

NIH Toolbox

Assessment of Neurological and Behavioral Function

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Sensation

Motor

Emotion

Cognition



Sensation and the NIH Toolbox

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This issue of the Toolbox newsletter is the second of two editions dedicated to the Sensory Domain and marks the final installment of our year-long series highlighting the four major Toolbox domains. We have established six separate sensory scientific teams in Audition, Somatosensation, Taste, Olfaction, Vestibular Balance, and Vision. Work in the latter three areas is overseen internally by Jerry Slotkin, PhD, and highlighted here. Dr. Slotkin coordinates the activities of three independent scientific teams whose membership is listed in the following pages.

In other news, the NIH Toolbox was mentioned in eight stimulus grants within the new initiative under the NIH Challenge Grants in Health and Science Research. As we move ahead, researchers are looking forward to using the Toolbox measures in their clinical studies. Please feel free to contact me with any questions or interest you may have regarding the use of the NIH Toolbox.

Olfaction

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The human olfactory system allows us to detect odors, to recognize and discriminate odor quality, and to identify the source of odors in our world. It is believed that humans are capable of detecting and discriminating thousands of different odorant molecules, many at extremely low concentrations (i.e., ppb or ppt levels). Our sense of smell provides us with information about our environment and food quality that is critical to our health and safety, a nutritious diet, and psychological well-being.

Smell or olfaction occurs when volatile chemicals stimulate olfactory receptor neurons located on a relatively small patch of specialized epithelial tissue high in the nasal cavity. These sensory neurons have an axon that travels as the olfactory nerve (Cranial Nerve I) to terminate in the olfactory bulb. In turn, the olfactory bulb projects more centrally and contributes inputs for higher cortical processing, which results in olfactory perception. Odorants reach the olfactory receptors in two ways; they can enter

the nostrils during normal inhalation (orthonasal route) or travel from the back of the oral cavity toward the roof of the mouth via the nasal pharynx (retronasal route). The perception of food flavor involves a combination of olfactory activation caused by odorous compounds released into the retronasal route through chewing or drinking, and the blending of taste (salty, sour, bitter, sweet) and other oral somatosensory sensations (texture, heat, cold). Nasal blockage and swelling can prevent odors from entering the retronasal stream, resulting in a shift of flavor toward blandness. Reported taste loss is more typically a loss of food flavor due to the blockage of this retronasal route than a decrement in taste perception.

There are a variety of ways to assess olfactory capabilities and olfactory loss in humans. Odor detection is evaluated by measuring the lowest concentration of an odorant at which an individual (a) can just detect the odor's presence or (b) can discriminate it from a sample of odorless air. The concentration at which this occurs is considered the detection threshold for that compound and the detection value can be compared with normative data gathered on other individuals to determine whether an

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Vision

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Vision is a complex sensation that provides us with a personal conscious representation of our surrounding environment. Loss of vision or blindness may limit a person’s ability to complete normal, daily activities and decrease overall quality of life. Visual impairment can impose various limitations on a person’s functional ability including reading, mobility (which includes driving), visual information processing (also called “seeing”), and visually guided motor behavior (also called “manipulation”).

Loss of vision due to disease or disorders of the visual system can result in problems associated with resolution of detail, field of view, appearance of contrast, appearance of colors, appearance of motion, resolution of depth, seeing in dim light, and disablement from glare. While each of these aspects of vision is important, visual acuity and visual fields are key aspects of vision that are commonly tested in clinical settings. Visual acuity tests are used to measure impairments in visual resolution or focus that can be caused by blurring of the retinal image, neural processing disorders, or damage to neurons in the retina or other parts of the visual pathway. Visual acuity is measured as the ratio of the viewing distance to the size of the smallest letters that can be read or smallest symbols that can be recognized on a standard vision chart. Visual field tests are measures of impairments in the person’s field of view that can be caused by disorders of the retina (e.g., retinal detachments), optic nerve (e.g., glaucoma), or visual parts of the brain (e.g., stroke). Visual fields are measured by mapping out blind or visually impaired areas in visual space. The person being tested is asked to report when spots of light or various types of patterns presented at different viewing angles in every direction can be seen while the person is looking straight ahead.

The impact of vision loss on functional abilities can be evaluated with visual performance measures or patient-reported measures. A questionnaire can be used to assess a patient’s own perception of his or her ability to perform specific types of activities in everyday life. Functioning and well-being are often assessed by using questionnaires such as

the National Eye Institute’s Visual Function Questionnaire (NEI VFQ). The instrument typically uses a list of statements about specific activities that are answered in terms of frequency of occurrence, level of agreement, perceived difficulty or some other response to each item using a categorical response rating scale.

For the NIH Toolbox, we have selected three instruments for vision assessment: a measure of visual acuity, a measure of visual field, and a self-reported measure of functional ability and well-being. Visual acuity will be evaluated using the ETDRS visual acuity test, an existing standardized instrument designed to allow for comparison of data across research studies. The measure will be embedded within the Dynamic Visual Acuity Test being used to assess vestibular balance. For younger children, the letters H-O-T-V and symbols will be used.

Visual field detection will be measured with a modified motion perimetry instrument specifically designed for NIH Toolbox. Motion detection perimetry is a computer program developed at the University of Iowa that maps the visual field by measuring a subject’s ability to detect a coherent shift in position of dots in a defined circular area against a background of fixed dots. The main outcome measure, motion size threshold, is defined as the smallest detectable circular area in which dot motion is detected. The NIH Toolbox version is a binocular test of the central 40° of the visual field. The next steps in the development of the motion perimetry instrument include test validation and determination of normative limits.

A modified instrument to measure visual function based on existing vision-specific quality of life instruments was developed for NIH Toolbox using the PROMIS approach (De Walt, 2007). A systematic review of relevant quality of life instruments was conducted. *(continued on page 4)*

Vision Instruments

- Visual Acuity
- Motion Detection Perimetry Test
- Visual Function Questionnaire

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Upcoming 2009 Conference Presentations

July 11-16, 2009

International Conference on
Alzheimer's Disease
Vienna, Austria

The NIH Toolbox:

*Assessment for Neurological
and Behavioral Function*

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October 7-11, 2009

American Congress of
Rehabilitation Medicine

American Society of
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Denver, CO

*Disability Access and the
NIH Toolbox: Evaluation
and Implementation of Acces-
sibility Guidelines in Health
Outcome Measurement*

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Vestibular Balance

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In developing an operational definition of vestibular function, the Vestibular Team determined that physiological and functional issues and the multimodal interdependence evident in the functions that vestibular input is involved in be addressed. The vestibular system is bilateral, with central and peripheral neural components. Those in the canals have major contribution for the vestibular ocular reflex (VOR), which corrects for retinal slip, preventing oscillopsia (gaze stabilization) when the head is moving. Those in the otoliths have primary contribution to the vestibulospinal (Vsp) reflexes, which maintain muscle tone and execute appropriate muscle responses to prevent a loss of balance. The central system involves the interpretation of vestibular inputs and the integration with other sensory inputs to enable these functions (e.g., balance and gaze stabilization). This multimodal integration and the interplay between the cortex, cerebellum, brain stem and spinal cord must be considered when developing tools to measure vestibular function. Furthermore, age-related changes (either developmental or decline due to advanced age) and injury or pathology occur in the senses and motor abilities that affect balance, spatial orientation and gaze stability. These changes have been referred to as multisensory system abilities or impairments. Therefore, it is important that the tests selected are valid and sensitive to the identification of vestibular gaze stability and vestibular balance, and that the measures are sensitive to typical changes across the lifespan.

Based on a comprehensive literature review, the Vestibular Team identified 33 potential tests. Six were screened out due to the reliance on self-report, high cost or expertise required to complete the test. An in-depth review on the remaining 27 tests, which were categorized by contribution to gaze stability (VOR function) or vestibular balance (Vsp

function) resulted in additional test elimination due to lack of reliability, sensitivity or high cost. The Vestibular Team decided on two tests for inclusion in the Toolbox: 1) dynamic visual acuity (DVA) as a measure of vestibular gaze stability and 2) a modified test of sensory interaction for balance to measure vestibular balance.

In the current development and validation phase, it was agreed that the DVA and vestibular balance measure provide measures that can be used as part of the Vision domain (acuity) and the Motor domain (balance), respectively. Thus, coordination is on-going between the Vestibular and Vision Teams and between the Vestibular and Motor Teams to develop and validate tests. While these measures have a well established history of use in clinical practice and research, inclusion in the Toolbox requires some modification and development. These tests are being developed and validated for use in the Toolbox:

DVA: A minimal cost computerized test that incorporates a pediatric version and minimizes motor, language, and cultural effects is being developed. Within this phase, we will determine at what age the use of letters versus symbols to test acuity is most effective, reliable and valid.

The test requires that an individual identify the optotype (letter or symbol) first with the head kept stationary (standard visual acuity test) and again with the head moving to the left or right at 120-180 degrees (*continued on page 4*)

Vestibular Balance Team

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Vestibular Balance Instruments

Dynamic Visual Acuity Test
Modified Test of Sensory Interac-
tion for Balance

Olfaction (continued from first page) individual's olfactory sensitivity falls within normal ranges. Odor identification is evaluated by presenting individuals with a variety of recognizable odors at supra-threshold concentrations (i.e., above the detection level for most subjects) and requiring them to choose the correct identity of the odor from a set of possible names or pictures. Performance can be compared with age- and gender-adjusted norms. The quality or hedonic valence of an odor is another important element of olfactory perception and, particularly among children, can be measured using scales of hedonic judgments of odors.

While the instruments available for evaluating smell ability are not as plentiful as those for other sensory domains (e.g., vision/audition), there are several standardized instruments which have been used to evaluate olfaction in both adults and children. Following an extensive literature review, the domain team determined that for adults, several of these tests were suitable for further investigation or development: the Brief Smell Identification Test (B-SIT, 12 item scratch 'n sniff format) and the San Diego Odor Identification Test (SDOIT- 8 everyday food or confection items placed in opaque plastic jars). The 12 items on the B-SIT do not overlap with those in the SDOIT, thus allowing us to identify the best 8 or 10 odors for a brief olfactory assessment. The San Diego Odor Identification Test was originally developed for children between 5-12 years of age, and children in this age group could identify the eight items with high reliability. Given the need to extend the pediatric assessment down to age 3, however, additional validation of the familiarity of these items for the younger cohort was needed, as well as several changes to the stimuli and response format. Specifically, we (1) have added four odors, bringing the total to twelve, although each child only evaluates six; (2) are now embodying them in standardized micro-encapsulated scratch 'n sniff stickers; and (3) are asking each child to choose the best match for each odor from only four pictures representing the correct and three distractor odor sources.

Olfaction Team

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Olfaction Instruments

Adult Odor Identification
Pediatric Odor Identification

Vestibular Balance (cont'd)

per second (monitored by a rate sensor on a headband). The difference in scores achieved between the two conditions is the DVA score, which represents vestibular contribution to gaze stability.

Balance: A tool that quantifies postural sway using an accelerometer is being developed. The test involves asking subjects to stand still under varying conditions of vision (eyes open and eyes closed), stance (single leg and double leg), and surface (solid floor, thick cushion). Collaboration and coordination with the Motor Domain will be on-going to finalize test parameters, protocol for use across the lifespan, and measurement algorithms to test vestibular

versus general balance abilities.

Vision (cont'd) Questionnaire items were binned into groups according to meaning and construct latency, followed by a reduction of items to a unique, but comprehensive set of questions. To refine the instrument, cognitive interviews were completed in a small set of individuals to obtain feedback on item comprehensibility, language, ambiguity, and relevance. The modified instrument will be validated in a set of normal youth and adults.

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