Neuropsychological Profiles in Toxicant-Induced Encephalopathies

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Roberta F. White, PhD, ABPP

How do we diagnose these disorders?

- Exposure history
- Medical history
- Domain-specific neuropsychological test findings
- Differential diagnosis
- Taxonomy
  - Lead encephalopathy
  - Solvent encephalopathy

Classification of Toxicant-Induced Encephalopathies (TE) (1)

(Modified from White et al., 1991)

I. Acute organic mental disorders
   A. Acute intoxication
      1. Duration: minutes
      2. Residua: none
      3. Symptoms: CNS depression, psychomotor or attentional deficits

Classification of TE (2)

I. Acute organic mental disorders
   B. Acute encephalopathy
      1. Symptoms: confusion, coma, seizures
      2. Pathophysiology: cerebral edema, CNS capillary damage
      3. Residua: permanent cognitive deficit may occur

Classification of TE (3)

II. Chronic organic mental disorder
   A. Organic affective syndrome
      1. Symptoms: mood disturbance (depression, irritability, fatigue, anxiety)
      2. Duration: days to weeks
      3. Residua: none

Classification of TE (4)

II. Chronic organic mental disorder
   B. Mild chronic encephalopathies
      1. Symptoms: fatigue, mood disturbance, cognitive complaints
      2. Course: insidious onset
      3. Duration: months to years

Classification of TE (5)

II. Chronic organic mental disorder

B. Mild-moderate chronic encephalopathies

4. Cognitive deficits: may include attentional impairment, motor slowing or in-coordination, visuospatial deficits, short-term memory loss
5. Residua: improvement may occur in absence of exposure but permanent mild cognitive deficits can be seen

Classification of TE (6)

II. Chronic organic mental disorder

C. Severe chronic encephalopathies

1. Symptoms: cognitive and affective change sufficient to interfere with daily living
2. Cognitive deficits: same as in mild chronic encephalopathies but more severe
3. Neurologic deficits: abnormalities seen on neurophysiologic measures (e.g., CT, EMG, MRI, EEG)

Classification of TE (7)

II. Chronic organic mental disorder
   C. Severe toxic encephalopathies
      4. Course: insidious onset, irreversible
      5. Residua: permanent cognitive dysfunction

Pesticides, organophosphates and AChE Inhibitors

Exposed populations

- Forest workers
- Greenhouse workers
- Pesticide manufacturing workers
- Suicide attempts
- Food contamination
- Water contamination
- Nerve gas agent manufacturing workers
- Nerve gas agent exposure (sarin, tabun, VX)

What does the research literature show?

Research Findings

- Evidence of residual CNS impairment in absence of obvious physical disease and years after exposure
- Prominent domains
  - Mood
  - Motor (fine manual motor speed)
  - Visuospatial (visual constructional)
  - Visual memory (learning, retrieval)
  - (Attention/executive/working memory)

What does the clinical literature tell us?

- Neurological manifestations of OP intoxication
- Neuropsychological sequeale of acute or chronic exposures in individual patients

OP Intoxication

- 1) acute cholinesterase crisis
- 2) intermediate syndrome
- 3) delayed peripheral neuropathy

Acute cholinergic crisis (ACC)

- Onset within hours of exposure
- Duration: up to 96 hours
- Mechanism: inhibition of neural AChE

ACC symptoms--2

- Muscarinic (inhibitory) receptor stimulation by ACh
  - Decreased visual acuity
  - Lethargy
  - Ataxia (loss voluntary movements)
  - Seizures
  - (Coma)

Intermediate Syndrome (IS)

- Onset 24-96 hours post-exposure
- Duration: up to 6 weeks
- Mechanism: prolonged stimulation at neuromuscular junction

Intermediate syndrome symptoms

- Muscle weakness (proximal limbs, neck)
- Reflex abnormalities
- Cranial nerve abnormalities
- Depressed respiratory muscle function
- (Death)
- (Muscle fiber necrosis)

Organophosphate-induced delayed neuropathy (OPDIN)

- Onset 1-5 weeks post-exposure
- Mechanism: inhibition of neuropathy target esterase

OPIDN symptoms

- Muscle weakness
- Paresthesias (tingling, pain)
- Diminished reflexes
- Recovery in reverse order from onset

Neurophysiological diagnosis

- EEG: > theta (subclinical), > spike waves (with seizures)
- Evoked potentials: abnormal visual and auditory EPs
- Nerve conduction studies: subclinical neuropathy
- EMGs: normal in intermediate stage, abnormal in OPIDN

Clinical Neuropsychological Manifestations of Neurotoxicity: Case Findings

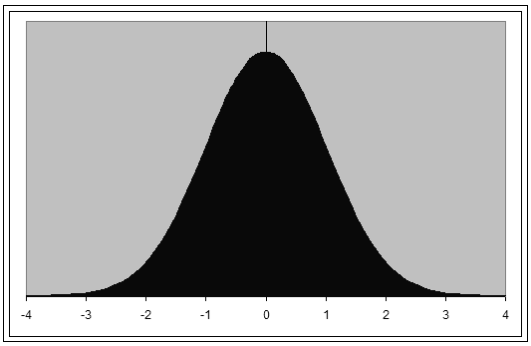
- Mood changes/fatigue
- Motor dysfunction
- Visual-constructional deficits
- Visual memory (learning retrieval)
- (Attention/executive working memory)
- Intact language

- Parkinsonian syndromes

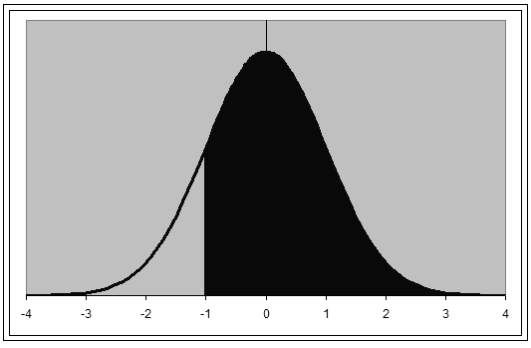
How do the clinical and epidemiological findings fit together?

- Same neuropsychological domains affected but different levels of deficit required for “significance” when interpreting findings

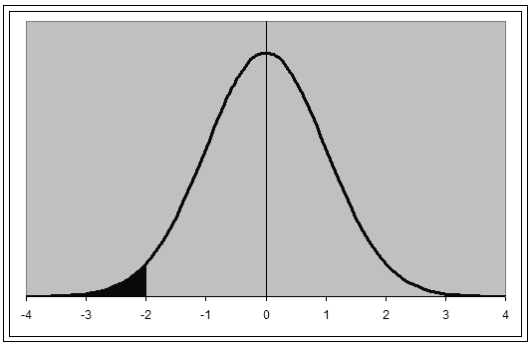
Epidemiological - 1



Epidemiological - 2



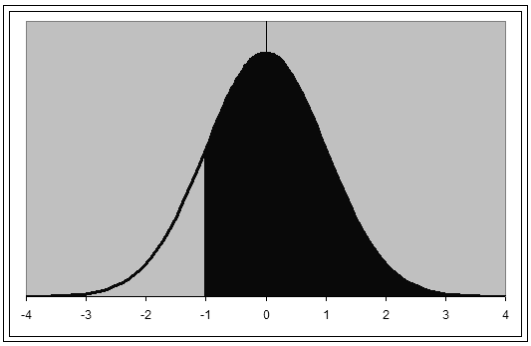
Clinical -1



Clinical Issues

- Patients can have abnormal neuropsychological or brain imaging results
- However, they can also have results that are interpreted as being in the normal range but be symptomatic and have critical functional issues in daily life

Subclinical



Questions?