reflect central nervous system activity comparable to that of epilepsy in humans and could be defined as neurotoxicity. Occasionally, other toxic actions of compounds, such as direct effects on muscle, might mimic some convulsion-like behaviors. In some cases, convulsions or convulsion-like behaviors may be observed in animals that are otherwise severely compromised, moribund, or near death. In such cases, convulsions might reflect an indirect effect of systemic toxicity and are less clearly indicative of neurotoxicity. As discussed in the section on neurophysiological measures, electrical recordings of brain activity could be used to determine specificity of effects on the nervous system.

(5) Specialized tests for neurotoxicity. Several procedures have been developed to measure agent-induced changes in specific neurobehavioral functions such as motor, sensory, or cognitive function (Tilson, 1987; Cory-Slechta, 1989). Table 6 lists several well-known behavioral tests, the neurobehavioral functions they were designed to assess, and agents known to affect the response. Many of these tests in animals have been designed to assess neural functions in humans using similar testing procedures.

TABLE 6.—EXAMPLES OF SPECIALIZED BEHAVIORAL TESTS TO MEASURE NEUROTOXICITY

Function	Procedure	Representative agents
Neuromuscular:		
Weakness	Grip strength; swimming endurance; suspen- sion rod; discriminative motor function.	n-Hexane, methl n-butylketone, carbaryl.
Incoordination	Rotorod, gait measurements, righting reflex	3-Acetylpyridine, ethanol.
Tremor	Rating scale, spectral analysis	Chlordecone, Type I pyrethroids, DDT.
Myoclonia spasms	Rating scale, spectral analysis	DDT, Type II pyrethroids.
Sensory:		
Auditory	Discrimination conditioning Reflex modification	Toluene, trimethyltin.
Visual	Discrimination conditioning	Methylmercury.
Somatosensory	Discrimination conditioning	Acrylamide.
Pain sensitivity	Discrimination conditioning (titration); func- tional observational battery.	Parathion.
Olfactory	Discrimination conditioning	3-Methylindole, methylbromide.
Learning/Memory:		
Habituation	Startle reflex	Diisopropyl-fluorophosphate (DFP) Pre/ neonatal methylmercury.
Classical conditioning	Nictitating membrane	Aluminum.
	Conditioned flavor aversion	Carbaryl.
	Passive avoidance	Trimethyltin, IDPN.
	Olfactory conditioning	Neonatal trimethyltin.
Operant conditioning	One-way avoidance	Chlordecone.
	Two-way avoidance	Pre/neonatal lead.
	Y-maze avoidance	Hypervitaminois A.
	Biel water maze	Styrene.
	Morris water maze	DFP.
	Radial arm maze	Trimethyltin.
	Delayed matching to sample	DFP.
	Repeated acquisition	Carbaryl.
	Visual discrimination	Lead.

A statistically significant chemically induced change in any measure in Table 6 is presumptive evidence of adverse effect. Judgments of neurotoxicity may involve not only the analysis of changes seen but the structure and class of the chemical and other available neurochemical, neurophysiological, and neuropathological evidence. In general, behavioral changes seen across broader dose ranges indicate more specific actions on the systems underlying those changes, i.e., the nervous system. Changes that are not dose dependent or that are confounded with body weight changes and/or other systemic toxicity may be more difficult to interpret as neurotoxic effects.

(a) Motor function: Neurotoxicants commonly affect motor function. These effects can be categorized generally into (1) weakness or decreased strength, (2) tremor, (3) incoordination, and (4) spasms, myoclonia, or abnormal motor movements (Tilson, 1987; Cory-Slechta, 1989). Specialized tests used to assess weakness include measures of grip strength, swimming endurance, suspension from a hanging rod, and discriminative motor function. Rotarod and gait assessments are used to measure incoordination, while rating scales and spectral analysis techniques can be used to quantify tremor and other abnormal movements.

(b) Sensory function: Gross perturbations of sensory function can be observed in simple neurological assessments such as the FOB. However, these tests may not be sufficiently sensitive to detect subtle sensory changes. Psychophysical procedures that study the relationship between a physical dimension (e.g., intensity, frequency) of a stimulus and behavior may be necessary to quantify agentinduced alterations in sensory function. Examples of psychophysical procedures include discriminated conditioning and startle reflex modification.

(c) Cognitive function: Alterations in learning and memory in experimental animals must be inferred from changes in behavior following exposure when compared with that either seen prior to exposure or with a nonexposed control group. Learning is defined as a relatively lasting change in behavior due to experience, and memory is defined as the persistence of a learned behavior over time. Table 6 lists several examples of learning and memory tests and representative neurotoxicants known to affect these tests. Measurement of changes in learning and memory must be separated from other changes in behavior that do not involve cognitive or associative processes (i.e., motor function, sensory capabilities, motivational factors). In addition, any apparent toxicant-induced change in learning or memory should ideally be