

## Individual-Administered Human Behavioral Test Batteries to Identify Neurotoxic Chemicals<sup>1</sup>

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Most research demonstrating behavioral effects of occupational chemical exposures is produced in established laboratories using a consistent set or battery of tests. Exemplifying this tradition are batteries developed at Finland's Institute of Occupational Health, Milan's Institute of Occupational Health, Sweden's National Institute of Occupational Health, Australia's National Institute of Occupational Safety and Health, and at universities in the United States and other countries. In 1983, under the World Health Organization (WHO) aegis, experienced human occupational researchers recommended the Neurobehavioral Core Test Battery (NCTB) as a screening instrument to be administered by an individual to subjects exposed to chemicals believed to be neurotoxic. Health professionals from 50 cities in 27 countries distributed on every large continent have been trained to administer the NCTB according to its Operational Guide. Six issues need to be addressed regarding human-administered test batteries: (a) The critical role of individual-administered batteries to screen chemically exposed populations in a field increasingly dominated by computer-administered batteries; (b) selection criteria for tests to assess known and unknown chemicals; (c) utility of baseline data for study analysis and interpretation; (d) test battery validation; (e) availability and cost of inexpensive test batteries; and (f) equivalence of computer- and human-administered variants of the same tests. © 1993 Academic Press, Inc.

### INTRODUCTION

Research assessing occupationally exposed persons with behavioral tests began in the 1960s (Hänninen, 1966) and has been consistently productive since the 1970s (Anger, 1990). Various laboratories and agencies developed their own test batteries early in this area of research (e.g., Hänninen and Lindström, 1979), a process that has continued through the 1980s and into 1990 (e.g., Gamberale *et al.*, 1990; Williamson *et al.*, 1982; Williamson, 1990; Almirall-Hernández, *et al.*, 1987; Hogstedt *et al.*, 1980; Valciukas and Lilis, 1980; Hänninen and Lindström, 1979; Hänninen, 1990). Research in various countries where laboratories use a consistent set or battery of tests produces the majority of findings demonstrating behavioral effects of occupational chemical exposures (Anger, 1990).

Behavioral test batteries that have been employed in neurotoxicology research or that were developed by members of the behavioral neurotoxicology community are listed in Table 1. The table is divided into batteries administered by a person (top) and those administered by a computer (bottom). The use of computer-

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TABLE 1  
HUMAN TEST BATTERIES IN BEHAVIORAL NEUROTOXICOLOGY

Battery name	Country of origin	Source
Individual-administered batteries		
—[Information Theory Battery]	Australia	Williamson <i>et al.</i> , 1982; Williamson, 1990
London School of Hygiene Battery	Britain	Cherry <i>et al.</i> , 1984
Finland Institute of Occupational Health (FIOH) Battery	Finland	Hänninen and Lindström, 1979, 1989
Neuropsychological Screening Battery (NPS) <sup>a</sup>	Finland	Hänninen, 1990
Test Battery for Investigating Functional Disorders (TUFF)	Sweden	Hogstedt <i>et al.</i> , 1980; Ekberg and Hane, 1984
—[Mt. Sinai 1970s–1980s battery]	United States	Valciukas and Lilis, 1980
Neurobehavioral Core Test Battery (NCTB)	World Health Organization	Johnson <i>et al.</i> , 1987
Pittsburgh Occupational Exposures Test Battery (POET) <sup>a</sup>	United States	Ryan <i>et al.</i> , 1987a
CNS-B <sup>a</sup>	United States	Bowler <i>et al.</i> , 1986
IMT	Cuba	Almirall-Hernández <i>et al.</i> , 1987
—[Milan IOH Battery]	Italy	Angotzi <i>et al.</i> , 1980
Computer-administered batteries		
Neurobehavioral Evaluation System (NES)	United States	Letz and Baker, 1986; Letz, 1990
Armed Forces Cooperative Performance Assessment Battery (UTC-PAB)	United States	Englund <i>et al.</i> , 1987
Microtox Test System (MTS)	United States	Eckerman <i>et al.</i> , 1985
Milan Automated Neurobehavioral System (MANS)	Italy	Cassitto <i>et al.</i> , 1989
Swedish Performance Evaluation System (SPES)	Sweden	Gamberale <i>et al.</i> , 1990
Cognitive Function Scanner	Denmark	Laursen, 1990
Automated Performance Test System (APTS)	United States	Kennedy <i>et al.</i> , 1987

<sup>a</sup> Neuropsychological battery.

administered test batteries (described by Letz in this volume) has grown with tremendous rapidity and has tended to dominate the field in recent years. This domination is due in part to the influence of publication in journals from industrialized countries where this interest is centered and where microprocessors are widely available and inexpensive.

Test batteries administered by a human do not achieve the level of efficiency or

presentation consistency as do computer-administered batteries. However, aided by precision equipment, human- or individual-administered batteries can be equivalent, or in some cases, superior to their computer-implemented clones. Reasons include the capability of the individual-administered batteries to employ a wider range of tests, the capacity of a human tester to elicit cooperation and responding from nervous, reluctant, or poorly literate subjects, and the greater potential for detecting subtle subject responses leading to important follow-up testing recommendations. Obviously, a combination of human administration and use of precision instruments (e.g., as employed by Williamson *et al.*, 1990, and Gamberale *et al.*, 1990) is the most effective approach. This suggests that the frequently mentioned distinction between human- and computer-administered batteries has a degree of artificiality and is unnecessarily limiting. Improved technology should be used to test subjects whenever it is appropriate; human judgment is needed to evaluate results and is often desirable for test administration.

#### *Individual-Administered Human Behavioral Batteries*

Hänninen developed the first behavioral test battery used in worksite research in her early studies of carbon disulfide-exposed workers (Hänninen, 1966, 1971, 1974). A handbook describing the battery and its implementation is available from the Finnish Institute of Occupational Health (FIOH) (Hänninen and Lindström, 1989) where it has been modified and refined over the years. Following the development of Hänninen's FIOH battery, there was a period of aggressive development of test batteries by scientists at other institutions, as reflected in Table 1. The batteries listed in Table 1 can be divided into neuropsychological test batteries, batteries that are no longer used actively, batteries that have been replaced by other (computer-implemented) batteries, and batteries undergoing active development and use. Supplementing the batteries in Table 1 are new batteries appearing in the literature in recent years. Each of these batteries is described below.

*Neuropsychological batteries.* Hänninen (1990) has developed the Neuropsychological Screening Battery (NPS), a more focused screening test battery, as distinct from a research tool (the FIOH battery). She has initiated a series of longitudinal studies in Finland, installing the battery in factories where it is given by in-plant occupational health professionals. The NPS is comprised of seven neuropsychological tests (Finger Tapping, Flanagan Coordination, Mira test, Block Design, Memory for Design, Digit Span, and Associative Learning) and its sensitivity to neurotoxic chemicals has been demonstrated in solvent-exposed workers at five manufacturing plants in Finland. The battery is now used routinely in select Finnish industries where its administration is triggered by worker complaints or evidence of high-concentration exposures.

Two other neuropsychological test batteries (Bowler *et al.*, 1986; Ryan *et al.*, 1987a) have been recommended for assessing neurotoxicity in working populations (Table 1). Both rely heavily on the Wechsler Memory Scale (WMS) and Wechsler Adult Intelligence Scale (WAIS) subtests, plus other cognitive and visual/motor (e.g., pegboard) tests. These batteries have been employed recently in worksite research (Ryan *et al.*, 1988; Bowler *et al.*, 1991) and have been used in methodological assessments (e.g., Law *et al.*, 1990). The use of neuropsycholog-

ical batteries is increasing in worksite research, due particularly to the need to evaluate individual subjects for worker compensation decisions and to identify individuals in need of follow-up care. Such judgmental decisions cannot be accomplished by screening batteries at present, rather clinical neuropsychologists select tests in order to provide such individual diagnosis and assessment.

*Batteries not used in recent years.* Two of the individual-administered batteries in Table 1 appear to have fallen into disuse in recent years as their developers turned to other interests. The London School of Hygiene Battery (Cherry *et al.*, 1984) employs a combination of neuropsychological and experimental psychology tests that have been used in Britain to study solvents. This battery includes perceptual/motor (grooved pegboard, simple reaction time, dotting) and cognitive function tests (visual search, Digit Symbol, Buschke Memory, Block Design, British National Reading test). The battery used in a series of studies by Valciukas and Lilis at Mt. Sinai in the 1970s and 1980s included only two WAIS tests (Digit Symbol and Block Design) and the Embedded Figures test (drawings of simple figures with distracting lines through them), which they adapted from neuropsychological testing. Research with these batteries has not been published in several years.

*Batteries replaced.* The test battery for Investigating Functional Disorders (TUFF) was developed in Sweden in an aggressive campaign to assess industrial exposures. The TUFF developed the most widely used symptoms questionnaire (Anger, 1990), and it employs a broad array of 15 motor ([manipulation of] bolts, cylinders, pins), perceptual/motor (Dots/cancellation), and cognitive tests (Figure Classification, Block Design, unfolding, visual gestalt, Digit Symbol, Same Number, Benton Visual Retention, Auditory Perception/Retention, Synonyms, opposites) (Hogstedt *et al.*, 1980). However, the computer-implemented Swedish Performance Evaluation System (SPES) (Gamberale *et al.*, 1990) has taken the major role in recent worksite evaluations in Sweden (e.g., Iregren, 1990). A similar fate has befallen the Milan IOH battery developed in the 1980s (Angotzi *et al.*, 1980) which is now used primarily for individual neuropsychological testing. For population assessments, it has been replaced by the computer-implemented Milan Automated Neurobehavioral System and the Neurobehavioral Core Test Battery, both described below.

*Batteries in active development.* The IMT was developed in Cuba (Almirall-Hernández, *et al.*, 1987). It includes motor and cognitive tests adapted from familiar English-language precursors. Testifying to the fact that the battery has been extensively evaluated in Cuba, the test manual includes baseline data for IMT tests (Almirall-Hernández, *et al.*, 1987). There is interest in Latin America in using this Spanish-language battery for neurotoxicity evaluations. Williamson and co-workers (1982, 1990) developed a battery based on information processing theory that is the most firmly grounded in experimental psychology of the batteries now in use. Tests are critical flicker fusion, vigilance, hand steadiness (stylus in hole), Simple Reaction Time, visual pursuit, sensory store memory, Sternberg memory test, and Paired Associates (short- and long-term memory). Key factors have been carefully assessed. Test-retest reliability exceeds 0.8 in most tests, and the effects of potential study confounders age, sex, education, job type, and

length of residence have been evaluated using multivariate linear regression analysis (7–26% of the variance was explained by these factors on the various tests). Finally, test sensitivity was evaluated in working populations exposed to mercury and lead. The tests show specificity for these chemicals and show promise for the development of hypotheses about the brain function or area where damage is producing the performance deficits.

*Recently described batteries.* New batteries appear poised to supplement the more established individual-administered batteries in Table 1, particularly in Germany (Triebig, 1989; Seeber *et al.*, 1990). These batteries employ standard neuropsychological tests (e.g., Digit Symbol), established experimental psychology tests (e.g., simple and choice reaction time), modifications of widely used vigilance tests (e.g., d2) (Seeber *et al.*, 1990), and unique tests based on cognitive theory (e.g., WES, KAI) (e.g., Triebig, 1989).

### *Strategies of Test Selection*

More important than the method of presentation is the strategy employed for selecting tests into a battery. Information about health effects of the chemical and symptoms of the chemically exposed group under study likely serve as a guide to test selection in most studies (e.g., Anger, 1985), although the rationale for test selection in any given study is rarely addressed in published reports. Some behavioral test batteries provide a menu of choices (e.g., the computer-implemented Neurobehavioral Evaluation System by Letz and Baker, 1986) with only limited guidance on test selection. Others have addressed the strategy for test selection. Eckerman *et al.* (1985) selected cognitive tests based on a factor analysis of a large sample of cognitive test results, identifying eight cognitive factors (Eckerman and Gullion, 1986). Williamson and co-workers (1982, 1990) took a theoretical approach, as noted above, selecting tests that could be interpreted within the constructs of information processing theory. Recommendations of expert gatherings also serve as an important test selection guide for many researchers.

### *International Recommendations*

Although appropriate concern has been voiced over limiting development of new methods (e.g., Letz and Singer, 1985), the use of standardized test instruments has been encouraged by many scientists at many international meetings (Laties, 1973; Dews, 1975), including the series of triennial meetings termed International Symposia on Neurobehavioral Methods (and Effects) in Environmental and Occupational Health (Johnson *et al.*, 1985; Eckerman, 1990). While behavioral test batteries to assess neurotoxic effects are used primarily in the country in which they are developed, events in the 1980s have begun to concentrate international interest on two test batteries (Anger, 1990; Letz, 1990). One, the Neurobehavioral Core Test battery, has been recommended by an international group of experts and has now been used in 10 countries in an evaluation of its feasibility for international use (Cassitto *et al.*, 1990; Liang *et al.*, 1990; Anger *et al.*, 1993). The other is the Neurobehavioral Evaluation System which is the most extensively used worksite research behavioral test battery in the world (Letz,

1990). The unifying element was the 1983 meeting at the National Institute for Occupational Safety and Health (NIOSH) in Cincinnati of experienced human occupational researchers convened from around the world under the aegis of the World Health Organization (WHO) (Johnson, 1983).

At the 1983 meeting in Cincinnati, scientists who had conducted behavioral research in working populations proposed a "core" test battery which could be used as a screening instrument to detect (and characterize in a limited way) a wide range of neurotoxic effects in human populations. The tests selected had been among the most useful in discriminating between groups exposed to the neurotoxic chemicals lead, mercury, and carbon disulfide in past research, and the tests could further be administered in even primitive settings by trained technicians. The proposed test battery was named the World Health Organization (WHO)-recommended Neurobehavioral Core Test Battery (NCTB) and consisted of seven tests: Digit Span, Digit Symbol, Simple Reaction Time, Pursuit Aiming II, Santa Ana dexterity, Benton Visual Retention, and Profile of Mood States (Johnson *et al.*, 1987). Since the NCTB was developed by many prominent researchers in the field of neurotoxicology, its tests were used individually in studies long before formal publication of the Battery's reference monograph in 1987.

#### *WHO NCTB Cross-Cultural Assessment*

A small group (Xintaras, Cassitto, Hänninen, Anger, Johnson, and Lindström at various stages) involved in recommending the NCTB subsequently met in Geneva to develop an Operational Guide for the NCTB. The Guide described the administration procedures, pitfalls, and general analysis of results. Members of this group also developed a plan to institute a two-phase Cross-Cultural Assessment (CCA) of the NCTB to address their primary concerns regarding the feasibility of using the battery worldwide. Since the NCTB tests were developed and validated in Western European and derivative populations, the CCA was focused on evaluating the NCTB's feasibility in a broad range of culturally diverse subject populations. Phase 1 was aimed at developing baseline or normative data in populations unexposed to chemicals at work, and phase 2 (which has not been implemented) was intended to demonstrate the sensitivity of the battery in people exposed at their workplace to established neurotoxic chemicals, both in a broad range of cultures (WHO, 1986a).

WHO's Office of Occupational Health under Drs. M. El-Batawi and C. Xintaras, and subsequently Dr. T. Ng, provided administrative support for the initial stages of phase I. The CCA proposal was distributed to all WHO Collaborating Centres and an article was published to further broaden contacts in Africa (Cassitto *et al.*, 1987). WHO's Office of Occupational Health collected the applications to participate in the CCA and distributed them to CCA coordinators. Applications to participate in the Cross-Cultural Assessment were received from 16 countries (Table 2, left two columns). Contacts with several applicant countries were successful and ultimately led to conducting the CCA in the countries listed in the right-hand columns of Table 2.

Training classes in administration of the NCTB were conducted by CCA coordinators Drs. Cassitto, Hänninen, or Anger to provide a measure of consistency in test application. A report (unpublished) describing a full-featured training pro-

TABLE 2  
INITIAL APPLICANTS AND FINAL PARTICIPANTS IN WHO-SPONSORED CROSS-CULTURAL  
ASSESSMENT (CCA) OF THE NCTB

Initial applicants		Final participants	
Country	Proposed site	Country	Final study site
Africa			
Egypt	Cairo		
Kenya	Nairobi		
America (Central)			
Cuba	Havana	Nicaragua	Leon Maracay
America (North)		United States	Salt Lake City Cincinnati Portland, OR Montréal
America (South)		Canada	
Brazil	Sao Paolo		
Asia			
India	Tiruchiripalli		
People's Republic of China	Beijing Shanghai	People's Republic of China	Beijing Shanghai
Thailand	Bangkok		
Europe (East)			
Poland	Lodz	Poland	Lodz
Europe (West)		Hungary	Budapest
		Austria	Innsbruck
		France	Paris
		Italy	Bari Chieti Milan Poggibonsi Potenza
Germany	Berlin	The Netherlands	The Hague
Oceania			
Australia	Sydney		

gram was prepared by Drs. R. Gilioli and M. Cassitto (1986) at Milan's Institute of Occupational Health. At least 75 people have been trained to administer the NCTB by one of the three CCA coordinators in the manner prescribed in the NCTB Operational Guide (WHO, 1986b). Countries from which personnel were trained are listed in Table 3. There is now a large coterie of trained NCTB administrators distributed in all permanently inhabited continents, except Oceania.

#### *Extensions of WHO NCTB Implementation*

The WHO-recommended NCTB has had its greatest impact in the People's Republic of China. Dr. Chen Zi-qiang of Shanghai Medical University learned to

TABLE 3  
 TRAINEES TAUGHT BY DRs. CASSITTO, ANGER, OR HÄNNINEN FOR THE NCTB  
 CROSS-CULTURAL ASSESSMENT

<b>Africa</b>	<b>Poland</b>
Kenya	Lodz
Nairobi	Portugal
Tanzania	Anodia
Dar Es Salaam	Coimbra
South Africa	<b>North America</b>
Cape Town	Canada
<b>Asia</b>	Toronto (2)
China	United States
Beijing (2)	Atlanta, GA (>10)
Shanghai	Baldwin, MD
Guangzhou	Blacksburg, VA
India	Cincinnati, OH (6)
Lucknow	Los Angeles, CA
Japan	Madison, WI
Tokyo	Portland, OR (4)
Korea	Salt Lake, UT (6)
Seoul	Seattle, WA
<b>Europe</b>	Washington, DC
Austria	<b>South America</b>
Innsbruck	Argentina
Bulgaria	Buenos Aires (2)
Sofia	Brazil
Czechoslovakia	Sao Paolo
Prague	Chile
Greece	Santiago
Athens	Columbia
Hungary	Bogota
Budapest	Venezuela
Italy	Maracay
Bergamo	<b>Central America</b>
Bologna	Cuba
Desio	Havana
Grosseto	Dominican Republic
Milan	San Domingo
Naples	Mexico
Lecco	Iztocala
Lodi	Nicaragua
Novara	Leon
Rome	<b>Middle East</b>
Siena	Israel
Sondrio	Jerusalem (2)
Volterra	<b>Oceania</b>

*Note.* Numbers in parentheses indicate number of people from city receiving training.

administer the NCTB at NIOSH in Cincinnati. Returning to Shanghai with an NCTB kit, he and Dr. Liang You-xin, with colleagues, undertook phase I of the Cross-Cultural Assessment to evaluate the NCTB's feasibility in unexposed workers. They quickly pressed on to evaluate the battery's sensitivity to lead

exposures (Liang *et al.*, 1990), the proposed phase 2 of the Cross-Cultural Assessment. Dr. Kuang Shou-ren of the Institute of Occupational Medicine in Guangzhou was also trained at NIOSH to administer the NCTB and began studying manganese-exposed workers.

In Beijing, Professor He Fengsheng of the Institute of Occupational Medicine arranged for local construction of the most expensive instrument in the NCTB, the Simple Reaction Time device, to minimize costs. She also conducted, along with members of her Institute and from Shanghai Medical University, NCTB training classes for health professionals in China. Cities represented at the training class by at least one person are listed in Table 4. Availability of an economical test battery and the support of scientists through publications and presentations from widely respected institutions in China built interest in the battery. A large cadre of trained NCTB test administrators are now distributed among more cities than in any other country, suggesting the likelihood of widespread use in the People's Republic of China.

#### *Test Batteries Based on the NCTB*

Two prominent members in the 1983 WHO-sponsored meeting in Cincinnati, Drs. E. Baker and R. Letz, then of Harvard School of Public Health, were at the time selecting behavioral tests to assess neurotoxicity in human populations. They implemented their tests in a computer format for reasons of efficiency and application consistency (Baker *et al.*, 1985). This battery of 19 tests named the Neurobehavioral Evaluation System (NES) includes computer-implemented variants of five of the seven NCTB tests. The NES, and its recent successor, the NES II (22 tests), has now been translated into several languages and has been employed in diverse countries and cultures. It has become the most widely used human behavioral neurotoxicology test battery in the world (Letz and Baker, 1986; Letz, 1990), as publications will soon demonstrate. A users group has been developed

TABLE 4  
CITIES OF RESIDENCE (BY PROVINCE) OF TRAINEES AT BEIJING'S INSTITUTE OF OCCUPATIONAL  
MEDICINE-SPONSORED NCTB TRAINING CLASS

Province	City	Province	City
Liaoning	Shenyang (4)	Fujian	Fuzhou
Liaoning	FuShun	Fujian	Nanping
Liaoning	Jinxi	Qinghai	Xining
Jilin	Jilin (2)	Shanxi	Xian (5)
Jilin	Qiqihar	Hubei	Wuhan
Heilongjiang	Harbin (4)	Hubei	Yichang (2)
Jiangsu	Nanjing (3)	Hainan	Hainan (2)
Shanxi	Datong	Shandong	Jinan
Sichuan	Chengdu (2)	Shandong	Qingdao
Sichuan	Panzhihua	Hebei	Qinhuangdao
Henan	Zhengzhou (2)	Hunan	Changsha (2)
Henan	Xinxiang (2)	Anhui	Hefei
Henan	Houyang	Yunan	Kunming
Henan	Luoyang		Beijing (2)

and centralized distribution of the software assures control over this battery's development. However, since the developers do not recommend use of a particular subset of NES tests in all investigations, the tests used in any given study may include a wide variety of tests from the NES menu. Ongoing research is directed at assessing whether the computer-implemented (NES) variants produce the same results as the same test given by an individual (e.g., in the NCTB) (e.g., Hooisma *et al.*, 1990). Of course, this was the form in which the tests were originally developed and validated.

Drs. M. Cassitto and R. Gilioli at the Institute of Occupational Health in Milan focused exclusively on the WHO-recommended NCTB. They developed a computer-implemented presentation of the NCTB cognitive tests which they named the Milan Automated Neurobehavioral System (MANS). This battery has been used in seven projects undertaken by its developers, and it is also being translated for use in Greece (Cassitto *et al.*, 1989). The MANS has been used in a multicenter study conducted by scientists in the Federal Republic of Germany, Italy, the United Kingdom, and the United States to study exposures to solvent mixtures due to growing concern over this problem (Triebig *et al.*, 1990).

### DISCUSSION

Test batteries have been employed in human behavioral neurotoxicology since 1966 (Hänninen, 1966). The development of standardized test instruments has been encouraged by many scientists, particularly in the series of triennial meetings termed International Symposia on Neurobehavioral Methods (and Effects) in Environmental and Occupational Health (Laties, 1973; Dews, 1975). This was strongly reaffirmed in 1988, at the third such meeting: "After vigorous discussion, the [clinical and field-testing batteries workshop] group recommended inclusion of the World Health Organization (WHO) Neurobehavioral Core Test Battery (NCTB) in all clinical and field studies of neurobehavioral function. This recommendation was offered without dissent." The primary reasons, closely paraphrased, given for this recommendation were (a) provision of a reference point for interstudy comparisons, (b) inclusion of tests of demonstrated sensitivity in all studies, and (c) the potential development of normative data for selected tests (Eckerman, 1990).

The development of technology has had a significant impact on the field of behavioral neurotoxicology, including the largest segment of research, field, or worksite epidemiological assessments. Computer-administered batteries will likely dominate the field for many reasons, particularly ease, consistency, and efficiency of administration, recording, and analysis. However, this reliance on computer-administered batteries will be constrained by high initial costs, the frequent need for competent computer service now widely available only in highly industrialized countries and the need to assess motor and sensory functions not easily elicited or measured by current computer hardware. This trend to computer-implemented tests should not limit research in locations where such hardware is unavailable because many of the same tests administered by a computer can be administered with equal competence and greater subject acceptability by a human administrator.

There is a clear need for administration of behavioral tests by both computers and humans (e.g., Williamson, 1990). Several test batteries administered by a human can be employed to study neurotoxic exposures to working populations. The WHO-recommended Neurobehavioral Core Test Battery (NCTB) is the most widely distributed individual-administered test battery and employs field-proven tests for research where humans are the test administrator of choice or where there are constraints on computer administration.

While test batteries administered by an individual have a significant niche in the field, at least six issues need to be addressed regarding such test batteries:

(a) The critical role of human-administered test batteries for screening working populations exposed to chemical agents in a field increasingly dominated by computer-administered test batteries;

(b) Selection criteria for tests to study the effects of known and unknown chemicals in humans;

(c) Utility of baseline or normative data for analysis and interpretation of future studies;

(d) The need for international validation of test batteries such as the NCTB (proposed as Phase II of the Cross-Cultural Assessment) and as a comparison for findings with unknown chemicals;

(e) Availability and cost of inexpensive test batteries for developing countries or underfunded researchers;

(f) Equivalence of computer- and human-administered variants of the same tests.

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#### REFERENCES

- Almirall-Hernández, P., Mayor-Rios, J., del Castillo-Martin, N., Rodriguez-Notario, R., and Román-Hernández, J. (1987). "Manual de Recomendaciones Para La Evaluación Psicológica en Trabajadores Expuestos A Sustancias Neurotóxicas." Ministerio de Salud Publica, Instituto del Trabajo, Departamento de Psicología. Havana.
- Anger, W. K. (1985). Neurobehavioral tests used in NIOSH-supported worksite studies, 1973-1983. *Neurobehav. Toxicol. Teratol.* 7, 359-368.
- Anger, W. K. (1990). Worksite behavioral research: Results, sensitive methods, test batteries and the transition from laboratory data to human health. *Neurotoxicology* 11, 629-720.
- Anger, W. K., Cassitto, M. G., Liang, Y-x, Amador, R., Hooisma, J., Chrislip, D. W., Mergler, D., Keifer, M., and Hörtnagl, J. (1993). Comparison of performance from three continents on the WHO-recommended Neurobehavioral Core Test Battery (NCTB). *Environ. Res.* in press.
- Angotzi, G., Cassitto, M. G., Camerino, D., Cioni, R., Desideri, E., Franzinelli, A., Gori, R., Loi, F., and Santorelli, E. (1980). Rapporti tra esposizione a mercurio e condizioni di salute in un gruppo di lavoratori addetti alla distillazione di mercurio in uno stabilimento della provincia di Siena. (Correlations between exposure to mercury and health in a group of workers at a mercury distillation plant in the province of Siena). *Med. Lav.* 71, 463-480.
- Baker, E. L., Letz, R., and Fidler, A. (1985). A computer-administered neurobehavioral evaluation system for occupational and environmental epidemiology: Rationale, methodology, and pilot study results. *J. Occup. Health* 27, 206-212.

- Bowler, R. M., Mergler, D., Huel, G., Harrison, R., and Cone, J. (1991). Neuropsychological impairment among former microelectronics workers. *Neurotoxicology* 12, 87-104.
- Bowler, R. M., Thaler, C. D., and Becker, C. E. (1986). California Neuropsychological Screening Battery (CNS/B I & II). *J. Clin. Psychol.* 42, 946-955.
- Cassitto, M., Anger, W. K., Hänninen, H., and Xintaras, C. (1987). Field evaluation of WHO Neurobehavioral Core Test Battery. *East Afr. Newslett.* 15 April/Issue 1, 26.
- Cassitto, M. G., Camerino, D., Hänninen, H., and Anger, W. K. (1990). International collaboration to evaluate the WHO neurobehavioral core test battery. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 203-223. Lewis, Chelsea, MI.
- Cassitto, M. G., Gilioli, R., and Camerino, D. (1989). Experiences with the Milan Automated Neurobehavioral System (MANS). *Neurotoxicol. Teratol.* 11, 571-574.
- Cherry, N., Venables, H., and Waldron, H. A. (1984). Description of the tests in the London School of Hygiene Test Battery. *Scand. J. Work Environ. Health Suppl.* 10(1), 18-19.
- Dews, P. (1975). An overview of behavioral toxicology. In "Behavioral Toxicology" (B. Weiss and V. Latic, Eds.), pp. 439-445. Plenum Press, New York.
- Eckerman, D. A. (1990). What should clinical and field-testing batteries for neurobehavioral screening encompass? In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 477-480. Lewis, Chelsea, MI.
- Eckerman, D. A., Carroll, J. B., Foree, D., Gullion, C. M., Lansman, M., Long, E. R., Waller, M. B., and Wallsten, T. S. (1985). An approach to brief field testing for neurotoxicity. *Neurobehav. Toxicol. Teratol.* 7, 387-393.
- Eckerman, D. A., and Gullion, C. M. (1986). Field testing. In "Neurobehavioral Toxicology" (Z. Annau, Ed.), pp. 288-330. Johns Hopkins Univ. Press, Baltimore, MD.
- Englund, C. E., Reeves, D. L., Shingledecker, C. A., Thorne, D. R., Wilson, K. P., and Hegge, F. W. (1987). "Unified Tri-Service Cognitive Performance Assessment Battery (UTC-PAB) I. Design and Specification of the Battery." Naval Health Research Center Report No. 87-10, Naval Health Research Center, San Diego, CA.
- Ekberg, K., and Hane, M. (1984). Test battery for investigating functional disorders—The TUFF battery. *Scand. J. Work Environ. Health Suppl.* 10(1), 14-17.
- Gamberale, F., Iregren, A., and Kjellberg, A. (1990). Computerized performance testing in neurotoxicology: Who, what, how, and where to? The SPES Example. In "Behavioral Measures of Neurotoxicity" (R. W. Russell, P. E. Flattau, and A. M. Pope, Eds.), pp. 359-394. National Academy Press, Washington, DC.
- Gilioli, R., and Cassitto, M. G. (1986). Training course on the neurobehavioral assessment theory and practice [outline]. Unpublished, University of Milan, Milan, Italy.
- Hänninen, H. (1966). Psychological tests in the diagnosis of carbon disulfide poisoning. *Work Environ. Health* 2, 16-20.
- Hänninen, H. (1971). Psychological picture of manifest and latent carbon disulphide poisoning. *Br. J. Ind. Med.* 28, 374-381.
- Hänninen, H. (1974). Behavioral study of the effects of carbon disulfide. In "Behavioral Toxicology: Early Detection of Occupational Hazards" (C. Xintaras, B. L. Johnson, I. deGroot, Eds.), pp. 73-80. USDHEW (NIOSH) Publication No. 74-126. NIOSH Publication Office, Cincinnati, OH.
- Hänninen, H. (1990). The neuropsychological screening test battery: Validation and current uses in Finland. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 257-262. Lewis, Chelsea, MI.
- Hänninen, H., and Lindström, K. (1979). "Neurobehavioral Test Battery of the Institute of Occupational Health." Institute of Occupational Health, Helsinki. [1989 revised].
- Hogstedt, C., Hane, M., and Axelson, O. (1980). Diagnostic and health care aspects of workers exposed to solvents. In "Developments in Occupational Medicine" (C. Zenz, Ed.), pp. 249-258. Year Book Medical Pub. Chicago, IL.
- Hooisma, J., Emmen, H. H., Kulig, B. M., Muijser, H., Poortvliet, D., and Letz, R. (1990). Factor analysis of tests from the Neurobehavioral Evaluation System and the WHO Neurobehavioral

- Core Test Battery. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 245-255. Lewis, Chelsea, MI.
- Iregren, A. (1990). Psychological test performance in foundry workers exposed to low levels of manganese. *Neurotoxicol. Teratol.* **12**, 673-675.
- Johnson, B. L. (1983). Report of international meeting on neurotoxicology. *Neurotoxicology* **4**(4), 177-178.
- Johnson, B. L., Anger, W. K., and Xintaras, C. (1985). Progress report on the WHO/NIOSH neurotoxicology programme. In "Neurobehavioral Methods in Occupational and Environmental Health: Symposium Report" (P. Grandjean, Ed.), pp. 6-10. World Health Organization Regional Office for Europe, Copenhagen.
- Johnson, B. L., Baker, E. L., El Batawi, M., Gilioli, R., Hänninen, H., Seppäläinen, A. M., and Xintaras, C. (1987). "Prevention of Neurotoxic Illness in Working Populations." Wiley, New York.
- Kennedy, R. S., Wilkes, R. L., Dunlap, W. P., and Kuntz, L. A. (1987). Development of an automated performance test system for environmental and behavioral toxicology studies. *Percept. Mot. Skills* **65**, 947-962.
- Laties, V. G. (1973). On the use of reference substances in behavioural toxicology. In "Adverse Effects of Environmental Chemicals and Psychotropic Drugs" (E. M. Horvath, Ed.), pp. 83-88. Elsevier, New York.
- Laursen, P. (1990). A computer-aided technique for testing cognitive functions. *Acta Neurol. Scand.* **82**(131), 1-108.
- Law, D., Lash, A. A., Bowler, R., Estrin, W., and Becker, C. E. (1990). Evaluation of the construct validity of examiner-administered and computer-administered neuropsychological tests. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 263-271. Lewis, Chelsea, MI.
- Letz, R. (1990). The neurobehavioral evaluation system: An international effort. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 189-201. Lewis, Chelsea, MI (USA).
- Letz, R. (1993). Covariates of computerized neurobehavioral test performance in epidemiologic investigations. *Environ. Res.* **61**, 124-132.
- Letz, R., and Baker, E. L. (1986). Computer-administered neurobehavioral testing in occupational health. *Semin. Occup. Med.* **1**, 197-203.
- Letz, R., and Singer, R. (1985). Neuropsychological tests [Report of Discussion Groups]. In "Neurobehavioral Methods in Occupational and Environmental Health: Symposium Report" (P. Grandjean, Ed.), pp. 17-18. World Health Organization Regional Office for Europe, Copenhagen.
- Liang, Y-x., Chen, Z-q., Sun, R-k., Fang, Y-f., and Yu, J-h. (1990). Application of the WHO Neurobehavioral Core Test Battery and other neurobehavioral screening systems. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 225-243. Lewis, Chelsea, MI.
- Ryan, C. M., Morrow, L. A., Bromet, E. F., and Parkinson, D. K. (1987a). Assessment of neurological dysfunction in the workplace: Normative data from the Pittsburgh Occupational Exposures Test battery. *J. Clin. Exp. Neuropsychol.* **9**, 665-679.
- Ryan, C. M., Morrow, L., Parkinson, D., and Bromet, E. (1987b). Low level lead exposure and neuropsychological functioning in blue collar males. *Int. J. Neurosci.* **36**, 29-39.
- Ryan, C. M., Morrow, L. A., and Hodgson, M. (1988). Cacosmia and neurobehavioral dysfunction associated with occupational exposure to mixtures of organic solvents. *Am. J. Psychiatry* **145**, 1442-1445.
- Seeber, A., Kiesswetter, E., Neidhart, B., and Blaszkewicz, M. (1990). Neurobehavioral effects of a long-term exposure to tetraethyllead. *Neurotoxicol. Teratol.* **12**, 653-655.
- Triebig, G. (1989). Occupational neurotoxicology of organic solvents and their mixtures. *Neurotoxicol. Teratol.* **11**, 575-578.

- Triebig, G., Lehl, S., and Barocka, A. (1990). International multicenter cross-sectional studies on chronic CNS effects of solvents in paint industries. In "Advances in Neurobehavioral Toxicology: Applications in Environmental and Occupational Health" (B. L. Johnson, W. K. Anger, A. Durao, and C. Xintaras, Eds.), pp. 297-304. Lewis, Chelsea, MI.
- Valciukas, J. A., and Lilis, R. (1980). Psychometric techniques in environmental research. *Environ. Res.* **21**, 275-297.
- Williamson, A. M. (1990). The development of a neurobehavioral test battery for use in health evaluations in occupational settings. *Neurotoxicol. Teratol.* **12**, 509-514.
- Williamson, A. M., Teo, R. K. C., and Sanderson, J. (1982). Occupational mercury exposure and its consequences for behavior. *Int. Arch. Occup. Environ. Health* **50**, 273-286.
- World Health Organization (WHO) (1986a). Field evaluation of WHO Neurobehavioral Core Test Battery. Unpublished. [Available from W. K. Anger]
- World Health Organization (WHO) (1986b). Operational Guide for WHO Neurobehavioral Core Test Battery. Unpublished. [Available from W. K. Anger]