Baehr & Frotscher, 2012). These deficits include attention difficulties, decreased sense of advanced planning, and inability to adapt to changing circumstances (Baehr & Frotscher, 2012). Although dysfunction of the

prefrontal cortex is typically the result of a traumatic brain injury, there is strong evidence that alcoholism and cocaine addiction also result in prefrontal cortex dysfunction (Lyvers, 2000). Additionally, the frontal lobes were found to be a primary site of action for opiates, such as heroin and morphine (Kuhar, Pert, & Snyder, 1973; Lewis et al., 1981).

The activation of the frontal lobes with opioid use indicated that pain medications influence the functioning of the prefrontal cortex. This discovery prompted further investigation into the details surrounding opioid-induced deficits of executive functioning, specifically if the severity of deficit was related to the severity of opioid dependence. Previous research by Lyvers and Maltzman (1991) suggested that the Wisconsin Card Sorting Test (WCST), an index of executive cognitive functioning, is sensitive to the effects of low doses of alcohol and nicotine. Lyvers and Yakimoff (2003) used the frequency of perseverative responses (PR) and perseverative errors (PE) on the WCST as a comparison to severity of opioid dependence. Two groups of methadone maintenance patients were compared. The first group was tested 90 minutes after receiving methadone and the second group, considered to be in "early withdrawal," was tested 24 hours after receiving methadone (Lyvers & Yakimoff, 2003). The participants' severity dependence, indicated by scores on the Severity of Opiate Dependence Questionnaire, was compared to the number of PRs and PEs made. Patients who indicated a more severe dependence were found to make more PRs and PEs. When further controlled for dependence severity, methadone patients in early withdrawal exhibited significantly higher rates of PRs and PEs during the WCST compared to the

group who had already received their daily methadone dose (Lyvers & Yakimoff, 2003). The severity of opioid dependence, as reported by the patients, directly affected the number of perseverative responses and errors; the production of these responses and errors was a significant indicator of deficits in executive functioning. In addition to the influence of dependence severity, patients in early withdrawal were also observed to have significant deficits in executive functioning skills. These results further support evidence of impaired executive functioning in relation to opioid use. The positive relationship between severity of dependence and level of impairment suggests that early withdrawal has a disruptive effect on frontal lobe functioning.

In addition to the research on cognition during the first 24 hours of opioid withdrawal, Rapeli et al. (2006) provided an examination of cognitive function during the first two weeks of abstinence from opioids. High positive correlations were found between the number of days of withdrawal and the participants' fluid intelligence performance (complex working memory performance), indicating that the cognitive effects of opioid use could be transient and reduced with continued abstinence.

Given the current literature, it has been found that opioids decrease cognitive functioning during periods of use and withdrawal, but researchers have now started to examine the long-term effects of opioids on abstinent ex-users in an attempt to define the permanent and transient impairments associated with the medications. Darke, McDonald, Kaye, and Torok (2012) compared the cognitive performance of current opioid maintenance patients to that of abstinent opioid users and a control group of non-opioid users. The opioid maintenance group consisted of patients receiving either methadone or

buprenorphine, an opioid also used for treating addiction. Opioid users exhibited poorer performance in the areas of executive function, information processing speed, verbal learning, and non-verbal learning when compared to ex-users and non-users, without any substantive differences between the methadone and buprenorphine maintenance patients (Darke et al., 2012). Due to the consistency of results between the two types of opioids, these results suggest that research completed on methadone-users can be generalized to users of other opioids. Further, Darke et al. (2012) found that abstinent ex-users did not significantly differ in level of executive functioning from that of non-opioid-using individuals, providing evidence that the negative effects of opioids on executive functioning are transient.

These results are supported by research done by Mintzer, Copersino, and Stitzer (2005), who found that abstinent opioid users scored in between current methadone maintenance groups and non-user groups on tasks of executive functioning, suggesting that recovery of cognitive functioning may improve with abstinence. Although there is promising evidence of executive function recovery with opioid abstinence, it is crucial to consider the detrimental effects of current opioid-use on the cognitive aspects of communication in the patients we treat.

In a study conducted by Ersche et al. (2006), the executive and memory functioning in opiate-dependent individuals was compared to that of amphetamine-dependent individuals, as well as abstinent ex-users and healthy non-using controls. The opiate-dependent group consisted of 42 participants who chronically used one or more of the following opioids: methadone, buprenorphine, dihydrocodeine, diamorphine,

morphine sulfate, or heroin. The amphetamine-dependent group consisted of 25 chronic amphetamine users, who were taking either D-amphetamine (Dexedrine) or street amphetamines. Dexedrine is a substitute treatment used for amphetamine dependence in the UK (Ersche et al., 2006). The ex-user group included 26 participants who were abstinent from all drugs of abuse for an average of 8.2 years. Within the ex-user group, five participants were ex-opiate users, eight were ex-amphetamine users, and 13 had been dependent on both. The Tower of London (TOL) planning task and the 3D-IDED attentional set-shifting task were administered to assess aspects of executive function, while the Paired Associates Learning (PAL) and Delayed Pattern Recognition Memory tasks were used to assess visual memory function.

When compared to controls, Ersche et al. (2006) found drug-using participants to show marked impairments in spatial planning, PAL, and visual pattern recognition. Former drug users did not perform significantly different from current drug users on any task measure, suggesting that neurocognitive impairments may be relatively permanent. The persisting impairments in cognition after years of abstinence may also indicate involvement of the frontal and temporal lobes (Ersche, et al., 2006). Additionally, correlational analyses found that years of drug use and years of abstinence were not associated with any outcome measure. These results contradict findings in the previously discussed studies and indicate a need for more extensive research regarding the long-term effects of opioids.

Mercuri et al. (2015) further examined how a specific executive function called episodic foresight, or mentally traveling forward in time, is affected in chronic opioid-

users. Participants included 48 long-term heroin users who were currently enrolled in an opioid maintenance program involving either methadone, suboxone, or naloxone and 48 healthy controls. Three measures were used to examine executive control: the Trail Making Test (TMT) measured mental flexibility, the Hayling Sentence Completion test measured inhibitory control, and a verbal fluency test measured cognitive initiation. An adaption of the Autobiographical Interview (AI) was then used to examine episodic and non-episodic foresight in both the past and future temporal phase conditions. Mercuri et al. (2015) found that opioid-using participants generated fewer episodic details when imagining novel future situations, compared to non-using controls. In fact, opiate-using participants generated more non-episodic details than episodic details despite explicit instructions in the AI to only provide episodic information (Mercuri et al., 2015). This indicates that opiate-users are more likely to retrieve "off-target" memories when attempting tasks that involve episodic foresight. The capacity to construct and work through varied hypothetical scenarios before initiating any goal-directed action is an anticipatory element of episodic foresight (Mercuri et al., 2015). With opiate-users being impaired in this ability, their choice of actions to achieve desired goals is restricted, ultimately contributing to maladaptive decision-making. Consequently, opiate users are more likely to give priority to the fulfillment of current needs rather than meeting future goals that could potentially provide greater rewards. Results from Mercuri et al. (2015) also indicated that long-term opiate users had much more difficulty imagining their own futures when compared to controls. Due to episodic foresight's reliance on prefrontal and

medial temporal neural regions, these results further support the notion that long-term opioid use affects these neural regions.

Effects of Opioids on Language Perception

For an individual to successfully perceive and process language, many executive functioning skills must be utilized. Executive functioning skills necessary for language perception include: attention, organization, memory, problem solving, and regulation of behavioral input. (Baehr & Frotscher, 2012). Due to the co-dependent relationship between executive function and language, the existing research regarding the effects of opioids on executive functioning can be applied to language perception; however, there is a very limited amount of research that has specifically examined language processing in patients who take opioids. The current literature regarding the relationship between opioids and language processing primarily focuses on the pragmatic domain. McDonald, Darke, Kaye, and Torok (2012) compared the emotional perception and social inference skills in opioid maintenance patients with abstinent ex-users and a non-heroin-using control group. Opioid maintenance patients were found to be impaired in emotional perception and social inference compared to ex-users and non-users. However, the ex-user and non-user groups did not differ in either category, which suggests that the negative effects of opioids on emotional perception and social inference skills could be transient.

In a similar study, Craparo et al. (2016) studied the role of alexithymia ability to detect facial expressions of emotion in 31 heroin addicts undergoing methadone

maintenance treatment and 31 healthy controls. In their study, the defined alexithymia as a deficit in the cognitive processing of emotions that reduce an individual's ability to identify, describe, and regulate feelings (Craparo et al., 2016). Researchers measured the participants' accuracy and reaction times when detecting affective expressions. Participants filled out the Toronto Alexithymia Scale (TAS-20) and were asked to evaluate and categorize facial emotion expressions elicited from the photos representing the basic emotions. The TAS-20 is a self-report scale composed of three subscales: Difficulty identifying feelings (DIF), Difficulty describing feelings (DDF), and Externally oriented thinking (EOT) (Craparo et al., 2016). Overall, they found that heroin addicts are less accurate and slower in the recognition of facial expressions of emotions when compared to healthy controls. Craparo et al. (2016) suggest that the slowed performance in emotion recognition originates from heroin exposure to neural circuits critical to emotion processing, such as the insula, amygdala, orbitofrontal cortex, the anterior cingulated cortex, and the basal ganglia.

After a social cue, such as a facial expression, is identified, it must be stored in an individual's memory while the person continues processing and responding to the cue. Syal et al. (2015) examined individuals' memory for reward cues following acute buprenorphine administration. 38 participants performed an emotional face relocation task after administration of buprenorphine and a placebo in a randomized placebo-controlled within-subjects design. The results of the study showed that buprenorphine administration significantly improves memory for happy faces, therefore increasing short-term memory for social reward cues (Syal et al., 2015).

This evidence is supported by research conducted by Bershard, Seiden, and De Wit (2015), who examined the effects of buprenorphine on three aspects of social processing: responses to simulated social rejection, attention to emotional facial expressions, and emotional responses to images with and without social content. 36 healthy adults were administered a placebo or 0.2mg sublingual buprenorphine in a randomized, double-blinded study. Participants then completed three behavioral tasks ninety minutes after drug administration. The first task was a virtual ball-toss game in which the participants were first included by other players, but then excluded. The second task examined attention in which the participants were shown pairs of faces, one emotional and one neutral, and the direction of their gazes was recorded with electrooculography. The third task was a picture-viewing task in which participants rated standardized images with or without social content. Results found that buprenorphine decreased perceived social rejection during the ball-toss game and reduced initial attention to fearful facial expressions during the attention task, without affecting attention to angry, happy, or sad faces (Bershard, Seiden, & De Wit, 2015). It was also found that buprenorphine increased ratings of positivity towards images with social content without influencing ratings of nonsocial images (Bershard, Seiden, & De Wit, 2015). The results of this study indicate that opioids reduce responses to some types of negative social stimuli while increasing positive responses to social stimuli, ultimately supporting the role of the opioid system in mediating responses to social rejection and reward. Due to the very low dose administered in this study, it can be assumed that buprenorphine's

effects on responses to social stimuli were produced independently of any euphoric mood effects of the drug.

The studies included in this review primarily account for perception of social cues when examining the effects of opioids and language perception. While perception of social cues is a vital aspect of language processing and may indicate the way in which other language cues are perceived in opiate-users, future research should aim to expand the research question to assess other aspects of language, both expressive and receptive, such as following directions and telling a narrative.

Summary

As the use of long-term opioid pain medications continues to increase, awareness of the associated side effects should also increase in clinicians and healthcare providers across all domains of care. Evidence of opioid influence on hearing, executive functioning, and social language perception ultimately indicates the negative effects of opioids on communication. As the primary interventionists in communication domains, it is imperative for speech language pathologists and audiologists to account for the use of pain medications in adult patients and to advocate for further research, education, and prevention in this area.

Chapter 2: Methodology

The current study is aimed at compiling data from previous studies to provide a comprehensive review of the current literature. It is hypothesized that opioid pain medications negatively affect overall communication abilities, specifically in the areas of hearing, executive functioning, and language processing. Numerous studies that support this hypothesis have been published, but have been unable to generalize to a larger population due to research design.

Research Questions

1. Does a relationship exist between opioid use and deficits in hearing, executive function, and language?
2. Does a relationship exist between the duration and quantity of opiate use and deficits in hearing, executive function, and language?
3. Does a relationship exist between the type of opioid pain medication and effects on hearing, executive function, and language?
4. Are the adverse effects of opioids on hearing, executive function, and language permanent or transient?

Inclusion and Exclusion Criteria

This thesis is a mixed-methods systematic review of previous studies conducted by researchers in the field. As such, the methods in this present study include the

inclusionary and exclusionary criteria used in the selection of participants, as well as the previous methods that were used in the included studies.

Inclusion criteria for participants was as follows: Articles utilized in this systematic review of the literature were identified through a search of the PubMed database for literature published between January 1970 and January 2016. The opioid medication search terms used were as follows: 'codeine,' 'heroin,' 'hydrocodone,' 'hydrocodone/acetaminophen,' 'methadone,' 'opioid,' 'oxycodone,' and 'polysubstance narcotics.' Related substance search terms used in conjunction with the opioid terms, using the Boolean AND rule, included: 'acetaminophen,' 'alcohol,' 'cocaine,' and 'nicotine.' Each medication search term was combined with the following general search terms: 'addiction,' 'adverse effects,' 'cognition,' 'executive functioning,' 'hearing loss,' 'memory,' 'toxicity,' 'receptor,' and 'receptor binding.' Participants presenting with congenital hearing loss or developmental delays were excluded from the study.

The relevant papers were examined for additional articles related to the topic. References were selected for inclusion in this review based on publication year and relevance concerning the development of an overview of the relationship between opioid use and hearing, cognition, and language. A total number of 28 articles were found using these criteria. The following article categories were included: those assessing the effects of opioids on the hearing mechanism (N=17), executive functioning (N=7), and language processing (N=4). Additionally, articles including information pertaining to high quality clinical trials, reports of adverse effects, and both preclinical and clinical research that

characterized the mechanisms underlying the effects of opioids were included in the systematic review.

Instrumentation

Instrumentation for the current study included that used in articles included in this review. The methods used to assess hearing function in patients of the included case studies are shown in Table 6. The methods used to assess executive functioning in the included studies are shown in Table 7. Table 8 lists the methods used to assess cognitive abilities related to language processing in studies included in this review.

Table 6. Instruments used to measure hearing function in participants of case studies included in the review

Instrumentation
otoacoustic emissions testing
pure-tone audiometry
stapedius reflex test
tympanometry

Table 7. Methods Used to Measure Cognitive Domains Related to Executive Function in Participants of Articles Included in the Review

Instrumentation
Autobiographical Interview (AI)
Benton Visual Retention Test
Color Trails Test (CTT)

Complex Figure of Rey

Controlled Oral Word Association Test

Culture Fair Intelligence Test (CFIT)

Delayed Logical Memory, WMS-revised

Delayed Pattern Recognition Memory (PRM), Cambridge Neuropsychological Test Automated Battery (CANTAB)

Digit Span (forwards and backwards), Wechsler Test of Adult Intelligence Scale (WAIS-III)

Digit Span, WMS-revised

Digit Symbol, Wechsler Test of Adult Intelligence Scale (WAIS-III)

Haylings Sentence Completion Test

Key Search

Logical Memory I and II, Wechsler Memory Scale (WMS)

Matrix Reasoning

Modified Stroop task

One-Touch Tower of London (TOL)

Paired Associate Learning (PAL), Cambridge Neuropsychological Test Automated Battery (CANTAB)

Paired Associates I and II, Wechsler Memory Scale (WMS)

Porteus Maze Test (PMQS)

Rey Auditory Verbal Learning Task

Ruff Figural Fluency Test

Serial Seven Subtraction Test (SSST)

Three-dimensional IDED
Trail Making Test (TMT)
Verbal Fluency task
Wisconsin Card Sorting Test (WCST)

Table 8. Methods Used to Measure Cognitive Domains Related to Language Processing in Participants of Articles Included in the Review

Instrumentation
Attention Bias task
"Cyberball" simulated social rejection task
Emotional Images task (using the International Affective Picture System)
Emotional Recognition task
Object Relocation task
The Awareness of Social Inference Test (TASIT)
Toronto Alexithymia Scale (TAS-20)

Materials

PubMed by National Center for Biotechnology Information (NCBI), U.S. National Library of Medicine will be used for participant selection and data collection. Microsoft Excel 2007® by Microsoft Corporation, Seattle, WA will be used to record and graph data.

Categories

Participants were separated into three groups for analysis: opioid-users, abstinent ex-users, and non-using controls. Opioid-users will then be separated by deficit: opioid-users with hearing loss, opioid-users with executive function deficits, and opioid-users with language deficits. Within each group, participants will be further differentiated by type of opioid used, duration of opioid-use, deficit characteristics, and permanent versus transient outcomes.

Analysis of Data Set

Data from each study was analyzed for level of evidence and opioid type. Case studies regarding opioid-induced hearing loss were further analyzed for participant age, duration of use, type and progression of loss, associated conditions, initial treatments, and hearing outcomes.

Studies examining the effects of opioids on executive function and language were analyzed for effect size measured in Cohen's d. Using the effects sizes reported in Cohen's d, the current study compared the effects of opioids across studies.

Chapter 3: Results

The purpose of this study was to review the data set provided by previous researchers and compile evidence relating the use of opiate analgesics to vital aspects of communication. Additionally, this study aimed to explore any relationships between reported communication deficits and opiate type, duration of use, dosage, and recovery outcomes. Data from 28 previous studies was collated and presented for analysis in the present study. Case study analysis and effect size comparisons were utilized to analyze the collected data.

Articles Analyzed

Data included in the present study was compiled from a number of publications. A total number of 17 articles were found to specifically examine the relationship between opioids and hearing loss. These articles primarily consisted of case reports, with one case-control nonintervention study. Between these publications, a total number of 156 participants were analyzed for auditory function in the current study, with 44 case studies included in the analysis.

In the analysis of opioid effects on executive function and cognition, a total number of seven articles were found to specifically examine the relationship. All seven articles provided evidence at the nonintervention level. A total number of 597 participants were included in the executive function group.

A total number of four articles were found to examine the relationship between opioids and aspects of language perception, with 361 total participants. Two of the

included articles provided evidence at the nonintervention level and two provided evidence at the level of randomized, controlled trials.

Table 9. Studies Examining the Relationship Between Opioid Use and Hearing Loss

Study	Level of Evidence	Opioid Type	# of participants
Blakely & Schilling (2008)	(V) Case Report	Codeine/Acetaminophen	3
Christenson & Marjala (2010)	(V) Case Report	Methadone	2
Fowler & King (2014)	(V) Case Report	Heroin	1
Freeman et al. (2009)	(V) Case Report	Codeine	10
Friedman et al. (2000)	(V) Case Report	Hydrocodone/Acetaminophen	12
Ho, Vrabec, & Burton (2007)	(V) Case Report	Hydrocodone/Acetaminophen	5
Lupin (1976)	(V) Case Report	Propoxyphene hydrochloride	1
Muller et al. (2007)	(IV) Case-Control Nonintervention	Methadone	112
Nair et al. (2010)	(V) Case Report	Heroin	1
Oh et al. (2000)	(V) Case Report	Hydrocodone/Acetaminophen	2
Rigby & Parnes (2008)	(V) Case Report	Oxycodone/Acetaminophen	1
Saifan et al. (2013)	(V) Case Report	Methadone	1
	(V) Case Report	Heroin	1

Schrock et al. (2008)			
Sweitzer et al. (2011)	(V) Case Report	Heroin	1
Shaw et al. (2011)	(V) Case Report	Methadone	1
Van Gaalen, Compier, & Fogeloo (2009)	(V) Case Report	Methadone	1
Vorasubin et al (2013)	(V) Case Report	Methadone	1

Table 10. Studies Examining the Relationship Between Opioid Use and Deficits in Executive Functioning

Study	Level of Evidence	Opioid Type	# of participants
Darke et al. (2012)	(IV) nonintervention study	Methadone, Buprenorphine	225
Ersche et al. (2006)	(IV) nonintervention study	Methadone	93
Lyvers and Yakimoff (2003)	(IV) nonintervention study	Methadone	39
Mercuri et al. (2015)	(IV) nonintervention study	Heroin, Methadone	96
Mintzer, Copersino, & Stitzer (2005)	(IV) nonintervention	Methadone	59
Pau, Lee, & Chan (2001)	(IV) nonintervention study	Heroin	55
Rapeli et al. (2006)	(IV) nonintervention study	Methadone	30

Table 11. Studies Examining the Relationship Between Opioid Use and Language Deficits

Study	Level of Evidence	Opioid Type	# of participants
Bershad, Seiden, & Wit (2015)	(II) double-blinded, prospective, randomized, controlled clinical trial	Buprenorphine	36
Craparo et al. (2015)	(IV) non-intervention	Heroin	62
McDonald et al. (2012)	(IV) non-intervention	Methadone, Buprenorphine	225
Syal, et al. (2014)	(II) double-blinded, prospective, randomized, controlled clinical trial	Buprenorphine	38

Case Study Analysis

44 case studies examining the relationship between opioid use and hearing loss were analyzed for the following data: age, sex, opioid type, duration of use, hearing loss, associated conditions, initial treatment, outcomes, and audiometric data. The reported age of hearing loss participants ranged from 18-57 years and included both males and females. The following opioids were present in the included case studies: codeine, codeine/acetaminophen, hydrocodone/acetaminophen, heroin, methadone, oxycodone, oxycodone/acetaminophen, and propoxyphene hydrochloride. The reported duration of opiate use prior to hearing loss ranged from 1-2 months to 30 years. All 44 case studies reported sensorineural hearing losses; however, both unilateral and bilateral losses were

reported, as well as both sudden and progressive losses. Initial treatments included oral steroids and opiate abstinence. Various outcomes reported included: deterioration of speech reception thresholds, full and partial recovery of auditory function, fitting for hearing aids, and cochlear implantation. Case study summary tables are located in Appendix A.

Effect Sizes

Articles addressing executive functioning in opioid-users, abstinent non-users, and non-using controls were analyzed for effect sizes. When comparing opioid-users to non-using controls, three tasks produced small effect sizes, three tasks produced medium effect sizes, and 19 tasks produced large effect sizes. The high number of large effect sizes found in this data set indicate that executive functioning is significantly impaired in opioid users when compared to controls. Table 12 displays the results of the opioid and control group comparison.

When comparing the opioid group to the abstinent group, seven tasks produced small effect sizes, four tasks produced medium effect sizes, and two tasks produced large effect sizes. The limited number of large effect sizes found in this group comparison indicate that the effects of opioids on executive functioning do not significantly differ between current and abstinent opioid users. Further, this suggests that deficits in executive functioning may be permanent, even with abstinence from opioids. Table 13 displays the results of the opioid and abstinent group comparison.

When comparing the abstinent ex-user group to the control group, four tasks produced small effect sizes, three tasks produced medium effect sizes, and 12 tasks produced large effect sizes. The high number of large effect sizes found in this data set indicate abstinent ex-users performed significantly worse than the control group, further supporting the permanence of executive function impairments. The results of the abstinent and control group comparison are displayed in Table 14.

Table 12. Effect Sizes Found in Executive Functioning Studies (Opioid vs. Control)

Small d	Medium d	Large d	Test	Study
		d=0.75	Haylings	Darke et al. (2012)
		d=1.06	Matrix Reasoning	Darke et al. (2012)
		d=0.90	Digit Span (information processing speed)	Darke et al. (2012)
		d=0.72	Immediate Logical Memory (verbal learning)	Darke et al. (2012)
		d=0.93	Delayed Logical Memory (verbal learning)	Darke et al. (2012)
		d=0.79	Complex Figure Test Recall (non-verbal learning)	Darke et al. (2012)
		d=0.95	TOL (perfect solutions at 1st attempt)	Ersche et al. (2006)
	d=0.46		TOL (mean attempts, 1-3 moves)	Ersche et al. (2006)
		d=0.64	TOL (mean attempts, 4-6 moves)	Ersche et al. (2006)
d=0.13			3D-ID/ED (IDS mean errors)	Ersche et al. (2006)
		d=0.89	PAL (1st trial memory score, mean)	Ersche et al. (2006)

		d=0.85	PAL (total trials to success, mean)	Ersche et al. (2006)
		d=0.64	PRM (immediate)	Ersche et al. (2006)
		d=0.97	PRM (delay)	Ersche et al. (2006)
d=0.27			Verbal Fluency Test	Mercuri et al. (2015)
	d=0.38		Trail Making Test	Mercuri et al. (2015)
		d=0.63	Haylings	Mercuri et al. (2015)
d=0.22			SSST: time spent	Pau et al. (2002)
		d=0.55	SSST: number of errors	Pau et al. (2002)
		d=0.74	CTT1: time spent	Pau et al. (2002)
		d=0.54	CTT2: time spent	Pau et al. (2002)
		d=0.50	WCST: number of perseverative errors	Pau et al. (2002)
		d=0.85	WCST: number of categories completed	Pau et al. (2002)
	d=0.43		WCST: number of trials	Pau et al. (2002)
		d=0.80	Porteus Maze Qualitative Scores	Pau et al. (2002)
(N= 3)	(N= 3)	(N= 19)		

Table 13. Effect Sizes Found in Executive Functioning Studies (Opioid vs. Abstinent)

Small d	Medium d	Large d	Test	Study
	d=0.46		Key Search	Darke et al. (2012)
		d=0.51	Haylings	Darke et al. (2012)
	d=0.49		Matrix Reasoning	Darke et al. (2012)
	d=0.35		Digit Span (information processing speed)	Darke et al. (2012)
		d=0.67	Complex Figure Test Recall (non-verbal learning)	Darke et al. (2012)
d=0.22			TOL (perfect solutions at 1st attempt)	Ersche et al. (2006)
	d=0.32		TOL (mean attempts, 1-3 moves)	Ersche et al. (2006)
d=0.02			TOL (mean attempts, 4-6 moves)	Ersche et al. (2006)
d=0.15			3D-ID/ED (IDS mean errors)	Ersche et al. (2006)
d=0.18			PAL (1st trial memory score, mean)	Ersche et al. (2006)
d=0.14			PAL (total trials to success, mean)	Ersche et al. (2006)
d=0.08			PRM (% of correctly recognized patterns, immediate)	Ersche et al. (2006)
d=0.08			PRM (% of correctly recognized patterns, delay)	Ersche et al. (2006)
(N= 7)	(N= 4)	(N= 2)		

Table 14. Effect Sizes Found in Executive Functioning Studies (Abstinent vs. Control)

Small d	Medium d	Large d	Test	Study
		d=0.96	TOL (perfect solutions at 1st attempt)	Ersche et al. (2006)
		d=0.84	TOL (mean attempts, 1-3 moves)	Ersche et al. (2006)
		d=0.74	TOL (mean attempts, 4-6 moves)	Ersche et al. (2006)
d=0.04			3D-ID/ED (IDS mean errors)	Ersche et al. (2006)
		d=0.70	PAL (1st trial memory score, mean)	Ersche et al. (2006)
		d=0.82	PAL (total trials to success, mean)	Ersche et al. (2006)
		d=0.61	PRM (immediate)	Ersche et al. (2006)
		d=0.81	PRM (delay)	Ersche et al. (2006)
d=0.12			Stroop (executive function)	Rapeli et al. (2006)
		d=0.83	RFFT unique (executive function)	Rapeli et al. (2006)
d=0.22			RFFT perseverative errors (executive function)	Rapeli et al. (2006)
		d=1.26	PASAT (attention)	Rapeli et al. (2006)
d=0.15			WMS-R Digit Span (attention)	Rapeli et al. (2006)
		d=0.56	RAVLT trials 1-3 (memory)	Rapeli et al. (2006)
		d=0.61	RAVLT delayed recall (memory)	Rapeli et al. (2006)
	d=0.30		WMS-R Logical Memory, immediate	Rapeli et al. (2006)
	d=0.40		WMS-R Logical Memory, delayed recall	Rapeli et al. (2006)

	d=0.41		BVRT, number of right figures (memory)	Rapeli et al. (2006)
		d=0.90	CFIT (fluid intelligence)	Rapeli et al. (2006)
(N= 4)	(N= 3)	(N=12)		

Of the studies included in this review, three reported effect sizes regarding language function in opiate users compared to either a control or abstinent group. In tasks that compared language functions in the opioid group to those of a control group, one task produced a medium effect size and five tasks produced large effect sizes. These results indicate that opioid users performed significantly lower than controls in areas of recognizing, processing, and regulating emotions. These studies and the reported effect sizes are shown in Table 15.

When comparing the opioid group to the abstinent group, one task produced a medium effect size and one task produced a large effect size. Although based on a limited number of studies, these results found opioid users to also perform significantly lower than abstinent ex-users in tasks of social and emotional perception, indicating that perceptual function may recover with abstinence. These studies and the reported effect sizes are shown in Table 16.

Table 15. Effect Sizes Found in Language Studies (Opioid vs. Control)

Small d	Medium d	Large d	Test	Study
		d=1.13	Alexithymia Index	Craparo et al. (2015)
		d=3.44	Emotions Recognition Task	Craparo et al. (2015)
		d=3.13	Emotion Recognition RTs	Craparo et al. (2015)
		d=0.56	TASIT 1 (emotional perception)	McDonald et al. (2012)
	d=0.38		TASIT 2 (social inference)	McDonald et al. (2012)
		d=0.63	Object Relocation Task	Syal et al. (2014)
(N=0)	(N=1)	(N=5)		

Table 16. Effect Sizes Found in Language Studies (Opioid vs. Abstinent)

Small d	Medium d	Large d	Test	Study
	d=0.40		TASIT 1 (emotional perception)	McDonald et al. (2012)
		d=0.59	TASIT 2 (social inference)	McDonald et al. (2012)
(N=0)	(N=1)	(N=1)		

Chapter 4: Discussion

The purpose of this study was to analyze case reports of hearing loss in opioid users, as well as analyze executive functioning and language data from opioid-users, abstinent ex-users, and non-using controls. Additionally, this study aimed to determine a relationship between communication impairments and duration of use, quantity, and type of opioid. The final aim of this study was to determine if deficits associated with opioid use are permanent or transient. Following is a discussion of the study's success in achieving these goals, as well as the investigative and clinical implications of the projected findings.

Research Hypotheses

1. H_0: No relationship exists between opioid use and deficits in hearing, executive function, and language.

   H_1: A relationship exists between opioid use and deficits in hearing, executive function, and language.

2. H_0: No relationship exists between the duration and quantity of opiate use and deficits in hearing, executive function, and language.

   H_1: A relationship exists between the duration and quantity of opiate use and deficits in hearing, executive function, and language.

3. H_0: No relationship exists between the type of opioid pain medication and effects on hearing, executive function, and language.

   H_1: A relationship exists between the type of opioid pain medication and effects on hearing, executive function, and language.

4. H_0: The adverse effects of opioids on hearing, executive function, and language are transient.

   H_1: The adverse effects of opioids on hearing, executive function, and language are permanent.

Research Findings

1. Does a relationship exist between opioid use and deficits in hearing, executive function, and language?

A relationship does appear to exist between opioid use and deficits in hearing, executive functioning, and aspects of language. Therefore, this study successfully rejected the null hypothesis. A relationship between opioid use and hearing loss was indicated in the case study analysis; however, the nature of this relationship is not clear in the present study. The data compiled in the case study analysis found opioid-induced hearing loss to be sensorineural in all participants. The relationship between opioid use and decreased executive functioning was seen in the effect size comparison, with opiate users performing significantly lower than controls across studies. More specifically, opioid use was found to significantly decrease performance in verbal and nonverbal

learning, information processing speed, spatial planning, paired associate learning, visual pattern recognition, and episodic foresight. Similarly, analysis found primarily large effect sizes when comparing opioid users to controls in tasks of social and emotional perception across studies, suggesting a relationship between opioid use and language perception deficits. This data set found opiate use to reduce responses to some types of negative social stimuli while increasing positive responses to social stimuli, providing evidence of the role of the opioid system in mediating responses to social rejection and reward.

2. Does a relationship exist between the duration and quantity of opiate use and deficits in hearing, executive function, and language?

The present study failed to reject the null hypothesis regarding a relationship between the duration and quantity of opiate use and communication deficits. Duration of opiate use did not appear to have a relationship with any of the examined deficits, with participants in all three data sets reporting varying lengths of opiate use. Opiate dosage, or quantity taken at any one time, was not found to have a relationship with level of deficit in either executive functioning or language perception. Further, results of these data sets indicate this relationship even at very low doses, suggesting that cognitive deficits are not related to feelings of euphoria.

The exception to this relationship appears to be opioid-induced hearing loss. Results of the case study analysis indicate a strong relationship between opiate overdose and loss of hearing function. Therefore, a relationship does appear to exist between the

quantity of opiates consumed and deficits in auditory function, specifically when an individual exceeds the recommended dosage.

3. Does a relationship exist between the type of opioid pain medication and effects on hearing, executive function, and language?

The present study failed to reject the null hypothesis that no relationship exists between the type of opioid used and effects on hearing, cognition, and language. This is primarily supported by data extracted from hearing loss case studies, in which a variety of opioids all resulted in sensorineural hearing loss. The data sets used to analyze executive function and language deficits consisted of methadone, buprenorphine, and heroin. Participant performance was not found to differ across opioid type, indicating that deficits associated with one opiate pain medication can be generalized to other opiates, despite differences in chemical structure.

4. Are the adverse effects of opioids on hearing, executive function, and language permanent or transient?

Results from this study failed to reject the null hypothesis regarding the effects of opioid use being transient. Due to the nature of case study reports, the present study was inconclusive in determining if auditory deficits due to opiates are permanent or transient. The data set included both permanent and transient hearing losses, with unclear evidence regarding the role of opioid abstinence or oral steroid treatment in the recovery of auditory function. Data regarding the long term effects of opioid use on executive

function were also inconclusive, with evidence supporting cognitive recovery with abstinence contradicted by evidence supporting persisting cognitive deficits following long periods of abstinence.

In analyzing language deficits, one study examined an abstinent ex-user group and found abstinent participants to perform similarly to the control group. Although the evidence is limited, results from this data set indicate that opioid-induced language deficits may be transient.

Study Limitations

The current study had several limitations regarding sample, level of evidence, and data collection. Sample size was relatively small due to the limited amount of previous publications on the topic, especially in the area of opioid-related language impairments. Studies included in the hearing loss group consisted primarily of case studies, therefore providing low levels of evidence. Regarding data collection, this review included numerous studies conducted by varying researchers over a span of many years. Due to the large number of contributing studies, variation in data collection is present and may account for inconsistencies in results.

General Findings and Clinical Implications

The present study found opioid pain medications to adversely affect the hearing mechanism, executive functioning, and social perception skills necessary for language.

These findings ultimately suggest an overall negative impact on the speech chain required for successful human communication.

The results of this study are particularly relevant to speech language pathologists working with adult patients in medical settings. Opioids have historically been included in the treatment plans of patients with head and neck cancer, but can also be prescribed in the instance of neck and back pain due to injury, traumatic brain injury, and neuropathy. The wide range of individuals who may be prescribed opiates emphasizes the need for a thorough case history when providing rehabilitation services to the adult population.

As research continues to develop in this topic area, it will be critical for therapists and other medical professionals to determine the proper course of treatment for patients who are currently on or recently abstinent from opiates. In regards to tasks of executive functioning and social language cues, clinicians must evaluate the effectiveness of targeting these areas in therapy when working with clients who are chronic opioid users. This study also emphasized the importance of clinical follow-up sessions in patients with opioid-related deficits, as these deficits can be permanent and can negatively impact an individual's quality of life.

Recommendations for Future Research

A large, multidimensional research study is required to clearly determine the relationship between opiate pain medications and neurocognitive aspects of communication. It it recommended that a double-blinded, prospective, randomized, controlled study be completed with a maintenance opioid such as methadone or

buprenorphine. To examine the permanent and transient effects of opioid use, it is recommended that future studies compare four participant group: current opioid users, ex-users in early abstinence (<24 hours), ex-users in late abstinence, and non-using controls. Tasks to measure cognitive and language performance in participants should include those presented in the present study, as well as tasks that specifically assess both expressive and receptive language functions. Regarding the relationship between opiate use and hearing loss, animal studies are recommended to study the underlying mechanism, as well as its relationship to dosage.

In regards to treatment, future research should aim to evaluate the effects of cognition and language therapy in this population. Due to opioid involvement of the prefrontal cortex and deficits similar to that exhibited in patients with traumatic brain injury (TBI), it is recommended that future studies examine the effectiveness of traditional TBI therapy in patients with opioid dependence. It is also recommended that future research determine effective treatment methods in patients with opioid-induced sensorineural hearing loss.

Chapter 5: Conclusions

The present review analyzed auditory and cognitive data from 28 studies and reported the findings, as well as relationships between communicative deficits and both quantity of opioids and persistence of impairment. This study reviewed and reported on relevant studies to provide evidence on how opiate pain medications may affect communication and the need for further research on this population and the associated deficit areas.

Data analysis demonstrated connections between opioid use and breakdowns in the communication chain. These connections were based on qualitative and quantitative measures of communicative functions. Qualitative data was collected through observation and interviews in individual studies and contributed to evidence denying a relationship between communication outcomes and both opiate type and duration of use. Quantitative data was collected in the form of effect sizes found in studies examining executive functioning and aspects of language perception. Quantitative measurements allowed the present study to examine the relationship between current opioid users and abstinent ex-users, suggesting that deficits in executive function may be permanent and deficits in social perception may be transient.

A pattern of relationships regarding opiate pain medications and communication deficits emerged throughout the course of this study. The findings imply there is a potential for opioids to increase an individual's risk level for hearing loss and cognitive deficits. With the presented implications, opioid dependence becomes a condition with

long term communication consequences which should be accounted for, educated on, and remediated in clinical settings.

References

American Speech-Language-Hearing Association (ASHA). (2015). *Sensorineural hearing loss*. Retrieved from http://www.asha.org/public/hearing/Sensorineural-Hearing-Loss/

Baehr, M., & Frotscher, M. (2012). *Duus' topical diagnosis in neurology*. New York, NY: Thieme.

Bershard, A. K., Seiden, J. A., & De Wit, H. (2015). Effects of buprenorphine on responses to social stimuli in healthy adults. *Psychoneuroendocrinology, 63*, 43-49. doi: 10.1016/j.psyneuen.2015.09.011

Butts, D. A., & Goldman, M. S. (2006). Tuning curves, neuronal variability, and sensory coding. *PLOS Biology, 4*(4), e92. doi: 10.1371/journal.pbio.0040092

Calvert, G. A., Bullmore, E., Brammer, M. J., Campbell, R., Williams, S. C. R., McGuire, P. K., Woodruff, P. W. R., Iversen, S. D., & David, A. S. (1997). Activation of auditory cortex during silent lipreading. *Science, 276*, 593–596. doi:10.1126/science.276.5312.593

Campbell, K. C. M. (2007). Mechanisms of toxicity in the cochlea (Including physical, free radical: Oxidative and anti-oxidative mechanisms, protein interactions, and defense mechanisms). In *Pharmacology and ototoxicity for audiologists* (p. 71). New York: Thomson Delmar Learning.

Chen, W. T., Lee, J. W., Yuan, C. H., & Chen, R. F. (2015). Oral steroid treatment for idiopathic sudden sensorineural hearing loss. *Saudi Medical Journal, 36*(3), 291-296. doi: 10.15537/smj.2015.3.9940

Christenson, B. J., & Marjala, A. R. P. (2010). Two cases of sudden sensorineural hearing loss after methadone overdose. *Annals of Pharmacotherapy*, *44*, 207-210. doi: 10.1345/aph.1M250

Craparo, G., Alessio, G., Dell Aera, S., Costanzo, G., Fasciano, S., Tomasello, A., & Vicario, C. M. (2016). Impaired emotion recognition is linked to alexithymia in heroin addicts. *Peer Journal, 4*:e1864. doi: 10.7717/peerj.1864

Cummins, E. (2012). The effects of acute and steady state methadone on memory retrieval in rats. *Psychopharmacology*, *222*, 225-235. doi: 10.1007/s00213-012-2638-8

Curhan, S. G., Eavey, R., Shargorodsky, J., & Curhan, G. C. (2012). Analgesic use and the risk of hearing loss in women. *American Journal of Epidemiology, 176*(6), 544-554.

Curhan, S. G., Eavey, R., Shargorodsky, J., & Curhan, G. C. (2010). Analgesic use and the risk of hearing loss in men. *American Journal of Medicine, 123*(3), 231-237. doi: 10.1016/j.amjmed.2009.08.006

Darke, S., McDonald, S., Kaye, S., & Torok, M. (2012). Comparative patterns of cognitive performance amongst opioid maintenance patients, abstinent opioid users and non-opioid users. *Drug and Alcohol Dependence, 126*, 309-315. doi:10.1016/j.drugalcdep.2012.05.032

Denes, P. B., & Pinson, E. N. (2012). *The speech chain: The physics and biology of spoken language* (pp. 86-140). Montana: Literary Licensing, LLC.

Didone, D. D., Garcia, M. V., Oppitz, S. J., Finamor da Silva, T. F., Neujahr do Santos, S. Bruno, R. S., Valentins do Santos Filha, V. A., & Coser, P. L. (2016). Auditory evoked potential P300 in adults: Reference values. *Einstein, 14*(2), 208-212. doi: 10.1590/S1679-45082016AO3586

Ersche, K. D., Clark, L., London, M., Robbins, T. W., & Sahakian, B. J. (2005) Profile of executive and memory function associated with amphetamine and opiate dependence. *Neuropsychopharmacology*, *31,* 1036-1047. doi:10.1038/sj.npp.1300889

Fowler, C. G., & King, J. L. (2008). Sudden bilateral sensorineural hearing loss following speedballing. *Journal of the American Academy of Audiology, 19,* 461-464. doi: 10.3766/jaaa.19.6.2

Friedman, R. A., Gherini, S., House, J. W., Luxford, W. M., & Mills, D. (2000). Profound hearing loss associated with hydrocodone/ acetaminophen abuse. *American Journal of Otolaryngology*, *21*, 188-191. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10733182

Gray, L. (1997). Neuroscience online: An electronic textbook for the neurosciences. *Chapter 10: Vestibular System: Structure and function. Department of Neurobiology and Anatomy, The University of Texas Health Science Center at Houston (UT Health).* Retrieved from http://neuroscience.uth.tmc.edu/s2/chapter10.html

Gray, L. (1997). Neuroscience online: An electronic textbook for the neurosciences. *Chapter 12: Auditory system: Structure and function. Department of*

Neurobiology and Anatomy, The University of Texas Health Science Center at Houston (UT Health). Retrieved from http://neuroscience.uth.tmc.edu/s2/chapter12.html

Ho, T., Vrabec, J. T., & Burton, A. W. (2007). Hydrocodone use and sensorineural hearing loss. *Pain Physician Journal, 10*, 467-472. Retrieved from www.painphysicianjournal.com

Jongkamonwiwat, N., Phansuwan-Pujito, P., Casalotti, S. O., Dodson, H., Forge, A., & Govitrapong, P. (2006). The existence of opioid receptors in the cochlea of guinea pigs. *European Journal of Neuroscience*, *23*, 2701-2711. doi:10.1111/j.1460-9568.2006.04810.x.

Kosten, T. R., & George, T. P. (2002). The neurobiology of opioid dependence: Implications for treatment. Science & Practice Perspectives, 13-20.

Kuhar, M. J., Pert, C. B., & Snyder, S. H. (1973). Regional distribution of opiate receptor binding in monkey and human brain. *Nature, 245*, 447–450. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/4127185

Lewis, M. E., Mishkin, M., Bragin, E., Brown, R. M., Pert, C. B., & Pert, A. (1981). Opiate receptor gradients in monkey cerebral cortex: Correspondence with sensory processing hierarchies. *Science, 211*, 1166–1169. doi:10.1126/science.6258227

Lopez, I. A., Ishiyama, A., & Ishiyama G. (2012). Sudden sensorineural hearing loss due to drug abuse. *Seminars in Hearing, 33*(3), 251-260. doi:10.1055/s-0032-1315724

Lupin, A. J. & Harley, C. H. (1976). Letter: Inner ear damage related to propoxyphene ingestion. *Canadian Medical Association Journal, 114*(7), 596.

Lyvers, M. (2000). Loss of control in alcoholism and drug addiction: A neuroscientific interpretation. *Experimental and Clinical Psychopharmacology, 8*(2), 225-249. doi:10.1037/1064-1297.8.2.225

Lyvers, M., & Maltzman, I. (1991). Selective effects of alcohol on Wisconsin Card Sorting Test Performance. *British Journal of Addiction, 86*, 399–407. doi: 10.1111/j.1360-0443.1991.tb03417.x

Lyvers, M., & Yakimoff, M. (2003). Neuropsychological correlates of opioid dependence and withdrawal. *Addictive Behaviors, 28*, 605–611. doi:10.1016/S0306-4603(01)00253-2

Manchikanti, L., Helm, S., Fellows, B., Janata, J. W., Pampati, V., Grider, J. S., & Boswell, M. V. (2012). Opioid epidemic in the united states. *Pain Physician Journal, 15*, 9-38. Retrieved from http://painphysicianjournal.com/current/pdf?article=MTcwNA%3D%3D&journal=68

Mayo Foundation for Medical Education and Research. (2016). *Diseases and conditions*: *Prescription drug abuse*. Retrieved from http://www.mayoclinic.org/diseases-conditions/prescription-drug-abuse/basics/complications/con-20032471

McDonald, S., Darke, S., Kaye, S., & Torok, M. (2012). Deficits in social perception in opioid maintenance patients, abstinent opioid users and non-opioid users. *Addiction, 108*, 566-574. doi:10.111/add.12040

McGurk, H., & MacDonald, J. W. (1976). Hearing lips and seeing voices. *Nature, 264*, 746–748. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed?term=1012311

Mercuri, K., Terrett, G., Henry, J. D., Bailey, P. E., Val Curran, H., & Rendell, P. G. (2015). Episodic foresight deficits in long-term opiate users. *Psychopharmacology, 232*, 1337-1345. doi: 10.1007/s00213-014-3772-2

Mintzer, M. Z., Copersino, M. L., & Stitzer, M. L. (2005). Opioid use and cognitive performance. *Drug and Alcohol Dependence, 78*(2), 225-230. doi:10.1016/j.drugalcdep.2004.10.008

Muller, B. W., Specka, M., Steinchen, N., Zerbin, D., Lodemann, E., Finkbeiner, T., & Scherbaum, N. (2007). Auditory target processing in methadone substituted opiate addicts: The effect of nicotine in controls. BMC Psychiatry, 7(63), 1-10. doi: 10.1186/1471-244X-7-63

Musacchia, G., Sams, M., Nicol, T., & Kraus, N. (2005). Seeing speech affects acoustic information processing in the human brainstem. *Experimental Brain Research*, *168*, 1–10. doi:10.1007/s00221-005-0071-5

Nair, E. L., Cienkowski, K. M., & Michaelides, E. (2010). The impact of sudden hearing loss secondary to heroin overdose on fitting outcomes. *American Journal of Audiology*, *19*(2), 86-90. doi:10.1044/1059-0889(2010/09-0020)

Oh, A. K., Ishiyama, A. & Baloh, R. W. (2000). Deafness associated with abuse of hydrocodone/acetaminophen. *Neurology, 54*(12), 2345. doi: 10.1212/WNL.54.12.2345

Palmer, R., Carrell, D., Cronkite, D., Saunders, K., Gross, D., Masters, E., Hylan, T., & VonKorff, M. (2014). The prevalence and characteristics of patients with indicators of opioid abuse within an integrated group practice. *The Journal of Pain, 15*(4), S25.

Rapeli, P., Kivisaari, R., Autti, T., Kahkonen, S., Puuskari, V., Jokela, O., & Kalska, H. (2006). Cognitive function during early abstinence from opioid dependence: A comparison to age, gender, and verbal intelligence matched controls. *BMC Psychiatry, 6*(9), 1-10. doi:10.1186/1471-244X-6-9

Rigby, M. H., & Parnes, L. S. (2008). Profound hearing loss associated with oxycodone-acetaminophen abuse. *American Journal of Otolaryngology-Head and Neck Medicine and Surgery, 37*(6), 161-162. Retrieved from https://www.ncbi.nlm.nih.gov/pubmed/19128688

Rosenblum, L. D. (2008). Speech perception as a multimodal phenomenon. *Current Directions in Psychological Science, 6,* 405-409. doi:10.1111/j.1467-8721.2008.00615.x.

Saifan, C., Glass, D., Barakat, I., & El-Sayegh, S. (2013). Methadone induced sensorineural hearing loss. *Case Reports in Medicine*, *2013*, 1-5. doi:10.1155/2013/242730

Schow, R. L., & Nerbonne, M. A. (2013). *Introduction to audiologic rehabilitation*. United States of America: Pearson.

Schrock, A., Jakob, M., Wirz, S., & Bootz, F. (2008). Sudden sensorineural hearing loss after heroin injection. *European Archives of Otorhinolaryngology*, *265*(5), 603–606. doi:10.1007/s00405-007-0495-6

Schweitzer, V. G., Darrat, I., Stach, B. A., & Gray, E. (2011). Sudden bilateral sensorineural hearing loss following polysubstance narcotic overdose. *Journal of the American Academy of Audiology, 22*(4). doi: 10.3766/jaaa.22.4.3

Shaw, K. A., Babu, K. M., & Hack, J. B. (2011). Methadone, another cause of opioid-associated hearing loss: A case report. *The Journal of Emergency Medicine, 41*(6), 635-639. doi: 10.1016/j.jemermed.2010.11.014

Syal, S., Ipser, J., Terburg, D., Solms, M., Panksepp, J., Malcom-Smith, S., Bos, P. A., Montoya, E. R., Steing, D. J., & Van Honk, J. (2015). Improved memory for reward cues following acute buprenorphine administration in humans. *Psychoneuroendocrinology, 53*, 10-15. doi: 10.1016/j.psyneuen.2014.11.009

Truax, B. (1999). Handbook for acoustic ecology. *World Soundscape Project,* Simon Fraser University and ARC Publications. Retrieved from https://www.sfu.ca/sonic-studio/handbook/index.html

Van Gaalen, F. A., Compier, E. A., & Fogeloo, A. J. (2009). Sudden hearing loss after a methadone overdose. *European Archives of Otorhinolaryngology*, *266*(5), 773-774. doi: 10.1007/s00405-009-0935-6

Vorasubin, N., Calzada, A. P., & Ishiyama, A. (2013). Methadone-induced bilateral severe sensorineural hearing loss. *American Journal of Otolaryngology-Head and Neck Medicine and Surgery 34*, 735-738. doi: 10.1016/j.amjoto.2013.08.011

Woodman, G. F. (2010). A brief introduction to the use of event-related potentials in studies of perception and attention. *Attention, Perception, & Psychophysics*, 72(8), 2031-20-46. doi: 10.3758/APP.72.8.2031

Appendix A: Summary of Opioid-Induced Hearing Loss Case Studies

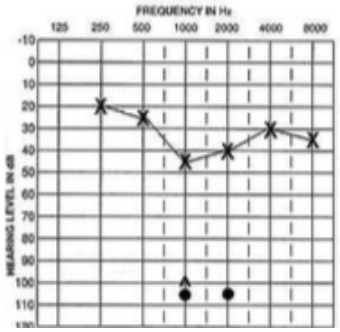
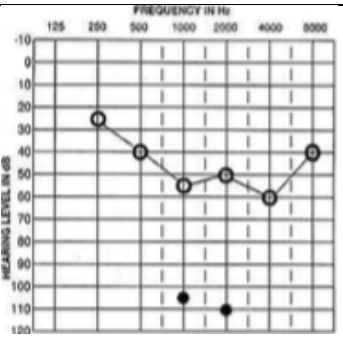
Author (Year)	Case Study: Patient 1							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Blakely & Schilling (2008)	37	M	Acetaminophen Codeine	2 years	Progressive Sensorineural Right Ear (pre-existing hearing loss in left ear)	None	None	Speech Reception Thresholds deteriorated to no response over 9 months
	Initial Speech Reception Threshold: Left Ear					**Initial Speech Reception Threshold: Right Ear**		
	80 dB					90 dB		

Author (Year)	Case Study: Patient 2							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Blakely & Schilling (2008)	45	F	Acetaminophen Codeine Oxycodone	22 years	Progressive Sensorineural	Tinnitus	None	Speech Reception Thresholds deteriorated to averages of 150 dB 2 months later
	Initial Speech Reception Threshold: Left Ear					**Initial Speech Reception Threshold: Right Ear**		
	80 dB					85 dB		

Author (Year)	Case Study: Patient 3							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Blakely & Schilling (2008)	37	F	Acetaminophen Codeine	2 years	Progressive Sensorineural Right Ear (pre-existing hearing loss in left ear)	Tinnitus Imbalance	None	Speech Reception Thresholds deteriorated to averages of 95 dB (right ear) and 110 dB (left ear)
	Initial Speech Reception Threshold: Left Ear					**Initial Speech Reception Threshold: Right Ear**		
	80 dB					85 dB		

Author (Year)	Case Study: Patient 1							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Christenson & Marjala (2010)	30	M	Methadone THC	Unknown	Bilateral Sudden Sensorineural	None	None	Recovery of hearing function 24 hours post-arrival
	No audiometric data available							

Author (Year)	Case Study: Patient 2							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Christenson & Marjala (2010)	25	F	Methadone THC	Unknown	Bilateral Sudden Sensorineural	None	None	Hearing function began to return 4 hours post-arrival
	No audiometric data available							

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Fowler & King (2014)	40	M	Heroin Cocaine	20 years	Bilateral Sudden Sensorineural	Tinnitus	Abstinence unknown	Unknown
	Initial Left Ear Audiogram					**Initial Right Ear Audiogram**		
								

Author (Year)	Case Study: Patient 1							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	8 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	No audiometric data available							

Author (Year)	Case Study: Patient 2							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	> 1 year	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	No audiometric data available							

Author (Year)	Case Study: Patient 3							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	Unknown	Bilateral Sudden Sensorineural	Vertigo initially	Unknown	Cochlear Implantation
	No audiometric data available							

Author (Year)	Case Study: Patient 4							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	> 2 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	Deafness in right ear occurred 3 weeks after deafness in left ear							

Author (Year)	Case Study: Patient 5							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	30 years	Bilateral Rapidly Progressive Sensorineural	None	Unknown	Cochlear Implantation
	Bilateral loss of vestibular function 6 years after hearing loss.							

Author (Year)	Case Study: Patient 6							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	10 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	Gradual hearing loss over 2 years in both ears before sudden sensorineural hearing loss (SSHL) occurred. SSHL in left ear occurred one month after SSHL in right ear.							

Author (Year)	Case Study: Patient 7							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	3 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	Hearing loss in left ear occurred 2 months after hearing loss in right ear.							

Author (Year)	Case Study: Patient 8							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	30 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	Gradual hearing loss over 4 years in both ears before SSHL occurred. SSHL in left ear occurred one year after SSHL in right ear.							

Author (Year)	Case Study: Patient 9							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	15 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	Hearing loss in right ear occurred 2 months after hearing loss in left ear.							

Author (Year)	Case Study: Patient 10							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Freeman, Bray, Amos, & Gibson (2009)	Unknown		Codeine	12 years	Bilateral Sudden Sensorineural	None	Unknown	Cochlear Implantation
	Rapidly progressing sensorineural hearing loss over 6 months in both ears before SSHL occurred. SSHL in right ear occurred one month after SSHL in left ear.							

Author (Year)	Case Study: Patient 1 (MF)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	42	M	Hydrocodone Acetaminophen	Unknown	Unilateral Sudden Sensorineural	None	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response					250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response		

Author (Year)	Case Study: Patient 2 (LS)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	52	M	Hydrocodone Acetaminophen	> 10 years	Unilateral Progressive Sensorineural	Tinnitus Dizziness	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response					250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response		

Author (Year)	Case Study: Patient 3 (PM)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	45	F	Hydrocodone Acetaminophen	> 10 years	Unilateral Progressive Sensorineural	Tinnitus	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response					250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response		

Author (Year)	Case Study: Patient 4 (JL)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	47	F	Hydrocodone Acetaminophen	Unknown	Bilateral Progressive Sensorineural	Tinnitus	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= 85 500 Hz= 100 1 kHz= 110 2 kHz= 120 3 kHz= 120 4 kHz= no response					250 Hz= no response 500 Hz= no response 1 kHz= 110 2 kHz= 100 3 kHz= 110 4 kHz= 115		

Author (Year)	Case Study: Patient 5 (MC)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	39	F	Hydrocodone Acetaminophen	2 years	Bilateral Progressive Sensorineural	None	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response					250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response		

Author (Year)	Case Study: Patient 6 (CD)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	43	F	Hydrocodone Acetaminophen	5 years	Bilateral Progressive Sensorineural	Tinnitus	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= 95 500 Hz= 105 1 kHz= 120 2 kHz= no response 3 kHz= no response 4 kHz= no response					250 Hz= 105 500 Hz= 110 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response		

Author (Year)	Case Study: Patient 7 (ED)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Treatment**	**Outcome**
Friedman et al. (2000)	32	F	Hydrocodone Acetaminophen	Unknown	Bilateral Progressive Sensorineural	Tinnitus	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response					250 Hz= no response 500 Hz= no response 1 kHz= no response 2 kHz= no response 3 kHz= no response 4 kHz= no response		

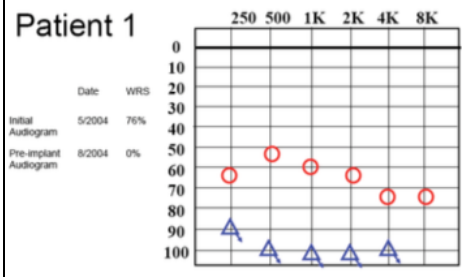
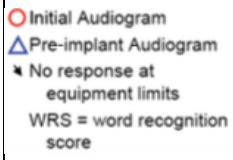
Author (Year)	Case Study: Patient 8 (RH)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	54	F	Hydrocodone Acetaminophen	Unknown	Bilateral Progressive Sensorineural	None	None	Successful cochlear implantation
	Unaided Preoperative Hearing Thresholds: Left Ear					**Unaided Preoperative Hearing Thresholds: Right Ear**		
	250 Hz= 95 500 Hz= 100 1 kHz= 115 2 kHz= 120 3 kHz= no response 4 kHz= no response					250 Hz= 95 500 Hz= 95 1 kHz= 115 2 kHz= 120 3 kHz= no response 4 kHz= no response		

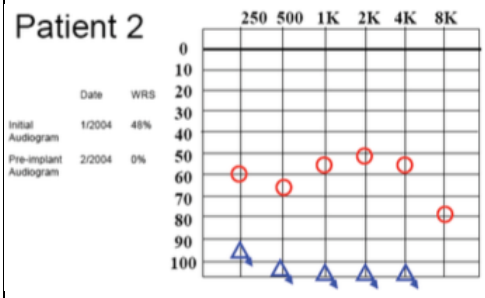
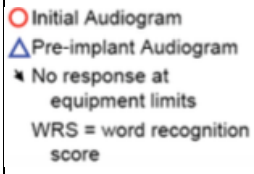
Author (Year)	Case Study: Patient 9 (IV)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	45	F	Hydrocodone Acetaminophen	6 years	Bilateral Progressive Sensorineural	Tinnitus Dizziness	Unknown	Unknown
	No audiometric data available							

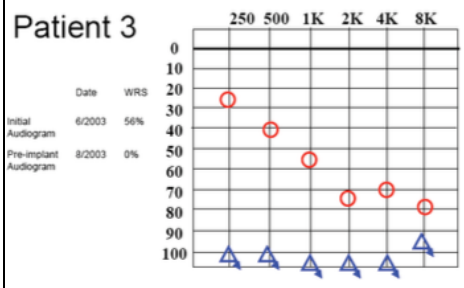
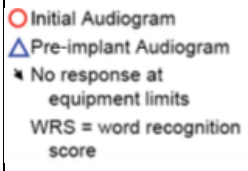
Author (Year)	Case Study: Patient 10 (GI)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	34	F	Hydrocodone Acetaminophen	2 months	Bilateral Progressive Sensorineural	Tinnitus	Unknown	Unknown
	No audiometric data available							

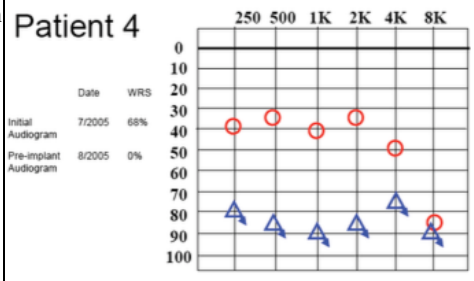
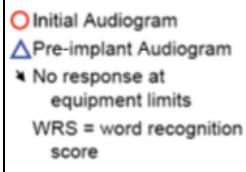
Author (Year)	Case Study: Patient 11 (LH)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	39	F	Hydrocodone Acetaminophen	4 years	Bilateral Progressive Sensorineural	None	Unknown	Unknown
	No audiometric data available							

Author (Year)	Case Study: Patient 12 (DS)							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Friedman et al. (2000)	33	M	Hydrocodone Acetaminophen	4 years	Unilateral Sudden	Tinnitus	Unknown	Unknown
	No audiometric data available							

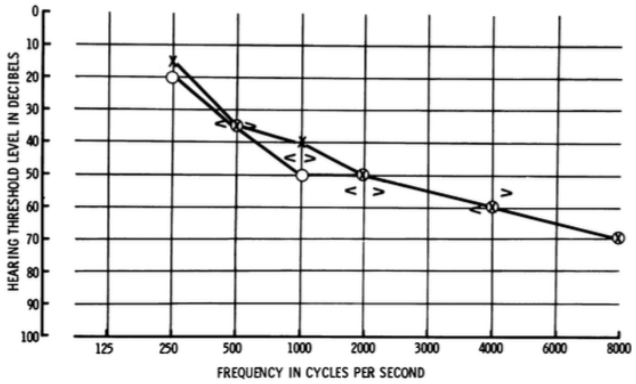
Author (Year)	Case Study: Patient 1							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Ho, Vrabec, & Burton (2007)	28	F	Hydrocodone Acetaminophen	> 2 years	Bilateral Progressive Sensorineural	Tinnitus	Steroids, Abstinence unknown	No spontaneous recovery, cochlear implantation
	Audiogram Comparison					**Legend**		
								

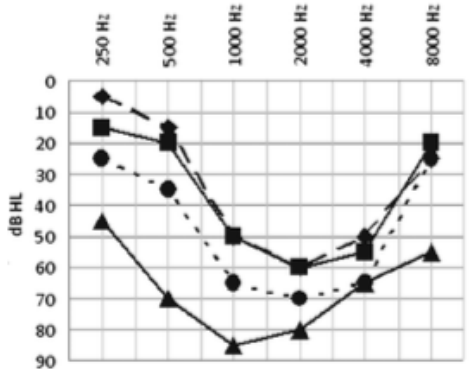
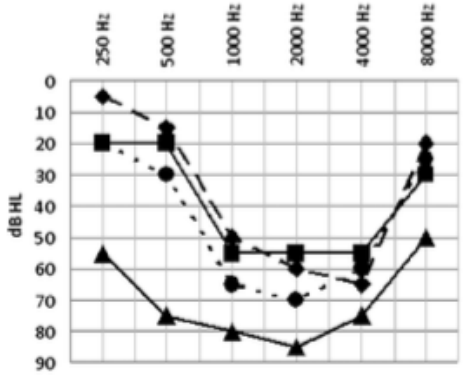
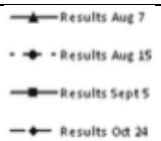
Author (Year)	Case Study: Patient 2							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Ho, Vrabec, & Burton (2007)	47	M	Hydrocodone Acetaminophen	> 1 year	Bilateral Progressive Sensorineural	Tinnitus	Steroids, Abstinence unknown	No spontaneous recovery, cochlear implantation
	Audiogram Comparison					**Legend**		
								

Author (Year)	Case Study: Patient 3							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Ho, Vrabec, & Burton (2007)	49	M	Hydrocodone Acetaminophen	1-2 months	Bilateral Progressive Sensorineural	None	Steroids, Abstinence unknown	No spontaneous recovery, cochlear implantation
	Audiogram Comparison					**Legend**		
								

Author (Year)	Case Study: Patient 4							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Ho, Vrabec, & Burton (2007)	48	F	Hydrocodone Acetaminophen	> 5 years	Bilateral Progressive Sensorineural	Headache	Steroids, Abstinence unknown	No spontaneous recovery, cochlear implantation
	Audiogram Comparison					**Legend**		
								

Author (Year)	Case Study: Patient 5							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Ho, Vrabec, & Burton (2007)	57	M	Hydrocodone Acetaminophen	Unknown	Bilateral Progressive Sensorineural	Tinnitus	Unknown	Unknown
	No audiometric data available							

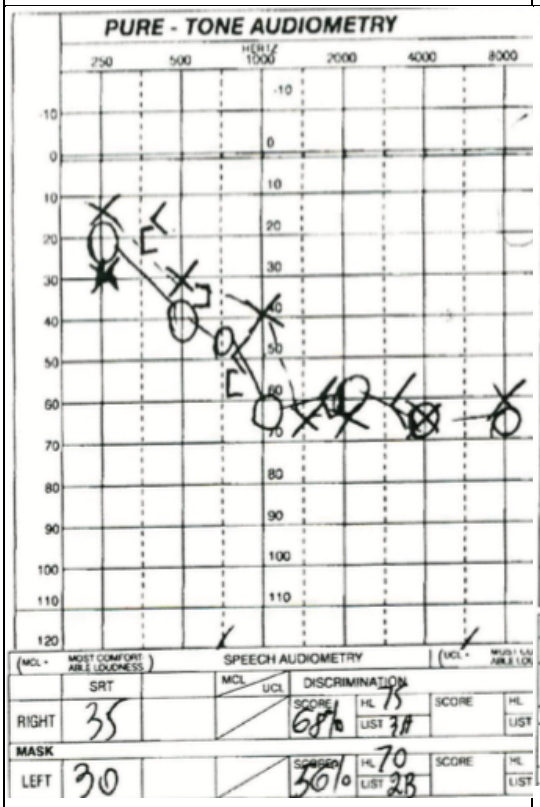
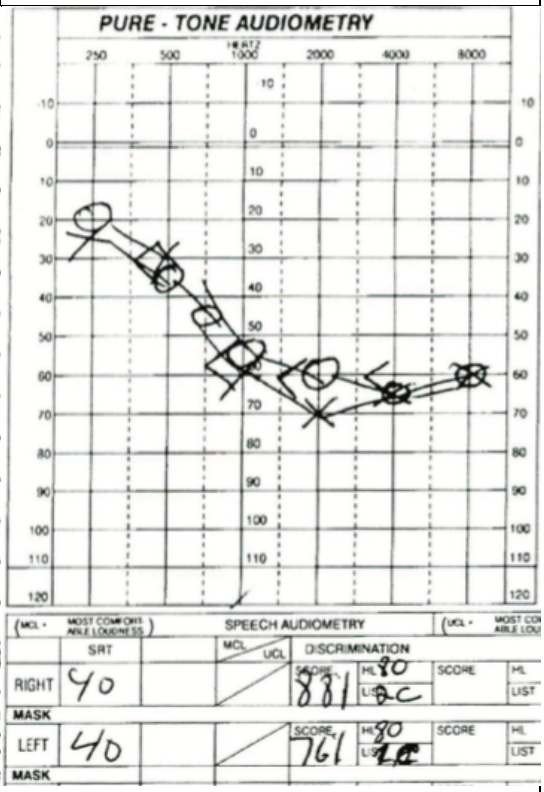
Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Lupin (1976)	22	M	Propoxyphene hydrochloride	130mg/2hr for 6 days	Bilateral Sudden Sensorineural	Tinnitus	None	Persistent hearing loss
	Audiogram							
								

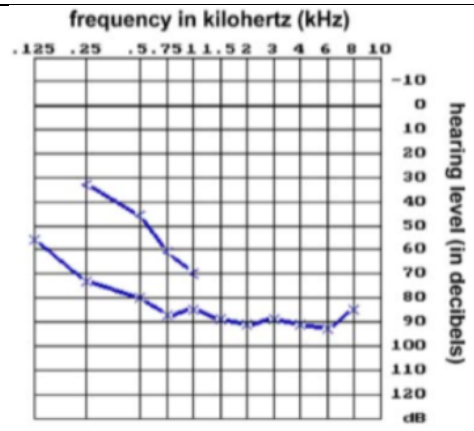
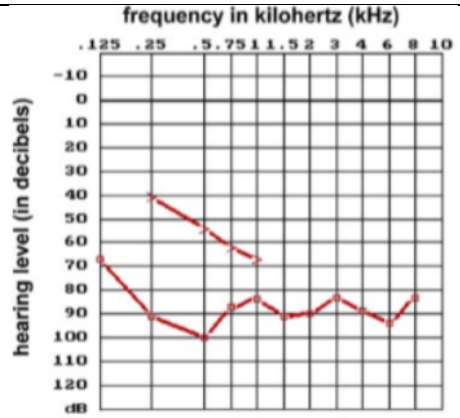
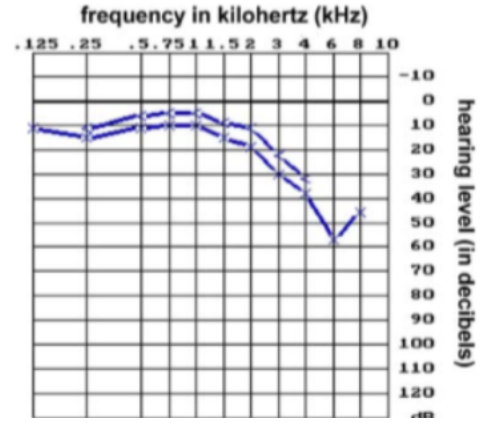
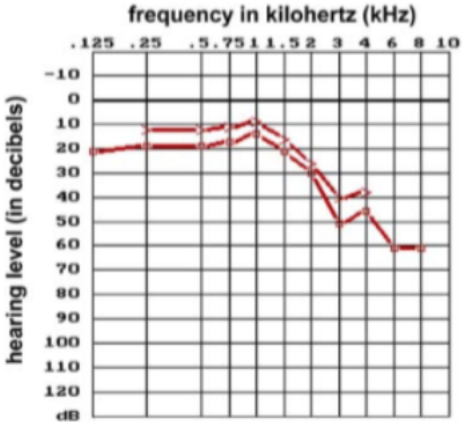
Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Nair, et al. (2010)	29	F	Heroin	Unknown	Bilateral Sudden Sensorineural	Tinnitus	Oral Steroids	Some improvement with initial treatment, ultimately fitted with binaural amplification
	Left Ear Thresholds					**Right Ear Thresholds**		
								
	Legend							
								

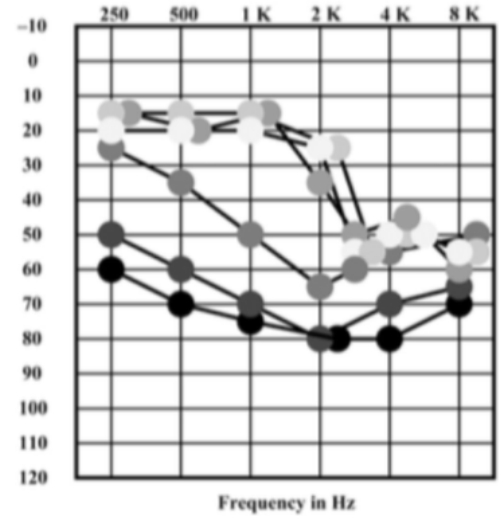
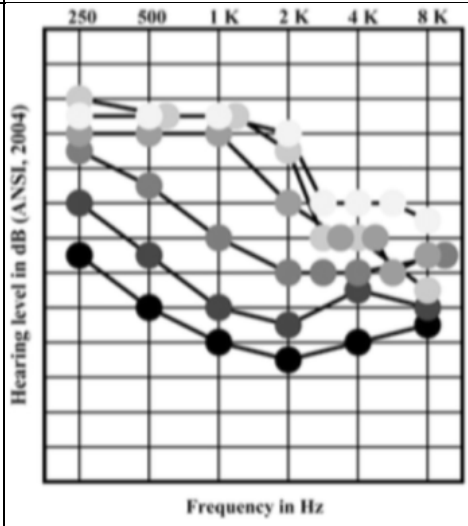
Author (Year)	Case Study: Patient 1							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Oh, et al. (2000)	34	F	Hydrocodone Acetaminophen	3 years	Bilateral Profound Rapidly Progressing Sensorineural	None	Oral prednisone	No response to steroid treatment; successful cochlear implantation
	Began to notice hearing loss after 3 years of regular Vicodin abuse. One month later, she noted a severe decrease in hearing bilaterally.							

Author (Year)	Case Study: Patient 2							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Oh, et al. (2000)	32	M	Hydrocodone Acetaminophen	8-9 years	Bilateral Progressive Sensorineural	Intermittent tinnitus	Oral prednisone	No response to steroid treatment
	Began to notice acute fullness and mild hearing loss in left ear, followed by multiple deteriorations in hearing in the left ear with periods of stabilization lasting 2-3 days. Simultaneously, the right ear experienced 2 sudden large declines in hearing with a period of stabilization lasting 1 week. Complete deafness occurred within 4 weeks of onset. Progressed to profound bilateral hearing loss 1 month later.							

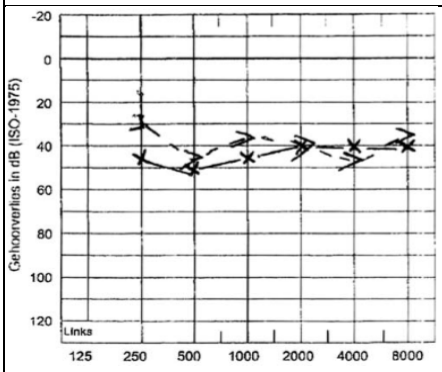
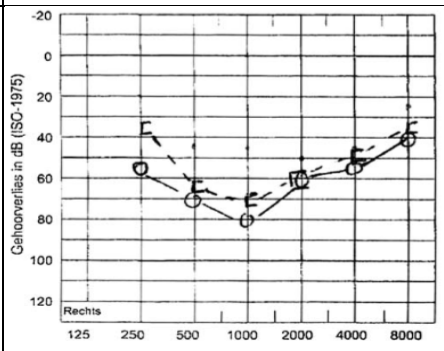
Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Rigby & Parnes (2008)	55	F	Oxycodone Acetaminophen	1.5 years	Bilateral Rapidly Progressing Sensorineural	Mild tinnitus in right ear	Abstinence	Persistent hearing loss 8 months following initial hearing loss
	Initial audiometric data					**Audiometric data 6 months later**		
	right ear = moderate-severe hearing loss left ear = moderate hearing loss					right ear = profound hearing loss left ear = severe-profound hearing loss		

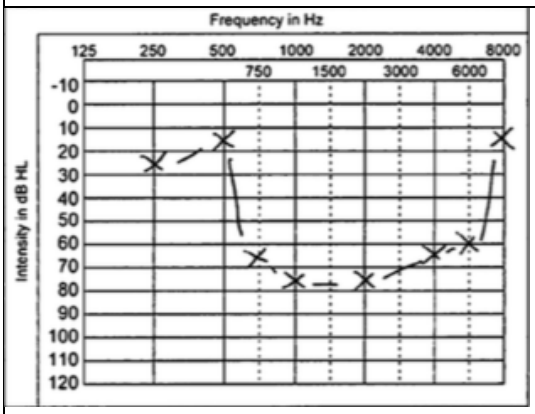
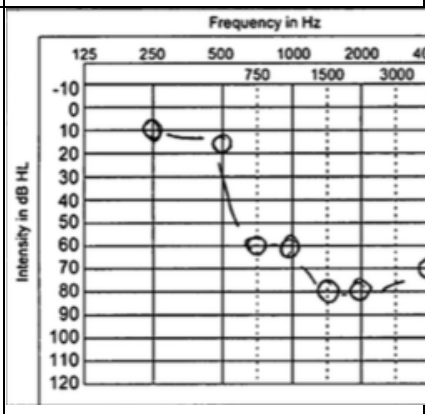
Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Saifan, et al. (2013)	31	M	Methadone	Unknown	Bilateral Sudden Sensorineural	None	None	Persistent profound hearing loss; prescribed binaural hearing aids
	Audiometry 1 month after discharge					**Audiometry 2 months after discharge**		
								

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Schrock, et al. (2006)	23	M	Heroin	2 g/day 2 years	Bilateral Sudden Sensorineural	None	Corticoids, vasoactive substances	Persistent symmetric high frequency hearing loss 3 days later
	Initial Audiogram and TEOAE: Left Ear					**Initial Audiogram and TEOAE: Right Ear**		
								
	Audiogram and TEOAE after 3 days treatment: Left Ear					**Audiogram and TEOAE after 3 days treatment: Right Ear**		
								

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Schweitzer, et al. (2011)	18	F	Heroin Benzodiazepine Cocaine	3 years	Bilateral Moderately-Severe Sudden Sensorineural	Intermittent tinnitus	Prednisone (1 month) Pentoxifylline (10 months)	Hearing sensitivity improved, Residual high frequency hearing loss
	Left Ear Audiogram Comparisons					**Right Ear Audiogram Comparisons**		
								
	Legend							
								

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Shaw et al. (2011)	20	M	Methadone	Unknown	Bilateral Sudden Sensorineural	Unknown	None	Complete resolution of hearing loss after 4 days
	No audiometric data available							

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Van Gaalen et al. (2009)	37	M	Methadone	Reported no previous use	Bilateral Sudden Sensorineural	Mild tinnitus	None	Normal audiometry 10 days later
	Audiogram 1 day after overdose: Left Ear					**Audiogram 1 day after overdose: Right Ear**		
								

Author (Year)	Case Study							
	Age	**Sex**	**Substance**	**Duration of Use**	**Hearing Loss**	**Associated Conditions**	**Initial Treatment**	**Outcome**
Vorasubin, et al. (2013)	23	M	Methadone	Unknown	Bilateral Sudden Sensorineural	None	Steroids	No change in audiograms at 9 month follow-up
	Initial Audiogram: Left Ear					**Initial Audiogram: Right Ear**		
								
	Speech Audiometry	**Right**	**Left**			**Tympanometry**	**Right**	**Left**
	Speech Threshold (dB HL) (SRT) SAT	15	25			Probe tone 226 Hz – 1000 Hz		
	Word Recognition (%)	12/.	16/.			Peak Pressure (daPa)	15	PE tube
	@ dB HL Presentation Level	55	55			Equivalent Volume (cm3)	2.0	6.8
	Word Recognition (%)	64/.	52/.			Gradient		
	@ dB HL Presentation Level	90	90			Static Admittance (mmho)	1.0	—