Research and clinical criteria for development of neurobehavioral test batteries

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Research and Clinical Criteria for Development of Neurobehavioral Test Batteries

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Because neuropsychological testing can detect subtle changes in central nervous system function resulting from occupational and environmental exposure to toxic chemicals, it has been widely used in behavioral neurotoxicologic investigations. However, work in this field often has ignored the distinction between clinical and research testing when applying these assessment techniques. Experimental studies generally compare groups of subjects on specific outcome measures, whereas clinical work usually is focused on diagnosis and treatment of individual patients. Therefore, the inclusion criteria applicable to the selection of neuropsychological test batteries are different in research and clinical settings. Issues germane to test selection in research settings include sensitivity to neurotoxins, psychometric standards, sensitivity to central nervous system dysfunction, overview of cognitive functions, sampling of cognitive processing, sampling of output modalities, and examination of theoretical constructs. The usual questions asked in the clinical setting can be addressed most efficiently when the following issues are considered in test selection: sensitivity to specific toxicant exposure, estimation of native ability patterns, differential diagnosis, developmental specificity of tests and exposure effects, and description of patterns of cognitive strengths and weaknesses.

Although many recent publications have focused on the use of behavioral test batteries to investigate the central nervous system (CNS) effects of occupational and environmental exposure to neurotoxins, it is clear there is a great deal of confusion concerning the settings in which specific batteries should be used.

Based on a critical review of the literature, it is apparent that at least three errors are frequently made in behavioral neurotoxicologic studies using neuropsychological methods. One, batteries developed for research studies of exposure to neurotoxic substances are applied to clinical settings. Two, clinical batteries are inappropriately used in epidemiologic research studies. Three, investigators fail to clearly explicate the hypotheses they intend to entertain through the application of particular neurobehavioral tests or test batteries.

The two situations in which psychoneurological test batteries are frequently used (the epidemiologic investigation of CNS effects of known or suspected neurotoxins and the clinical investigation of possible CNS impairment in individual patients with neurotoxin exposure) demand different information from neuropsychological testing and involve different constraints on testing. Research situations usually attempt to define behavioral outcomes in groups; clinical
Evaluations generally focus on individual diagnoses and treatment. Therefore, the criteria for determining test batteries vary for the two situations. In a previous article, we discussed criteria for selecting neuropsychological tests for epidemiologic studies and evaluated existing neurobehavioral batteries using these criteria. In this article, we briefly review those previously published criteria for test selection in epidemiologic studies and then discuss clinical battery test selection in detail.

**Epidemiologic Study Batteries**

A number of different test batteries are being used in epidemiologic study designs to quantify the CNS effects of specific neurotoxins. Each battery has its own strengths and weaknesses in terms of what it will reveal about neurobehavioral effects of toxin exposure. When selecting an appropriate battery of tests in an epidemiologic study, the investigator should consider a number of specific issues (Table 1).

**Sensitivity to Neurotoxins**

Test batteries designed for studies in behavioral neurotoxicology most commonly have been developed to include tests that the experimenter, by reviewing the research literature, knows to be sensitive to the neurotoxin(s) in question. Although this is the most common criterion used, it often is not the most informative. Using this inclusion criterion, tests have been used repeatedly in studies with no new information being acquired after several repetitions.

**Psychometric Concerns**

(1) Consideration of the quantitative measures of validity (eg sensitivity, specificity, predictive value) and the reliability of the specific tests selected should be recognized in development of the battery. (2) Appropriate attention to statistical measures concerning the distribution of test scores is necessary. (3) Tests with a reasonable range of performance outcome measures should be included in batteries. That is, the tests should have continuous scores as their outcome; “impaired” versus “unimpaired” categories are relatively uninformative. (4) Finally, tests included in the battery should have a reasonable “floor” and a reasonable “ceiling” so that restriction of range is not confined to one end of the range.

**Sensitivity to Central Nervous System Dysfunction**

Tests included in a neurotoxicologic study of neurobehavioral outcome should include tests that are known from previous research or clinical work to be sensitive to CNS dysfunction. Although it is often assumed that any behavioral test measures CNS function, this is not always so. Some tests can be failed because of motor deficits secondary to peripheral neuropathy; eg, a subject with solvent exposure may be slowed on a block design test because of numbness in the fingers, not because of a centrally based loss of spatial problem solving. Other tests may reflect more about background cultural or demographic variables than about CNS function. Information is available on the brain-behavior relationships revealed by many neuropsychological tests, ie, research indicates that specific types of neuropathology (lesion sites, disease states, pathological degeneration of certain types) are associated with impairment on specific neuropsychological tests. When choosing a behavioral task as a measure of CNS function, it is essential to know both that the task has been shown to be sensitive to brain damage in other studies and to know the specific brain-behavior relationships that may be revealed by the task. For some batteries used in epidemiological studies in behavioral neurotoxicology to date, investigators have now shown that the tests used have been validated in these ways.

**Overview of Cognitive Functions**

Especially when evaluating the effects of a new substance suspected to be neurotoxic, it often is valuable to design a test battery that will sample enough different types of cognitive abilities to provide an accurate picture of impaired versus retained abilities in the face of the exposure. The battery should thus include some sampling of as many cognitive domains as possible. These domains are clearly listed in the World Health Organization/National Institute for Occupational Safety & Health (WHO/NIOSH) recommended full test battery and in a recent article on toxic assessment and include: (1) attention and executive function, (2) visuospatial skills, (3) affect, (4) memory (anterograde and retrograde), (5) language abilities and reasoning, and (6) motor skills. When sufficient sampling of cognitive domains occurs, patterns of cognitive function begin to emerge when describing neurotoxic effects that may lead to predictions about cerebral sites of neurotoxic effects.

**Sampling of Underlying Cognitive Processes**

Test batteries in epidemiologic studies should include tasks that allow the investigator to consider specific cognitive processing deficits that may
Contribute to the intellectual loss observed during testing. For example, attentional problems can cause impaired scores on short-term memory tasks or motor problems can affect performance on visuospatial construction tasks. It is necessary to consider as many underlying processing deficits as possible when designing a test battery and interpreting results once a battery has been used.

Multiple Output Modalities

Tests that allow more than one performance modality from the subject should be included. That is, batteries should not simply include tasks involving pushing buttons on a computer or tasks using verbal responses. Single modality testing severely constrains the range of neuropsychological responding available to the subject. Pushing computer buttons, for example, relies heavily on visual scanning and manual motor coordination; such testing usually involves reaction to highly structured test requirements. Spoken tests, in contrast, rely disproportionately on linguistic aptitudes and expressive retrieval of information from semantic memory.

Theoretical Constructs

Tests that allow the researcher to address theoretical questions should be included in epidemiologic batteries. For example, one could include tests that assess different aspects of information processing or that address different neuropsychological theories of the likely cerebral localization of brain damage associated with a specific neurotoxic exposure.

Of the published neurobehavioral test batteries used in behavioral neurotoxicology, very few address all the psychoneuropsychological inclusion issues outlined above. The full set of WHO/NIOSH recommended tests and the extensive clinical battery developed by Baker, White, and Murawski and by White et al. do allow a sufficient range of tests to address all seven issues. However, in individual epidemiologic studies it is essential to choose a battery specifically designed to answer the specific hypotheses raised by the study investigators. Generally, because of time/cost constraints this would not include all tests from any one of the above mentioned batteries, but choices should reflect a thoughtful selection on the part of the investigator based on consideration of the proposed inclusion issues.

Clinical Neurobehavioral Batteries

The purposes of a clinical neurobehavioral test battery are quite different from those of an epidemiologic battery. The focus is on diagnosis: describing cognitive changes within individual patients (rather than groups), determining a diagnosis, and providing a treatment plan for individual patients. Single case clinical studies may provide valuable clues to understanding the behavioral effects of neurotoxins and to developing theories of the underlying mechanisms of neurotoxic effects; however, they usually represent descriptions of carefully completed clinical evaluations, but their design is not oriented primarily toward research.

Issues to Consider in Test Selection

A patient with a history of neurotoxin exposure usually is referred for behavioral evaluation because the patient either complains about cognitive or personality abnormalities or shows such behavioral abnormalities during medical examination or interview. A sophisticated neuropsychological evaluation can provide a wealth of clinical information, including an elaborate description of a patient's mental status and diagnostic conclusions regarding any cognitive abnormalities observed. The usual questions asked when such a patient is referred are elaborated below.

1. Does the patient show any behavioral or cognitive abnormalities? If so, what are they?

A thorough neuropsychological examination can provide a great deal of information on cognitive functioning in the patient and can address changes in mood and personality. To be comprehensive, the battery of assessment techniques and interview format used must cover a range of cognitive functions including attention and executive functioning, verbal and language skills, visuospatial abilities, motor coordination, and memory (short-term and retrograde). Measures of personality and affective symptoms are also critical to a comprehensive examination. A summary of the types of tests that can be used to assess these behavioral domains is shown in Table 2.

2. What structures in the brain show evidence of dysfunction on neuropsychological testing?

The practice of neuropsychology grew out of the early observation that structures of the brain have specific functions associated with them (notion of cerebral specialization). Broca noted in 1861 that lesions in the left hemisphere produced aphasic symptoms. Other investigators began to describe specific visuospatial deficits associated with lesions in the right cerebral hemisphere and reasoning impairments in patients with frontal lobe lesions. The study of cerebral specialization has been well developed in this century, and psychological testing has provided a powerful measurement tool in these studies. Psychological tests can be standardized in their administration and scoring and, when published and used clinically, have normative scores (e.g., percentiles, t scores) available to psychometrically interpret a person's raw scores. These normative scores often are adjusted by important demographic variables such as gender, age, and education. In addition, there are literally dozens of psychological tests that have been applied to patient groups with well-documented, specific types of brain damage; there is thus a great deal of information on which tests measure dysfunction in various brain structures. For example, the Trails Test is a task with two conditions. In condition A, the patient is required to draw a line connecting an array of numbered dots (1-2-3, etc.). In condition B, the patient must draw a line
<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Implications</th>
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</thead>
<tbody>
<tr>
<td><strong>General intellect</strong></td>
<td></td>
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<tr>
<td>Wechsler IQ tests(^{27}) (WAIS-R, WISC(^{36}), WPPS(^{39}))</td>
<td>Omnibus IQ measures</td>
<td>Overall level of cognitive function compared with population norms</td>
</tr>
<tr>
<td>Peabody Picture Vocabulary Test(^{38})</td>
<td>Single word comprehension</td>
<td>Robust measure of verbal intelligence in adults, can be sensitive to exposure in children</td>
</tr>
<tr>
<td>Stanford-Binet(^{40})</td>
<td>Omnibus IQ measure</td>
<td>Similar to Wechsler tests</td>
</tr>
<tr>
<td>Wide Range Achievement Test—Revised(^{41})</td>
<td>Academic skills in arithmetic, spelling, reading</td>
<td>Robust estimate of premorbid ability patterns in adults, can be sensitive to exposure in children</td>
</tr>
<tr>
<td><strong>Attention, executive functioning</strong></td>
<td></td>
<td>(Attention and executive functioning tasks are sensitive to many types of exposure)</td>
</tr>
<tr>
<td>Digit Span (WAIS-R)(^{27})</td>
<td>Digits forward and backward</td>
<td>Measures simple attention and cognitive tracking</td>
</tr>
<tr>
<td>Arithmetic (Wechsler tests)(^{27})</td>
<td>Oral calculations</td>
<td>Assesses attention, tracking, and calculation</td>
</tr>
<tr>
<td>Trail Making Test(^{12})</td>
<td>Connect-a-dot task requiring sequencing and alternating sequences</td>
<td>Measures attention, sequencing, visual scanning, speed of processing</td>
</tr>
<tr>
<td>Continuous Performance Test(^{42})</td>
<td>Acknowledgment of occurrence of critical stimuli in a series of orally or visually presented stimuli</td>
<td>Assesses attention</td>
</tr>
<tr>
<td>Paced Auditory Serial Addition(^{43})</td>
<td>Serial calculation test</td>
<td></td>
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<tr>
<td>Wisconsin Card Sorting Test(^{44})</td>
<td>Requires subject to infer decision-making rules</td>
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<tr>
<td><strong>Verbal, language</strong></td>
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<tr>
<td>Information (Wechsler tests)(^{27})</td>
<td>Information usually learned in school</td>
<td>Sensitive measure of attention and tracking speed</td>
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<tr>
<td>Vocabulary (Wechsler tests)(^{27})</td>
<td>Verbal vocabulary definitions</td>
<td>Tests ability to think flexibly</td>
</tr>
<tr>
<td>Comprehension (Wechsler tests)(^{27})</td>
<td>Proverb definitions, social judgment, problem solving</td>
<td>(Language tests are sometimes sensitive to exposure in children but are usually robust in adult exposure, except as noted)</td>
</tr>
<tr>
<td>Similarities (Wechsler tests)(^{27})</td>
<td>Inference of similarities between nominative words</td>
<td>Robust estimate of native abilities in adults</td>
</tr>
<tr>
<td>Controlled Oral Word Association(^{45})</td>
<td>Word list generation within alphabetical or semantic categories</td>
<td>Fairly robust estimate of verbal intelligence although sensitive to concreteness associated with brain damage (including toxic encephalopathy)</td>
</tr>
<tr>
<td>Boston Naming Test(^{49})</td>
<td>Naming of objects depicted in line drawings</td>
<td>Sensitive to reasoning skills; can be impaired after exposure to neurotoxicants</td>
</tr>
<tr>
<td>Reading Comprehension (Boston Diagnostic Aphasia Exam)(^{46})</td>
<td>A direct screening test of simple reading comprehension</td>
<td>Sensitive to reasoning skills; can be impaired after exposure to neurotoxicants</td>
</tr>
<tr>
<td>Writing Sample(^{46})</td>
<td>Patient writes to dictation or describes a picture</td>
<td>Assesses flexibility, planning, arousal, processing speed, ability to generate strategies, somewhat sensitive to exposure</td>
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<tr>
<td><strong>Note:</strong></td>
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<tr>
<td>Tests Commonly Used in Clinical Assessment of Possible Encephalopathy Secondary to Exposure to Toxic Chemicals. (Boston Extended Neurotoxicologic Battery—Clinical)</td>
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<tr>
<td>Domain</td>
<td>Description</td>
<td>Implications</td>
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<tr>
<td>Visuospatial, visuo-motor</td>
<td>Identification of missing details in line drawing</td>
<td>(Visuospatial and visuomotor tasks are frequently sensitive to exposure in adults and children) Measures perceptual analysis</td>
</tr>
<tr>
<td>Picture Completion (Wechsler tests)</td>
<td>Coding task requiring matching symbols to digits</td>
<td>Complex task assessing motor speed, visual scanning, working memory Measures visual sequencing, ability to infer relationships from visuospatial/social stimuli Assesses abstract visual construction ability and planning</td>
</tr>
<tr>
<td>Picture Arrangement (Wechsler tests)</td>
<td>Sequencing of cartoon frames to represent meaningful stories</td>
<td>Measure of concrete visual constructional skills, Gestalt recognition Measures constructional abilities, motor functioning Sensitive to Gestalt integration processing Sensitive to deficits in visuospatial planning and construction Measures motor speed and coordination Sensitive to lateralized manual motor speed (New learning and retention are often sensitive to toxicants; retrograde memory of prior events is more complexly related to exposure) Sensitive to new learning and retention of newly learned information Measures abstract verbal list learning, retention</td>
</tr>
<tr>
<td>Block Design (Wechsler tests)</td>
<td>Assembly of 3-D blocks to replicate 2-D representations of designs</td>
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<tr>
<td>Object Assembly (Wechsler tests)</td>
<td>Assembly of puzzles</td>
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<tr>
<td>Boston Visuospatial Quantitative Battery</td>
<td>Drawings of common objects spontaneously and to copy</td>
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<tr>
<td>Hooper Visual Organization Test</td>
<td>Identification of correct outline of drawings of cut up objects</td>
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<tr>
<td>Rey-Osterreith Complex Figure (copy condition)</td>
<td>Drawing of a complicated abstract visual design</td>
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<tr>
<td>Santa Ana Formboard Test</td>
<td>Knobs in a formboard are turned 180° with each hand individually and both hands together</td>
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<tr>
<td>Finger tapping</td>
<td>Speed of tapping with each index finger</td>
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<tr>
<td>Memory</td>
<td>Recall of paragraph information read orally on an immediate and 20-minute delayed recall</td>
<td></td>
</tr>
<tr>
<td>Logical Memories—Immediate and Delayed Recall (IR, DR) (Wechsler Memory Scales)</td>
<td>Two paired words are presented in a list of pairs; subject must recall second word; test is presented on immediate and delayed recall</td>
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<tr>
<td>Verbal Paired Associate Learning, IR, DR (Wechsler Memory Scales)</td>
<td>Multiple choice recognition of visual designs immediately after initial presentation</td>
<td></td>
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<tr>
<td>Figural Memory (Wechsler Memory Scales)</td>
<td>6 visual designs are paired with 6 colors; recognition memory is tested immediately after the 6 are presented on learning trials and at delayed recall</td>
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</tr>
<tr>
<td>Visual Paired Associate Learning, IR, DR (Wechsler Memory Scales)</td>
<td>Visual designs are drawn immediately after presentation and on delayed recall</td>
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</tr>
<tr>
<td>Visual Reproductions, IR, DR (Wechsler Memory Scales)</td>
<td>Based on delayed nonmatching to sample paradigm, discs are moved about on a board to assess recognition memory for words, color, spatial locations</td>
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<tr>
<td>Delayed Recognition Span Test</td>
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</table>
TABLE 2

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<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peterson Task(^\text{54})</td>
<td>Words or consonants are presented and must be recollected after a period of distraction</td>
<td>Measures sensitivity to interference in new learning</td>
</tr>
<tr>
<td>California Verbal Learning Test(^\text{55})</td>
<td>Subject is presented with list of 16 words (which can be semantically related) over multiple learning trials and an interference list</td>
<td>Provides multiple measures of new learning, recall, recognition memory, use of strategies and sensitivity to interference</td>
</tr>
<tr>
<td>Rey-Osterreith (IR, DR)(^\text{11})</td>
<td>Complex design is drawn from IR immediately after it has been copied and at a 20-minute delayed recall</td>
<td>Assesses memory for visual information which is difficult to encode verbally</td>
</tr>
<tr>
<td>Personality, Mood</td>
<td>65 single word descriptors of affective symptoms are endorsed by degree of severity on 6 scales</td>
<td>Sensitive to clinical mood disturbance and to affective changes secondary to toxicant exposure</td>
</tr>
<tr>
<td>Profile of Mood States(^\text{58})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Minnesota Multiphasic Personality Inventory (R)(^\text{57})</td>
<td>True-false responses provided on personality inventory summarized on multiple clinical dimensions</td>
<td>Provides description of current personality function, some scales sensitive to exposure</td>
</tr>
</tbody>
</table>

alternately connecting numbered and lettered dots in an array (1-A-2-B-3-C etc). Age and gender-adjusted norms are available for this test. It is also well established that poor performance on this test is associated with dysfunction of the frontal lobes due to direct structural damage to the frontal lobes or due to damage to parts of the brain that are connected to the frontal lobes.\(^{11}\)

Because of research evidence linking impaired performance on specific tests to certain types of brain dysfunction and the accumulation of clinical knowledge of brain-behavior relationships gained from observing the test performance of many patients with specific types of brain damage, the experienced neuropsychologist can draw conclusions about the likely locations of cerebral dysfunction in individual patients based on impairments observed during careful testing.

3. What is the likely etiology of the cognitive and behavioral abnormalities observed during assessment? Are they due to toxic exposure or some other etiology?

Frequently, the referral source questions whether a patient shows behavioral abnormalities because of toxic poisoning or for some other reason. Because patterns of retained and impaired performance on neuropsychological tests have been described for many neurologic and psychological conditions,\(^{11,13}\) the neuropsychologist often is able to render a diagnostic conclusion on the likely etiology of the behavioral abnormalities observed during testing.

The cognitive and test impairments observed with exposure to numerous neurotoxins such as lead,\(^{14-17}\) trichloroethylene,\(^{18}\) mercury,\(^{19,20}\) and carbon disulfide\(^{21-23}\) have been described in the literature. Many other types of exposure have been seen clinically by individual practitioners. Given this knowledge and this experience, diagnostic conclusions can be reached on the findings for individual patients.

It is not always the case, however, that a toxic encephalopathy is identified. In our experience, a significant number of patients referred for evaluation of possible toxic encephalopathy perform normally on neuropsychological tests and thus do not show an identifiable encephalopathy at the time of testing. Another significant portion of patients seen performs abnormally but the behavioral abnormalities are not typical of those seen in toxic encephalopathy: they appear to reflect another condition. Because a great deal is known about psychological test performance in many diagnosed groups, the neuropsychologist can still render a diagnostic opinion.\(^{24}\)

The kinds of disorders most commonly encountered in our experience include constitutional conditions such as learning disabilities or low intellectual endowment, neurologic disorders (congenital trauma, idiopathic seizures, head trauma, multiple sclerosis, Parkinson's disease, Alzheimer's disease), psychiatric disorders (depression, somatoform disorders, anxiety states, posttraumatic stress disorder, personality disorder, nonorganic psychosis), or conditions due to administration of neurotoxic substances other than that under consideration as the toxic agent (alcohol, street drugs, prescription drugs).\(^{24}\)

Patients can show behavioral abnormalities for multiple reasons. In such cases, diagnosis can be challenging but not impossible. For example,
a patient with a history of exposure to perchloroethylene may have a history of language-based learning disability; this patient may show problems in reading and writing (as would be expected based on history) but also show marked visual memory deficits typical in perchloroethylene exposure (but not for the learning disability).

Malingering is detectable with careful neuropsychological testing but is much less common than might be expected given the amount of attention it receives in the literature.

4. Has this patient shown any changes in behavioral function?

This question is most appropriately asked and most easily answered when the patient has undergone previous neuropsychological testing. Follow-up or longitudinal testing of individual patients is most useful in:

- describing recovery of function in toxic poisonings after periods of nonexposure to the toxin
- documenting any change in function after treatment of intoxication (eg, chelation)
- documenting cognitive status under conditions of continued exposure, after exposure to a new neurotoxin, or after changes in medical status.

5. What are the implications of the neuropsychological test results and diagnostic impressions for the patient’s care?

Beyond the level of clinical description and diagnostics, clinical neuropsychological examinations may also have implications for decisions regarding the patient’s care or for vocational planning. For example, a patient with a serious organic depression secondary to exposure may benefit from pharmacologic intervention although a patient with a stress reaction to an exposure may need psychotherapy. A patient whose exposure has produced circumscribed visuospatial deficits but who has strong verbal abilities may be employable in a job capitalizing on her verbal skills (eg, proofreading), but a patient with severe attentional and memory deficits may be disabled to work based on cognitive and behavioral change.

Criteria for a Clinical Battery

Given the questions that must be answered in a clinical battery, the tests chosen for administration in a given case must be designed to answer the clinical question at hand. Certain criteria may be used in developing such a battery (see Table 1).

Specificity of Cognitive Deficits to Toxin Exposure

Inclusion of tests that would not be sensitive to the toxin(s) in question ("hold tests") as well as tests known to be sensitive to the toxin(s) to which the patient has been exposed is necessary for a fair evaluation of toxic encephalopathy. If the patient fails hold tests (eg, if an adult patient with lead exposure has a language disorder) diagnostic possibilities other than toxin exposure must be considered in determining the etiology of at least some of the deficits noted. As discussed above, multiple causes of brain dysfunction can be encountered in an individual case; therefore, it may be inaccurate to attribute all the deficits observed to an exposure. The clinician should be specific in describing the relationship between exposure and resultant cognitive deficits.

Estimation of Native Ability Patterns

It is essential to include tests that allow the clinician to estimate native intellectual capacity. Unless there is pre-exposure testing (a rare event), the clinician must estimate native intellectual capacity based on tests little affected by exposure that are known to correlate well with native intellectual function or must estimate abilities based on education, occupation, or socioeconomic level. We have found the latter to be highly inaccurate in clinical assessment, although it is sometimes the only method available. The former method of estimation of native abilities is, in our experience, best accomplished by using tests of general academic knowledge (eg, Information subtest, Weschler Adult Intelligence Scale-Revised (WAIS-R)) or comprehension of word knowledge, eg, Peabody Picture Vocabulary test) to estimate native intellectual capacity.

To assess premorbid ability patterns more accurately, it may be necessary to include tasks that predict native verbal abilities (to rule out a longstanding language processing deficit) or that predict native nonverbal processing problems. Tests of academic skills such as reading and spelling (for verbal abilities) or arithmetic (correlated with nonverbal learning ability) can be useful in this regard as can tests of vocabulary (eg, WAIS-R Vocabulary subtest), naming (eg, Boston Naming test), or simple visuospatial analysis (eg, WAIS-R Picture Comprehension subtest). It may be somewhat trickier to uncover an adult residual attention deficit disorder and to dissociate such a disorder from effects of toxic exposure, but this usually can be done through inclusion of tests assessing simple and complex attention as well as eliciting any history of school attention problems or hyperactivity.

When attempting to estimate native intellectual abilities, clinical interview can provide essential information on school history of the patient and academic success of siblings, parents, and offspring that can be invaluable in determining diagnosis when combined with test data. School records also can be valuable in some cases.

Differential Diagnosis

The test battery should be complete enough to rule out other potential etiologies to deficits noted during neuropsychological assessment. As noted above, a subgroup of patients referred for evaluation may be diagnosed with other active neurologic or psychiatric conditions. To accurately assess these patients, the assessment battery must include tasks that are sensitive to other disorders. For this reason, it may be important to include tests of verbal and language skills (although most such tasks are not sensitive to neurotoxins in adults) to rule out neuropsychiatric disorders, including the A

ologic disorder. Mental of the A
da is a possibility that should be evaluated in patients with suspected neurotoxic involvement.
Degree and Types of Cognitive Strengths and Dysfunction

The assessment battery ideally will be extensive enough to describe the patient’s cognitive and behavioral strengths and weaknesses in sufficient detail to provide recommendations regarding any likely limitations on activities of daily living. If cognitive impairment is severe, the patient may require home care or monitoring to ensure safety. It may be necessary to determine whether it is safe for the patient to drive or whether the patient can handle his/her finances independently. If cognitive or motor deficits are severe or occur in functional domains particularly germane to the patient’s field of work, vocational planning and/or rehabilitation may be indicated. Especially in cases of severe encephalopathy or in those in which behavioral change is pre-eminent, retirement on disability may be necessary. Finally, psychiatric treatment may be indicated to optimize adjustment to cognitive change, or cognitive rehabilitation may be worth considering as a treatment possibility for remediation of cognitive loss.

Existing Test Batteries

Most test batteries described in the literature on behavioral neurotoxicology were designed for use in epidemiologic studies and are not appropriate for detailed clinical assessments carried out for the purpose of diagnosis of toxic encephalopathy. In most cases, the batteries are too brief and limited in scope to meet the criteria for a clinical battery, as elaborated above. Although some batteries that have been used in previous research studies on neurotoxins have been advocated as potential clinical assessment batteries, this is often inappropriate. Two examples of this error are the lead batteries used by Baker et al. and Ryan et al. The computerized test batteries developed for epidemiologic research such as the Neurobehavioral Evaluation System (NES) also are inappropriate as clinical assessment batteries because the tests have never been validated in computerized form on patients with known brain damage. Although some subtests of these batteries have been shown to be sensitive to toxic exposure in epidemiologic studies, their clinical utility for differential diagnosis of toxic encephalopathy versus other states in patients has not been demonstrated.

A careful sampling of the WHO/NIOSH recommended battery of tests will meet many of the criteria listed above, though those tests are limited in the areas of academic testing and personality assessment. A previously published battery of tests used at Boston University Medical Center Department of Neurology, and since revised, was designed to meet the inclusion criteria for clinical assessments. The battery is summarized in Table 2.

Acknowledgment

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