

cannot detect the rare variants of small or moderate effects, in either one or multiple genes, that might still comprise an important part of the whole picture.

**Vincenzo Bonifati**

Department of Clinical Genetics, Erasmus Medical Center, 3000 CA Rotterdam, Netherlands  
v.bonifati@erasmusmc.nl

I have no conflicts of interest.

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## Assessment of neurological and behavioural function: the NIH Toolbox

The National Institutes of Health Toolbox for the Assessment of Neurological and Behavioral Function (NIH Toolbox) initiative, part of the NIH Blueprint for Neuroscience Research (NIH Blueprint) initiative, is developing brief yet comprehensive instruments to measure motor, cognitive, sensory, and emotional function. When completed, the Toolbox should provide a standard set of concise, well validated measures that will be available in English and Spanish for longitudinal or epidemiological studies and also for prevention or intervention trials of people aged 3–85 years.

The need for brief and uniform instruments to facilitate the assessment of neurological and behavioural function in large-scale studies was initially identified by the trans-NIH Cognitive and Emotional Health Project (CEHP) Critical Evaluation Study Committee.<sup>1</sup> Although this Committee focused on cognition and emotion, most of its findings were also applicable to other domains such as motor and sensory health, and were incorporated into the NIH Blueprint development team's recommendations for the Toolbox. The underlying proposition was that a focus on optimum functioning and health might lead to the identification of a different set of risk factors and thus different prevention strategies, rather than the conventional focus on single disease outcomes. This approach could apply to studies on neurological and behavioural

function, and also to studies outside these areas (eg, cardiovascular research) that might wish to assess these functions in addition to their specific primary outcome measures. However, there are few assessment tools that reliably reflect everyday function and monitor health rather than identify illness and disability. Furthermore, current instruments for assessing brain function are not used uniformly, making comparison of data across studies difficult. This variability limits the ability to undertake combined analyses to design strategies that could both maintain health and prevent disease. The NIH Toolbox, envisioned as a standard set of measures of function, is intended to address these needs. Additionally, the NIH Toolbox is designed to be brief, inexpensive, reliable over time, and to incorporate state-of-the-art psychometric properties and advances in technology (eg, computerised administration and adaptive testing when applicable).

To ascertain the needs of potential end users, we first solicited expert input on criteria that the Toolbox should meet, and the specific areas (subdomains) of function it should target, and reviewed relevant existing measures. To date we have undertaken two internet-based interviews with NIH-funded researchers (n=150 and 143), one phone-based interview of a subset of those interviewees (n=44), and a systematic literature review for each of our targeted domains. These

For more on the NIH Blueprint see <http://www.neuroscienceblueprint.nih.gov>

investigations concluded that the Toolbox should take a maximum of 2 h to administer (30 min for individual domain batteries), be accurate across the range of normal function, be understandable for participants with low literacy and of diverse ethnic origin, and be easy to undertake, score, and interpret with minimal cost. After an extensive review of 1391 existing instruments, a combination of new and existing instruments has been assembled. A total of 48 assessments to measure the domains listed in the panel are under development.

These assessments have been reviewed by five independent US-based expert working groups, covering issues related to culture, language, accessibility, and use in paediatric and geriatric populations. Each of these groups evaluated and modified the instruments, ensuring that the items were culturally sensitive and conceptually appropriate to provide a harmonised Spanish translation, to ensure that the items were accessible for people with sensory and motor handicaps, and to ensure suitability for use from children to the elderly. Candidate measures without existing validity data are undergoing evaluation of psychometric properties, including calibration and external validity testing against gold-standard measures, with sample sizes ranging from 100 to 7500 per assessment. The selection of final measures will be based on the results of these studies. In late 2010, we will commence a stratified random sampling (n=4500) of the US general population to obtain normative information (including evaluation at 1 week and after a longer period to assess test-retest reliability and practice effects), in both English-speaking and Spanish-speaking populations. Furthermore, we are working with researchers outside our development group to assess the validity of the Toolbox measures in targeted disease groups.

Although developed in the USA, we hope that the NIH Toolbox will serve as an international resource. It will be freely available for further translation and normative activities. The entire range of instruments, scoring algorithms, and norms will be provided royalty-free for the international research community. Designed to be flexible, this resource could be used as a whole or at the individual domain level. The Toolbox is also designed to be dynamic—ensuring longitudinal data continuity over time, and adaptability in response to advances in science and technology. Our

#### Panel: Domains assessed by NIH Toolbox instruments\*

##### Cognitive function

- Executive function
- Episodic memory
- Working memory
- Processing speed
- Language
- Attention

##### Emotional health

- Negative affect
- Positive affect
- Social relationships
- Stress and coping

##### Motor function

- Locomotion
- Strength
- Non-vestibular balance
- Endurance
- Dexterity

##### Sensory function

- Vision
- Audition
- Vestibular balance
- Somatosensation
- Taste
- Olfaction

NIH=National Institutes of Health. \*The participating NIH Institutes, Centers, and Offices for the NIH Blueprint include NCCAM, NCCR, NEI, NIA, NIAAA, NIBIB, NICHD, NIDA, NIDCD, NIDCR, NIEHS, NIGMS, NIMH, NINDS, NINR, and OBSSR.

development team of more than 254 scientists from 96 academic institutions, numerous NIH Institutes, and other organisations with expertise in instrument development welcomes your comments at the Toolbox website and looks forward to sharing our validation data and final instruments with the scientific community in the coming months and years.

*Richard C Gershon, David Cella, Nathan A Fox,*

*Richard J Havlik, Hugh C Hendrie, Molly V Wagster*

Northwestern University, Department of Medical Social Sciences, Chicago, IL, USA (RCG, DC); University of Maryland, Department of Human Development, College Park, MD, USA (NAF); Westat, Rockville, MD, USA (RJH); Indiana University Center for Aging Research, Indianapolis, IN, USA (HCH); National Institute on Aging, Bethesda, MD, USA (MVW)  
gershon@northwestern.edu

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For more on the Toolbox and to submit your comments see <http://www.nihtoolbox.org>