Test Retest Repeatability of Contralateral Inhibition of Transient Evoked Otoacoustic Emissions

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CERTIFICATE

This is to certify that this dissertation titled "**Test Retest Repeatability of Contralateral Inhibition of Transient Evoked Otoacoustic Emissions"** is a bonafide work submitted in part fulfilment for degree of Master of Science (Audiology) of the student Registration Number: 14AUD002. This has been carried out under the guidance of a faculty of this institute and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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This is to certify that this dissertation titled **"Test Retest Repeatability of Contralateral Inhibition of Transient Evoked Otoacoustic Emissions"** has been prepared under my supervision and guidance. It is also been certified that this dissertation has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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DECLARATION

This is to certify that this dissertation titled **"Test Retest Repeatability of Contralateral Inhibition of Transient Evoked Otoacoustic Emissions"** is the result of my own study under the guidance of **Dr. Ajith Kumar U**, Reader in Audiology, Department of Audiology, All India Institute of Speech and Hearing, Mysuru and has not been submitted earlier to any other University for the award of any other Diploma or Degree.

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Dedicated to Amma

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Abstract

The test retest repeatability of transient evoked otoacoustic emission (TEOAE) was assessed for single probe-fit and multiple probe-fit modes in 30 male participants. In single probe-fit mode inhibition of TEOAEs amplitudes were measured twice without altering the position of the probe. In multiple probe-fit mode inhibition magnitudes were measured across different days. The global TEOAE amplitude, amplitude inhibition, SNR inhibition and normalized inhibition were measured in both the modes. High reliability was found for TEOAE amplitude for both modes. However, reliability estimates were less for inhibition magnitudes. Among the inhibition parameters assessed amplitude inhibition had better reliability estimates than normalized inhibition and SNR inhibition. Also, inhibition in the single probe-fit mode had higher reliability than the multiple probe-fit mode. Amplitude inhibition had the highest reliability and hence this measure of medial olivocochlear reflex (MOCR) should be considered for all clinical interpretations.

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Chapter 1

INTRODUCTION

The efferent system has two distinct neuronal pathways. Thin and unmyelinated efferent axons originate in the lateral superior olivary complex (LSOC) and synapse with afferent neurons near the cochlear inner hair cells (IHCs). Large and myelinated efferent axons are primarily from the medial olivary cochlear complex and project contralaterally through medial olivocochlear bundle (MOCB) and innervate the outer hair cells (Guinan, 2006). Of two descending pathways MOCB is most studied due to its accessibility. MOCB can be activated via noise/sound presented to ear or by direct electrical shocks delivered at the floor of the fourth ventricle. Activation of the MOCB results in reduction of the electro-motility of the cochlear outer hair cells and inhibit cochlear responses by reducing the gain from the cochlear amplifier (Guinan, 2006). This reduction of the OHC motility is manifested as reduced basilar membrane displacement, velocity (Russell & Murugasu, 1997), reduction in the magnitudes of otoacoustic emissions (OAEs) (Collet et al., 1994), and compound action potential of the auditory nerve fibers (Liberman, 1989).

Transient evoked otoacoustic emissions (TEOAEs) are byproducts from the active process of cochlear outer hair cells and can be recorded from the external auditory canal via a probe microphone. TEOAEs provide frequency-specific information about cochlear function and outer hair cell (OHC) motility (Kemp, 2002). OHC function seems to be directly influenced by the descending or efferent auditory pathway. Functioning of the MOCB can be assessed by monitoring the amplitudes of transient evoked otoacoustic emissions upon the application of the noise in the contralateral ear (Berlin et al., 1993; Collet et al., 1990). Typically, amplitudes of the

TEOAEs reduces upon the application of the noise in the contralateral ear and is termed as contralateral inhibition of TEOAEs (Berlin et al., 1993; Collet et al., 1990).

Auditory efferent system is hypothesized to play an important role in protecting cochlea from acoustic injury, speech perception in noise, learning new speech sounds. Therefore, measurement of the contralateral inhibition of TEOAEs may prove to be clinically useful in several applications such as screening individuals for susceptibility to acoustic trauma, as a weakened MOC effect has been observed in laboratory animals that are preferentially susceptible to noise-induced damage (Maison & Liberman, 2000). It can act as an index to monitor efficacy of auditory training (de Boer & Thornton, 2008; Veuillet, Magnan, Ecalle, Thai-Van, & Collet, 2007). Altered MOC inhibitions have been reported in individuals with auditory neuropathy (Starr, Picton, Sininger, Hood, & Berlin, 1996) auditory processing disorders (Muchnika et al., 2004; Sanches & Carvallo, 2006), learning disability (Garinis, Glattke, & Cone-Wesson, 2008), and tinnitus (Ceranic, Prasher, Raglan, & Luxon, 1998). Like- wise, enhanced functioning of the MOC system has been reported in musicians (Perrot & Collet, 2014). Studies have also provided evidence that assessment of the efferent system could be useful in the diagnosis of pontine lesions such as tumors, acoustic neuromas and vestibulocochlear nerve pathology (Prasher, Ryan, & Luxon, 1994; Quaranta, Wagstaff, & Baguley, 2004).

Few studies have assessed reliability of TEOAE inhibition. But, these studies have assessed the reliability of contralateral inhibition of OAEs over one or two recording sessions (Chan & Pherson, 2000; Franklin, McCoy, Martin, & Lonsbury-Martin, 1992; Mishra & Lutman, 2013; Vedantam & Musiek, 1991). However, it is important to evaluate the reliability of TEOAE inhibition over more number of

recording settings as the information derived through TEOAE inhibition can be applied to evaluate numerous clinical conditions. The literature suggests that the magnitude of OAE inhibition is very small in quantity that can be affected by a multitude of factors. As the applications of OAEs and its inhibition evolve, there is an augmented need to define and establish the repeatability and reliability of contralateral inhibition of OAEs so as to facilitate its use as a clinical tool in monitoring the auditory function over time.

This study aims at studying the test retest repeatability of contralateral inhibition of TEOAEs.

Objectives of the study

- To assess the test-retest reliability of contralateral inhibition of TEOAEs within session.
- To assess the test-retest reliability of contralateral inhibition of TEOAEs across sessions.

CHAPTER 2

REVIEW OF LITERATURE

The Efferent system

The efferent pathway consists of the medial olivocochlear (MOC) and lateral olivocochlear efferents (LOC). The cochleae receive thick myelinated MOC fibers that originate from the medial part of superior olivary complex (SOC) on both sides. From the SOC, they project to the cochlea, and innervate the outer hair cells (OHCs). On the contrary, the cochleae receive ipsilateral thin unmyelinated LOC fibers and these innervate the IHCs. The MOC and LOC fibers project into the cochlear nucleus and to brainstem vestibular nuclei as well (Guinan, 2006). These are based on animal experiments but can be extended to human efferent system (Moore, 1999; Schrott-Fischer, Egg, Kong, Renard, & Eybalin, 1994; Spoendlin & Schrott, 1989).

Physiology of the Auditory Efferent System

When stimulated, MOC fibers release neurotransmitters (primarily acetylcholine, ACh) into the synaptic cleft between MOC axons and OHC dendrites. ACh binds to receptors on OHCs, which allows calcium (Ca2+) ions that in turn cause potassium (K+) ions to flow out of the OHC (Sewell, 2011). Because OHCs have a negative resting potential, while endolymph has a positive resting potential, release of K+ causes the OHC to hyperpolarize and results in a decreased endocochlear potential (Guinan & Stankovic, 1996). This effect has a time course of approximately 100 ms, and is often termed the MOC "fast effect" (Guinan, 2006). There is also a "slow effect" that has a time course of >20 s (Sridhar, Liberman, Brown, Eye, & Infirmary, 1995), and is believed to be due to increased stiffness in OHCs due to changes in

prestin (Guinan, Backus, Lilaonitkul, & Aharonson, 2003; Guinan, 2006). Both effects result in reduced amplification of basilar membrane motion by OHCs.

When sound enters the cochlea, it is frequency analyzed along the length of the basilar membrane. The OHCs at each point on the basilar membrane amplify its motion through somatic electromotility and stereocilia motility. This forms the cochlear amplifier (Dallos, Zheng, & Cheatham, 2006). The MOC efferents that end on OHCs have the potential to modify the action of the OHCs and, through this, to control the gain of the "cochlear amplifier" (Guinan & Stankovic, 1996). MOC efferents, by making mechanical changes that inhibit the cochlear amplifier, change basilar membrane motion, thereby changing OAEs.

Efferent stimulation increases the amplitude of the cochlear microphonic (Fex, 1959) due to increased current flow through OHCs (Guinan & Stankovic, 1996). OAEs typically are reduced in amplitude with efferent stimulation (Guinan et al., 2003; Mott, Norton, Neely, & Bruce Warr, 1989). MOC stimulation can also cause phase leads and decreases in OAE latency, which is likely due to broadening of the traveling wave peak (Francis & Guinan, 2010; Giraud, Wable, Chays, Collet, & Chéry-Croze, 1997). OAEs are particularly useful for studying efferent effects in humans because they can be measured quickly and non-invasively.

Functional significance of MOCR

a. Hearing in noise

Animal work has found that auditory nerve responses to stimuli in noise can be increased in the presence of noise, likely due to efferent inhibition of the response to noise (Kawase, Delgutte, & Liberman, 1993; Kawase & Liberman, 1993; Winslow & Sachs, 1987). However, studies in humans have shown conflicting results. Kumar and Vanaja (2004) found that MOCR strength was positively correlated with

performance on a speech-in noise task in ten normal-hearing children. However, Wagner et al, (2008) found no significant correlation between MOCR strength and performance. Differences in the speech and noise stimuli and levels may partly explain the varying results, but the limited evidence suggests that the effect is not robust.

b. Protection from acoustic trauma

The MOCR reduces the enhancement of basilar membrane motion provided by the cochlear amplifier. One purpose proposed is that it serves as a protective mechanism from cochlear damage due to loud sounds. This notion has been supported by the results of animal work. Rajan (2000) measured noise-induced threshold shifts in cats before and after sectioning MOC fibers; threshold shifts were significantly larger after the efferents were sectioned. Similar results have been reported when using DPOAEs in the chinchilla (Zheng, Henderson, McFadden, & Hu, 1997). Rats with stronger (i.e., more effective) MOCR, as assessed by the magnitude of reduction in DPOAEs with versus without MOCR activation, had less severe threshold shifts after being exposed to high-level (109 dB SPL) sound (Maison & Liberman, 2000). The same relationship has also been found for mice exposed to less extreme sound levels (84 dB SPL) (Maison et al., 2012). Although the MOCR appears to provide protection, it has been argued that sound levels in nature are lower than the sound levels used experimentally, suggesting that efferent effects did not evolve to prevent noise damage (Kirk & Smith, 2003).

Darrow et al, (2007) hypothesized that LOC efferents may also have a role in protection from noise damage. They lesioned the LOC bundle of one hemisphere in mice but did not damage the MOC bundle. DPOAEs and ABRs were measured before and after noise exposure in both ears. DPOAEs were the same in both ears, suggesting

equal damage to OHCs on both side, but ABR thresholds were poorer in the ear that was the same side as the lesion. Given that LOC fibers terminate on auditory nerve fibers primarily on the same side, the LOC bundle reduces auditory nerve responses to noise and thus protects from noise damage at the level of the nerve (Darrow et al., 2007). There are limited studies on humans and have not shown a clear relationship between the MOCR and noise damage (Mertes, 2014).

c. Learning

Studies have reported that the top-down influences do not terminate at the auditory cortex but also extend from the auditory cortex toward subcortical nuclei (Palmer et al., 2007; Winer, 2006) via the extensive corticofugal system (Zhang & Suga, 2000; Zhou & Jen, 2000). Corticofugal influences reach even into the inner ear (Perrot et al., 2006; Suga, Xiao, Ma, & Ji, 2002) via the efferents of the medial olivocochlear bundle (MOCB) (Guinan, 2006), which originate from the brainstem and terminate inside the cochlea, where they modulate preneural amplification gain. It is thought that the corticofugal system contributes to learning-related plasticity by forming feedback circuits that initiate and reinforce altered neural sound presentations along the central auditory pathway (Suga et al., 2002).

Potential Clinical Utility of MOCR Measurements

Assessment of Clinical Populations

Various clinical populations demonstrate difficulty hearing in the presence of normal hearing. Given that the MOC system may provide benefit for hearing in noise, some researchers have speculated that these individuals may demonstrate reduced or absent MOCR function. MOCR effects on OAEs have been studied for various conditions, such as auditory processing disorder (Muchnika et al., 2004; Sanches & Carvallo, 2006), learning disabilities (Garinis et al., 2008), specific language

impairment (Clarke, Ahmmed, Parker, & Adams, 2006), dyslexia (Veuillet et al., 2007) and Asperger's syndrome (Kaf & Danesh, 2013). These studies compared MOCR-induced changes in OAEs between the clinical population and a normal control group. Some of these studies have shown smaller changes in OAEs for the clinical group (Muchnika et al., 2004; Sanches & Carvallo, 2006). Others have shown that the clinical group demonstrated more efferent activity in the left ear, whereas the control group demonstrated more activity in the right ear (Garinis et al., 2008; Kaf & Danesh, 2013; Veuillet et al., 2007). These results may suggest that reduced or abnormal MOC functioning may be present in some clinical conditions which exhibit difficulty in speech perception in noise. Auditory neuropathy spectrum disorder is another condition where measuring MOCR may have diagnostic significance.

Auditory neuropathy is a condition in which the auditory nerve cannot fire synchronously but OHC function is normal, and presents clinically as present OAEs, abnormal or absent ABR, and poor speech discrimination (Starr et al., 1996). Because the middle ear muscle reflex (MEMR) and MOCR pathways involve the auditory nerve, these reflexes are also abnormal or absent in patients with auditory neuropathy (Berlin et al., 2005; Hood, Berlin, Bordelon, & Rose, 2003). Diagnosis of auditory neuropathy requires ABR measurement (Hood et al., 2003), which typically requires sedation in older infants and younger children. MOCR testing may find use as a screening tool and/or addition to the test battery because it can be measured non-invasively without the need for sedation.

Assessing Outcomes of Auditory Training

In humans, several sources of evidence suggest that auditory training can strengthen efferent effects, presumably through a cortically mediated mechanism. Individuals with musical training have stronger effects than untrained individuals (Micheyl, Perrot, & Collet, 1997). Additionally, de Boer and Thornton (2008) found a relationship between MOCR strength and improvement on phoneme discrimination after an auditory training task. Individuals with weak baseline MOCR effects improved their performance after the training, and also had increases in MOCR strength after the task. Veuillet et al, (2007) examined the effect of auditory training on MOCR effects in children with dyslexia. At baseline, dyslexic children showed asymmetry in MOCR effects, where larger effects were seen in left ears relative to right ears. An opposite pattern was seen in a control group. After training on a phoneme discrimination task, the dyslexic children showed MOCR ear effects that were more similar to the control group. These results suggest that auditory training can both strengthen the MOCR and reduce abnormalities in MOCR asymmetry.

Kumar et al, (2010) investigated how the strength of feedback in the medial olivocochlear bundle (MOCB) affects perceptual learning of non-native speech sounds. Training was given for 12 days where the discrimination of non-native (Malayalam) speech sounds from its native (Hindi) counterparts was monitored. Contralateral inhibition of otoacoustic emissions were measured on the first and twelfth day of training. Results suggested that training significantly improved reaction time and accuracy of identification of non-native speech sounds. Findings suggested that during perceptual learning, feedback from the MOCB may fine tune the brainstem and/ or cochlea.

Shastri et al, (2014) investigated the ability of native listeners to identify subtle phonetic contrasts in nonsense words and its relationship with the contralateral inhibition of transient evoked otoacoustic emissions (TEOAE). The phone identification score and reaction time for four phonetic pairs in nonsense words were measured for each participant. The authors found that the phone identification score and global contralateral inhibition amplitude of TEOAE were significantly higher and reaction time was significantly shorter in high performers than that of low performers. Significant correlation was found between the phone identification score and contralateral inhibition of TEOAE. These results support the emerging view that top down influences from higher centers shapes the responses of lower centers. However, the mechanism for how this occurs is unclear and requires further study.

OAEs to measure the MOC effects

Factors Influencing MOCR Effects on OAEs

i. Ipsilateral, Contralateral, and Bilateral Activation

The MOCR is a bilateral reflex, so sound presented in either ear can activate the reflex and influence OHC function in both ears. The strongest MOCR effects occur when the reflex is elicited bilaterally, with weaker effects occurring for ipsilateral and contralateral activation (Berlin, Hood, Hurley, Wen, & Kemp, 1995). In humans ipsilateral and contralateral activation appears to have similar effects (Guinan, 2006). Most human studies use contralateral activation of the MOCR, which has the advantage of acoustically separating the MOCR and OAE activating stimuli.

ii. Stimulus Parameters

The MOCR can be activated by a variety of sounds, including pure tones, tone bursts, clicks, narrowband and broadband noise (Guinan et al., 2003). Efferent effects

become stronger as the stimulus bandwidth increases due to increased number of efferent fibers stimulated (Lilaonitkul & Guinan, 2009; Maison, Micheyl, Andéol, Gallégo, & Collet, 2000; Norman & Thornton, 1993; Velenovsky & Glattke, 2002). Therefore, broadband noise is typically used as the MOCR-eliciting stimulus. MOCR effects also become stronger as the level of the eliciting stimulus increases (Collet et al., 1990; Hood, Berlin, Hurley, Cecola, & Bell, 1996). Although intense, broadband stimuli seem ideal for eliciting MOCR, elicitation of the middle-ear muscle reflex (MEMR) also increases as stimulus bandwidth and level increases (Margolis & Wilson, 1980; Popelka, Karlovich, & Wiley, 1974). Activation of MEMR increases the impedance of the middle ear primarily below 1 kHz (Moller, 1962), reducing transmission of sound through the tympanic membrane in the forward and reverse direction. Activation of MEMR reduces OAE amplitudes (Whitehead, Martin, & Lonsbury-Martin, 1991), similar to MOCR activation. It can therefore be difficult to determine if decreases in OAE amplitudes were due to MEMR and/or MOCR. Methods have been proposed for disentangling these effects (Guinan et al., 2003), but it may be preferable to avoid MEMR elicitation. An additional confound is that OAE-eliciting stimuli, especially clicks, can also elicit the MEMR (Guinan et al., 2003; Rawool, 1995) as well as MOCR activity.

iii. OAE Frequency Effects

MOCR effects in humans have typically been found to be most prominent on OAEs in the 1-2 kHz region (Collet et al., 1990; Goodman, Mertes, Lewis, & Weissbeck, 2013; Hood et al., 1996). Effects are weak or absent above 4 kHz, although this may be due to poor signal to noise ratios (SNRs) of higher-frequency emissions (Goodman et al., 2013). This pattern of frequency effects may be related to the density of efferent

innervation (Robertson, Anderson, & Cole, 1987). It may also be related to the middle ear transfer function, which is most efficient in the 1 – 4 kHz region (Aibara, Welsh, Puria, & Goode, 2001; Moller, 1963). OAEs in this frequency region would be strongest and therefore changes would be most easily observable in this region.

iv. Lateralization of MOCR

MOCR effects tend to be stronger in right ears relative to left ears (Morlet et al., 1999). Administration of benzodiazepines, of which there are more receptors in the left hemisphere, reduced MOCR effects when measured in the right ear relative to the left ear (Morand-Villeneuve et al., 2005). These studies used contralateral MOCR activators, which primarily excites the uncrossed MOC fibers (Guinan & Stankovic, 1996).

v. Attention Effects

The presence of descending pathways from the cortex to the brainstem suggests that the cortex can influence efferent activity. Efferent effects are reduced or absent in the presence of sleep (Froehlich, Collet, Valatx, & Morgon, 1993) and anesthesia (Boyev, Liberman, & Brown, 2002; Chambers, Hancock, Maison, Liberman, & Polley, 2012). Auditory and visual attention tasks in animals and humans decrease the amplitude of evoked potentials and otoacoustic emissions relative to measurements made with no attention task (de Boer & Thornton, 2007; Delano, Elgueda, Hamame, & Robles, 2007; Harkrider & Bowers, 2009). It has been suggested that efferent activity will be strongest when it is advantageous to reduce sensitivity to auditory input (Guinan, 2011). For example, an individual attending to visual stimuli in the presence of distracting acoustic stimuli may benefit from the MOCR, whereas an individual

attending to soft acoustic stimuli would likely not benefit from the MOCR. This notion has been supported by studies that compared visual and auditory attention tasks, in which visual tasks were found to increase the amount of efferent activity more than auditory tasks (de Boer & Thornton, 2007; Delano et al., 2007). A reduction in auditory sensitivity may have been beneficial in order to attend to visual input. Additionally, auditory tasks that involved attending to stimuli in the ear in which OAEs were recorded from showed less efferent activity relative to attending to stimuli in the contralateral ear or no task (Harkrider & Bowers, 2009). In this type of task, reducing sensitivity in the contralateral ear would be expected to be beneficial, but not in the ipsilateral ear.

vi. Age Effects

Age appears to show the largest effect in older adults. MOCR effects in newborns are similar to those in young adults (Carolina Abdala, Mishra, & Garinis, 2013). Others have found decreasing MOCR strength with increasing age in adults (Jacobson, Kim, Romney, Zhu, & Frisina, 2003; Keppler et al., 2010; Kim, Frisina, & Frisina, 2002; Parthasarathy, 2001). These differences remained after controlling for hearing thresholds. Interestingly, a study in a mouse model of presbycusis found that MOCR effects on DPOAEs dissipated before DPOAEs (Zhu et al., 2007), suggesting that loss of MOCR may predict the onset of hearing loss prior to more well-established measures of auditory function.

Recommended protocol to measure MOCR effects

TEOAEs are elicited using transient stimuli which contain a broader bandwidth compared to pure tone stimuli and thus stimulate a broader region of the cochlea and provide more information about the OHC function in a shorter time period (Goodman, Fitzpatrick, Ellison, Jesteadt, & Keefe, 2009). These transient stimuli like clicks or tone pips can also be used to measure MOC effects (Collet et al., 1990). The nonlinear method is used to elicit TEOAEs which can cancel the ringing response of the click or tone-pip (Kemp & Bray, 1987). However, the nonlinear method also cancels out the linear part of the MOC effect. An alternative method is to record TEOAEs with and without MOC activity elicited by a contralateral sound, and to subtract one result from the other. The result would cancel the stimulus ringing and leave the MOC-induced change in the TEOAE (Guinan, 2006).

Chabert et al, (2002) studied the differences between OAEs and neural responses after MOC activation. Contralateral 50 dB SL broadband noise produced an approximately 10-dB shift in human auditory nerve responses measured during retrosigmoid surgery, whereas previously reported shifts in humans were 3.7 dB in TEOAEs and 0.5 to 2 dB in DPOAEs for the same contralateral sound (Abdala, Ma, & Sininger, 1999; Moulin, Collet, & Duclaux, 1993; Williams & Brown, 1997). Thus, it appears that MOC-induced OAE changes considerably underestimate MOC-induced neural changes.

For 60 dB SPL broadband noise elicitors, there is approximately 25 ms from sound onset (or offset) to the start of the MOC-induced change in the SFOAE (Backus & Guinan, 2006). Both ipsilateral and contralateral reflexes have similar time courses. Amplitude modulation of the elicitor produces OAE responses that are time

modulated to an extent consistent with MOC time constants in the same range (Backus & Guinan, 2006; S. Maison et al., 2000). Based on the above review, recommended protocol to measure MOC reflex is shown in Table 2.1

TABLE 2.1

Recommended Protocol

Parameter	**Setting**
Stimulus level	60 dB pe SPL
Contralateral acoustic stimulus level	60 – 65 dB SPL / 35 dB SL
Rate	50/s
Sweeps	260

Rationale for Assessing Repeatability of MOCR Effects

One important aspect of a clinically useful measurement is its high repeatability across time in a control population (e.g., normal hearing young adults with no noise exposure and no ear/hearing pathology). If changes in a metric across repeated measurements are to be of clinical value (e.g., detecting improvement in MOCR due to auditory training, or a decrement in MOCR due to hearing loss), then a healthy control population should demonstrate low variability and high repeatability in the measurements across time. A change in a measurement due to a pathology or intervention must be larger than the variability seen in a control population; smaller variability in the control population means that smaller changes can be detected and that the measurement may be clinically useful.

Repeatability of the MOC effects

Although efferent effects on OAEs in humans have been assessed for nearly 30 years, relatively few have investigated the repeatability of these effects across time. Typically, the test-retest reliability between two sessions has been examined (Berlin et al., 1993, 1995; de Boer & Thornton, 2008; Mishra & Lutman, 2013; Sanches & Carvallo, 2006). This has often been assessed within a single session. There are a few studies have examined the reliability for sessions spaced by several days (de Boer & Thornton, 2008; Mishra & Lutman, 2013).

Graham and Hazell (1994) were the first to examine repeatability across more than two sessions. They examined MOCR effects on TEOAEs in 6 adults with normal hearing; five were between 22-26 years old and one was 67 years old. Eighteen total measurements were taken: six measurements at three visits, with each visit spaced by three weeks. TEOAEs were elicited with 65 dB SPL clicks and the MOCR was elicited with 30 dB SL contralateral acoustic stimulation (CAS). MOCR was quantified as the amplitude difference between mean TEOAE waveforms obtained with and without CAS. Across all measurements, mean TEOAE shifts ranged from approximately 0.3 – 0.6 dB and the standard deviations ranged from 0.10 – 0.25 dB, indicating small but repeatable effects over time. Some of the drawbacks of this study were that the authors did not examine the statistical significance of MOC shifts in individuals or in the group. Individual data are reported, and some mean MOC shifts are close to 0 dB. It is likely that the 95% confidence intervals would include 0 in some instances, suggesting that the MOC shift was not significantly different from zero. Therefore, it is not known how many of the shifts reported were actually significant. Additionally, the SNRs of the TEOAEs were not reported, so it is not known how robust the emissions were.

Kumar et al, (2013) examined repeatability of MOC shifts using DPOAEs. Subjects were 24 normal hearing adult males ages 18-45 years. Ten measurements were taken across a two-week span: two measurements on the first day and one measurement taken on eight additional days. 2f1-f2 DPOAEs (f2/f1=1.2, L1/L2=65/55 dB SPL) were measured from 1-8 kHz (spaced by 1 kHz) with and without the presence of CAS presented at 40 dB SPL. Repeatability was examined statistically using multiple metrics, including repeated measures ANOVA, Cronbach's alpha and interclass correlation coefficient (ICC), standard error of measurement (SEM, in dB), and the smallest detectable difference (SDD, in dB). DPOAE amplitudes without CAS had SEMs ranging from 0.7 – 1.4 dB across sessions and frequencies, suggesting stable emissions and consistency with previous reports of DPOAE amplitude stability. However, poor repeatability was seen for MOC shifts. Within a single session without probe re-insertion, Cronbach's alpha values ranged from 0.2 to 0.7 and ICC values ranged from 0.1 to 0.6 (for both metrics, 1.0 indicates perfect reliability). SEMs, which were calculated using Cronbach's alpha and the standard deviation, were 1 dB or less. Given that these values were relatively low, this indicates that the standard deviations of measurements were small while the Cronbach's alpha was large. SDD values ranged from 1.7 to 2.7 dB, which are large relative to most previous reports of MOCR effects that often show changes of 1 dB or less. When repeatability across multiple sessions was examined, increases in Cronbach's alpha (ranging from 0.5 to 0.8) but decrements in the ICC (ranging from 0.1 to 0.3) were found. The reason for the discrepancy in these measurements was not explained. SEMs were slightly larger (1.6 dB or less), and SDDs also increased (ranged from 1.6 to 4.3 dB). The authors concluded that the results were too variable

within and across subjects for DPOAEs to be clinically useful for assessing MOCR effects.

Short comings of this study are that the authors reported that DPOAEs were required to have a >6 dB SNR to be considered present, but the authors did not report the measured SNRs. They reported that DPOAE measurements lasted 30 seconds per frequency, which may have resulted in relatively low SNRs. The purported MOCR activator, which was broadband noise presented at 40dB SPL, may have been too low in level to elicit MOCR effects in most subjects. Studies have demonstrated that increasing the MOCR activator level increases the magnitude of change in OAE amplitudes (Collet et al., 1990). The authors examined the composite DPOAE rather than separating it into the distortion- and reflection-sources, which could explain why some subjects exhibited increases in DPOAE amplitude with efferent stimulation. DPOAE fine structure appears to be repeatable across time (Reuter & Hammershøi, 2006), so this may not account for the variability in MOCR effects.

Mishra and Lutman (2013) also examined the repeatability of MOCR effects on OAEs but concluded that the effects were highly repeatable and may be clinically usable. MOCR effects on TEOAEs were measured in 35 normal-hearing young adults. Two measurements were obtained per subject, with measurements separated by one to four days. TEOAEs were obtained at five levels ranging from 57-69 dB pSPL in 3 dB steps. The MOCR activator was CAS presented at 35 dB SL. The MOCR effect was quantified as the change in the overall TEOAE amplitude. TEOAE SNRs ranged from 6 to 17 dB, with a mean of 12 dB. When MOCR effects were expressed as the dB change in TEOAE amplitudes, Bland-Altman plots showed that effects changed by 0.03 – 0.07 dB across session for each stimulus level. Cronbach's

alpha was 0.8 for four stimulus levels and 0.7 for one level. The ANOVA revealed no main effect of test session, indicating that the mean MOCR effect did not change between sessions. Essentially similar results occurred when MOCR effects were expressed as the percentage of change in TEOAE amplitude without CAS. Repeatability results revealed low variability and high reliability across the two sessions. Limitations of this study are that the authors reported the measured SNRs but did not include SDDs. Therefore, it is not known if the shifts that were observed were statistically significant. Also, two measurements taken within five days do not give an indication of the repeatability over a longer time span. The genders of the participants are not mentioned. Finally, the authors only examined changes in overall TEOAE amplitude rather than within frequency bands.

Mertes (2014, 2015) studied the MOCR effects on TEOAEs and found it to be highly repeatable across a 5-week time span in a large majority of young normal-hearing subjects. The authors investigated the within- and across-subject variability of these measurements in a research setting. 24 normal-hearing young adults were included in the study. TEOAEs were elicited with 35 dB SL clicks and the CAS was 35 dB SL broadband noise. Across a 5-week span, changes in both TEOAE amplitude and phase evoked by MOCR activation (*MOC shifts*) were measured at four sessions. Other variables such as slow drifts in TEOAE amplitude across time, activation of the middle-ear muscle reflex, and changes in subjects' attentional states were controlled. In a large number of subjects the MOC shifts were statistically significant. However, some subjects showed within- and across-session variability that could not be explained by changes in hearing status, middle ear status, or attentional state. The measured variability of subsequent MOC shifts in subjects was often larger than expected (based on the variability present at baseline), indicating the presence of

additional variability at subsequent sessions. It appears that MOC shifts, as analysed in this study, may be too variable for clinical use, at least in some individuals. In this study although inclusion criteria were chosen to include young subjects with good hearing, it is not known how these results would generalize to other populations, such as older adults or individuals with some level of hearing loss. If reliable measurement of MOCR is limited to young adults with normal hearing, the clinical applications may be limited. Few studies have assessed MOCR effects in subjects with hearing loss, so it remains to be seen if these measurements hold promise for these populations.

Mishra and Abdala (2015) assessed the repeatability of a fine-resolution, distortion product otoacoustic emission (DPOAE)–based assay of the medial olivocochlear (MOC) reflex in normal-hearing adults. 4 (2 females, 2 males) normal hearing adults to assess short term stability and 5 (4 females, 1 male) normal hearing adults to assess long term stability were included. The four ears assessing short-term stability were tested daily for 4 consecutive days (4 × 4 = 16 sessions). The five ears included in the assessment of long-term stability were tested weekly for 4 weeks (5 × 4 = 20). Only right ears were tested. DPOAE recordings were made for frequencies between 500 and 4000 Hz using stimulus levels of 65 (L1) and 55 (L2) dB SPL and a constant stimulus frequency ratio (f2/f1) of 1.22. Broadband noise was used as contralateral acoustic stimulation (CAS) and was presented through an ER-2 insert transducer at 60 dB SPL. The DPOAE level and phase measurements were recorded with and without contralateral acoustic stimulation. MOC reflex indices were computed by (a) noting contralateral acoustic stimulation-induced changes in DPOAE level (both absolute and normalized) at fine-structure peaks, (b) recording the effect as a vector difference, and (c) separating DPOAE components and considering a

component-specific metric. Analyses indicated good repeatability of all indices of the MOC reflex in most frequency ranges. Short- and long-term repeatability was generally comparable. Normalized inhibition showed the greatest repeatability. These results suggested that fine-resolution DPOAE-based measures of the MOC reflex measured at strategic frequencies are stable, and natural variance from day-to-day or week-to-week durations is small enough to detect between-group differences and possibly to monitor intervention-related success. One factor that was not controlled was attention. The MOC effect was evoked without any attempt to monitor or control the subject's attention toward the contralateral noise activator. Controlling attention by including task-dependent measures might decrease intra-subject variability more effectively. The sample is less to be generalizing the findings and the short term versus long term stability was compared in different sets of participants.

Stuart and Cobb (2015) studied the reliability of measures of transient evoked otoacoustic emissions (TEOAEs) with contralateral suppression on 14 adult females and 14 adult males. They studied the parameters across three days. The testing consisted of four recordings (i.e., initial test; retest without probe removal; retest with probe removal on the same day and retest after 2 days). They also studied the effect of gender and ear. 60 dB peSPL linear click stimuli with and without a contralateral 65 dB SPL broadband noise suppressor was used. Absolute TEOAE suppression and a normalized index of TEOAE suppression (i.e., percentage of suppression) were examined. They found no statistically significant ($p > 0.05$) main effects of test, gender, and ear or interactions for both absolute dB and % TEOAE suppression values. Cronbach's alpha was greater than 0.90 across the four tests for both TEOAE measures. Mean test differences or bias (i.e., between the initial and subsequent tests) for absolute and % TEOAE suppression ranged from -0.05 to 0.11 dB and -1.5% to

1.1%, respectively. There was no proportional/ systematic bias with the mean differences of the first and subsequent measurements. Data herein were consistent with the view that bilateral TEOAE suppression measures are reliable across test sessions of 1–2 days among females and males and may provide a method to monitor medial olivocochlear efferent reflex status over time. However, the measurements in the study were done over a short period of time and thus, measurements of contralateral suppression of TEOAEs over longer time periods and with different populations have yet to be determined.

Chapter 3

METHODS

Participants

Thirty male participants in the age range of 18 to 25 years (mean age = 21.29 years; SD = 2.19 years) participated in the study. Females were excluded from the study as previous research has shown that oto-acoustic emission (OAE) amplitudes change with the hormonal changes owing to menstrual cycle (Bell, 1992; McFadden, Martin, Stagner, & Maloney, 2009; Yellin & Stillman, 1999). Through a structured interview, it was ascertained that none of the participants had any complaint or history of otological disorders, neurological disorders, noise exposure, ototoxicity or ear infections. Detailed audiological assessment was performed on all participants before recruiting them for the study.

Audiological evaluation consisted of otoscopy, otoacoustic emissions, pure tone audiometry, tympanometry and measurement of ipsilateral and contralateral acoustic reflex thresholds. All these participants had normal hearing sensitivity (less than 15 dB HL) at octave frequencies between 250 Hz and 8000 Hz for air conduction and between 250 Hz and 4000 Hz for bone conduction. Also, all participants had 'A' type tympanogram with static compliance between 0.3 to 1.5cc and peak pressure between +60 and -100 daPa (Margolis & Heller, 1987) and normal ipsilateral as well as contralateral acoustic reflexes at 500, 1000, 2000 and 4000 Hz frequencies. All participants had a mean contralateral acoustic reflex threshold for broad band noise of 70.83 dB HL (SD = 4.37). All participants were right handed on administering the Edinburgh's Handedness Inventory and passed screening test for central auditory processing disorders on the Screening Checklist for Auditory Processing in Adults (SCAP-A) (Vaidyanath & Yathiraj, 2014).

All the tests were conducted in sound treated audiological test rooms (ANSI, 2008). The audiometric and tympanometric evaluations were conducted three times: at the beginning of the experiment, once on the fifth day and at the end of the experiment (15^{th} day).

Equipment

A calibrated dual channel (Inventis Piano with Telephonics TDH 49 supra-aural headphones housed in MX 41R cushions) audiometer was used for air conduction threshold estimation and speech audiometry. A bone vibrator (Radio-ear B71) connected to the same audiometer was used for bone conduction threshold estimation. Calibrated (ANSI S3.39-1987 (R2012) middle ear analyzer (Grason-Stadler Incorporation Tympstar middle ear analyzer) with default probe assembly and contralateral insert earphones was used for conducting tympanometry and reflexometry. The Otodynamics ILO V6 was used to record and analyze the OAE and its contralateral inhibition. The calibrated probe of the OAE system was used to deliver the stimulus to the test ear. EAR- 3A insert earphones connected to a calibrated audiometer (Grason-Stadler Incorporation Audiostar Pro) was used to present noise to the contralateral ear. The use of insert earphones avoided the likelihood of inter-aural crossover.

Stimulus

The Otodynamics ILO v6 system was used to deliver the TEOAE stimulus and record the responses. Clicks of 65 dB peak SPL, at repetition rate 50/s for 260 averages presented in linear mode was used to elicit OAEs. These protocols were selected as previous research has shown that these stimulus parameters are more efficient in eliciting contralateral inhibition (Berlin, Hood, Hurley, Wen, & Kemp,

1995; Goodman, Mertes, Lewis, & Weissbeck, 2013; Guinan, 2006; Hood, Berlin, Hurley, Cecola, & Bell, 1996; Kumar, Hegde, & Mayaleela, 2010; Kumar, Methi, & Avinash, 2013; Kumar & Vanaja, 2004). The broadband noise presented at 60 dB SPL to the contralateral ear served as inhibitor. Suppressor stimuli that are of the same intensity or 5dB greater than the TEOAE eliciting stimuli are effective in maximizing the suppression effect (Berlin et al., 1993).

Procedure

Basic audiological evaluation

1. Pure tone hearing thresholds at octave frequencies from 250 Hz to 8000 Hz for air conduction and 250 Hz to 4000 Hz for bone conduction were obtained using modified version of Hughson and Westlake procedure (Carhart & Jerger, 1959).
2. Speech recognition thresholds (Rajashekar, 1976) and speech identification scores (Vijayalakshmi & Yathiraj, 2005) were determined using standardized materials in Kannada Ascending method was used to determine participant's uncomfortable level for both ears through the headphones.
3. Tympanometry was measured at probe tone frequency of 226Hz. Ipsilateral and contralateral acoustic reflex thresholds were measured for 500 Hz, 1000 Hz, 2000Hz and 4000 Hz. Contralateral acoustic reflex threshold for broad band noise was also elicited.

All these measurements were done thrice: first day, fifth day and the last (15th) day from the commencement of the testing.

Contralateral inhibition of TEOAE

Participants were made to sit in a comfortable chair and the OAE probe was placed in the test ear and ER 3A insert earphones connected to the audiometer was placed in the contralateral ear. A good seal was ensured and the emissions were recorded with and without noise in the contralateral ear. Participants were instructed not to swallow or make any kind of movement during the testing. The 'auto-adjust stimulus' option was selected before each recording to ensure that the stimulus intensity did not vary more than 2dB from the set criteria.

Each session consisted of three recordings: the first and the third recordings were without contralateral acoustic stimulation (CAS) and the second recording was with CAS. After the first session, participants were given a break of 5-10 minutes and a second session of the same three series of recordings was done. During the break, position of the probe in the test ear was unaltered. This yielded the single probe-fit mode. Following this, experiment (two sessions per day i.e., each session consisting of 2 TEOAE without CAS and 1 TEOAE with CAS recording) was repeated on the next four consecutive days. A gap of 5 to 6 days (average gap = 5.29 days) was provided after the first set of measurements and same protocol was repeated from day 11 to 15. These experiments yielded the values for multiple probe-fit mode. Entire series of experiments was completed within 15 days from its commencement.

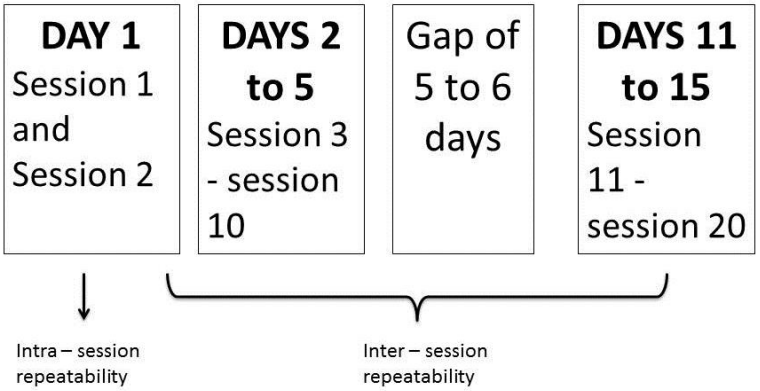

Figure 3.1: Block diagram of experimental protocol

Analyses

The noise (dB SPL), SNR (dB) and the response amplitude (dB SPL) at frequencies 1000, 1500, 2000, 3000 and 4000Hz with and without contralateral noise for the frequencies were noted. Also, the total OAE response amplitude (dB SPL) and total noise (dB SPL) were noted. The difference between TEOAE magnitudes with and without contralateral noise was considered as the magnitude of inhibition. The data was analyzed separately for the intra and inter session recordings.

The following statistical analyses were considered:

1. Repeated measures of ANOVA: to analyze the magnitude of contralateral inhibition.

2. Reliability coefficients Cronbach's alpha and interclass correlation coefficients (ICC): to assess the test/retest reliabilities of contralateral inhibition of TEOAEs.

3. Standard error of measurement (SEM): to calculate 95% confidence intervals of TEOAE inhibition magnitudes. It was calculated using the following equation:

$$SEM = SD \times \sqrt{(1-q)}$$

Where SD is the standard deviation of the set of the observed values, q is the reliability coefficient. SEM was used to calculate 95% confidence intervals of TEOAE inhibition magnitudes.

4. Smallest detectable difference (SDD): The smallest detectable difference is the minimum difference in the inhibition magnitudes that can be considered as real (due to any experimental manipulations), and not due to measurement error or random variations. It was calculated using the formula:

$$SDD = 1.96 \times SEM \times \sqrt{2}$$

5. Normalized inhibition: Calculated as ratio of amplitude inhibition to average of amplitudes without CAS.

Chapter 4

RESULTS

Primary aim of the study was to evaluate the test retest repeatability of the contralateral inhibition of otoacoustic emissions (OAEs). For this purpose, transient evoked otoacoustic emissions (TEOAEs) were measured with and without contralateral acoustic stimuli (CAS) in multiple sessions. Before analyzing the data, 2 participants who were identified as outliers in the box plots in SPSS were removed and all analyses was performed only on 28 participants. Normality of the data was assessed via Shapiro-Wilk test. As data was normally distributed, parametric statistics were used.

Audiological findings

Pure tone hearing thresholds and immittance evaluations were repeated thrice (1^{st} day, 5^{th} day and 15^{th} day of recording) during the experiment to check the hearing and middle ear status. A repeated measures analysis of variance showed that there was no significant main effect of evaluations (1^{st}, 2^{nd} and 3^{rd}) on pure tone average [$F(2, 54) = 1.23$, $p > 0.05$], tympanometric peak pressure [$F(2, 54) = 0.59$, $p > 0.05$] and static compliance [$F(2, 54) = 1.80$, $p > 0.05$]. These results indicate that hearing thresholds and middle ear status of the participants did not change significantly during the course of the experiment which otherwise would have influenced amplitudes of OAEs.

TEOAE Amplitude

Single Probe-fit mode

TEOAE global amplitudes were noted for all the participants. Figure 4.1 represents the global TEOAE amplitudes obtained (without CAS condition) in single-probe-fit condition across all participants. Figure 4.2 represents the mean and one standard deviation of global TEOAE amplitudes for single probe-fit condition. From the Figures 4.1 and 4.2 it can be seen that TEOAE amplitude did not change much between two recordings in most of the participants. Maximum change observed between two recordings was 3 dB in participant 7. In about 82% of the participants change was less than 1 dB between two recording sessions. Paired t test was done to assess the significance of difference in TEOAE amplitude between two recording sessions. Results revealed no significant difference between the global TEOAE amplitudes between two recording conditions [$t(27) = -0.70$, $p > 0.05$]. To check the reliability Cronbach's alpha and interclass correlation (ICC) coefficients were calculated for single probe-fit mode. Both Cronbach's alpha (0.99) and ICC (0.99) revealed very high reliability for single probe-fit condition.

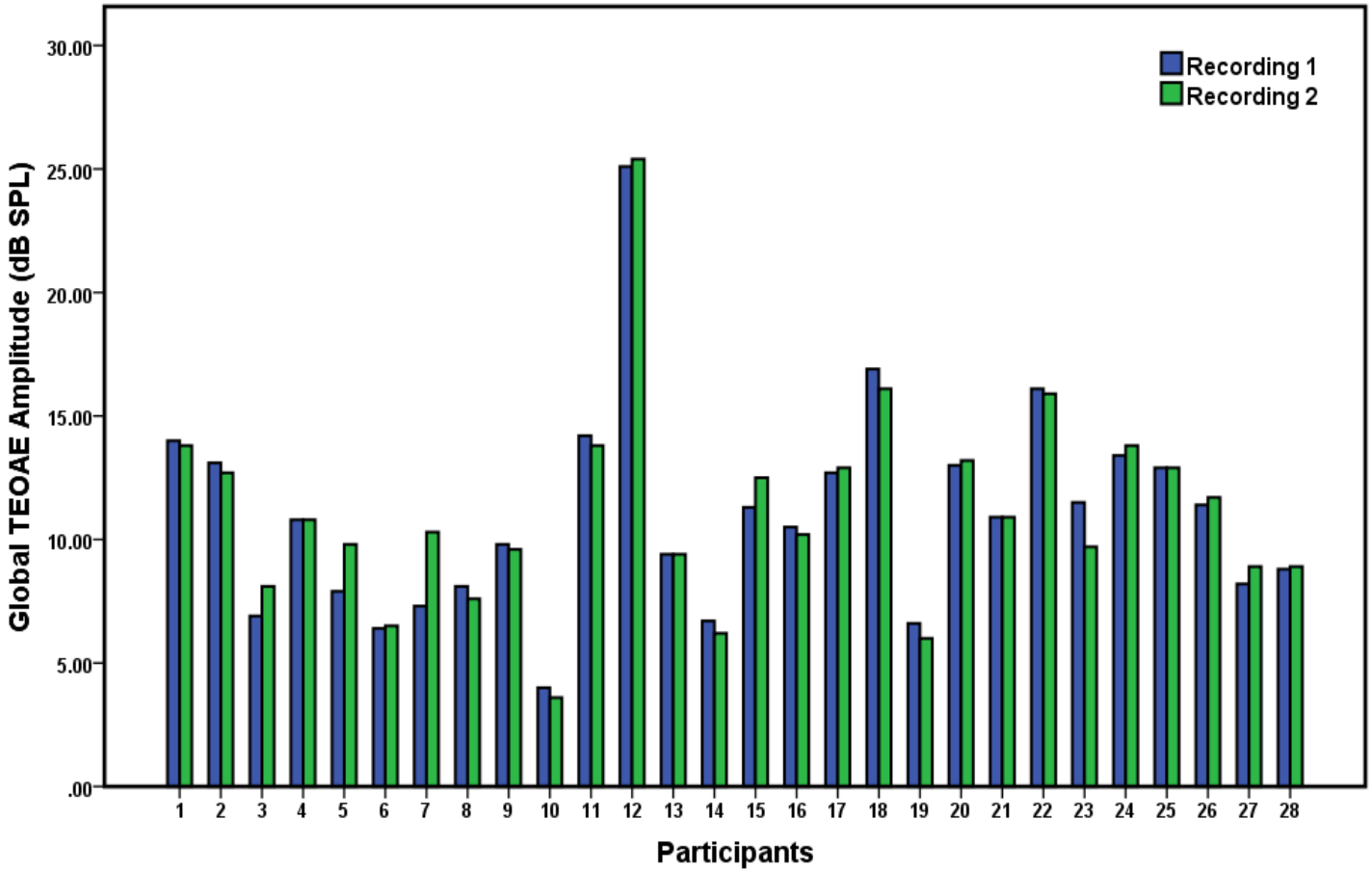

Figure 4.1: Global TEOAE amplitudes for the single probe-fit mode in dB SPL across all participants (recording 1 and 2).

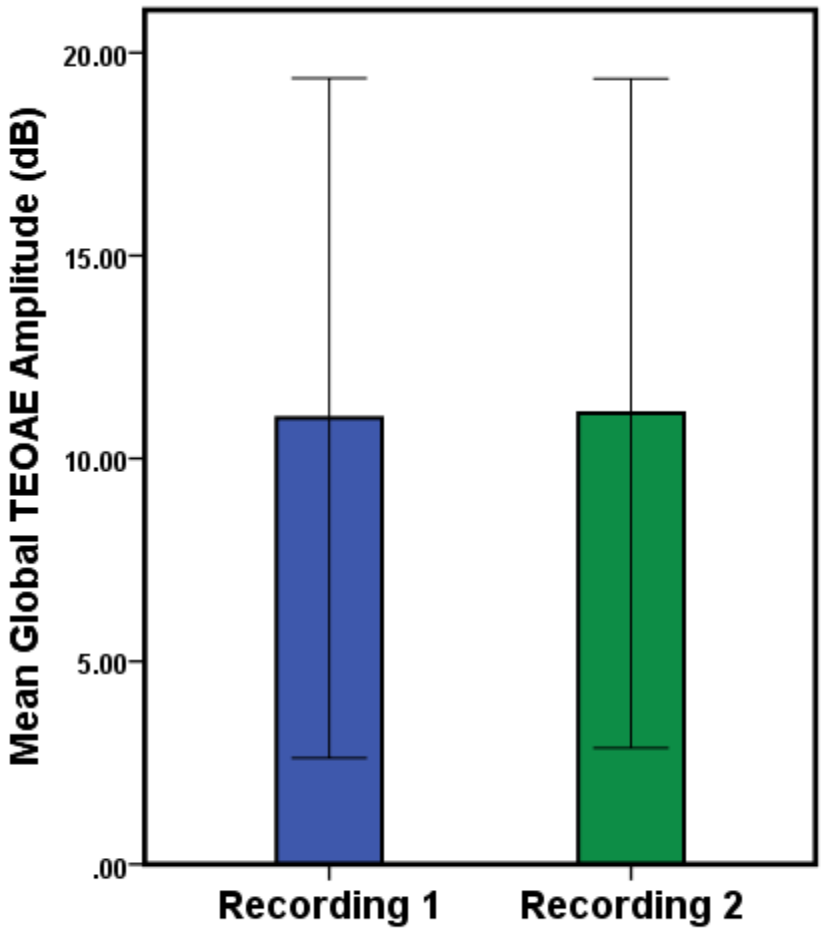

Figure 4.2: Mean and standard deviations of global TEOAE amplitudes for single probe-fit (recording 1 and 2). Error bars indicate one standard deviation.

Multiple Probe-fit mode

Figure 4.3 represents the global TEOAE amplitudes obtained in multiple probe-fit condition. Figure 4.4 shows mean and one standard deviation of TEOAE amplitudes obtained in multiple probe-fit condition. From the Figures 4.3 and 4.4 it can be seen that TEOAE amplitude did not vary much across different recording conditions. In 39% of participants variation in amplitude was less than 3 dB, in 39% of participants variation was less than 5dB across recording conditions. Maximum variation was 9.5 dB for participant 17. A repeated measures ANOVA was performed to assess the significance of differences in TEOAE amplitudes across recording conditions. Results showed no significant main effect of recording conditions on global TEOAE amplitude [$F(5,136) = 0.563$, $p > 0.05$]. Reliability measures are depicted in Table 4.1. From the Table 4.1 it can be inferred that TEAOE amplitudes are highly reliable across different recording sessions.

TABLE 4.1

Reliability measures for global values in multiple probe-fit mode

Cronbach's alpha	0.99
Single measure ICC	0.91
SEM	0.39
SDD	1.08

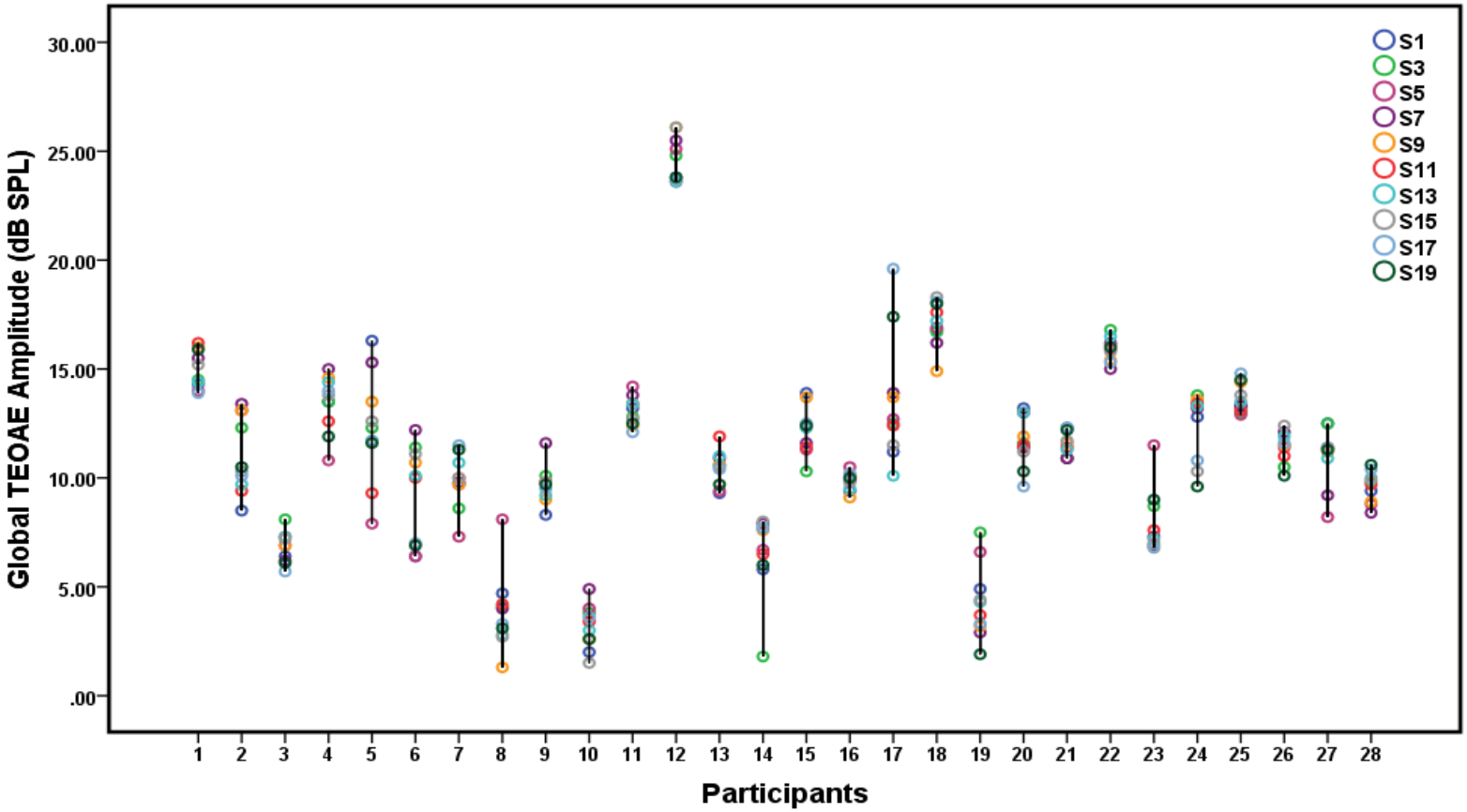

Figure 4.3: Global TEOAE amplitudes for multiple probe-fit mode across all participants.

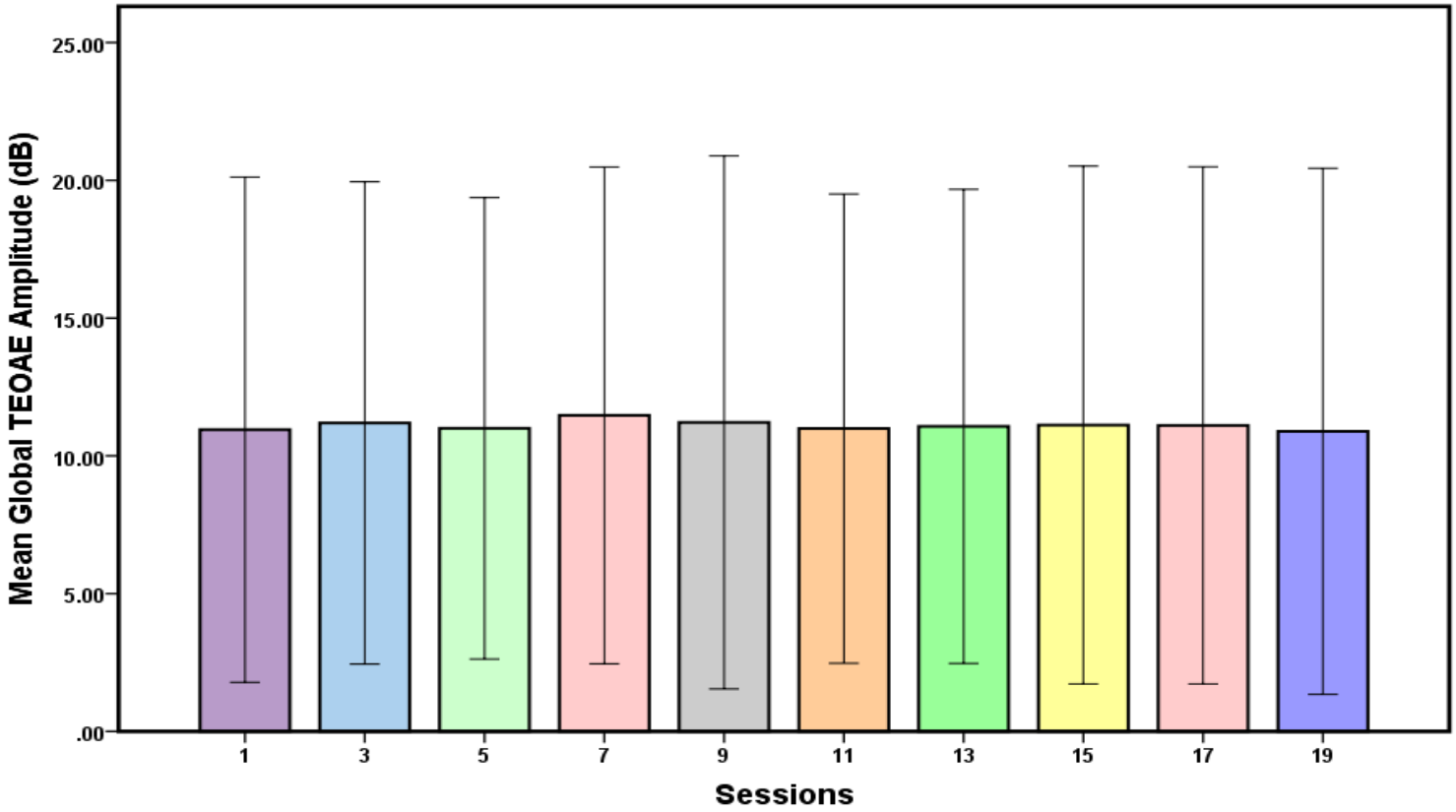

Figure 4.4: Mean and standard deviations of Global TEOAE amplitudes for multiple probe-fit mode. Error bars indicate one standard deviation.

TEOAE Amplitude Inhibition

Single probe-fit mode

Contralateral inhibition magnitude was calculated as difference between TEOAE amplitudes without CAS condition (average of two recordings) and TEOAE amplitudes with CAS condition. Figure 4.5 represents the global amplitude inhibition values across all participants for the single probe-fit mode. Figure 4.6 depicts the mean and one standard deviation of global TEOAE amplitude inhibition in single probe-fit mode. From the Figure 4.5 and 4.6 it can be seen that the inhibition values varied across the individuals and also between the recording sessions. CAS typically reduced amplitudes in majority of the participants. However, in a few participants (7, 10, 25 and 27) CAS enhanced TEAOE amplitudes. Maximum variation in inhibition was 1.15 dB for participant 17. The paired-t test revealed no significant difference between the global TEOAE inhibition between two recordings [$t(27) = 0.51$, $p > 0.05$]. To check the reliability Cronbach's alpha and interclass correlation (ICC) coefficients were calculated for single probe-fit mode. Both Cronbach's alpha (0.89) and ICC (0.82) revealed moderate reliability for single probe-fit condition.

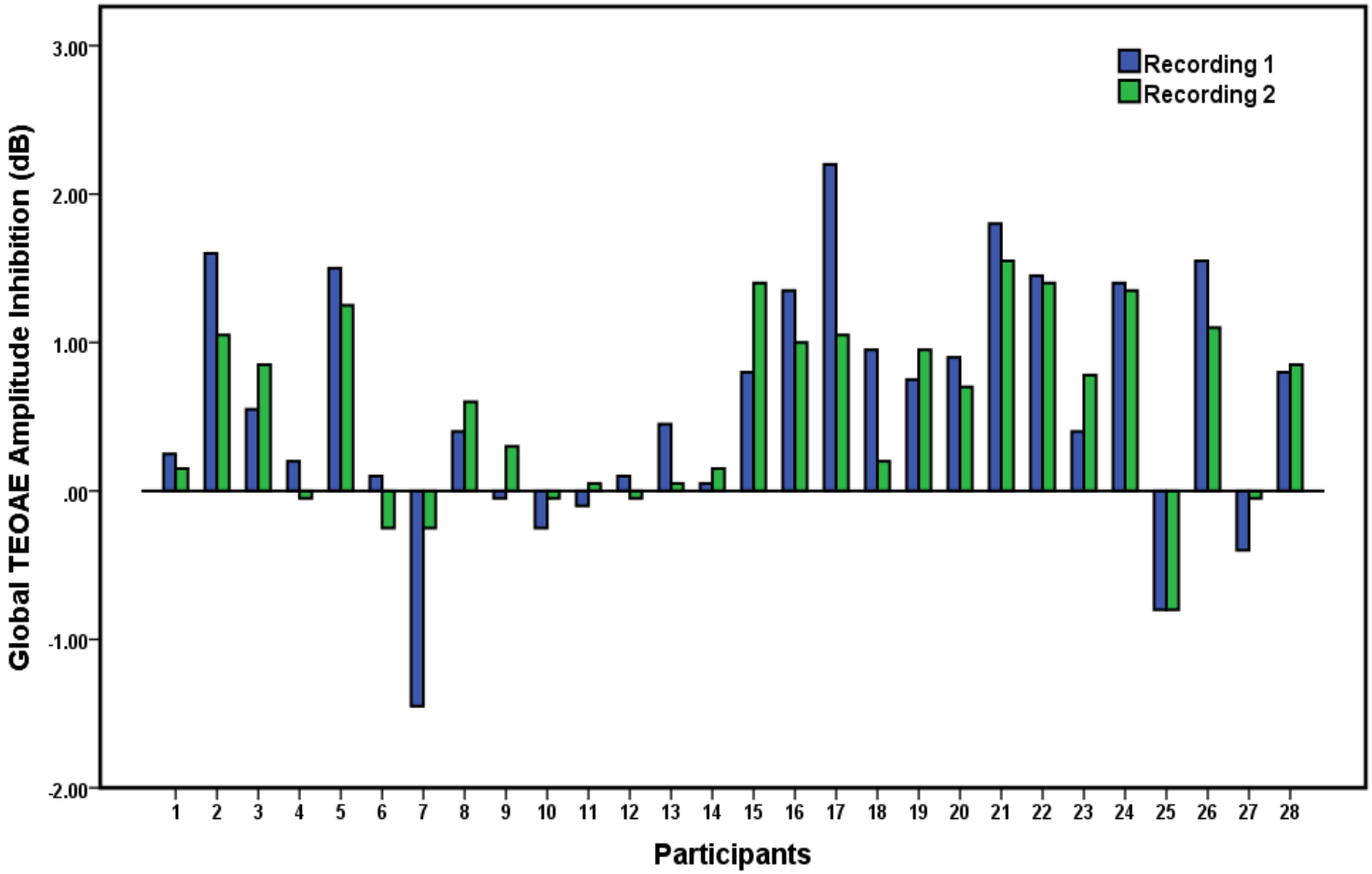

Figure 4.5: Global TEOAE amplitude inhibition for the single probe-fit mode across all participants (recording 1 and 2).

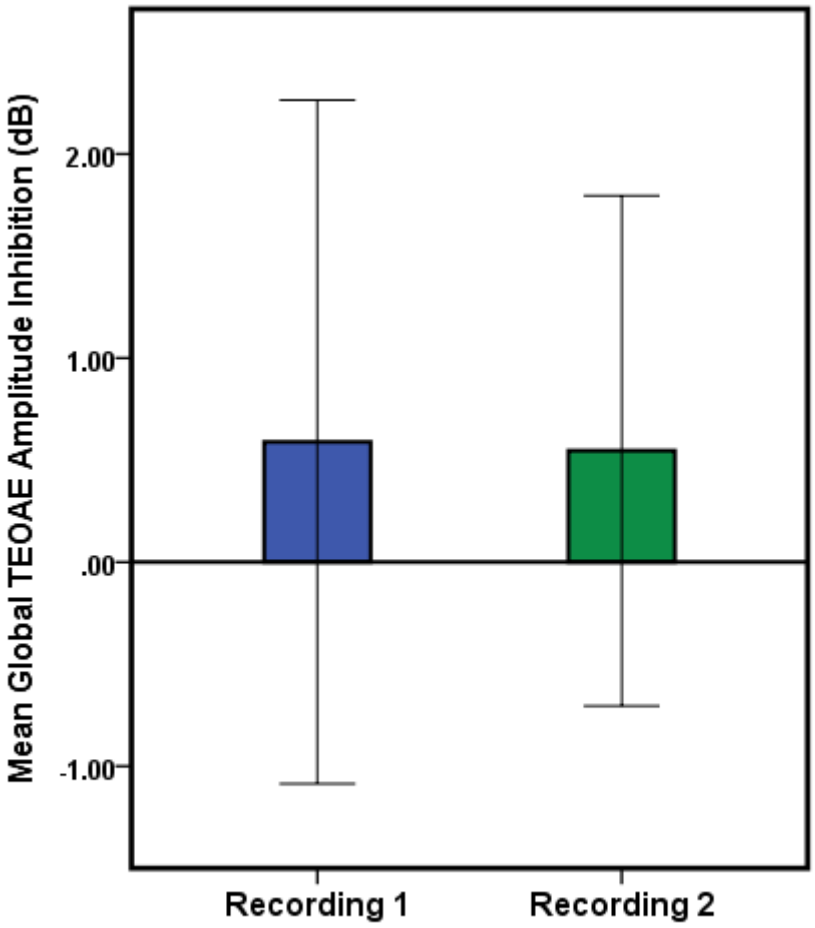

Figure 4.6: Mean and standard deviations of global TEOAE amplitude inhibition for single probe-fit (recording 1 and 2). Error bars indicate one standard deviation.

Multiple probe-fit mode

Figure 4.7 represents the global TEOAE amplitude inhibition values in multiple probe-fit mode across all participants. Figure 4.8 represents the mean and one standard deviation of global amplitude inhibition values for multiple probe-fit recordings. From the Figures 4.7 and 4.8 it can be seen that the TEOAE inhibition varied across different recording conditions. In 82% of participants variation in amplitude was less than 3 dB, in 18% of participants variation was less than 5 dB across recording conditions. The maximum variation seen was 4.6 dB for participant 17. A repeated measures ANOVA was performed to assess the significance of differences in TEOAE amplitude inhibitions across recording conditions. Results showed no significant main effect of recording conditions on global TEOAE amplitude inhibition [$F(5,161) = 1.42$, $p > 0.05$]. Reliability measures are depicted in Table 4.2. From the Table 4.2 it can be inferred that TEAOE amplitude inhibition are poor to moderately reliable across different recording sessions.

TABLE 4.2

Reliability measures for global values in multiple probe-fit mode

Cronbach's alpha	0.86
Single measure ICC	0.37
SEM	0.27
SDD	0.75

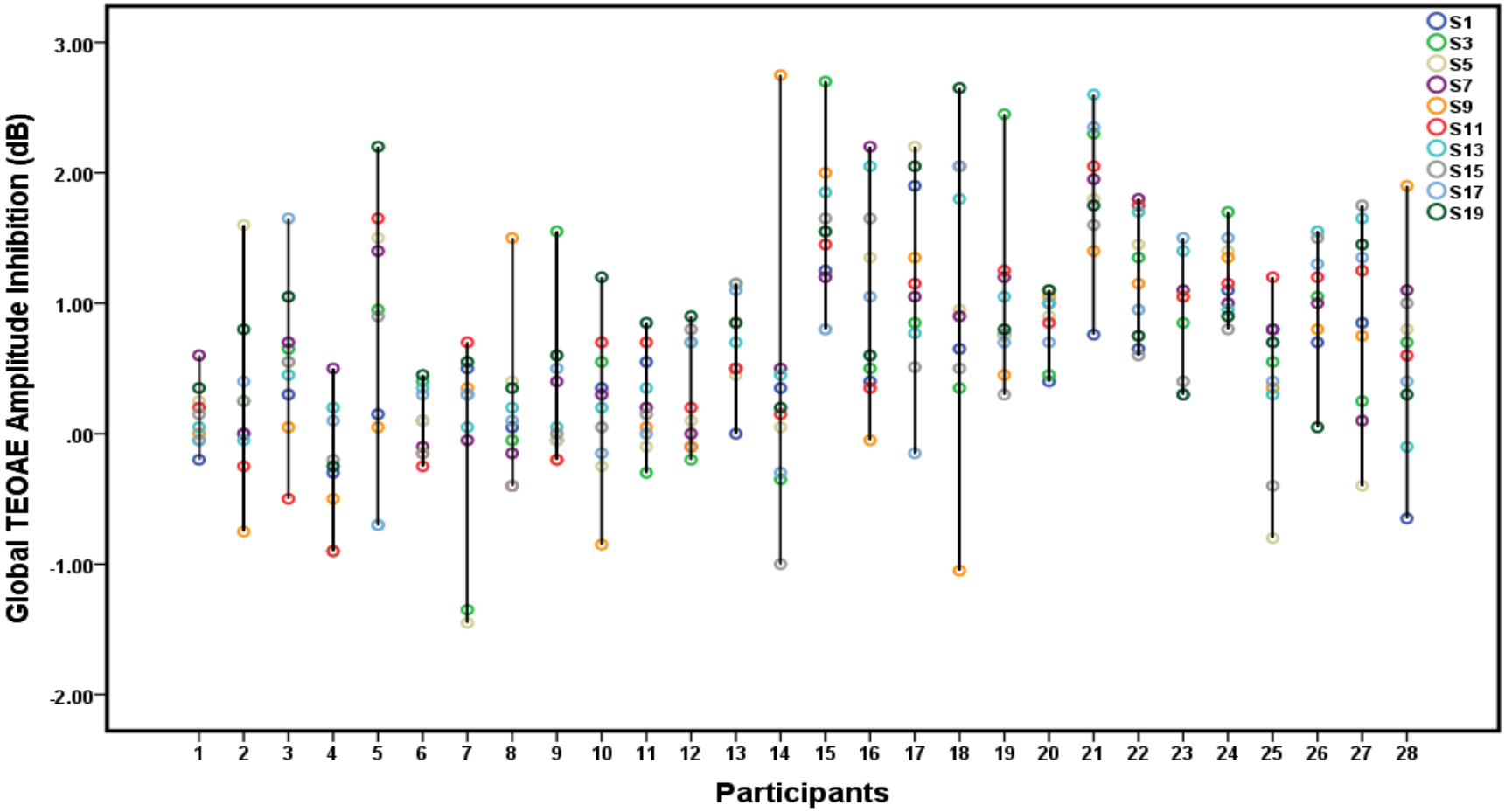

Figure 4.7: Global TEOAE amplitude inhibition for multiple probe-fit mode across all participants.

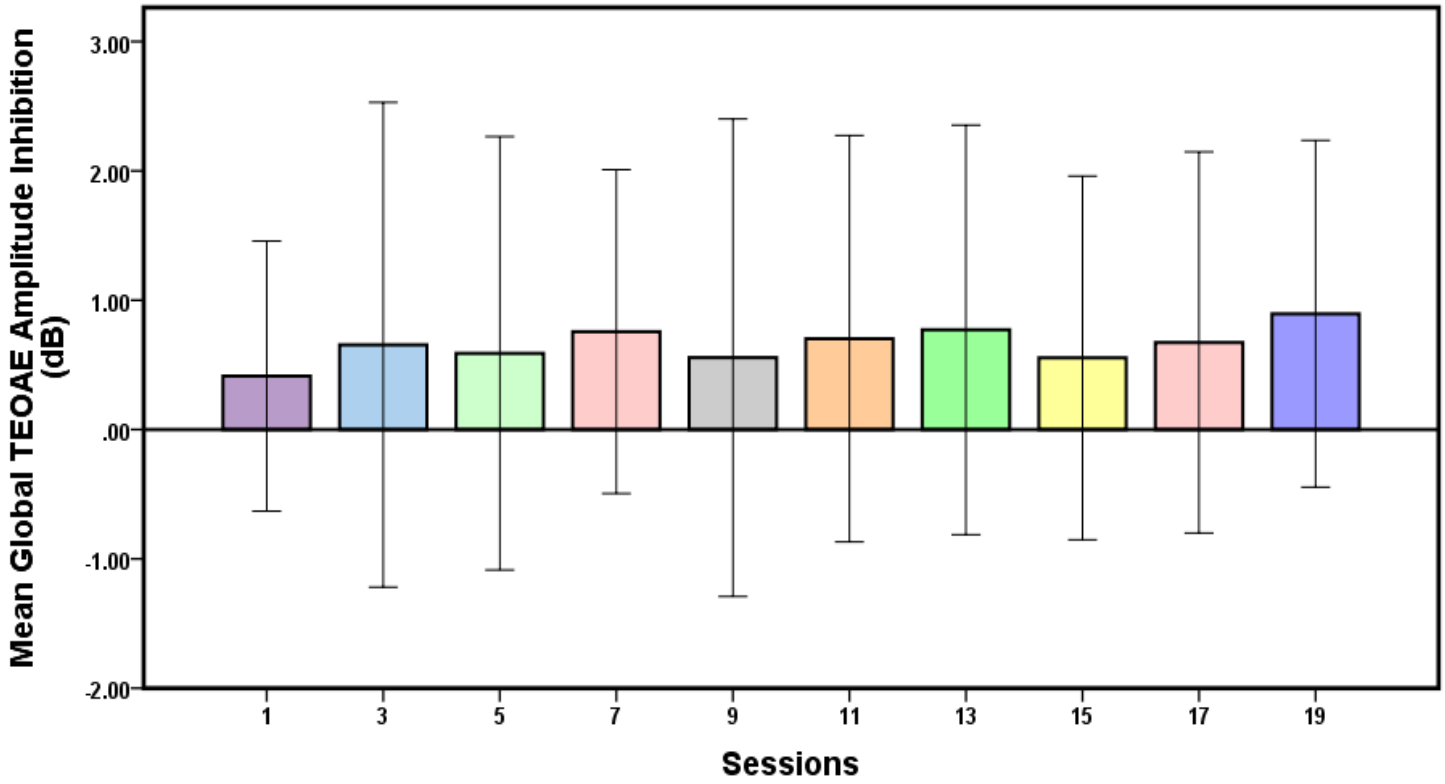

Figure 4.8: Mean and standard deviations of global TEOAE amplitude inhibitions for the multiple probe-fit mode. Error bars indicate one standard deviation.

TEOAE Normalized Inhibition

Single probe-fit mode

Normalized inhibition magnitude was calculated as a ratio of global TEOAE amplitude inhibition to TEOAE amplitudes without CAS condition (average of two recordings). This was done to eliminate the effect of absolute OAE amplitudes on inhibition. Figure 4.9 represents the normalized inhibition values across all participants for the single probe-fit mode. Figure 4.10 depicts the mean and one standard deviation of TEOAE normalized inhibition in single probe-fit mode. From the Figures 4.9 and 4.10 it can be seen that the inhibition values varied across the individuals and also between the recording sessions. Maximum variation in inhibition was 0.14 dB for participant 6. The paired-t test revealed no significant difference between the TEOAE normalized inhibition between two recordings [$t(27) = 0.24$, $p > 0.05$]. To check the reliability Cronbach's alpha and interclass correlation (ICC) coefficients were calculated for single probe-fit mode. Both Cronbach's alpha (0.88) and ICC (0.79) revealed moderate reliability for single probe-fit condition. Variation in inhibition amplitudes and reliability measures were similar to that observed for not normalized OAE amplitude.

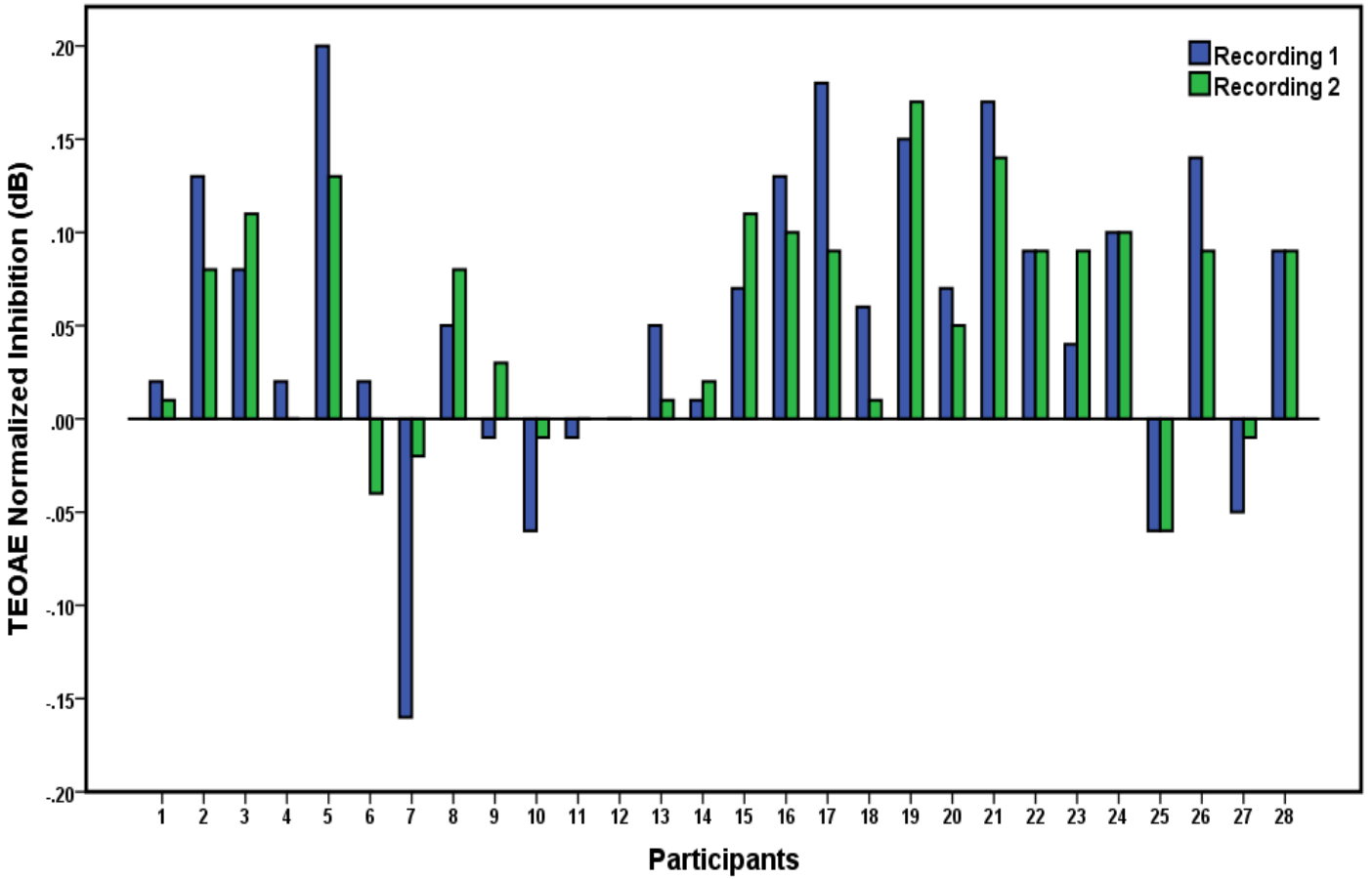

Figure 4.9: TEOAE normalized inhibition for the single probe-fit mode across all participants (recording 1 and 2).

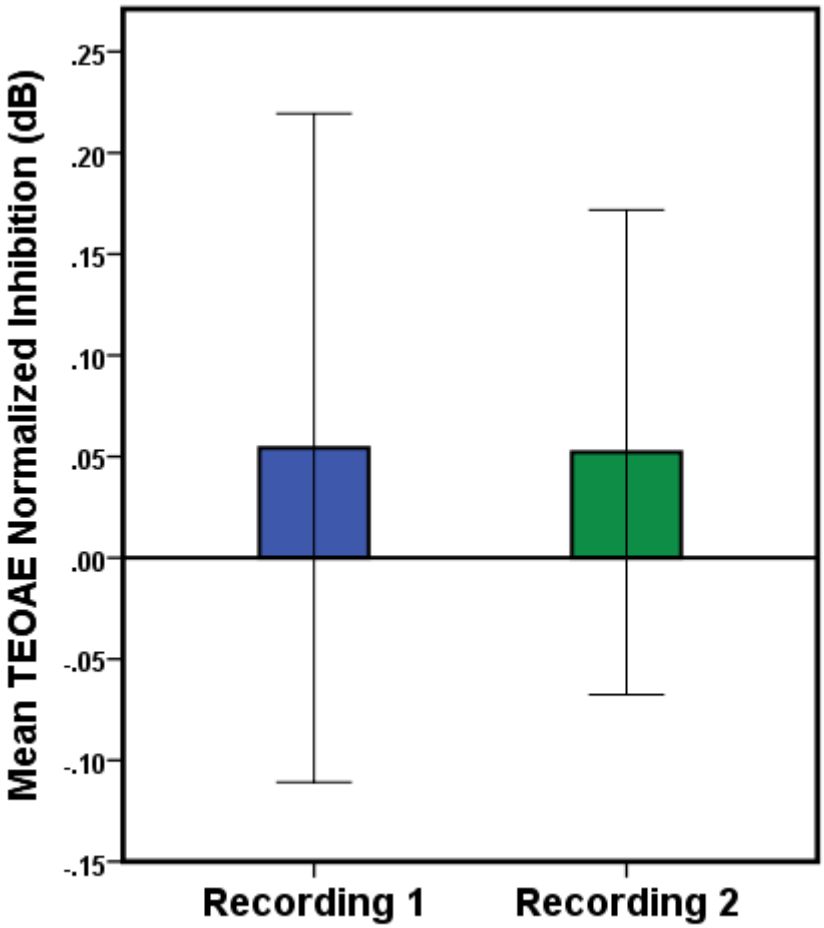

Figure 4.10: Mean and standard deviations of TEOAE normalized inhibition for single probe-fit mode (recording 1 and 2). Error bars indicate one standard deviation.

Multiple probe-fit mode

Figure 4.11 represents the TEOAE normalized inhibition values in multiple probe-fit mode across all participants. Figure 4.12 represents the mean and one standard deviation of normalized inhibition values for the multiple probe-fit recordings. From the Figures 4.11 and 4.12 it can be seen that the TEOAE normalized inhibition varied across the different recording conditions. In 89% of participants variation in amplitude was less than 0.5 dB, in 11% of participants variation was less than 1.5 dB across recording conditions. Maximum variation was 1.29 for participant 8. A repeated measures ANOVA was performed to assess the significance of differences in TEOAE normalized inhibitions across recording conditions. Results showed no significant main effect of recording conditions on TEOAE normalized inhibition [$F(2,64) = 0.26$, $p > 0.05$]. Reliability measures are depicted in Table 4.3. From the Table 4.3 it can be inferred that TEAOE normalized inhibition are poor to moderately reliable across different recording sessions. Variation in inhibition amplitudes and reliability measures were poorer than that observed for not normalized OAE amplitude.

TABLE 4.3

Reliability measures for global values in multiple probe-fit mode

Cronbach's alpha	0.68
Single measure ICC	0.18
SEM	0.04
SDD	0.12

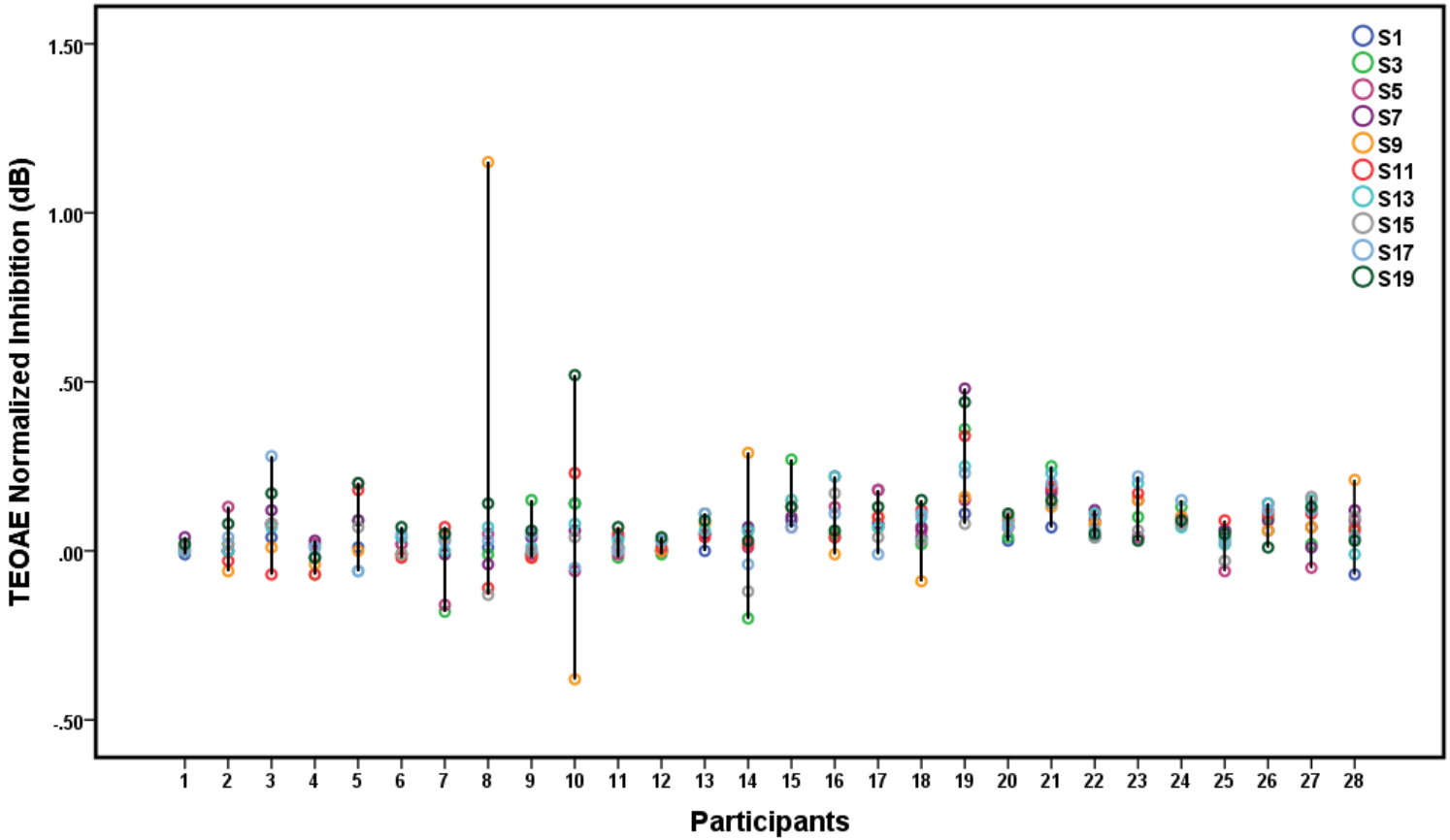

Figure 4.11: TEOAE normalized inhibition values for multiple probe-fit mode across all participants.

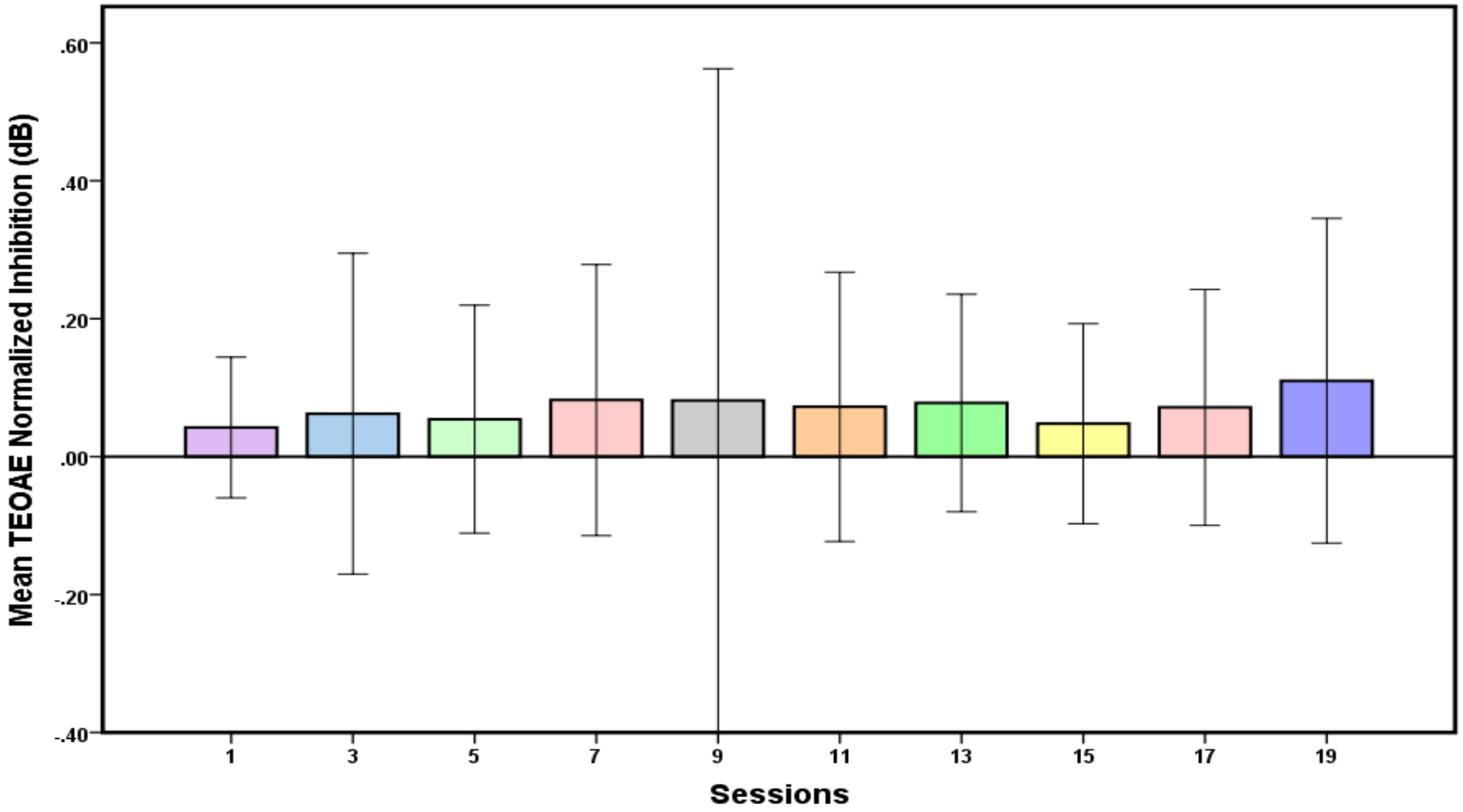

Figure 4.12: Mean and standard deviations of TEOAE normalized inhibition for multiple probe-fit recordings. Error bars indicate one standard deviation

TEOAE SNR Inhibition

Single probe-fit mode

Contralateral SNR inhibition was calculated as difference between TEOAE SNRs without CAS condition (average of two recordings) and TEOAE SNR with CAS condition. Figure 4.13 represents the global SNR inhibition values for the participants for the single probe-fit mode. Figure 4.14 depicts the mean and one standard deviations of global TEOAE SNR inhibition for the single probe-fit mode. From Figures 4.13 and 4.14 it can be seen that the SNR values varied highly across the participants and across the recording sessions. Maximum variation in SNR inhibition between recordings was 7.05 dB for participant 17. Paired t test revealed no significant difference between the global TEOAE SNR inhibition for single probe-fit [$t(27) = 0.15$, $p > 0.05$]. To check the reliability Cronbach's alpha and interclass correlation (ICC) coefficients were calculated for single probe-fit mode. Both Cronbach's alpha (0.40) and ICC (0.25) revealed poor reliability for single probe-fit condition.

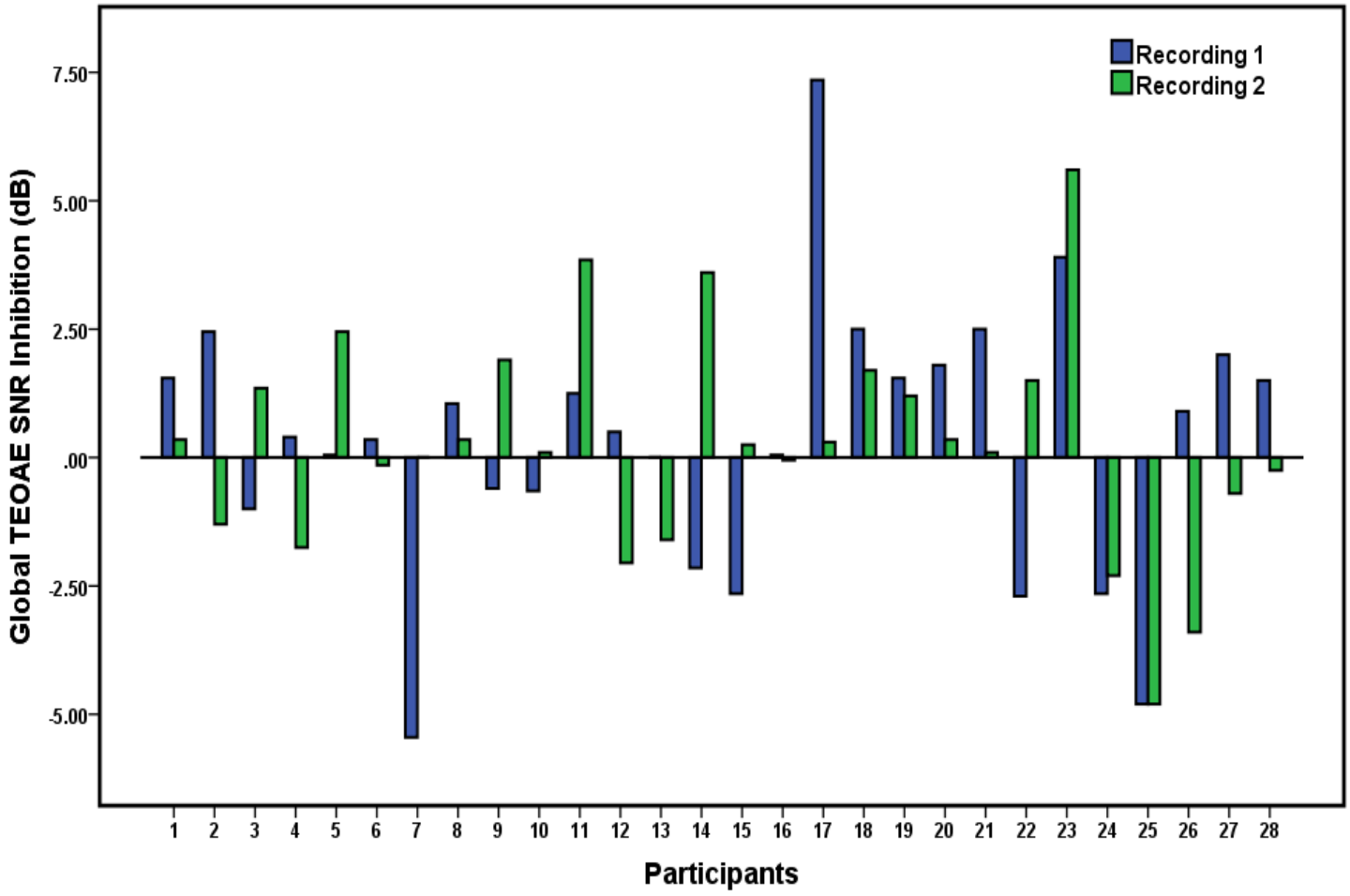

Figure 4.13: Global TEOAE SNR inhibition for the single probe-fit mode across all participants (recording 1 and 2).

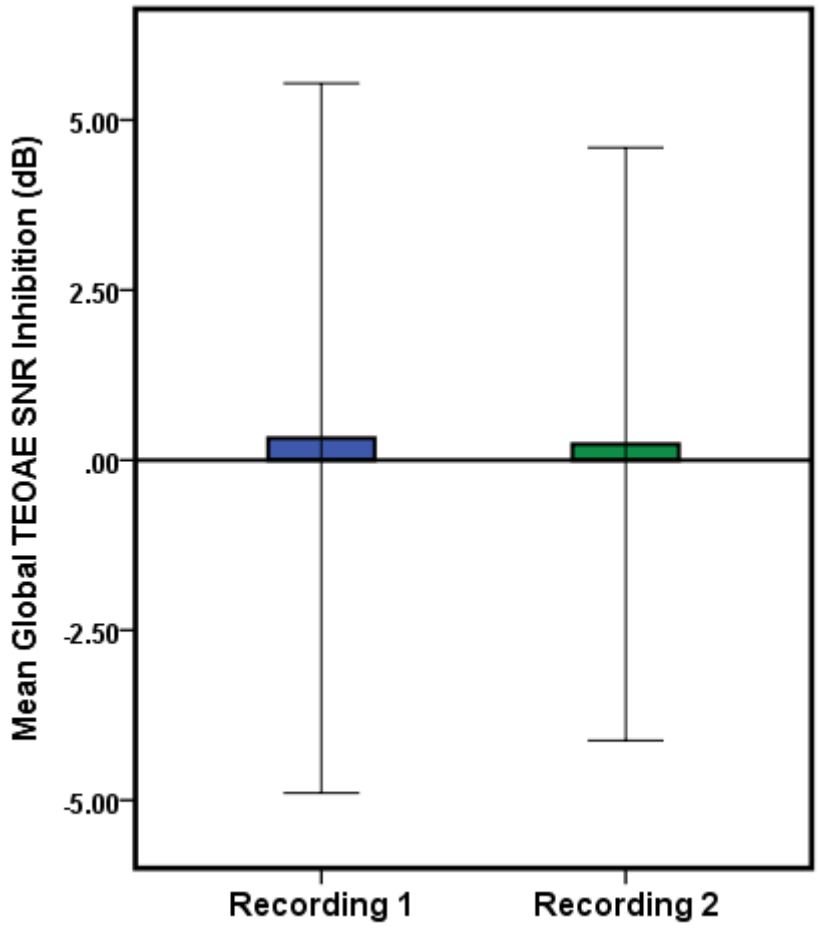

Figure 4.14: Mean and standard deviations of global TEOAE SNR inhibition for single probe-fit mode (recording 1 and 2). Error bars indicate one standard deviation.

Multiple probe-fit mode

Figure 4.15 represents the global SNR inhibition values in multiple probe-fit mode. Figure 4.16 represents the mean and one standard deviations of global SNR inhibition for all the multiple probe-fit recordings. From Figures 4.15 and 4.16 it can be seen that the TEOAE SNR inhibition varied highly across the different recording conditions. In 11% of participants variation in SNR inhibition was less than 5 dB, in 18% of participants variation was less than 7 dB across recording conditions. In 71% of the participants variation was more than 5 dB. Maximum variation was as much as 15.25 dB in participant 13. A repeated measures ANOVA was performed to assess the significance of differences in TEOAE SNR inhibitions across recording conditions. Results showed no significant main effect of recording conditions on global TEOAE SNR inhibition [$F(6,176) = 1.10$, $p > 0.05$]. Reliability measures are depicted in Table 4.4. From the Table 4.4 it can be inferred that TEAOE SNR inhibitions are poorly reliable across different recording sessions.

TABLE 4.4

Reliability measures for global values in multiple probe-fit mode

Cronbach's alpha	0.29
Single measure ICC	0.04
SEM	1.88
SDD	5.20

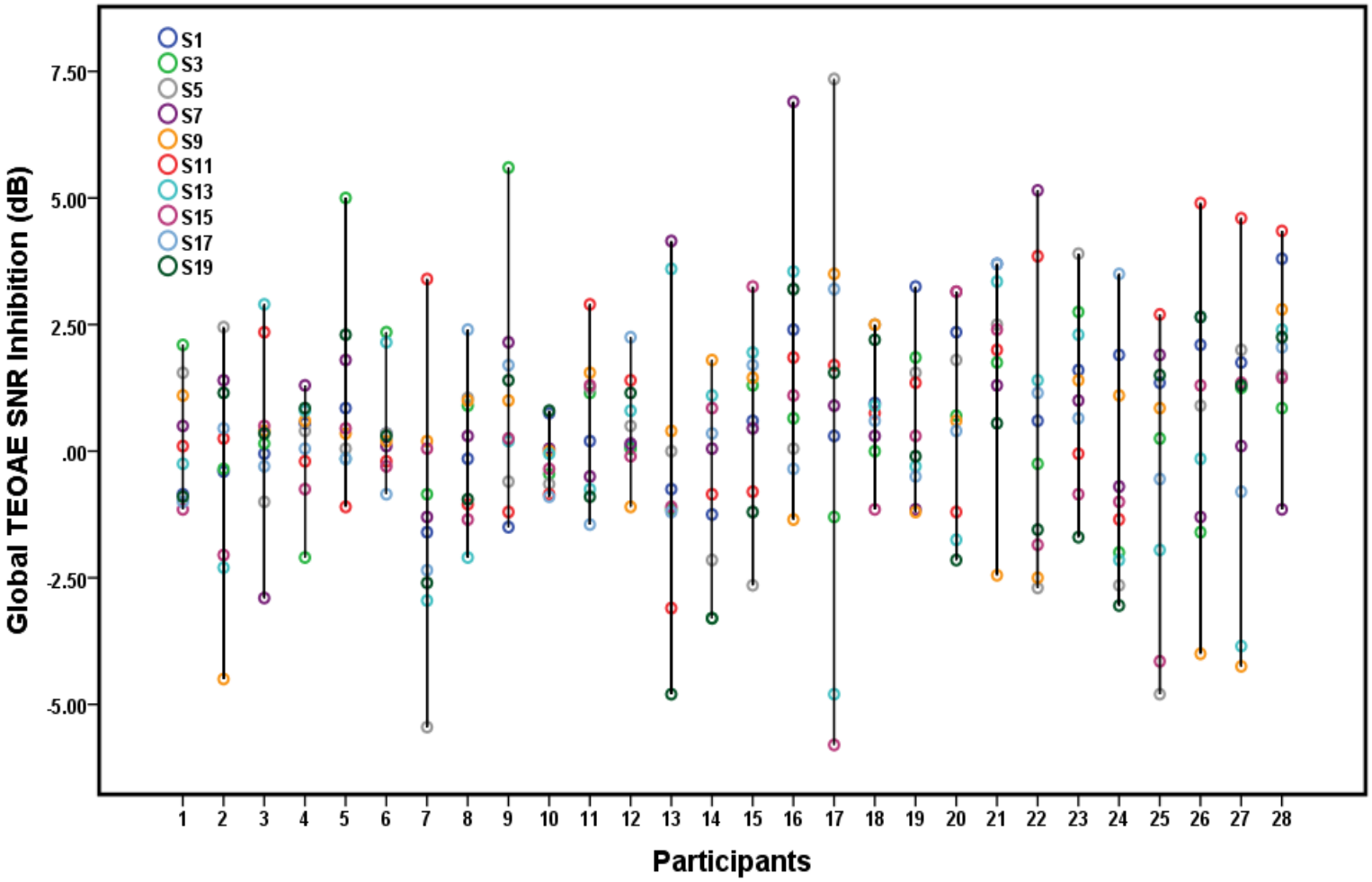

Figure 4.15: Global TEOAE SNR inhibition values for multiple probe-fit mode across all participants.

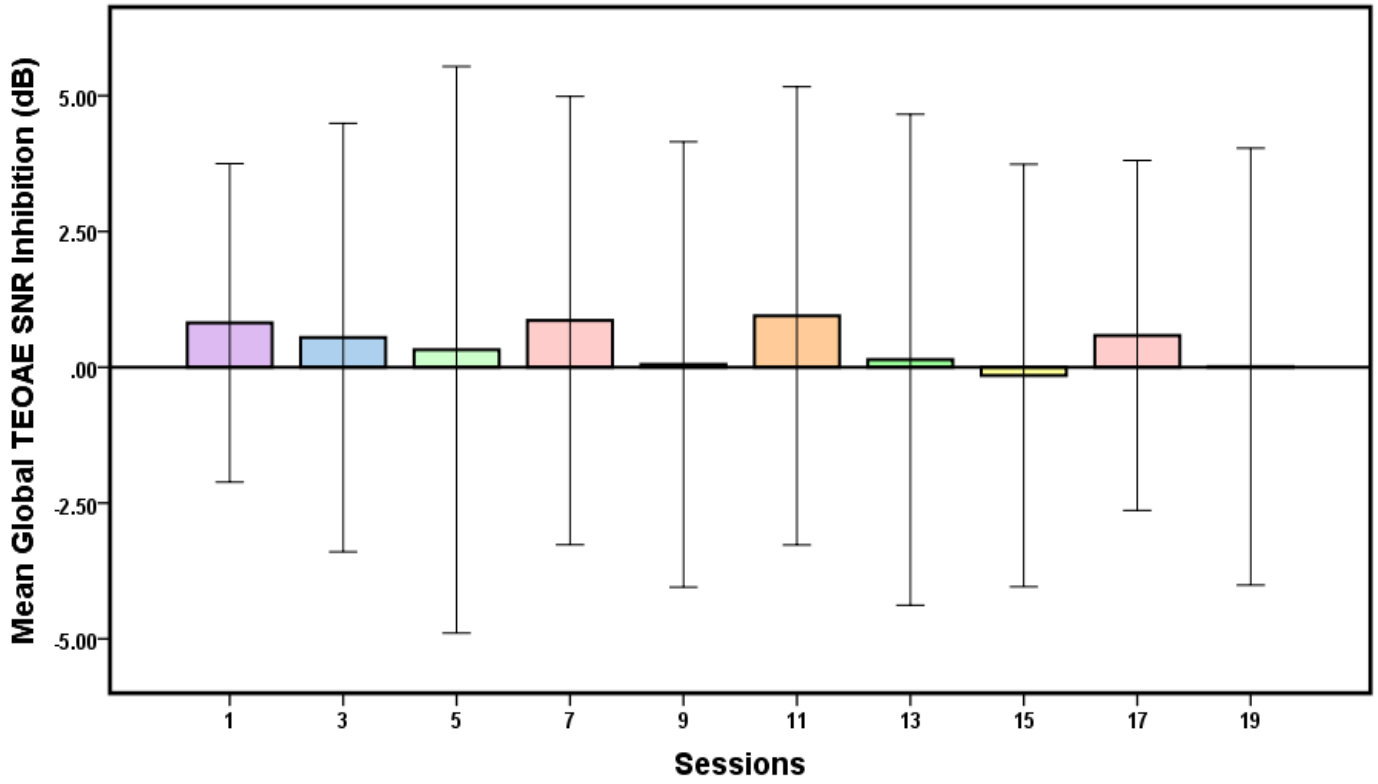

Figure 4.16: Mean and standard deviations of global TEOAE SNR inhibition for multiple probe-fit recordings. Error bars indicate one standard deviation.

To summarize, TEOAE amplitudes were quite reliable over different recording sessions. But, inhibition magnitudes varied substantially across recording sessions on all measures.

Chapter 5

DISCUSSION

The test retest repeatability of contralateral inhibition of transient evoked otoacoustic emissions (TEOAE) was studied in 30 male participants. The global TEOAE amplitude, amplitude inhibition, signal to noise ratio (SNR) inhibition and normalized inhibition were checked in both single probe-fit mode and multiple probe-fit modes.

TEOAE Amplitude

The results for the single probe-fit mode revealed high reliability of TEOAE amplitudes between two recordings. In majority of the participants variation was less than 1 dB. In the multiple probe-fit mode the TEOAE amplitude was slightly more variable than single probe-fit condition. These findings are in accordance with previous research (Franklin et al., 1992; Hurley & Musiek, 1994; Keppler et al., 2010; Marshall & Heller, 1996; Vedantam & Musiek, 1991). Marshall et al (1996) studied the reliability of TEOAEs in 25 normal ears for 10 sessions. They found the intra session amplitude correlation to be as much as 0.86. Franklin et al (1992) assessed the test retest reliability of TEOAEs in 12 participants (7 males and 5 females). TEOAEs were recorded on four consecutive days and they report a reproducibility index as high as 0.9. In another study, Vedantam et al (1991) checked the reliability of TEOAEs on 100 normal ears. The retest was done however on 30 ears and 1.5 hours post initial test. They report a Spearman's correlation coefficient of 0.991.

The slightly less reliability could be due to certain calibration issues inherent to current OAE technology. Despite the auto calibration of the probe before every recording, the intensity level of the stimulus might have varied slightly across the recordings. This is probably due to the presence of evanescent waves at the probe.

Evanescent waves are those waves that do not reach termination (Souza, Dhar, & Neely, 2014). The variations in the stimulus delivered and the response spectrum elicited might have led to the variations in the amplitude recorded and resulting reduced reliability in multiple probe-fit conditions.

TEOAE Inhibition

Mean amplitude of inhibition observed in current investigation was 0.56 dB. Even in single probe-fit mode more than 60 % of the participants had inhibition changes more than this value. Though the reliability of the inhibition was high on group data (Cronbach's alpha = 0.89, ICC = 0.82), inspection of the individual inhibition magnitudes showed high variability in few subjects. In few participants, the inhibition varied as much as 1.15 dB (participant 17) even in single probe-fit mode. In the multiple probe-fit mode the reliability was poor to moderate (Cronbach's alpha = 0.86, ICC = 0.37) as a group. On visual examination of individual data, inhibition magnitudes showed high variability in majority of the participants across recording sessions. The maximum variation seen was 4.6 dB for participant 17. Variations in the inhibition magnitudes increased when SNR or normalized amplitudes were considered to calculate the magnitude of inhibition. Our results are not consistent with some of the previous investigation (Graham & Hazell, 1994; Mertes, 2014; Mishra & Lutman, 2013; Stuart & Cobb, 2015). Graham and Hazell (1994) found that across all measurements, mean TEOAE shifts in inhibition ranged from approximately 0.3 – 0.6 dB and the standard deviations ranged from 0.10 – 0.25 dB, indicating small but repeatable effects over time. Mishra and Lutman (2013) reported that when MOCR effects were expressed as the dB change in TEOAE amplitudes, Bland-Altman plots showed that effects changed by 0.03 – 0.07 dB across session for each stimulus level.

Cronbach's alpha was 0.8 for four stimulus levels and 0.7 for one level. Mishra and Abdala (2015) also found good long term repeatability of contralateral suppression of distortion product otoacoustic emissions. Stuart and Cobb (2015) report a Cronbach's alpha greater than 0.9 and normalized percentage of TEOAE suppression from absolute amplitude ranging from -1.5% to 1.1%. These findings are in contradiction to that reported by Mishra and Lutman (2013). They found a higher reliability for normalized inhibition compared to the amplitude inhibition.

Reasons for differences between our study and previous research are not clear to us. Some of the possible reasons may be methodology and procedural differences across the studies. For example, Graham and Hazell (1994),was conducted only on 6 participants with wide age range. Similarly, Stuart and Cobb (2015) measured only short term reliability. Moreover all studies mentioned above have looked at reliability measures on group data. Our analyses of group data showed reliability of inhibition magnitudes were moderate to good. But inspection of individual data indicated that variations observed were substantial.

Our results are more consistent with (Kumar et al., 2013; Mishra & Abdala, 2015). Kumar et al, (2013) for DPOAE inhibition magnitudes found that within a single session without probe re-insertion, Cronbach's alpha values ranged from 0.2 to 0.7 and ICC values ranged from 0.1 to 0.6. SEMs, which were calculated using Cronbach's alpha and the standard deviation, were 1 dB or less. SDD values ranged from 1.7 to 2.7 dB. Across multiple sessions Cronbach's alpha ranged from 0.5 to 0.8 and ICC was between 0.1 and 0.3. SEMs were slightly larger (1.6 dB or less), and SDDs also increased (ranged from 1.6 to 4.3 dB). They concluded that variation in the

inhibition magnitudes was large and DPOAE inhibition should not be used for clinical purpose.

In the present study care was taken to eliminate other extraneous variables. Females were excluded from the study and the middle ear status of all the participants were monitored throughout. One of the factors that might have contributed to the observed large variations in the magnitude of DPOAE inhibition is attentional states of the participants which were not controlled. Maison et al, (2001) reported that selective attention to an auditory task significantly enhanced the inhibition magnitudes of transient-evoked OAEs. Khalfa et al, (2001) reported the altered MOC activity in individuals whose Heschl's gyrus, amygdale, and hippocampus was surgically removed. These results indicate the role of higher cortical centres in the inhibition of otoacoustic emissions.

The results of the present study revealed high reliability of TEOAE amplitude and lesser reliability of TEOAE inhibition. The high variability in contralateral inhibition of SNR compared to that of amplitude highlights the importance of utilizing the amplitude measures for clinical purposes rather than SNR measures.

Chapter 6

SUMMARY AND CONCLUSIONS

The aim of this study was to assess the test retest repeatability of contralateral inhibition of TEOAEs. The test retest repeatability was assessed for single probe-fit and multiple probe-fit modes in 30 male participants (mean age = 21.29 years). All the tests were conducted in sound treated audiological test rooms. The audiometric and tympanometric evaluations were conducted three times: at the beginning of the experiment, once on the fifth day and at the end of the experiment (15^{th} day). Each session consisted of three recordings: the first and the third recordings were without contralateral acoustic stimulation (CAS) and the second recording was with CAS. After the first session, participants were given a break of 5-10 minutes and a second session of the same three series of recordings was done. A gap of 5 to 6 days (average gap = 5.29 days) was provided after the first set of measurements and same protocol was repeated from day 11 to 15. Thus the study included one single probe-fit recording and ten multiple probe-fit recordings. The global TEOAE amplitude, amplitude inhibition, SNR inhibition and normalized inhibition were checked in both the modes. High reliability was found for TEOAE amplitude for both modes and across all participants. The reliability of amplitude inhibition was higher than that of normalized inhibition. SNR inhibition had the poorest reliability. Also, inhibition in the single probe-fit mode had higher reliability than the multiple probe-fit modes. Amplitude inhibition had the highest reliability and hence this measure of medial olivocochlear reflex (MOCR) should be considered for all clinical interpretations.

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