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Special Series Introduction: NIH EXAMINER and the Assessment of Executive Functioning

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Executive functions are of increasing interest and importance in cognitive neuroscience and clinical assessment. Broadly, executive functioning has been defined as the ability to organize and engage in goal-directed behavior. These multi-faceted and integrated functions support the organization, initiation and control of cognition and behavior, facilitate awareness of and adherence to social norms, and contribute to emotion regulation. They are mediated by broad neuro-anatomical systems that include lateral and medial frontal lobes, frontal-subcortical loops, frontal-parietal networks, and underlying white matter tracts. A multitude of neuro-behavioral conditions impact executive functions, and executive impairment may be the core cognitive deficit in disorders like attention-deficit/hyperactivity disorder (Barkley, 1997), behavioral variant frontotemporal dementia (Rascovsky et al., 2011), subcortical ischemic vascular disease (Reed et al., 2004), traumatic brain injury (Levin & Hanten, 2005), Huntington's disease (Peinemann et al., 2005), and schizophrenia (Altshuler et al., 2004). Improvement in executive abilities over childhood and decline during late life are salient and ecologically meaningful features of typical lifespan development.

Executive functioning is critical for successful adaptation, and the importance of targeting these skills in clinical research cannot be overstated. However, clinical investigators interested in measuring executive functioning face several challenges. The sheer number of available tasks purported to measure executive function is overwhelming, and there is little consensus on how executive functioning can be best parsed into meaningful components. Variability in instrumentation also makes it more difficult to merge datasets from different investigators. Clinical neuropsychological instruments are often multifactorial, drawing on several non-executive component skills, and psychometric properties (e.g., test–retest reliability), imperative for clinical trials, are often not well specified.

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In recognition of the need for broadly accepted measurement tools, the National Institutes of Health (NIH) committed to the development of psychometrically robust measures of executive function that would be accepted by the neurology clinical trials and clinical research communities. NIH identified a need for an executive function battery that was applicable to a broad range of neurological conditions and ages, assessed multiple domains of executive functioning, could be modified to meet specific research needs, provided English and Spanish versions, and was related to functional outcomes. The NIH EXAMINER (Executive Abilities: Measures and Instruments for Neurobehavioral Evaluation and Research) is the product of this initiative. NIH EXAMINER consists of a series of both computerized and paper-and-pencil tasks that target working memory, inhibition, set shifting, fluency, insight, planning, social cognition, and behavior. In addition to individual test scores, composite scores based on item response theory are available. NIH EXAMINER was part of a broader NIH effort to develop widely accepted assessment tools, including the Patient Reported Outcomes Measurement Information System (PROMIS®), a system of patient-report measures of physical, mental, and social well-being, and the NIH Toolbox, which features self-contained batteries that assess cognition, sensation, movement, and emotion (Weintraub et al., 2013).

This special series presents several articles that describe NIH EXAMINER and illustrates ways in which the battery can be used in clinical research. The first article by Kramer and colleagues describes the methodology underlying the conceptual basis for battery development. The authors outline each targeted domain of executive functioning and review the tasks that were included in the final battery. They also describe the data collection phase of the project that involved several sites across the country and included over 1200 subjects, approximately a third of whom were under 17 years of age, and approximately half of whom carried a neurologic or neurobehavioral diagnosis. The article also provides an overview of the rationale and methods for combining individual test scores into an Executive

Composite score and Working Memory, Fluency, and Cognitive Control scores; more details about scale construction are available in an online supplement.

This methods paper is followed by a validation study by Possin and colleagues. Important goals for any neuropsychological test are to predict real world behavior and help generate hypotheses about underlying neuroanatomy. Possin et al. used the NIH EXAMINER'S Executive Composite score, which combines measures of inhibition, set-shifting, fluency, and working memory into a single, psychometrically robust score. They tested the validity of the Executive Composite score in two ways. First, they used the Frontal Systems Behavior Scale (FrSBe) (Malloy & Grace, 2005), an informant-based measure, as an index of real-world executive behavior, and showed that after controlling for demographic variables, the Executive Composite accounted for 28% of the variance in the FrSBe. The composite score remained a significant predictor of the FrSBe even after including two widely used executive function tests (Trails B and Stroop) as covariates. Second, Possin et al. used voxel-based morphometry to show that lower Executive Composite scores were associated with smaller dorsolateral prefrontal volumes bilaterally.

The remainder of the papers in this series used NIH EXAMINER as a tool in clinical research studies. Two studies looking at different pediatric populations used the psychometrically equivalent Working Memory, Cognitive Control, and Fluency scores. Schatz et al. studied a group of children with sickle cell anemia, a group with a high degree of cerebrovascular morbidities. While cognitive deficits (attention, executive functioning) have been documented in individuals with sickle cell disease (Berkelhammer et al., 2007), it is not entirely clear whether they are due to the indirect effects of social and environmental disadvantages and chronic illness or due to underlying cerebrovascular injury. Schatz et al. used the NIH EXAMINER to assess executive functioning in children with sickle cell disease, hypothesizing that performance would be associated with the degree of cerebrovascular injury. They specifically targeted the size of the corpus callosum in light of their previous work showing that it serves as a robust index of general white matter integrity that is associated with neurologic disease in SCD (Schatz & Buzan, 2006). They studied 32 children with sickle cell anemia with varying degree of neurologic morbidity and 60 matched controls. Performance on the Executive Composite and the Working Memory, Cognitive Control, and Fluency scores declined with increasing clinical history of neurologic morbidity. In addition, the NIH EXAMINER scores were inversely correlated with midsagittal corpus callosum area.

Schreiber and colleagues posed the question as to whether specific aspects of executive function are differentially affected in ADHD. To date, given that executive functioning is broadly defined, there is not a widely accepted pattern of performance on measures of executive functioning in the ADHD population (Doyle, 2006; Wodka et al., 2008). This study compared 32 children ages 8–15 years diagnosed with ADHD and no comorbid learning or conduct disorders, with 60 age and gender matched healthy controls. Children with ADHD performed worse on the Working Memory score compared with controls, whereas no differences were found on the Cognitive Control or Fluency scores. For children with ADHD, poorer working memory, but not cognitive control or fluency, predicted parent report of child learning problems.

Because executive functioning is so broadly defined, measuring the neural correlates of executive functioning has been challenging. Robinson et al. used individual NIH EXAMINER tasks to investigate the underlying neuroanatomy of different aspects of executive functioning. They grouped NIH EXAMINER tasks into three general domains: Cognitive, social/emotional, and insight. They hypothesized that cognitive measures of executive functioning would be associated with dorsolateral prefrontal cortex and that social/emotional and insight would be associated with ventromedial prefrontal cortex. Subjects were 37 patients with focal lesions to the frontal lobes and 25 patients with non-frontal focal lesions. Using voxel-based lesion-symptom mapping, their hypothesis were confirmed, as they found that damage to the ventromedial prefrontal cortex was predominately associated with deficits in social/emotional aspects of executive functioning, while damage to dorsolateral prefrontal cortex and anterior cingulate was predominately associated with deficits in cognitive aspects of executive function.

How to best conceptualize and operationalize executive functioning continues to be debated in the neuropsychological literature. Although there is general agreement that executive functioning reflects the capacity to engage in goal-oriented behavior, clinicians and researchers apply a broad range of tasks that tap constructs like fluency, set shifting, inhibition, working memory, abstract reasoning, organization, planning, novel problem solving, insight, and conflict monitoring (Lezak, Howieson, Bigler, & Tranel, 2012). Considerable methodological heterogeneity is evident even within a specified subdomain. Working memory tasks, for example, encompass backward spans, dual-task costs, self-ordered pointing tests, delayed match to sample, and listening span tests (Chiappe, Hasher, & Siegel, 2000), and these tasks differentially emphasize on-line storage of information, inhibition or manipulation of information, and updating. The confluence of executive functioning within other cognitive domains is evidenced by the observation by Rabin et al. (2005) that measures of episodic memory and figure copy were included in clinicians' ratings of the most used executive function tests. Some investigators suggest that the construct of executive functioning may overlap so much with processing speed and fluid intelligence as to be redundant (Salthouse, 1996; Salthouse, Atkinson, & Berish, 2003).

The goal of NIH EXAMINER was not to resolve this debate, but rather to provide a brief, readily available, and psychometrically sound set of instruments that would prove useful to researchers and clinical trial specialists. Studies to date are promising. Reliability data reported in the manual indicate that the scales are robust enough for clinical trials. Research reported in this series demonstrates an association with functional status and suggests that lateral and medial frontal regions, frontal-parietal networks, and underlying white matter are important neuroanatomical substrates (Luks et al., 2010; Possin, LaMarre, Wood, Mungas, & Kramer, 2013). Work by Robinson et al. and others (Krueger et al., 2011; Possin, Feigenbaum et al., 2013) highlight the value of considering both cognitive and social/emotional aspects of goal-oriented behavior. Ultimately, of course, the utility of any measurement instrument depends on an accumulated body of empirical support, and additional studies using NIH EXAMINER to assess behavior, understand clinical populations, predict anatomy, and show cognitive change in response to interventions are required.

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