Longitudinal Cognitive and Neurobehavioral Functional Outcomes Before and After Repairing Otic Capsule Dehiscence

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METHODS

DIAGNOSTIC TESTING

Comprehensive testing was performed pre- and postoperatively with the tuning fork, audiometry, electrocochleography (ECoG), cervical vestibular evoked myogenic potential (cVEMP) assessment, vestibular autorotation testing (VAT), moving platform pressure testing, computerized dynamic posturography, computed tomography (CT), and for a limited number of patients, magnetic resonance imaging.

Tuning Fork Testing

As a screening tool for patients with SSCDS/OCDS symptoms, a low-frequency tuning fork was applied to their knees and elbows, and they were asked if they could hear or feel the vibration in their head. A 256-Hz tuning fork was used (8).

Audiometry

Pure-tone audiometry was performed over the frequency ranges of 250 to 8,000 Hz for air conduction and 250 to 3,000 Hz for bone conduction. Testing was performed in a sound-proof booth. Appropriate masking was used for bone conduction and, when needed, for air conduction. Tympanometry was also performed, and acoustic reflexes were tested for ipsilateral and contralateral presentation of tones.

Electrocochleography

Preoperative ECoG was performed with gold foil tiptrodes (Etymotic Research; Elk Grove Village, Ill.), which were placed adjacent to the tympanic membrane in the external auditory canal and stabilized at the foam tip of the insert audio transducer. Unfiltered clicks of 100 μsec duration were presented at an intensity of 85 dB nHL. Two replications of averaged responses elicited by 1,500 clicks presented at a rate of 11.7/sec were obtained. Responses were band-pass filtered (20 to 1,500 Hz) and averaged, and the summating potential to action potential (SP/AP) ratio was calculated. An SP/AP ratio of greater than 0.4 was defined as abnormal for purposes of this study, based on commonly used standards for clinical testing (29).

Acoustic cVEMP Stimuli and Recording Techniques

A commercial auditory evoked potential software system (v. 6.2.1d; Bio-Logic Systems; Mundelein, Ill.) was used for acoustic cVEMP testing. Sound stimuli were delivered monaurally via an intra-auricular transducer with foam earphones (E-A-RLink Insert Earphones; E-A-R Auditory Systems, Indianapolis) as described previously (30).

During the recording protocol, the subjects were seated upright. The skin in the areas of electrode placement was cleansed with alcohol preps prior to electrode placement. The cVEMP measurements were recorded on disposable, self-adhesive, pre-gelled electrodes (Red Dot Ag/AgCl electrodes; 3M Canada; London, Ont.) and lead wires from Bio-Logic. The electrode montage consisted of an active electrode on the top third of the sternocleidomastoid muscle, a reference electrode at the sternoclavicular junction, and a ground electrode on the sternal notch.

During the cVEMP instruction, patients were asked to rotate their head toward the shoulder contralateral to the stimulus, and tilt their head approximately 30° to maximize the contraction of the sternocleidomastoid muscle. The clinician applied the maximum amount of manual resistance that each patient could tolerate while visually confirming the muscle contraction during stimulus delivery.

During the cVEMP measurements, air-conducted stimuli were delivered with a 1,000-Hz, 100-dB-nHL tone burst of positive polarity at a repetition rate of 4.3/sec (a 2 msec rise/fall time and a 2 msec plateau). Evoked myogenic potentials were amplified by 1,000 and band-pass filtered (10 to 1,500 Hz). An average of approximately 80 to 150 sweeps were made per test.

The response parameters were defined as (1) the cVEMP p13 potential being the first distinctive trough in the waveform, anticipated to occur at approximately 10 to 14 msec following the stimulus, and (2) the n23 potential being the first distinctive peak in the waveform, occurring at approximately 19 to 23 msec after stimulus onset. Peak-to-peak amplitude was calculated with the Bio-Logic software after peaks were labeled and the amplitude difference between the two peaks was measured. The threshold was defined as the lowest dB SPL at which a p13 and n23 response could be recorded. For reporting purposes, the cVEMP was considered positive when an increase in amplitude and decrease in threshold were observed.

Vestibular Autorotation Testing

The horizontal and vertical vestibulo-ocular reflexes (VORs) of each patient were tested by the VAT, which is a computerized test based on active head movements over a frequency range from 2 to 6 Hz. At frequencies higher than 2 Hz, the VORs represent the primary systems for ocular gaze fixation because other ocular movement systems (e.g., smooth pursuit) are minimally effective in this range of frequencies.

For the VAT protocol, patient were seated and fitted with conventional electro-oculographic (EOG) electrodes. Then a lightweight headband was attached to a rotational velocity sensor and an EOG amplifier. Horizontal eye movements were recorded by bilateral electrodes positioned at the outer canthi and by a reference electrode positioned above the bridge of the nose. Vertical eye movements were recorded by electrodes placed above and below one eye. Head velocity was recorded by a calibrated velocity sensor that was fixed to the headband. A computer-generated tone was used as an audible cue to direct the frequency of head motion while the computer program swept the frequencies from 0.5 to 6.5 Hz during the 18-second test epoch. Two instructions were given: (1) "stare at the wall-mounted target" (a 1-cm disk) and (2) "move your head smoothly from side to side in time to the computer generated tone."

After a 30-second rest, the same procedure was performed twice more for a total of three evaluations of horizontal head movements, and then it was performed three more times with vertical head movements in a "nose up, nose down" direction. Eye position and head velocity data were amplified and digitized. Data from the first 6 seconds were used for EOG calibration. Gain and phase were computed during the final 12 seconds of the test epoch. In brief, *gain* is defined as the eye velocity amplitude divided by the head velocity amplitude. *Phase* is the time lag in degrees of the eye velocity in relation to the head velocity. *Asymmetry* is the amount of drift of the eye toward one side. All three characteristics are frequency-dependent. An ideal VOR result would be expressed as gain = 1 and phase = 180° with no asymmetry.

An inability of eye velocity to follow head velocity can indicate pathology when gains and phases differ from normal. Eye drifts to the right or left might indicate pathology when they occur systematically toward one side. A VAT result is considered clinically abnormal if two or more means and standard deviations of gain or phase datapoints show error bars that are clearly separable from those of the normal group in one or more of the four plotted graphs: horizontal and vertical, gains and phases. Asymmetry plots are generated from each patient's data by determining the ratio of the eye position deviation from the straight-ahead position and the amount of spectral energy at each frequency as a percentage; and Fourier analysis ascertains this. Asymmetry in VORs suggests that the number of neural impulses per unit of time that contributes to the extraocular muscles is lower on one side, which causes the eye to drift in the orbit to that side during active head movement. Asymmetry suggests the presence of a unilateral lesion, and the direction of the eye drift is toward the side of the lesion.

Moving Platform Pressure Test

Most patients underwent moving platform pressure testing (fistula test) preoperatively as described by Black et al. (2,31).

Computed Tomography of the Temporal Bone

All 17 patients underwent temporal bone CT on a helical high-resolution scanner (Somatom Sensation 64-slice scanner; Siemens; Malvern Pa.) with a collimation of 12 × 0.6 mm and a reconstruction increment of 0.3 mm. Axial imaging was obtained with reconstructions in sagittal and coronal planes. The images were optimized with a very sharp kernel and a specific window level dedicated to the inner ear (Seimens PLM Software).

Next, the axial 0.6-mm raw dataset was loaded onto a viewer (AquariusNET; TeraRecon; Foster City, Calif.) in three-dimensional (3-D) mode. Using the 3-D controls, the left and right superior semicircular canals were manipulated to a "best view in plane" position with the circumference of the canal. The entire bony otic capsule, including the superior semicircular canals, was then evaluated with two different 3-D rendering modes. The first was a gray-scale minimum-intensity projection mode at 1-mm thickness. The second was a color 3-D volume-rendering mode, also at 1-mm thickness. The character and size of the dehiscence was measured using the best-view-in-plane images on the workstation. The bone overlying the superior semicircular canal on each side and with each 3-D rendering mode was characterized as either *normal, thin, small* (SCD ≤2 mm), *medium* (2 to 4 mm), or *large* (≥4 mm. For reporting purposes, an image was classified as *normal* if no dehiscence could be seen in any of the three semicircular canals or anywhere else in the bony otic capsule.

Magnetic Resonance Imaging

Magnetic resonance imaging (Tim Trio 3.0 T MRI; Siemens) was performed in 4 patients (patients 9-12) who underwent SCD plugging via the middle cranial fossa and subsequently developed no-iOCD and recurrence of their symptoms, to determine if their superior semicircular canals remained plugged. The semicircular canal sequence used to determine if a semicircular canal was patent or plugged was CISS (constructive interference in steady state) 0.6-mm axial acquisitions, which were then evaluated in both 2-D and 3-D volume rendering on the Tera AquariusNet viewer. The 3-D volumes were then evaluated with maximum-intensity projection slabs ranging from 10 to 20 mm. These high-resolution sequences were used to determine whether or not fluid was present within the superior semicircular canals.

Dizziness Handicap Inventory

All 17 patients were asked to complete the Dizziness Handicap Inventory (DHI). The patients were studied retrospectively on one occasion following their surgical procedures. They were contacted by email and sent two copies of the DHI, with standard instructions on how to complete it; patients were assured of their privacy and of data confidentiality in the study. For one copy, they were asked to respond, to the best of their abilities, as they would have responded before they underwent the surgery for their otic capsule dehiscence(s). A second copy was to be completed to reflect their status at the

present time. They were instructed to return the questionnaire electronically or via facsimile. For the 3 groups, 6 (75%) no-iOCD patients, 4 both SCD and no-iOCD patients, and 4 (80%) SCD only patients returned their DHI questionnaires. The DHI questionnaires were scored by a neutral observer who was not involved in patient care, who used the scoring system validated by Jacobson and Newman for this instrument ("Yes" = 4 points; "Sometimes" = 2 points; "No" = 0 points) (32). The pre- and post-treatment scores were then totaled, both for the combined total and for each domain score (physical, functional, emotional), difference scores were calculated, and all were entered into an Excel database for analysis. All data were examined with standard descriptive statistics (mean, SD, range). When comparisons between the pre- and post-treatment scores were made, the data were analyzed using repeated-measures analysis of variance and least significant differences tests for paired comparisons, establishing 0.05 as the criterion level of significance.

The Dizziness Handicap Inventory (DHI)

Name _____ **Date** _____

		Now
P1.	Does looking up increase your problem?	o Yes o Sometimes o No
E2.	Because of your problem, do you feel frustrated?	o Yes o Sometimes o No
F3.	Because of your problem, do you restrict your travel for business or recreation?	o Yes o Sometimes o No
P4.	Does walking down the aisle of a supermarket increase your problems?	o Yes o Sometimes o No
F5.	Because of your problem, do you have difficulty getting into or out of bed?	o Yes o Sometimes o No
F6.	Does your problem significantly restrict your participation in social activities, such as going out to dinner, going to the movies, dancing, or going to parties?	o Yes o Sometimes o No
F7.	Because of your problem, do you have difficulty reading?	o Yes o Sometimes o No
P8.	Does performing more ambitious activities such as sports, dancing, household chores (sweeping or putting dishes away) increase your problems?	o Yes o Sometimes o No
E9.	Because of your problem, are you afraid to leave your home without having without having someone accompany you?	o Yes o Sometimes o No
E10.	Because of your problem have you been embarrassed in front of others?	o Yes o Sometimes o No
P11.	Do quick movements of your head increase your problem?	o Yes o Sometimes o No
F12.	Because of your problem, do you avoid heights?	o Yes o Sometimes o No
P13.	Does turning over in bed increase your problem?	o Yes o Sometimes o No
F14.	Because of your problem, is it difficult for you to do strenuous homework or yard work?	o Yes o Sometimes o No
E15.	Because of your problem, are you afraid people may think you are intoxicated?	o Yes o Sometimes o No
F16.	Because of your problem, is it difficult for you to go for a walk by yourself?	o Yes o Sometimes o No
P17.	Does walking down a sidewalk increase your problem?	o Yes o Sometimes o No
E18.	Because of your problem, is it difficult for you to concentrate?	o Yes o Sometimes o No
F19.	Because of your problem, is it difficult for you to walk around your house in the dark?	o Yes o Sometimes o No
E20.	Because of your problem, are you afraid to stay home alone?	o Yes o Sometimes o No
E21.	Because of your problem, do you feel handicapped?	o Yes o Sometimes o No
E22.	Has the problem placed stress on your relationships with members of your family or friends?	o Yes o Sometimes o No
E23.	Because of your problem, are you depressed?	o Yes o Sometimes o No
F24.	Does your problem interfere with your job or household responsibilities?	o Yes o Sometimes o No
P25.	Does bending over increase your problem?	o Yes o Sometimes o No

Headache Impact Test

All 17 patients were also asked to complete the Headache Impact Test (HIT-6). The patients were studied retrospectively on one occasion following their surgical procedures. They were contacted by email and sent two copies of the HIT-6, with standard instructions on how to complete it; patients were assured of their privacy and of data confidentiality in the study. They were asked to recall and complete one copy, to the best of their abilities, as they would have responded before they underwent the surgery for their otic capsule dehiscence(s). A second copy was to be completed to reflect their status at the present time. They were instructed to return the questionnaire electronically or via facsimile. For the three groups, 6 (75%) no-iOCD patients, 4 both SCD and no-iOCD patients, and 4 (80%) SCD only patients returned their HIT-6 questionnaires. The HIT-6 questionnaires were scored by a neutral observer who was not involved in patient care, who used the scoring system validated for this instrument ("Never" = 6 points; "Rarely" = 9 points; "Sometimes" = 10 points; "Very often" = 11 points; "Always" = 13 points) (33,34). The final HIT-6 score was obtained from simple summation of the six items and ranges between 36 and 78, with larger scores reflecting greater impact. Headache impact severity level was categorized using score ranges based on the HIT-6 interpretation guide (33,34). The four headache impact severity categories are little or no impact (49 or less, [Class I]), some impact (50–55, [Class II]), substantial impact (56–59, [Class III]), and severe impact (60–78, [Class IV]). The pre- and post-treatment scores were examined with standard descriptive statistics (mean, SD, range). When comparisons between the pre- and post-treatment scores were made, the data were analyzed using repeated-measures analysis of variance and least significant differences tests for paired comparisons, establishing 0.05 as the criterion level of significance.

HIT-6 Questionnaire (Evaluation of headache disability)

Name _____ **Date** _____

This questionnaire was designed to help you describe and communicate the way you feel and what you cannot do because of headaches.

INSTRUCTIONS :
To complete, please circle one answer (or mark X next to the answer) for each question.

1. When you have headaches, how often is the pain severe?

Never Rarely Sometimes Very often Always

2. How often do headaches limit your ability to do usual daily activities including household work, work, school, or social activities?

Never Rarely Sometimes Very often Always

3. When you have a headache, how often do you wish you could lie down?

Never Rarely Sometimes Very often Always

4. In the past 4 weeks, how often have you felt too tired to do work or daily activities because of your headaches?

Never Rarely Sometimes Very often Always

5. In the past 4 weeks, how often have you felt fed up or irritated because of your headaches?

Never Rarely Sometimes Very often Always

6. In the past 4 weeks, how often did headaches limit your ability to concentrate on work or daily activities?

Never Rarely Sometimes Very often Always

Column 1 6 points each	Column 2 9 points each	Column 3 10 points each	Column 4 11 points each	Column 5 13 points each
_____	_____	_____	_____	_____

To score, add points for answers in each column. **Total Score**: _____

Class I: 36-49, **Class II**: 50-55, **Class III**: 56-59, **Class IV**: 60 and more.

Computerized Dynamic Posturography

Postural performance was measured in eight no-iOCD patients, three both SCD and no-iOCD patients (one patient exceeded the weight limit of the test system) and five SCD only patients before and after surgical intervention with an EquiTest platform (NeuroCom International Inc, Clackamas, OR). Subjects stood centered on the movable platform with shoes off, feet shoulder width apart, and the medial malleolus aligned with the rotational axis of the support surface and visual surround. The support surface consisted of a dual force plate with four force transducers (strain gauges) mounted symmetrically to measure the distribution of vertical forces sampled at 100 Hz. Subjects were instructed to maintain upright stance with arms folded and their head in a natural upright orientation. Center-of-mass (COM) sway angles were derived from anterior-posterior (AP) and medial-lateral (ML) center-of-pressure positions using a low pass Butterworth filter (2^{nd} order, cutoff frequency at 0.85 Hz), with the height of the COM estimated at 55% of the subject height (35).

During platform testing, sensory organization tests (SOTs) were administered. SOTs pose a set of increasingly challenging conditions to assess a patient's ability to make effective use of visual, vestibular, and somatosensory information in order to maintain an upright stance. Testing is done under six sensory conditions:

- 1: fixed support surface, eyes open and fixed on a target;
- 2: fixed support, eyes closed;
- 3: fixed support, vision sway-referenced;
- 4: support sway-referenced, eyes open and fixed;
- 5: support sway-referenced, eyes closed; and
- 6: support sway-referenced, vision sway-referenced (36).

During some SOTs, the support surface and/or the visual surround was rotated in direct proportion to the patient's instantaneous anteroposterior sway, which is referred to as *sway referencing.* Postural sway was measured during 20-second trials; testing included combinations of <u>two</u> somatosensory conditions (fixed-support and sway-referenced support) and <u>three</u> visual conditions (eyes open, eyes closed, and sway-referenced vision). Three trials of each condition were performed. The anteroposterior peak-to-peak sway angle, q (in degrees), was used to compute a continuous equilibrium (EQ) score, as follows:

$$EQ = (1-(q / 12.5)) \times \% \text{ trial completed},$$

where 12.5° is the maximum theoretical peak-to-peak AP sway and the range of normalized values was between 0 and 100 (37). Falls were marked when subjects moved their feet, began to take a step, or raised their arms. In addition to the Continuous EQ scores for each SOT condition, a weighted composite score was calculated for each CDP session. Due to the skewed distribution of the EQ scores, nonparametric repeated measures Wilcoxon Signed Rank test was used to compare pre- versus postoperative posture performance, and independent samples Kruskal-Wallis test was used to compare scores across SCD, no-iOCD and Both groups using IBM SPSS Statistics software (version 22).

SURGICAL TECHNIQUES

Superior Semicircular Canal Dehiscence Surgical Techniques

The same surgical technique was used for all nine patients. A traditional middle cranial fossa (MCF) approach with craniotomy centered on the zygomatic root and craniectomy to the skull base was used after intravenous administration of 10 mg of Decadron (dexamethasone) and 0.5 gm/kg of Osmitrol (mannitol). The dura was elevated with an Adson periosteal elevator and a Fisch MCF retractor was placed with the retractor tip just past the petrous ridge. Using microsurgical techniques, the superior canal was inspected. If the dehiscence was not seen on the superior aspect of the canal, further dural elevation and subsequent use of a Buckingham mirror to identify a dehiscence was completed. The canal was plugged using temporalis fascia or periosteum. The superior canal was resurfaced with OsteoVation hydroxylapatite bone cement (OsteoMed, Addison, TX). Gelfoam (Pfizer, New York, NY) was then used to fill the middle ear if the ossicles were in contact with the herniated temporal lobe and dura. Likewise Gelfoam was used to fill all of the remaining temporal bone defects. After removing the Fisch retractor, DuraGen X Dural Regeneration Matrix (Integra, Plainsboro, NJ) was used to cover all of the exposed temporal lobe dura. If there were any dura defects present the dura was repaired with either a fascia graft or a medial graft fashioned from DuraGen. A single piece of Gelfoam was used to cover all of the exposed dura at the craniotomy/craniectomy site before titanium mesh (Synthes North America, West Chester, PA) was secured to the skull. OsteoVation calcium phosphate cement (OsteoMed, Addison, TX) was then used to complete the cranioplasty prior to wound closure. The temporalis muscle was closed with simple interrupted 3-0 Vicryl suture (Ethicon, Somerville, NJ). The galeal and subcutaneous layers were closed with inverted interrupted 4-0 Monocryl suture (Ethicon). The skin was closed with a running locked 5-0 fast absorbing plain gut suture (Ethicon).

Round Window Reinforcement Surgical Techniques

The same surgical technique was used for all 12 patients undergoing RWR. A posterior auricular incision was made. Loose areolar tissue was harvested, and then minced into 0.25 mm pieces using a No. 10 Beaver blade. TISEEL, a two component fibrin sealant, (Baxter Healthcare Corporation, Westlake Village, CA) was used for coating the pieces. One component is a sealer protein solution that contains human fibrinogen and a synthetic fibrinolysis inhibitor, aprotinin, which helps prevent premature degradation of the fibrin clot. The other component is a human thrombin solution and calcium chloride. Each of these solutions is prepared and kept isolated into petri dishes into which the minced tissue is divided. In addition, perichondrium was harvested and thinned using a fascia press. A 2 mm conchal cartilage graft was harvested using a 2 mm biopsy punch (Miltex, Inc., York, PA) and then split in half. The subcutaneous layer was closed with inverted interrupted 4-0 Monocryl suture (Ethicon). The skin was closed with a running locked 5-0 fast absorbing plain gut suture (Ethicon).

After entering the middle ear, the bone was drilled off of the RW niche using a 0.8 mm diamond bur to fully expose and visualize the RW membrane. A laser was used

to denude all of the mucosa around the RW niche and also around the anterior portion of bone surrounding the OW annular ligament. A Lumenis Spectra II (Lumenis Inc., San Jose, CA) laser was used with a Lumenis® Acculite™ EndoOto™ hand held laser probe (Horn, 24 ga 20° angled, SubMiniature Type A [SMA] 906 connector, 200µm). The Selecta II has a red 635nm (<5 mW) He NE aiming beam; and a Q-switched frequency doubled 1064 nm Nd:YAG, (532 nm [green wavelength]) diode-pumped solid state laser as its treatment beam. The specific treatment settings used were: power 1000 mW; pulse duration of 0.3 seconds; and pulse interval of 0.3 seconds.

The thinned perichondrium was placed directly on the surface of the RW membrane and extended onto the otic capsule with the mucosa denuded using the laser. The split conchal cartilage graft was placed on top of the perichondrial graft and seated over the round wind membrane. The minced loose areolar tissue was then circumferentially placed in a manner of a gasket around the cartilage and onto the perichondrium.

After placement of the reinforcement materials, the defocused laser was also used to further coagulate and denature these materials at the periphery so that greater adherence to the temporal bone was achieved. The OW reinforcement was accomplished by draped grafts around the anterior crus and holding them in place with Gelfoam. Too much tissue was intentionally placed in the RW niche and also around the stapes knowing that some will be resorbed during the healing and connective tissue remodeling phases. Following reinforcement, the middle ear was filled with Gelfoam and tympanomeatal flap returned to the anatomic position. Strips of dry Gelfoam were placed across the intact skin and the skin of the tympanomeatal flap and a small amount of antibiotic ointment is placed over this. Ofloxacin (Floxin) 0.3% otic solution is then placed into the external auditory canal. No additional dressing materials were required.

NEUROPSYCHOLOGY TEST BATTERY

Beck Depression Inventory, 2nd Edition

The Beck Depression Inventory, Second Edition (BDI-II) is consistent with the depression criteria of the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM–IV) (18). The Beck Depression Inventory is extremely rapid, taking only five minutes to complete, and is the most widely used instrument for detecting depression.

The BDI has been used for over one-half century to identify and assess depressive symptoms, and has been reported to be highly reliable regardless of the population (19-22). The BDI has a high coefficient alpha, (0.80) its construct validity has been established, and it is able to differentiate depressed from non-depressed patients. For the BDI-II the coefficient alphas (0.92 for outpatients and 0.93 for the college students) were higher than those for the BDI-I and BDI-IA.

The BDI-II consists of 21 items to assess the intensity of depression in clinical and normal patients. Each item is a list of four statements arranged in increasing severity about a particular symptom of depression. BDI-II was initially standardized using a large clinical sample (N = 500), of individuals from rural and suburban settings (21). BDI-II replaced earlier versions and includes items intending to index symptoms of severe depression, which would require hospitalization. Items indicate increases or decreases in sleep and appetite, agitation, concentration difficulty and loss of energy. When being assessed with the BDI-II, the patient is asked to consider each statement as it relates to the way they have felt for the past two weeks, which more accurately corresponds to the DSM-IV criteria. Total score of 0-13 is considered minimal range, 14-19 is mild, 20-28 is moderate, and 29-63 is severe.

Wide Range Intelligence Test

Intelligence consists of a general factor underpinning all purposeful thinking and behavior together with certain specific factors. It may be better defined as a person's capacity for processing information. Intelligence is measured in terms of Intelligence Quotient (IQ).

The national average score for IQ is 100 with 34% of the population having IQs between 85 and 100 and 34% of the population having IQs between 100 and 115. This is known as the 'average' range. About 16% have IQs above 115 and about 3% above 130. The Wide Range Intelligence Test (WRIT) is a highly reliable individually administered battery of four subtests of cognitive abilities: verbal analogies, vocabulary, matrices, and diamonds (23). It assesses both verbal and non-verbal abilities by means of Verbal and Visual Scales. Each scale consists of two sub-tests each addressing a group of specific abilities. Verbal items are all oral with no reading or writing involved. Verbal IQ measures the functioning of the left hemisphere of the brain which is the hemisphere usually responsible for speech and language. The Performance IQ measures the functioning of the right hemisphere which is usually responsible for practical, creative, artistic and visual thinking skills. The WRIT can be used between the ages 4 to 85, providing measures of crystallized and fluid intelligence. The test can be completed in 30 minutes.

Standardized on 2,285 individuals, the WRIT produces IQs that are highly correlated with those from traditional and much lengthier cognitive measures, including the Wechsler Intelligence Scale for Children III (0.90) and the Wechsler Adult Intelligence Scale III (0.91) (24).

Many intelligence tests utilize similar subtests, particularly some of the subtests that constitute the Wechsler Adult Intelligence Test (23,24).

The WRIT is comprised of four subtests:

1) Diamonds. To complete the diamonds subtest, patients must construct specific designs in a limited time using pieces shapes as diamonds. It is regarded as an excellent measure of spatial ability;

2) Vocabulary. Vocabulary and general knowledge and vocabulary, such as *"What does 'to swim' mean?*";

3) Matrices. Picture concepts in which patients must select one picture from a larger set of alternatives that share a common theme; and

4) Verbal Analogies. Verbal analogies assess abstract, verbal reasoning, and includes questions like *"Chaff is to wheat as dregs are to _____?"*

Wide Range Assessment of Memory and Learning, 2nd Edition

The WRAML2 is a carefully standardized psychometric instrument which allows the user to evaluate an individual's memory functioning (25). The WRAML2 affords evaluation of both immediate and delayed memory ability, as well as the acquisition of new learning.

The WRAML2 Core Battery is composed of two Verbal, two Visual, and two Attention/Concentration subtests, yielding a Verbal Memory Index, a Visual Memory Index, and an Attention/Concentration Index. Together, these subtests yield a General Memory Index. A new Working Memory Index has been added, which is comprised of the Symbolic Working Memory and Verbal Working Memory subtests.

The WRAML2 is normed for children, adolescents, and adults, ages 5 to 90 years. The normative sample was constructed using a national stratified sampling technique, controlling for age, sex, race, region, and education of 1200 children and adults. The WRAML2 includes standard scores, scaled scores, and percentiles. Age equivalents are provided for the child and pre-adolescent age groups. It takes an average of 90 minutes to administer. Alpha reliabilities for the Core Battery Verbal Memory Index, Visual Memory Index, and Attention/Concentration Index are 0.92, 0.89, and 0.86, respectively. The alpha reliability for the General Memory Index is 0.93. The Working Memory Index had an alpha reliability ranging from 0.86-0.94; a range of 0.91-0.94 was obtained in the 14 to 17 and 25 to 89 age range groups.

The WRAML-2 is comprised of these four indices:

- ***Verbal Memory Index:*** demonstrates the ability to learn and recall both meaningful and rote verbal information.

  Subtests:

  - ***Story Memory***

    Examinee listens to a series of two brief stories, each one to two paragraphs in length; examinee is then asked to recall in detail the events of each story.

  - ***Verbal Learning***

This is a list of 16 single syllable words; examinee listens to the list, and then verbally lists every word remembered. This task is repeated four times; after 15 minutes, examinee is again asked to list each word from the list.

- ***Visual Memory Index:*** demonstrates the ability to learn and recall both meaningful, e.g., pictorial, and minimally related, rote, e.g., design, visual information.

  Subtests:

  - ***Picture Memory***

    Four scenes of everyday life: zoo, living room, classroom, and garage/driveway.

    Pictures are shown to the examinee for 10 seconds, after which, a picture similar to the one shown is placed in front of examinee, who then crosses out each item that has been changed, moved or added.

  - ***Design Memory***

    Five cards, each with its own design varying in complexity. Designs are shown to the examinee for five seconds, after which a blank card is placed in front of examinee who then replicates the design from memory.

- ***Attention/Concentration Index:*** demonstrates the ability to learn and recall rote, sequential information either visually or aurally. Subtests:
  - ***Finger Windows***

    A laminated card, 8 ½ by 11" with holes one inch in diameter punched in random locations, is placed in front of examinee.

    Evaluator pokes finger through holes in a pattern; and the examinee is asked to repeat the same pattern. The number of holes in each pattern gradually increases in length.

  - ***Number-Letter***

    Examinee is asked to repeat a series of mixed up numbers and letters; the length of each series increases gradually.

- ***Working Memory***: provides an estimate of the client's ability to operate on and retain information that is held in short-term memory.

  Subtests:

  - ***Verbal Working Memory***

Examinee listens to a list of words, some are animals and some are not.

The examinee is asked to repeat the list in this order: animals first, smallest to largest, then non-animals in any order.

The task increases in difficulty in two ways: length of list of words increases, and examinee is asked to order the words in this way: animals first, smallest to largest; then non-animals, smallest to largest.

- ***Symbolic Working Memory***

  Examinee listens to a series of mixed up numbers, and then asked to point to the numbers in the correct numerical order on a laminated card.

  Difficulty increases when letters are added to the series, and the examinee is asked to point to the numbers first in correct numerical order, and then the letters in the correct alphabetical order.

Delis-Kaplan Executive Function System

The Delis-Kaplan Executive Function System (D-KEFS) was the first nationally standardized set of tests to evaluate higher-level cognitive functions in both children and adults. (26-28). With nine stand-alone tests, the D-KEFS comprehensively assesses key components of executive functions believed to be mediated, primarily by the frontal lobe, including the detection of subtle executive function deficits (26).

Standardization was completed using a sample of 1,700 children and adults selected to match the demographic characteristics of the United States. Normative data has been collected for ages 8 to 89 years. Consistent reliability coefficients have been difficult to obtain, not only for the D-KEFS, but for other instruments that tap a wider spectrum of complex, effortful cognitive processes; and compared to more homogeneous, fundamental tasks such as the vocabulary or picture completion subtests, and as a result, the potential for performance variability or measurement error may be greater for more complex tests. However, it is often the complexity of these tasks that make them so sensitive to the detection of even mild brain damage. In addition, tests of executive functions and memory often pose special problems for calculating reliability in traditional ways (26). Although caution must always be exercised in ascribing brain damage to low scores on any test, especially for more complex tasks such as the D-KEFS tests and memory instruments, the utility of these instruments for detecting neurocognitive deficits has been demonstrated in numerous studies.

The D-KEFS Trail Making Test, overall, provides rigorous measures of four key fundamental skills that contribute to successful performance on the primary executive function task, *Condition 4: Number-Letter Switching*. These skills include *Motor Speed: Condition 5*. In this way, the clinician can assess empirically whether a deficient score on the switching task is related to a higher-level deficit in cognitive flexibility and/or to one

or more impairments in the fundamental component skills tapped by the task. The Trail Making Test places significant demands on cognitive switching. Over the past several decades, neuropsychological research with adult neurological patients has consistently revealed this finding: patients with focal frontal lobe damage often perform normally on IQ tests and other tests of basic cognitive skills, e.g., reading and spelling. Switching tasks reveal the examinee's flexibility of thinking, the ability to abandon one conceptual relationship in order to apprehend new ones. It is one of the key attributes that give human beings the mental freedom to engage in creative thought (26-28).

There are 240 seconds allotted to Condition 4: Number-Letter Switching, while 150 seconds are allotted to Condition 5: Motor Speed. For the Condition 4: Number-Letter Switching test, the examinee alternates between connecting numbers, and then letters, and so on, until the end letter /P/ on an 11" by 20"paper. For the Condition 5: Motor Speed test, the examinee traces a dotted line from circle to circle, making sure to touch each circle, on an 11" by 20" paper, as quickly as possible.

RESULTS

While not the focus of the present study, once each patient completed their final surgical procedure and medical management resolved any of the factors complicating their postoperative recovery, their presenting symptoms and signs were returned to their baseline before developing SSCDS/OCDS. In general, the pseudoconductive hearing loss in the SCD patients did not change and for those patients undergoing RWR surgery, additional conductive hearing loss resulted; however, these data are not reported in detail as the focus of this study is on cognitive dysfunction and cognitive recovery. Likewise we did not compare the cVEMP data since the RWR surgery and the associated soft tissue placed into the middle ear of 12 of the 17 patients did not allow a direct comparison of pre- versus postoperative since an air conduction stimulus was used and an additional conductive hearing loss was created. In the future, as a bone-conduction force-acceleration system for measuring cVEMPs and oVEMPs is developed, this limitation may be overcome (30).

DISCUSSION

Reporting the outcomes of surgical intervention for SCD itself is complicated and without a standardized approach (38). However, our present patient cohorts included patients with no-iOCD alone and patients who developed no-iOCD after plugging of their SCD. These latter two groups had RWR and therefore additional soft tissue placed in their middle ears which would produce a conductive hearing loss and associated decrease in cVEMP amplitude for air-conduction cVEMP and oVEMP studies. Reporting hearing outcomes in SCD plugging only patients is also not a straight-forward and standardized methodology (39).

Cognitive Functional Differences between SCD and no-iOCD Patients

The differences in WRAML verbal, visual and attention test performance between the SCD group and the no-iOCD group are of particular interest because they are

selective to particular tests. Although the WRAML visual scores did not differ preoperatively among groups, the scores improved postoperatively in the other two groups but not the SCD group. Conversely, the no-iOCD group had significantly lower scores on the WRAML attention test preoperatively, but they recovered postoperatively to match the other groups. The preoperative findings and postoperative courses did not differ significantly on the WRAML working memory test, D-KEFS motor scores, D-KEFS number and letter scores, or Wide Range Intelligence Test scores.

These selective cognitive test performance findings do not appear to be confounded with balance performance or headache issues. There were no concomitant, significant differences between these groups in performance during computerized dynamic posturography, Beck Depression Index or headache symptoms (HIT-6) or Dizziness Handicap Inventory. Diagnosis by exclusion is admittedly a risky venture; however, these findings indicate that there are test-selective cognitive performance differences between the no-iOCD and SCD patient groups.

In 1883, Bechterew reported different patterns of behavioral compensation for unilateral, serial bilateral and simultaneous bilateral damage to the vestibular periphery (50). The most striking effect has been termed the Bechterew phenomenon: after compensation for a unilateral peripheral vestibular lesion, a lesion of the intact side produces behavior suggestive of a functional input from the vestibular apparatus that was ablated initially. One underlying mechanism appears to be a rebalancing of commissural inhibitory connections between the vestibular nuclei ipsilateral and contralateral to the lesion (51). It is one manifestation of operations of compensatory mechanisms in the central nervous system that maintain (and restore) the symmetry of vestibular function (52,53). It is perhaps significant that compensatory mechanisms have been examined typically after a unilateral manipulation of all semicircular canals and otolith organs, which is arguable comparable to the functional consequences in the non-iOCD patients. The RWR operation can be conceived to be a restoration of function to the entire vestibular apparatus on one side by changing the inner ear compliance and effectively closing or minimizing an abnormal third window, which alters input to vestibular pathways that have compensated for the previous deficit. The SCD repair, by extension, closes the abnormal third window, but also alters the function of one semicircular canal.

The differences in WRAML findings between the SCD and no-iOCD patients raise the question of whether it may be more difficult to compensate for a functional change in a single superior semicircular canal than a complete unilateral effect. Dual task interference is a well-known phenomenon in human performance (54), including effects on cognitive task performance associated with demands of balance and postural control (55-57). The interference effects are mutual: cognitive task difficulty also impacts gait performance (58). These phenomena are regarded as indications of resource competition at bottlenecks that limit network processing capacity in sites that include prefrontal cortex (59). Because the WRAML tests in this study are cognitive tasks performed by initially symptomatic individuals with SCD or non-iOCD, our findings suggest that they differ in demands for verbal, visual and attentional memory and learning resources to as part of balance compensation processes. In this regard, the test results likely represent

differential “cognitive resource saturation”, indicating that different resources may be engaged by the SCD or non-iOCD patient groups to achieve similar performance on dynamic posturography and the other test batteries.

Clinically, cognitive alterations are nearly universal in patients with superior canal dehiscence syndrome, whether due to an actual SCD or a no-iOCD. In contrast to these disorders that result in gravitational receptor dysfunction type of vertigo, it is uncommon in patients with rotational receptor dysfunction type of vertigo such as with benign positional vertigo, vestibular neuronitis or other disorders producing true rotational vertigo. Patients with a no-iOCD and/or SCD often use the following descriptors when describing their cognitive function: *“fuzzy, foggy, spacey, out-of-it; memory and concentration are poor; difficulty reading – as if the words are floating on the page; trouble finding the right words; and forgetting what I wanted to say.”*

Gurvich and colleagues published an excellent review of the role of the vestibular system on cognition and psychiatry (60). The two key anatomical regions that provide links between the vestibular system and neural networks involved in cognitive and emotional processing are the parabrachial nucleus and the hippocampus (49,61-63); however, many of the neuroanatomical regions that are linked to the vestibular system are also implicated in several psychiatric illnesses. The past decade has seen an increased interest in the relationship between the vestibular system and mood, cognition and psychiatric symptoms with studies demonstrating vestibular stimulation can produce changes in mood, cognition and psychiatric symptoms (64-66). It is also the case that many individuals with SCDS have been assigned a neurological or psychiatric diagnosis before their vestibular disorder was diagnosed and have experienced resolution of their “psychiatric disorder” following surgical intervention (4,5,9-11) (Table 1). This unfortunately is common with children (4,5). The hippocampus is consistently implicated in cognition and models of psychiatric disorders and there is a large body of evidence supporting vestibular–hippocampal interactions (67-71).

Smith et al. and Zheng et al. have reported that modulation of memory, but not spatial memory, occurs with vestibular lesions and can be influenced by galvanic vestibular stimulation (72,73). These findings may lead to additional treatment strategies that may accelerate or maximize recovery after repairing a no-iOCD or SCD.

Of historical interest, Grimm and coworkers described PLF in mild head trauma and performed psychological affective tests such as the Minnesota Multiphasic Personality Inventory as well as IQ, memory and learning ability (74). They found statistically significant reductions in IQ, memory, learning ability and statistically significant higher scores for depression, hysteria, psychotic deviate, paranoia, and schizophrenia among others. They did not test their patients after PLF surgery, so it remains unknown if they improved, remained unchanged, or whether these abnormalities were due to their PLF, their mild head trauma, or their innate cognitive and psychiatric character. Gizzi and coworkers have reported that there is no causal relationship between vestibular disease and cognitive dysfunction (75). They studied 200 patients with “dizziness” – half with a history of brain trauma and half without. They concluded that in

patients with postconcussive dizziness, cognitive complaints are likely due to neurologic injury or affective disturbance; and in dizzy patients without brain trauma, cognitive complaints are likely due to concurrent affective disturbance. These findings conflict with our observations; however, in our series we have been studying cognitive dysfunction before and after intervention so that each subject has comparative data. Recorded video clips of consenting patients before and after intervention helps to further capture this obvious dysfunction in ways that complement standardized neuropsychology testing (4-12).

Altered Spatial Orientation

Patients with PLF, vestibular migraine, no-iOCD and/or SCD often use the following descriptors when describing their altered spatial orientation: *"trouble judging distances; feeling detached and separated or not connected, almost like watching a play when around other people; and even an out-of-body experience (in more severe gravitational receptor asymmetries)."* Several groups have begun studying this phenomenon. Clinically, this spatial disorientation reverses after surgery; however, Baek and colleagues reported that spatial memory deficits following bilateral vestibular loss may be permanent (76). There is also evidence that simulation of the vestibular system is necessary to maintain normal spatial memory (77). Deroualle and Lopez have explored the visual-vestibular interaction and in their 2014 review of the topic conclude that vestibular signals may be involved in the sensory bases of self-other distinction and mirroring, emotion perception and perspective taking (78). Clinically, patients with non-iOCD and/or SCD recognize changes in their personality. Smith and Darlington argue that these changes in cognitive and emotional occur because of the role of the ascending vestibular pathways to the limbic system and neocortex play in the sense of spatial orientation (79). They further suggest that this change in the sense of self is responsible for the depersonalization and derealization symptoms such as feeling "spaced out," "body feeling strange" and "not feeling in control of self."

Migraine Headache

Vestibular migraine (VM), also termed migraine-associated dizziness, has become recognized as a distinct clinical entity that accounts for a high proportion of patients with vestibular symptoms (for review see Furman et al. 80). A temporal overlap between vestibular symptoms, such as vertigo and head-movement intolerance, and migraine symptoms, such as headache, photophobia, and phonophobia, is a requisite diagnostic criterion. Physical examination and laboratory testing are usually normal in VM but can be used to rule out other vestibular disorders with overlapping symptoms such as with OCDS no-iOCD or SCD. Vestibular migraine patients do not have sound-induced dizziness and nausea or autophony; however, when these patients have endolymphatic hydrops, they can have sound sensitivity that borders on a Tullio phenomenon. For this reason, when a high-resolution temporal bone CT with color 3D volume rendering shows no evidence of SCD, all patients suspected as having no-iOCD should be treated as a VM patient, as were the patients in this study cohort, since medical management, if successful, avoids unnecessary surgery (3).

Vestibular migraine is an example of the integral overlap between vestibular pathways and migraine circuit triggers and central mechanisms for premonitory symptom generation. Information transmitted by peripheral vestibular sensory organs and the vestibular nerve to the medulla and pons is an external trigger within the migraine circuit construct proposed by Ho and coworkers (81). This model is based upon the distribution of the neuropeptide CGRP, which has a complex distribution within the vestibular periphery (82). Migraine headache is nearly always present in patients with gravitational receptor dysfunction type of vertigo caused by no-iOCD or SCD, but infrequently with rotational receptor dysfunction type of true rotational vertigo (3-6,9-12). This is an important concept as no-iOCD and SCD can induce migraine and the three variants of migraine – ocular migraine, hemiplegic migraine and vestibular migraine (3,6). As shown in Table 2, 33% (2/6) patients in each cohort had migraine variants; two no-iOCD patients had intermittent ocular migraines and one SCD had intermittent ocular migraines while the other had intermittent vestibular migraines. The latter explains why some patients with no-iOCD or SCD, who normally only have gravitational receptor dysfunction type of vertigo (disequilibrium) can have episodes of vestibular migraine and infrequent true rotational vertigo attacks. It should also be noted that the character of the migraine headaches was different between our two cohorts. The migraine headaches were characterized as "24/7" with exacerbation of the intensity of the headache in the no-iOCD group. These patients also had a greater degree of light sensitivity with many of the patients wearing sunglasses much of their waking day and physicians finding the room lights off when entering the examination room. In this series, as is the case in clinical practice, surgical management of no-iOCD and/or SCD resolves the migraine headaches; however, sometimes there is only a marked decrease of the frequency and intensity of the migraines, as migraine has a high incidence overall (3-7,9-11). The HIT-6 data revealed that there was a highly statistically significant improvement pre- versus postoperatively ($p<0.001$) overall and between groups (Fig. 3), yet there were 2 patients who quantitatively became Class II and one patient remained a Class IV. The remaining 11 patients became Class I.

Learning Effects

With regard to tests of emotional functioning and levels of distress, self-report measures, such as the BDI, are commonly given over the course of the intervention to track progress. Such measures are not generally vulnerable to practice effects because they are measures related to the participants' perceptions of psychological symptoms. As shown in Figure 5 the improvements in the BDI were robust and showed continued improvement over time.

In neuropsychological assessment, it is standard practice to use the same test repeatedly in order to track change. This is done for two reasons: 1) to assure that the same construct is being measured with each test; and 2) to assure that the mean scores established for each test remain constant (83). If the testing conditions were changed at each session, it could not be assured that the testing conditions and scoring procedures did not contribute to changes in performance. Although this is standard practice for tracking clinical change in both research and clinical settings, practice effects may inflate

scores obtained after repeated testing. A meta-analysis performed by Calamia and coworkers (84) indicated that neuropsychological domains, ages of participants, and length of the test–retest interval were associated with test results in many cases. With regard to domains of testing, the visual memory domain was most vulnerable to practice effects, and visual-spatial ability was least vulnerable. Practice effects were most noticeable when comparing the second administration to the first; however, in our study there was a surgical intervention and associated recovery between the pre- and first postoperative study which may temper this effect. In fact, it is common to see clinical studies with surgical or medical intervention repeating the neuropsychology testing at 3 to 6 month intervals. Recently Jessup and coworkers (85) used the WRAML2 and D-KEFS to assess neurocognitive deficits in newly diagnosed children and adolescents with type I diabetes with and without diabetic ketoacidosis with retesting at 8-12 week intervals. They did not observe learning effects. We intentionally used short repeat test intervals in this pilot study to better understand the rates of recovery between the 3 disease and treatment groups.

Future Directions

Based on these data, improved study design, incorporation of strategies designed to accelerate cognitive recovery and integration of rehabilitation techniques that target visual recovery in vestibular compensation and in memory and learning are all ripe opportunities to have a positive impact on our patients with otic capsule dehiscence syndrome. The introduction of fMRI and tract tracing MRI studies will likely add greater insight into how the brain function of each of these patients is impacted and how we can develop additional interventions based on these findings.

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