



The Carousel Network

**Chronic Neuroimmune Disease  
Information and Support for Sonoma County**  
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Santa Rosa, CA 95409  
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## **Protocol for Cognitive Assessment for CFIDS** **Curt A. Sandman, PhD and Stephanie Moore, PsyD**

A battery of standardized tests typically used by neuropsychologists to evaluate patients can be useful in documenting the deficits typically experienced by those diagnosed with chronic fatigue syndrome and/or multiple chemical sensitivity. In the absence of definitive laboratory tests, such neuropsychological batteries, which can differentiate between those suffering from primary depression, dementia, and other disorders, may be useful documentation of the disorder and deficits or organic brain damage resulting from chemical exposures.

*The Carousel Network (TCN) offers information on the various diseases and disorders associated with chronic neuroimmune diseases, such as chronic fatigue syndrome, fibromyalgia, multiple chemical sensitivity, autoimmune thyroid disease, etc. The information is intended to help patients and caregivers make informed decisions about the patient's health, diagnostic testing, and treatment in conjunction with their health care practitioners. TCN does not diagnose patients nor recommend specific medical or palliative treatments.*

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**Protocol for Cognitive Assessment for CFIDS**  
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Two basic questions can be resolved by performing neuropsychological evaluations in CFIDS patients. The first question is "What effects on the brain and behavior are specific and unique to CFIDS?" The second question is "Are there idiosyncratic effects of CFIDS related to patient strengths and weaknesses?" The implications of these questions are quite different, but both are important to answer.

The first question about the specific and unique effects of CFIDS provides basic information about the influence of the disease on the brain and behavior. Until the cause of CFIDS is known and a diagnostic test is available, these effects can serve as markers of the disease to assist in diagnosis. In addition, CFIDS-specific profiles are useful for explaining to patients what to expect and how to compensate for losses. These profiles are guides for research and are clues about which areas of the brain are compromised.

The second question about idiosyncratic effects of CFIDS relates to the interaction between the disease and patient history. Each patient has a unique life history with a special collection of strengths and weaknesses. The influence of CFIDS, as with other neurological and brain disorders, is manifested against this background. Because patients' backgrounds differ, this effect is highly individual.

To answer the first question, a series of tests are needed that are sensitive to the effects of CFIDS (can detect deficits) and can differentiate CFIDS from other diseases (specificity). The development of sensitive and specific test systems has been an elusive goal of neuropsychology. For instance, despite great efforts, no such neuropsychological test system is accepted for Alzheimer's Disease. In addition to requiring extensive effort, the development of such a test system requires serendipity.

Development of the ideal test system demands a large group of well-diagnosed CFIDS patients, groups of healthy subjects matched for age and education with the patients (control group), and at least one other disease group that may share symptoms with the CFIDS group. Tests must be selected that are relevant to the disease, or a large battery of tests can be administered and their diagnostic utility determined empirically. Our approach included all of these components.

We focused on memory because of the initial working case definition of the CDC and included depressed patients as a comparison group because depression was a common complaint of CFIDS patients. Further, there was (is) considerable debate in the literature about the relationship between CFIDS and depression. Our specific and unique effects of CFIDS were confined to the memory tests, but we have described briefly the entire test battery so the context for the conclusions is understood.

A battery of traditional neuropsychological tests were administered only to the CFIDS patients, including mental status examinations (Mini-Mental State Examination; Blessed; Benton; Temporal Orientation Test), Wechsler Adult Intelligent Scale-Revised, Wechsler Memory Scale-Revised, Wisconsin Card Sort Test, Trail-Making Test, Boston Naming Test, and the Visual-Function scale (C4) of the Luria Nebraska Neuropsychological Battery. Comparisons with normative groups were made.

The focused memory tests (Irvine Memory Battery) were administered to all groups with an interactive computer system (Computerized Memory and Interactive Dementia System; C-MIND, Neurocomp, Newport Beach, CA). Two separate studies have been completed with slightly different versions of the C-MIND system. Although the conclusions are identical, the effects were strongest with the latest version of the system. The procedures for the current version are described below.

## Recall

One of the primary questions to resolve about memory deficits is whether the difficulty is in making new memories (consolidation) or in locating memories (retrieval). Our test system has the ability to differentiate these two crucial processes by determining the utility of cues for recalling information. Briefly, patients with retrieval problems benefit from cues, while those with consolidation problems do not. To start the test, patients were told they would see 12 words on the screen and were then asked to estimate how many words they expected to recall (metacognitive estimate). Twelve words were presented on the computer screen, one at a time (one-second duration) and patients were asked to recall as they could. For the second recall test, patients were provided cues to assist recall. Word pairs (12) were presented, one pair at a time (i.e., "day-night"). Recall was cued by presenting the stem word (e.g., "day") on the screen. The third recall test was similar to the second test, except the patients were shown four words on the screen and asked to choose the associated word.

### Proactive Inhibition (PI)

The test of proactive inhibition required the patient to briefly retain three items in memory while being distracted by a computer game for ten seconds. The three items included a list of letters, numbers, and related words. The information appeared on the computer screen for a brief period, then a maze appeared and the patient had to "drag" (on a touch-sensitive screen) a target through the maze. The primary purpose of the game was to distract the patient and discourage active rehearsal of the three items. Normal, healthy controls retained the three items and were not influenced by the maze. Prevention of rehearsal in CFIDS patients resulted in confusion between previously learned information and recent information. Furthermore, if the recent information was similar to previous information, the probability of distortion was greater (PI error). This test allowed assessment of interference on memory and specifically: 1) the decay in memory when rehearsal was discouraged, and 2) the organization of memory when similar information was presented.

### Item Recognition

Mental efficiency decreases as the amount of information increases. This test assessed the effects on memory efficiency of increased mental load or information. Patients were asked to remember various amounts of information for a short time. Then a target appeared on the screen and the patient had to determine if the target was part of the information they were asked to remember. They pushed one key if the target was part of the memory set and another key if it was not. Reaction time for decision-making and visual scanning (i.e., mental speed) was separated from motor (or simple response) speed.

### Semantic Memory Test (SMT)

This test examined access to information accumulated over the course of a lifetime. Common categories (e.g., fabrics) were presented one at a time for 1200ms, followed by words that were (e.g., wool) or were not (e.g., desk) an example of that category. Patients pushed a key to signify their responses.

### Results

Although CFIDS patients had normal neuropsychological profiles (determined by classical neuropsychological tests), they exhibited memory deficits significantly different from depressed and control subjects. The most obvious difficulty was distractibility. CFIDS patients lost the ability to retain three-item lists when a simple, irrelevant 10-second task was interposed between the items and recall. A competing task erased their fragile memories of simple information. The performance of the CFIDS patients was seven-fold worse than either the control or depressed group, and 90 percent of the CFIDS patients made more errors than the mean value of healthy controls and depressed patients. The second major difficulty was making memories (consolidation). Unlike the healthy controls or depressed patients, the CFIDS patients failed to benefit from cues (priming or increasing context) in tests of recall. The CFIDS patients, who characteristically expected to recall more than they did, appeared to be uncertain and misinformed about their memory function. In addition, CFIDS patients exhibited significant delay in mental speed as information increased. In these specific tests of memory, but not in other widely used tests of general neuropsychological function, CFIDS patients had highly significant deficits in memory consolidation, were vulnerable to interference, slow or uncertain in decision-making, and relatively unaware of their difficulties. Apparently, CFIDS patients made weak memory traces that were very easily perturbed. These results indicated that the memory deficit in CFIDS was more severe than assumed by CDC criteria.

The pattern of weak consolidation and vulnerability to interference has been reported in patients with diseases affecting the medial temporal cortex, hippocampus, and structures of the limbic system, including Huntington's Disease and herpes simplex encephalitis. These relationships are particularly interesting because of the recent reports of temporal lobe hypoperfusion as measured with SPECT scans in CFIDS patients by Dr. Ismael Mena. Preliminary comparison of markers from our battery and from the SPECT scans yielded very high associations in six CFIDS patients examined.

As reviewed above, each patient has a unique personal history that adds dimensions to the effects of CFIDS. For instance, a physician who had frontal head trauma from a car accident that occurred in the 1960s, began manifesting frontal symptoms for the first time in the late 1980s, shortly after CFIDS developed. In addition to the classical CFIDS profile, he developed loss of executive functions, impulsivity, and aggression, typically not part of the CFIDS profile. Possibly, the dormant brain injury was exacerbated or "liberated" by CFIDS onset. These symptoms are not detectable without a comprehensive, general battery of test instruments.

## Summary

To summarize, the unique and specific effects of CFIDS included pathological overestimation of ability (metamemory), inability to recall information even with cues, serious distractibility and inability to concentrate, and slowed mental processing and decision-making. The protocol for these deficits involves three tests (and can be simplified). The most sensitive is the PI test (about 10 minutes). The recall test (about seven minutes) adds to the sensitivity of the profile. The item recognition test (10 minutes) produces a modest improvement on the utility of the specific battery to detect CFIDS deficits.