Out of the Gate

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This newsletter highlights the initial work done to identify and define the sub-domains which will make up the assessment of Cognitive Health to be included in the final NIH Toolbox for Health Assessment which measures emotional, cognitive, motor and sensory function. Since our last newsletter, we have conducted expert interviews with over 44 potential users, including both pediatric and aging specialists across our four primary domains. These data were combined with literature reviews and our initial request for information responses from 147 scientists to prioritize the individual sub-domains to be included in The Toolbox. The following pages highlight the conclusions of these efforts, including conceptual definitions of cognition sub-domains. Future issues of this newsletter will feature conceptual definitions of the remaining three primary domains - a focus on motor function will be next.

Our efforts are now taking on even stronger momentum as each domain working group has increased in size to include consultants with expertise in each of the selected sub-domains. Individual sub-domain working groups are in the process of reviewing their respective share of the 1300+ existing instruments which we have indentified thus far as having potential use as part of the Toolbox effort. As always, please contact me directly with any ideas or questions.

Cognition - and the NIH Toolbox

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Cognition is defined as “The process of knowing and, more precisely, the process of being aware, knowing, thinking, learning and judging. The study of cognition touches on the fields of psychology, linguistics, computer science, neuroscience, mathematics, ethology and philosophy.” (Webster’s Medical Dictionary) Cognition is not unitary but instead is comprised of a number of processes carried out by the brain that serve to represent the external world, create a “history” of the past to guide future behavior and decisions, and permit planning and execution of complex behaviors. Examples of the domains of mental function that make up cognition in its broadest sense are perception, attention, memory and learning, judgment, abstraction, reasoning, language in all its modalities, and executive functions. Some mental processes, such as those making up complex auditory, visual and somatosensory perception, serve to translate the external world into mental representations that can then be stored, manipulated and recreated. Others serve to translate thoughts into conventional symbols (e.g., words) so that they can be communicated to others. Yet others generally modulate the speed and fidelity of information processing resources.

The measurement of cognition is essential to any study of health and well-being. Even if the target of study is not cognition itself, for a number of reasons, measures of cognition should be included in large-scale epidemiologic studies and in experimental studies of health and development. First, many studies make the assumption of “normal” cognition in volunteer participants. Objective cognitive measures can provide information that can be used to further analyze results as they apply to individuals with a range of cognitive abilities. (cont'd page 4)
Cognitive Sub-domain Selection

Sub-domain selection was based upon literature reviews, expert interviews and a field survey of 147 NIH-funded researchers.

One hundred and two of the survey respondents indicated familiarity with cognitive function as follows:

Please indicate four areas of cognitive functioning that you think are most relevant for the Toolbox measures to assess in large scale longitudinal and epidemiological studies and clinical trials. For each, also indicate whether you think they should be evaluated by self-report, objective testing or both.

<table>
<thead>
<tr>
<th></th>
<th>4 most relevant areas</th>
<th>Best if assessed objectively</th>
<th>Best if assessed with self-report</th>
<th>Both objective and self-report</th>
</tr>
</thead>
<tbody>
<tr>
<td>General or global function</td>
<td>66%</td>
<td>55%</td>
<td>2%</td>
<td>41%</td>
</tr>
<tr>
<td>Memory</td>
<td>80%</td>
<td>58%</td>
<td>1%</td>
<td>37%</td>
</tr>
<tr>
<td>Executive Function</td>
<td>77%</td>
<td>59%</td>
<td>3%</td>
<td>36%</td>
</tr>
<tr>
<td>Language</td>
<td>70%</td>
<td>75%</td>
<td>4%</td>
<td>16%</td>
</tr>
<tr>
<td>Visiospatial</td>
<td>68%</td>
<td>84%</td>
<td>2%</td>
<td>11%</td>
</tr>
<tr>
<td>Attention</td>
<td>67%</td>
<td>59%</td>
<td>0%</td>
<td>31%</td>
</tr>
<tr>
<td>Processing Speed</td>
<td>60%</td>
<td>83%</td>
<td>0%</td>
<td>31%</td>
</tr>
</tbody>
</table>

Cognitive Sub-domains

In consultation with NIH representatives, the following sub-domains were selected for further exploration. Sub-domains were ranked such that the top 4 listed were identified as measuring distinct cognitive abilities.

Executive Function (EF): is defined as the capacity to plan, organize, and monitor the execution of behaviors that are strategically directed in a goal-oriented manner. Toolbox will focus on the following components of EF: 1) set shifting, or the capacity for switching among multiple aspects of a strategy or task; 2) inhibition of automatic response tendencies that may interfere with achieving a goal; and 3) fluency, the ability to utilize one or more strategies to rapidly generate specific exemplars of a response category (e.g., words that begin with specific letters or types of animals) while avoiding response repetition.

Episodic Memory (EM): refers to cognitive processes involved in the acquisition, storage and retrieval of NEW information. It involves conscious recollection of information learned within a context. The term “learning” refers to the acquisition of skills and knowledge while the term “memory” refers to the persistence of this learning over time and/or the facility with which one is able to spontaneously recall the information following a delay. EM can be verbal, as in remembering a conversation or a list of grocery items, or nonverbal, as in imagining a place one visited or a picture one saw a week ago.

Working Memory (WM): refers to a limited-capacity storage buffer that becomes overloaded when the amount of information exceeds capacity. The concept of working memory (WM) refers to the capacity of an individual to 1) process information across a series of tasks and modalities, 2) to hold the information in a short-term buffer, 3) to manipulate the information, and 4) to hold the products in the same short-term buffer. This concept updates the traditional construct of “short-term memory”, which refers to a passive storage buffer, to include the notion of an active computational workspace. WM overlaps with constructs of attention and EF.
Cognitive Sub-domains (cont’d)

**Processing Speed (PS):** is defined as either the amount of time it takes to process a set amount of information, or, conversely, the amount of information that can be processed within a certain unit of time. It is a measure that reflects mental efficiency. PS is central for many cognitive functions and domains, and is sensitive to change and/or disease.

**Language:** refers to a set of mental processes that serve to translate thought into symbols (words, gestures) that can be shared among individuals for purposes of communication. Toolbox will focus on two aspects of language. The first is vocabulary knowledge, which is fundamental to the growth of knowledge and which also has a very high association with overall intelligence, or what has been called the “G-factor”. The second is oral reading skill, which reflects level and quality of prior educational experiences, and provides a fairly robust indication of verbal intelligence that is relatively undisturbed by many medical conditions that affect the brain.

**Attention:** refers to the allocation of one’s limited capacities to deal with an abundance of environmental stimulation and is the foundation for all other types of mental processes. There are several different forms of attention, including sustained, selective, and divided. Sustained attention is closely linked to the level of wakefulness or the maintenance of an alert state. Selective attention serves to direct sensory and thought processes to a particular stimulus or sector of the visual field so that action can be taken. Divided attention is the ability to attend to more than one stimulus, spatial sector or modality simultaneously, and overlaps with EF.

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**Poster Recently Presented at the Alzheimer’s Disease Biomarkers Meeting**
*(an ancillary meeting of Alzheimer’s Association International Conference on Prevention of Dementia)*

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Secondly, in intervention studies that require subjects to follow instructions, cognition may be a “hidden variable” that could contribute to the success or failure of the intervention. Thirdly, adequate cognition is essential to autonomy, academic achievement, and career accomplishments and can be a powerful modulator of risks in epidemiologic studies. Fourthly, abnormalities of cognition are frequently an indicator of disease. Thus, cognitive measures can further characterize clinical samples.

And finally, cognition changes throughout the life span and thus measurement of cognition is especially important in characterizing different target age groups, as well as for longitudinal tracking of cohorts.

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