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Reconsideration of the WHO NCTB Strategy and Test Selection

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Abstract

The World Health Organization-recommended Neurobehavioral Core Test Battery (NCTB) became the international standard for identifying adverse human behavioral effects due to neurotoxic chemical exposure when it was first proposed in 1983. Since then the WHO NCTB has been repeatedly cited as the basis for test selection in human neurotoxicology research. A Discussion Group was held before the International Symposium on Neurobehavioral Methods and effects in Occupational and Environmental Health to review the NCTB and reconsider it's tests. The workshop made three consensus recommendations to the International Congress on Occupational Health (ICOH) Scientific Committee on Neurotoxicology and Psychophysiology (SCNP):

1. a 'screening' battery of broadly sensitive tests is needed as guidance to the field of human neurotoxicology
2. the SCNP should convene a panel to reconsider the functions measured and the tests in the WHO NCTB
3. Three disciplines should be represented in the panel recommending a revised NCTB: Neuropsychology; Experimental Psychology; Neurology

This recommendation will be pursued at the next meeting of the International Congress on Occupational Health (ICOH) Scientific Committee on Neurotoxicology and Psychophysiology (SCNP).

Keywords

NCTB; Neurotoxicology; neuropsychology; toxicology

Keywords

WHO NCTB; Neurobehavioral Core Test Battery; Behavioral Neurotoxicology

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1.1 Introduction

The World Health Organization (WHO) Neurobehavioral Core Test Battery (NCTB) is a test battery designed to identify neurotoxic effects in human populations. It was developed at a meeting held in Cincinnati in 1983 by the National Institute for Occupational Safety and Health (NIOSH) and WHO (Johnson et al. 1987; Anger et al. 2000). The organizers, chiefly Drs. Charles Xintaras, Barry Johnson and Renato Gilioli, with counsel from others, selected the 41 participants on the basis of published evidence of experience in testing occupational populations exposed to neurotoxic substances, and the meeting organizers attempted to get participation from throughout the world to represent diverse cultures. Participants came from North America (16 scientists), Europe (14), Asia/Southeast Asia (6), South America (3) and Africa (2). The meeting itself was not mentioned in the publication developed from the meeting (Johnson et al. 1987), but the names of the participants were listed as "contributors" in the publication. The author was a participant at that meeting.

The meeting was designed to identify a "core" set of tests to be used in every study in order to develop a body of evidence from the same set of tests, and to propose additional tests for in depth characterization of the effects of chemical exposures. The test selection guidelines for the core tests developed at the meeting were to choose tests that: (1) Measured functions affected by multiple neurotoxicants, (2) detected positive effects in published studies, (3) were reliable and have construct validity (test well-defined functions), (4) returned a reasonable amount of information for the time committed to the test, (5) were relatively culture-free, and (6) were motivating to take, or not boring (Johnson et al. 1987, page 174). Effectively, the functional domains were identified, and then the tests were selected that measured those domains. The additional requirement was that the tests selected could be used in a minimal setting, which was freely translated into 'no electricity required,' though batteries could be used to run a test. The tests in the WHO-recommended NCTB (i.e., the "core" tests) as they have been known since the 1983 meeting, are listed in Table 1.

While a tiered set of tests was recommended based on the test setting (i.e., lab, clinic or workplace), personnel available to administer the tests (e.g., scientists, clinicians, community members), and the purpose of the assessment (i.e., detect illness, identify affected individuals, perform diagnostic workups or to study mechanisms), the recommendation of the "core" set of tests listed in Table 1 became the most widely recognized recommendation of the meeting and publication, with limited attention to the recommendations of more advanced diagnostic tests and tests that could assess mechanisms. The meeting participants concluded that the core set of tests should be used without replacement or alternative so to "avoid dispersion of methodologies and to make interlaboratory data comparisons possible" (Johnson et al. 1987, page 175).

The WHO NCTB has been referenced frequently over the years since 1984, sometimes because the entire battery and sometimes elements of the battery were used in the studies referring to it. A search of PubMed using the term "NCTB" in the title or the abstract revealed 46 publications (Cassitto et al. 1989; Chen et al. 1990; Yokoyama et al. 1990; Waszkowska and Bazylewicz-Walczak 1992; Anger and Cassitto 1993; Anger et al. 1993; Dudek and Bazylewicz-Walczak 1993; Lee and Lee 1993; Nell et al. 1993; Reif et al. 1993;

Chia et al. 1994; Yang et al. 1994; Escalona et al. 1995; Maizlish et al. 1995; Tang et al. 1995; Chia et al. 1997; Liang et al. 1997; London et al. 1997; Niu et al. 1998; Anger et al. 2000; Cao et al. 2000; Kang 2000; Niu et al. 2000; Sun and Liang 2001; Shen et al. 2002; Zhou et al. 2002; He et al. 2003; He et al. 2003; Myers et al. 2003; Reif et al. 2003; Chia et al. 2004; Mohamed and Nordin 2004; Niu et al. 2004; Kim et al. 2005; Young et al. 2005; Yuan et al. 2006; Chia et al. 2007; Wang et al. 2007; Zhou et al. 2007; Nie et al. 2008; Wang et al. 2008; Gao et al. 2010; Niu et al. 2010; Zhang et al. 2011; Li et al. 2013; Qiu et al. 2013).

Table 2 lists the 46 articles in chronological order, by year. Eight of the articles were designed to study the NCTB as a method or evaluate it in a reference population. The remaining 38 were epidemiologic studies of chemical or physical agent exposures, primarily in workplace populations. Table 2 lists the population studied, chemical exposure or biomarker measured and the NCTB tests that (1) revealed significant differences between exposed and reference participants, (2) were correlated with biomarkers, or (3) were differentially correlated with external exposure levels.

Table 3 summarizes the data in Table 2 to show the number of studies in which the NCTB tests were reported to reveal a significant difference, and the chemicals to which each test was sensitive.

The NCTB was also a key reference point for the development of the computer-based test batteries in the 1980s, 1990s and 2000s (e.g., Baker et al. 1985; Cassitto et al. 1989; Yokoyama et al. 1990; Rohlman et al. 2003). The same strategy was used by the Agency for Toxic Substances and Disease Registry (ATSDR) when they developed their own broader battery of tests intended to address both occupational and the lower-level exposures in the environment, the Adult Environmental Neurobehavioral Test Battery (AENTB) (Anger and Sizemore 1993). The AENTB is the only other national/international expert-recommended test battery for detecting human neurotoxicity. It has seen limited use.

In 1999, at the 7th International Symposium on Neurobehavioral Methods and Effects in Occupational and Environmental Health (Iregren 2000), the series of meetings that was largely spawned by the development of the WHO NCTB and addressed changes in the battery (Anger and Boyes 2012), a lessons learned review was held (Anger et al. 2000). The speakers from Asia, the US, Europe, and Africa identified 94 studies published in the peer reviewed literature, most from China, that had used the NCTB. They concluded that populations with 12 or more years of education and from North American, Western European-derivative and some Asian cultures could be tested effectively with the NCTB but that African or aboriginal cultures could not be tested effectively with the battery. This was supported by the findings of the cross-cultural assessment of the NCTB conducted in 10 countries (Anger et al. 1993). Examiner drift was also a problem noted by the review group in 2000. The main recommendation of the group was to establish construct validity of the NCTB in a wide range of countries (Anger et al. 2000). This, however, was never attempted.

From our search that identified 38 epidemiological studies referencing the NCTB in the title or abstract, Table 1 reveals that 14 of those articles were published in the decade of the

1990s, 19 were published between 2000 and 2009, and 5 articles were published in 2010–2013, suggesting that the NCTB publications in the current decade would be projected to approximate the level in the 1990s (i.e., 5 publications in 2010–2013 is 1.25 publications per year or 12.5 publications in 10 years).

In order to estimate the current frequency of use of NCTB tests in worksite neurotoxicity studies that did not specifically employ or identify the NCTB as a testing system, a search was conducted via PubMed for articles published in 2000–2013 for research that employed the NCTB tests but did not employ the term "NCTB" in the title or abstract. The terms neurotoxicology, neurobehavioral toxicology or toxins, and established neurotoxicants (manganese, pesticides, lead, mercury) with 'neurobehavioral' or 'neurotoxicity' were employed, each with the term "humans" as a filter. The search yielded 1695 titles (with overlap across the different searches) and an initial sample of 66 articles drawn from that search met the criteria of epidemiologic studies of workers exposed to chemical or physical agents. The sample was unbiased in that they were the first identified in the list of candidate studies as meeting the criteria. Of the 66, 7 were also identified in the "NCTB" search (i.e., Table 1 above) and excluded from this assessment. Thus 59 articles were reviewed to determine if they used any NCTB tests and if they used at least 5 of the tests indicating they had substantially used the "core" set of NCTB tests (Dolbec et al. 2000; Letz et al. 2000; Lucchini et al. 2000; Schwartz et al. 2000; Steenland et al. 2000; Triebig et al. 2000; Deschamps et al. 2001; Ellingsen et al. 2001; Frumkin et al. 2001; Schwartz et al. 2001; Hwang et al. 2002; Polizzi et al. 2002; Wesseling et al. 2002; Bouchard et al. 2003; Carta et al. 2003; Gong et al. 2003; Kamel et al. 2003; Lucchini et al. 2003; Mascagni et al. 2003; Urban et al. 2003; Chuang et al. 2004; Kilburn 2004; Kilburn 2004; Kunert et al. 2004; Bast-Pettersen and Ellingsen 2005; Bast-Pettersen et al. 2005; Chen et al. 2005; Rohlman et al. 2005; Roldan-Tapia et al. 2005; Vouriot et al. 2005; Dorsey et al. 2006; Echeverria et al. 2006; Rothlein et al. 2006; Schofield et al. 2006; Winker et al. 2006; Bleecker et al. 2007; Blond et al. 2007; Bouchard et al. 2007; Eckerman et al. 2007; Iwata et al. 2007; Keski-Santti et al. 2007; Lee et al. 2007; Rohlman et al. 2007; Shin et al. 2007; Abdel Rasoul et al. 2008; Bouchard et al. 2008; Ellingsen et al. 2008; Scapellato et al. 2008; Wastensson et al. 2008; Chang et al. 2009; Cowan et al. 2009; Hilt et al. 2009; Kaukiainen et al. 2009; Kim et al. 2011; Lucchini et al. 2012; Lucchini et al. 2012; Rentschler et al. 2012; Starks et al. 2012; Wastensson et al. 2012). From the sample of 59, 37 studies (63%) used at least 1 NCTB test, and 5 (8.5%) used 5 or more NCTB tests.

Together these searches reveal that the WHO NCTB remains in use as a core battery of tests (Table 1) and that use has been somewhat constant in the three decades following its recommendation (1984) and publication (Johnson et al. 1987). Furthermore some of the NCTB tests remain frequently used in the field as a whole in the years from 2000–2013, but the hope of the NCTB framers for a pervasive use of the "core" set of tests to build a field-wide database for cross-study comparisons has not been realized.

1.2 2013 Discussion Group

In 2013, a Discussion Group was held at the twelfth international symposium on Neurobehavioral Methods and effects in Occupational and Environmental Health, in Cape

Town, South Africa. It is the subject of this report. The Discussion Group was titled a "reconsideration of the WHO NCTB strategy and test selection" to encourage raising questions about both the tests and the strategy for their selection. The Discussion Group was organized around 5 questions that the author had heard raised by the leading scientists in the field of human behavioral neurotoxicology but which had not been recorded in publications. (The NCTB review data in this manuscript was not available to the participants.) The purpose of the Discussion Group was to open up a discussion on these questions and either confirm them as key questions for the field or identify more pertinent questions. The questions follow.

1. Is direction [still] needed for the field as it was judged to be in 1983, or should investigators be encouraged to develop their own test batteries without regard to other investigators or existing tests?
2. What rationale should be used to select tests: Should the goal be to "screen" populations to identify neurotoxic effects in populations, or should the goal be to characterize effects or to identify mechanisms?
3. What approach should be used to select tests? Should the same course followed in 1983 be followed again, specifically to select functions known to be affected by a wide range of neurotoxic substances (e.g., proven in epidemiological studies)?
4. Should the tests be selected to be effective in assessing neurotoxic effects in any population, including those in developing countries?
5. Who should be represented on the panel to select the functions and tests?

The pre-conference Discussion Group, held before the meeting, was attended by 13 people, most experienced in testing human populations exposed to neurotoxic substances. The comments of the audience members are recorded here without references, to document the range of responses that are found in the research community as background for a reconsideration of the WHO NCTB. The comments have been reflected as accurately as possible. Indeed, some comments are diametrically opposed to other comments. The Discussion Group participants and their affiliations are listed in Table 4.

1.3 Results of the Discussion Group

The audience offered a number of general considerations about using a battery of neurobehavioral tests to assess neurotoxic chemicals that should be taken into account when reconsidering the NCTB:

- Socioeconomic status (SES) and education are the two main factors that affect test performance, especially in timed tests, so they should be documented in any research
- The tests should all sample different functions
- The intensity and duration of exposure are the main variables to be measured, to correlate with test performance

- The NCTB concentrated on occupational exposures and workers, but now there is little funding for workplace exposures. The National Institute for Occupational Safety and Health (NIOSH) in the US and the European Union (EU) provide limited funding to study workers with occupational exposures. The largest funding is for the adverse effects of environmental exposures. This leads researchers to focus on environmental effects somewhat preferentially when it comes to selecting tests for their research.
- Psychology test publishers haven't yet bought into the computer-based tests because they don't think they are sensitive
- Computer-administered tests allow you to scale, to study more and larger populations more economically than with individually-administered tests
- Computer-administered tests are satisfactory for testing a few functions, but not most. Other functions/domains that need to be tested for include memory and executive function. Tests of memory should be verbal and visual – short term memory and delay. Stroop and trailmaking are two recommended tests.
- The recommended tests should not be copyrighted; most of the NCTB tests are copyrighted and must be purchased to use them legitimately. An example of a public domain test would be the trailmaking test.
- Culture-free tests should be used.

Question 1: Is direction [still] needed for the field as it was judged to be in 1983, or should investigators be encouraged to develop their own test batteries without regard to other investigators or existing tests?

The audience voted on this question, with 13 of 13 voting yes. The following were the comments informing the vote:

- What would be the impact of changing the NCTB? Could changing the NCTB do damage, because people have built their testing around it?
- Korea uses computer-administered tests that are based on the individually-administered tests of the WHO NCTB
- It would be acceptable to refine the NCTB
- Survey the opinions of the ICOH Scientific Committee on Neurotoxicology and Psychophysiology (SCNP) members from different countries about these questions
- Survey the WHO Collaborating Centres to find out who's using the NCTB, including those that are funded
- The NCTB is needed for regulations that are based on neurobehavioral test results
- There is no consistency in tests across studies in some cases. There is also the problem of culture in that tests cannot be used in multiple cultures. However, a specific test battery of tests is needed to establish chemicals as neurotoxicants
- The mechanisms of the effects of many neurotoxicants are unknown

Question 2. What rationale should be used to select tests: Should the goal be to "screen" populations to identify neurotoxic effects in populations, or should the goal be to characterize effects or to identify mechanisms?

All 13 members of the audience voted in favor of a screening battery to identify neurotoxic effects in populations. The following were the comments informing the vote.

- The basis for selecting tests should be that they are sensitive to proven neurotoxic chemicals (i.e., the results of exposed and non-exposed participants differ when studied in cross-sectional or prospective epidemiologic research)
- Tests need to be sensitive to neurotoxicants. In general, scientists should use tests with greater specificity for different functions. Specificity is as important as sensitivity.
- The European Union expert group on solvents should be consulted to identify functions and domains. Need to define the domains and the tests for those domains.
- For guidance, off-the-shelf tests and training in how to administer them are needed
- For computer-based tests, the parameters are almost never specified. They should be specified in the future.
- The big issues now are air pollution including diesel exposures and nanoparticles, so tests should be sensitive to these exposures
- Animal research may play a role, in part because it is also important to provide information for regulations. Manganese health research was mentioned as a case in point.

Question 3. What approach should be used to select tests? Should the same course followed in 1983 be followed again, specifically to select functions known to be affected by a wide range of neurotoxic substances (e.g., proven in epidemiological studies)?

A vote was not taken on question 3, but broad agreement was reached that a consensus approach should be used for test selection. The following comments were made in response to this question:

- The basis for test selection should be to assess functions and domains
- There should be many domains, but few tests
- Need cognitive tests in the NCTB. There are too few of these now.
- Methods sections are just too brief. Sufficient details should be provided so that regulators can interpret the findings and consider them in a risk assessment context For example, the test parameters are not mentioned in the articles. Is the measure a time or a score? Need training for editors and publishers to get the correct information.
- There was general agreement that you always need a local control group as a comparison in epidemiologic research studies of neurotoxic exposures

- Need to address how to define an adverse effect. In this context, the norm needs to be defined. When norms are used in comparison to an exposed group, it is possible to detect clinical deficits or impairment with 2 SD below the normative data. A difference of 2 SDs from the average constitutes a clinically relevant deficit.
- What do you do for workers? You use test-retest data, or health surveillance, not research. Where we know the outcome, turn it into occupational monitoring. We need early monitoring of deficits in populations.
- Consider what a prominent neurotoxicologist has said: Shift the curve, and individuals move into the clinical range (i.e., at the extremes)

Question 4. Should the tests be selected to be effective in assessing neurotoxic effects in any population including developing countries?

The following comments were made in response to this question.

- Consider cost and developing countries
- Put the administration protocol and an example on “You Tube”
- Need a core set of tests to develop converging evidence to build the science of neurotoxicology
- Test broadly for diverse functions

Question 5. Who should be represented on the panel to select the functions and tests?

The consensus recommendation of the audience was to select panel members from three disciplines to reconsider the NCTB:

- Neuropsychology
- Experimental Psychology
- Neurology

Other disciplines or areas of experience and expertise that would increase the value of the panel were also mentioned: Regulatory community, Occupational medicine, industry, labor/unions, developing countries (for culture issues), imaging, animal research, exposure specialists (to neurotoxic chemicals)

1.4 Final Recommendation

The Discussion Group made three consensus recommendations to the International Congress on Occupational Health (ICOH) Scientific Committee on Neurotoxicology and Psychophysiology (SCNP):

1. a ‘screening’ battery of broadly sensitive tests is needed as guidance to the field of human neurotoxicology
2. the SCNP should convene a panel to reconsider the functions measured and the tests in the WHO NCTB

3. Three disciplines should be represented in the panel recommending a revised NCTB:
    - Neuropsychology
    - Experimental Psychology
    - Neurology

Recommendations and comments made in this Discussion Group should thus inform the reconsideration of the functions measured and the tests selected in the WHO NCTB. These recommendations will be addressed at the next meeting of the SCNP in 2015.

Scientists are encouraged to nominate themselves (and provide their credentials) for participation in the future meeting intended to re-assess the NCTB.

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Highlights

- The WHO NCTB, recommended in 1983, is in need of reconsideration
- A ‘screening’ battery of broadly sensitive tests is needed as guidance to the field of human neurotoxicology
- The functions measured and the tests should be reconsidered
- Three Disciplines should be represented on the panel: Neuropsychology, experimental psychology, neurology

Table 1

Functional Domains tested by the WHO NCTB

Motor steadiness	**Pursuit Aiming II**
Attention/response speed	Simple reaction time
Perceptual Motor Speed	Digit Symbol (WAIS-R)
Manual dexterity	Santa Ana (Helsinki version)
Visual perception/memory	Benton Visual Retention
Auditory memory	Digit span (WAIS-R)
Affect	Profile of Mood States (POMS)

Table 2

Populations studied with the NCTB, Chemical Exposures and Significant Test Results.

Reference	Population	Chemical/Physical Exposure	Results or Tests in which Adverse Effects Reported
Cassitto, Gilioli, & Camerino, 1989	Italy: na	na	Creating computer- based battery based on NCTB tests
Chen, Yu, & Cao, 1990	China: nd	unexposed	Evaluated effect of demographic variables on NCTB
Yokoyama et al., 1990	Japan: na	na	Development of NCTB for Japan
Waszkowska & Bazylewicz-Walczak, 1992	Poland: Painters	solvents	SRT, SA*, Aim*
W. K. Anger & Cassitto, 1993	na	na	Individuals in 27 countries trained to use NCTB
W.K. Anger et al., 1993	Reference population	not exposed to chemicals	Performance from 10 countries on NCTB
Dudek & Bazylewicz-Walczak, 1993	Poland: Greenhouse workers	organophosphorus pesticides	POMS, SRT, DigSym
Lee & Lee, 1993	Korea: Car painters	solvents	Benton, DigSym, SA
Nell, Myers, Colvin, & Rees, 1993	South Africa: Paint mfg	solvents	No comparisons reported
Reif et al., 1993	US: residents	mercury	No comparisons reported
Chia, Jeyaratnam, Ong, Ng, & Lee, 1994	Singapore*: Reinforced fiberglass mfg	styrene	Benton, DigSpan,
Yang, Liang, & Tang, 1994	China: workers	lead	DigSpan or Benton*, SA*
Escalona, Yanes, Feo, & Maizlish, 1995	Venezuela: Adhesive mfg	solvents	DigSym, POMS, SA, SRT
Maizlish, Parra, & Feo, 1995	Venezuela: smelter wkrs	inorganic lead	POMS
Tang, Liang, Hu, & Yang, 1995	China: Lead smelter and battery wkrs	lead	Aim, Benton, DigSym, SA, SRT
Chia, Chia, Ong, & Jeyaratnam, 1997	Singapore*: Lead battery wkrs	lead	Aim, DigSym, SA
Liang, Chen, Wang, Tang, & Yang, 1997	China: Lead-Exposed wkrs	lead	Aim, Benton, DigSym, SA, SRT
London, Myers, Nell, Taylor, & Thompson, 1997	South Africa: Agricultural wkrs	organophosphorus pesticides	Aim, SA
Niu, Dai, & Chen, 1998	China: Printing house wkrs	lead	None
W. Anger et al., 2000	na	na	Workshop for feedback on experience with NCTB
Cao, Liu, Li, & Zhao, 2000	Wkrs with cell phones	electromagnetic radiation	SRT
Kang, 2000	Korea: Wkrs	na	Review of studies using NCTB; found NCTB applicable in Korean wkrs
Niu et al., 2000	China: Lead-exposed wkrs	lead	Aim, DigSym, POMS, SRT
Sun & Liang, 2001	China: Dental patients	mercury	DigSpan, DigSym

Reference	Population	Chemical/Physical Exposure	Results or Tests in which Adverse Effects Reported
Shen, Zhou, Hu, & Zhang, 2002	China: Aircrew, interception personnel, postgraduate students	na	Evaluation of the NCTB as a method
W. Zhou, Liang, & Christiani, 2002	China: many occupational groups	mercury, lead, solvents	Summary of 39 studies; most sensitive: Mercury: Benton; Lead: Aim, POMS; solvents: Aim, DigSpan, DigSym
S. C. He, Qiao, & Sheng, 2003	China*: aluminum electrolytic wkrs	aluminum	Aim, DigSym, POMS
S. He, Zhang, Niu, Wang, & Chen, 2003	China*: aluminum electrolytic wkrs	aluminum	Aim, DigSym, POMS
Myers et al., 2003	South Africa: Mineworkers	manganese	none
Reif et al., 2003	US: residents	tricholoroeth ylene	Benton, DigSpan, DigSym, POMS, SRT
Chia, Yap, & Chia, 2004	China (and immigrants): lead wkrs	lead	none
Mohamed & Nordin, 2004	Malaysia: Police	lead	none
Niu et al., 2004	China: Welding shop wkrs	lead	SRT Aim, DigSpan, DigSym
Kim et al., 2005	Korea: welders, smelter wkrs, welding rod mfg wkrs	manganese	Aim, Benton, DigSpan, POMS SA,
Young, Myers, & Thompson, 2005	South Africa: Smelter wkrs	Manganese	DigSpan
Yuan et al., 2006	China: Welders	manganese	Aim, DigSpan, DigSym, POMS, SRT
Chia, Huijun, Theng, & Yap, 2007	Singapore: Mfg	Lead	Aim, SA
F. Wang et al., 2007	China: Coke oven wkrs		POMS +
D. L. Zhou et al., 2007	China: Vanadium wkrs	vanadium	Aim Benton, SA
Nie et al., 2008	China: Coke oven wkrs	polycyclic aromatic hydrocarbons (PAHs)	Aim, Benton, DigSpan, DigSym
X. L. Wang et al., 2008	China: Welders	lead, cadmium, manganese	Lead: DigSpan, POMS; Manganese: DigSpan, POMS
Gao, Lu, Li, & Tian, 2010	China: Storage battery wkrs	inorganic lead	DigSpan
Niu, Zhang, Li, & Li, 2010	China: Coke oven wkrs	benzo[a]pyrene	DigSpan
Zhang et al., 2011	China: Ethylbenzene-exposed wkrs	ethylbenzene	Benton, DigSpan, DigSym, POMS, SA
H. Li et al., 2013	China: Vanadium-exposed wkrs	vanadium	Aim, Benton, DigSpan, POMS, SRT
Qiu, Peng, Cheng, Xia, & Tu, 2013	China: Coke oven wkrs	benzo[a]pyrene	Aim, DigSpan, DigSym, SRT

na = not applicable; nd = not described;

* could not be confirmed

Industries: Mfg = manufacturing; wkrs = workers

Tests: SA = Santa Ana; Aim = Pursuit Aiming; SRT = Simple Reaction Time; POMS = Profile of Mood States; DigSym = Digit Symbol; Benton = Benton Visual Retention Test; DigSpan = Digit Span

Table 3

Number of studies reporting a significant effect adverse effect and the chemicals in which the effects were reported (multiple citations are noted in parentheses) for each NCTB test.

NCTB Test	Number of Studies	Chemical/Physical agents
Santa Ana	12	ethylbenzene, lead (5), manganese, organophosphorus pesticides, solvents (3), vanadium
Pursuit Aiming	18	aluminum (2), benzo[a]pyrene, lead (7), manganese (2), organophosphorus pesticides, polycyclic aromatic hydrocarbons, solvents (2), vanadium (2)
Simple Reaction Time	12	benzo[a]pyrene, electromagnetic radiation, lead (4), manganese, organophosphorus pesticides, solvents (2), trichloroethylene, vanadium
Digit Span	17	benzo[a]pyrene (2), ethylbenzene, lead (3), inorganic lead, manganese (4), mercury, polycyclic aromatic hydrocarbons, solvents, styrene, trichloroethylene, vanadium
Digit Symbol	18	aluminum (2), benzo[a]pyrene, ethylbenzene, lead (5), manganese, mercury, organophosphorus pesticides, polycyclic aromatic hydrocarbons, solvents (3), styrene, trichloroethylene,
Benton	12	ethylbenzene, lead (3), manganese, mercury, polycyclic aromatic hydrocarbons, solvents, styrene, trichloroethylene, vanadium (2)
Profile Of Mood States	14	aluminum (2), ethylbenzene, lead (3), inorganic lead, manganese (3), organophosphorus pesticides, solvents, trichloroethylene, vanadium
Methods and summary studies	8	

Table 4

Discussion Group Participants, their Affiliation and their Country.

Name	Affiliation	Country
W. Kent Anger	Oregon Health & Science University	US
Rosemarie Bowler	San Francisco State University	US
Ulrike Dydak	Purdue University and Indiana University School of Medicine	US
Zelda Holtman	University of Cape Town	South Africa
Eun A Kim	Korea Occupational Safety and Heath Agency (KOSHA)	Korea
Leslie London	University of Cape Town	South Africa
Roberto G. Lucchini	University of Brescia and Mt. Sinai School of Medicine, New York	Italy and US
Doreen McGough	International Manganese Institute	France
Monika Meyer-Baron	Leibniz Research Centre for Working Environment and Human Factors	Germany
Jonny Myers	University of Cape Town	South Africa
Aiwerasia Vera Ngowi	Muhimbili University of Health & Allied Sciences	Tanzania
Stephanie Juran	Karolinska Institutet	Sweden
Diane S. Rohlman	University of Iowa	US