

6. ADD DIAGNOSIS

CATEGORICAL VS DIMENSIONAL DIAGNOSIS

Information technology is classically binary: on or off, 0 or 1. So is medical diagnosis: the lesion is cancerous, or not; you are pregnant, or not; you either had a heart attack or you didn't. Cancer, pregnancy and heart attacks are what are called categorical diagnoses. You either fall into the category, or you don't.

Modern living, on the other hand, is largely concerned with disorders that are dimensional in nature. Obesity, hypertension, diabetes, hypercholesterolemia are examples of dimensional diagnoses. The conditions exist along a continuum, and beyond a certain point, they are said to be pathological and deserving of treatment. The pathological thresholds are necessarily arbitrary. They are established by committees of experts who base their decisions on statistical models of risk. If your waistline exceeds 36 inches, for example, you are likelier to have a myocardial infarction.¹ Every small increment in one's levels of HbA1c is associated with an increase in risk of heart failure and cardiovascular death.²

The tradition of categorical diagnosis arose during the centuries when physicians dealt primarily with diseases, and when patients didn't go to doctors until they were very, very sick. Smallpox, cancer, rheumatic heart disease and nephritis are overt diseases, and the signs and symptoms are explicable in terms of pathological anatomy and pathophysiology. The relationship between pathogens and infectious disease is direct, and the importance of specific etiologies has infused medicine with a deterministic streak that ill fits current circumstances. As a way of thinking, it is less pertinent to the present orientation of medicine, at least in the developed world, which is to the preservation of health, the prevention of disease, and the appreciation that most modern diseases can be anticipated by risk factor analysis. Risk factors contribute to the development of disease, but they are not etiological. In fact, studying the special cases where known risk factors do not lead to disease (e.g., the "French paradox") has been especially fruitful.

Neuropsychiatry is unique in medicine for its concentration of disorders that are dimensional rather than categorical in their structure. To the early psychiatrists, conditions like dementia praecox, catatonia, melancholia and manic-depression were obviously categorical; the ready availability of psychiatric treatment, especially drugs, has diminished the frequency with which these catastrophic conditions occur, however. Psychiatry is increasingly concerned with partial or subthreshold conditions that are more appropriately given to dimensional definition. Thus psychiatry struggles against the formidable challenge of fitting dimensional conditions into a categorical, Kraepelinian nosology. The next generation of diagnostic manuals is likely to merge dimensional features into a categorical system, but it is a formidable challenge.³

1 Circulation. 2008 Jul 29;118(5):482-90. Relation between body mass index, waist circumference, and death after acute myocardial infarction. Zeller M, Steg PG, Ravisy J, Lorgis L, Laurent Y, Sicard P, Janin-Manificat L, Beer JC, Makki H, Lagrost AC, Rochette L, Cottin Y; RICO Survey Working Group.

2 Arch Intern Med. 2008 Aug 11;168(15):1699-704. The hemoglobin A1c level as a progressive risk factor for cardiovascular death, hospitalization for heart failure, or death in patients with chronic heart failure: an analysis of the Candesartan in Heart failure: Assessment of Reduction in Mortality and Morbidity (CHARM) program. Gerstein HC, Swedberg K, Carlsson J, McMurray JJ, Michelson EL, Olofsson B, Pfeffer MA, Yusuf S; CHARM Program Investigators.

3 Eur Arch Psychiatry Clin Neurosci. 2008 Mar;258 Suppl 1:6-11. Refinement of diagnosis and disease classification in psychiatry. Lecrubier Y.

ADD is a good place to address of the problem of neuropsychiatric diagnosis, because it is so clearly a dimensional disorder: a relative weakness of certain regulatory systems that is aggravated or mitigated by endogenous and exogenous factors. All of the diagnostic tools in psychiatry, neurology and psychology have been brought to bear, with more or less success, as we shall see, but every method that has posed as a frog test for ADD has failed miserably. The clinicians who pronounce, "Yes, you have ADD" on the basis of some new technological marvel are no less than mountebanks. The role of the diagnostician, in this case, as in so many others in our field, is not "knowing thoroughly" and affecting a cure, but making sense of multiple data inputs and identifying a problem that may be amenable to improvement.

Fuzzy Sets & Centroid Averagers

Ever since Aristotle, a dominant theme in Western thinking has been the *law of the excluded middle*: that everything is, in principle at least, either A or not-A. *Of any subject, one thing must be either asserted or denied.* Fuzzy logic, however, is different from classical or Aristotelian logic. Fuzzy logicians grapple, in mathematical terms, with the behavior of complex systems, where, in reality, things may be a bit A and a bit not-A. Fuzzy set theory allows something to be partly a member of one set and partly a member of another. It is not simply a theoretical exercise. Applications of fuzzy set theory allow the digital computer to run complex systems, like climate-control systems in large buildings or mass transportation networks or voice recognition software, with a high degree of precision.

The founder of fuzzy set theory, Lofti Zadeh, was preoccupied with applying mathematical principles to the study of biological systems.⁴ His basic rule for dealing with complexity was to simplify. Not all available information needs to be used and an increased amount of uncertainty is accepted in order to create robust summary concepts. In fuzzy logic, the truth of any statement is a matter of degree.

The rules of fuzzy logic are clearly applicable to the study of the nervous system, a system of inordinate complexity, and where the relations between structure and function are obscure, to say the least. In the CNS, the idea of organization by serial and hierarchical control modules has been abandoned in favor of the idea of functional assemblies or syncytia of cells, whose aggregate behavior varies in nature and intensity in response to a host of internal and external constraints. Cells in one assembly are associated with cells in other assemblies; under certain circumstances, they have a partial association with one behavioral action, and in other circumstances have different amounts of association with other behavioral actions. The boundaries of structures within the CNS are imprecise because they participate, to varying degrees, in many behavioral programs. CNS structures, or cell assemblies are not well "insulated" one from another. They "leak."⁵

When a digital computer is programmed to operate by fuzzy logic, it uses an algorithm known as "centroid averaging." The relative importance of a host of dimensional inputs is computed and translated into an intelligent action step. This process is iterated and reiterated by feedback from the environment until the desired result is attained. It is appropriate to suggest that the neuron, too, is a centroid averager, processing input from synapses and extrasynaptic receptors, from glia and the extracellular fluid; and that cell assemblies are centroid averagers, processing input from other cell assemblies with which they are associated in different ways. Complex functional systems compute dimensional inputs from multiple sources, and the organism itself is the final or ultimate centroid averager.

4 Zadeh, L.A., "Outline of a new approach to the analysis of complex systems and decision processes," IEEE Transactions on Systems, Man, and Cybernetics, Vol. 3, No. 1, pp. 28-44, Jan. 1973.

5 Gualtieri, C.T. Brain Injury and Mental Retardation: Psychopharmacology and Neuropsychiatry. Lippincott, Williams & Wilkins, Baltimore, 2002.

Most neuropsychiatric disorders are, by their nature, dimensional. Even the outcomes of stroke and brain injury are determined by multiple dimensional inputs that are, in many cases, more important than the lesions themselves. In evaluating the clinical state of a brain injury patient, for example, the physician himself is a centroid averager, computing the relevance and importance of a host of dimensional inputs in order to generate an intelligent action step.

The diagnostic entities of Kraepelinian psychiatry are categories, by convention. In fact, they are centroid averages. They are the overt manifestation of a host of dimensional inputs. That is why their symptoms are so diverse and overlapping and why symptoms are mutable over time. All of the psychiatric disorders have a well-defined center and fuzzy boundaries; that is, pure types are readily diagnosable, but borderline conditions, with symptoms that are typical of different conditions, are very difficult to diagnose with precision.

So it is with ADD. It isn't a problem making the diagnosis in a child who never can sit still and whose attention span is less than a minute. It is a bit more problematic when the patient is a student who feels he studies long hours but is inefficient or a fellow who gets impatient and surly if a meeting lasts longer than 20 minutes. Or a patient who walks into your office, announces "I have ADD" and demands a prescription for amphetamines.

CONVENTIONAL APPROACHES TO ADD DIAGNOSIS

Fuzzy logic is a good way to approach the mild cognitive disorders in general and ADD in particular. So, this discussion of ADD diagnosis will be developed in detail, because an intelligent approach to ADD diagnosis can be applied, with only small modification, to all of the mild cognitive disorders. It is possible to be objective in diagnosing the condition, even though so much about it is subjective. The method is not probabilistic, it is fuzzy. Probability tells you how likely it is that a person with certain characteristics is ADD; that is, how likely the patient is to fall into that category. Fuzzy logic tells you to what degree the patient has problems with attention and executive control; that is, where he or she stands with respect to the various dimensions that comprise ADD.

ADD is a relative weakness in one's ability to regulate attention and executive control of behavior and emotional responding. The central elements of the disorder are functions that are outer-directed (attention, behavioral and emotional responding); for that reason, the difficulties that patients experience are usually in their adaptation to external events. For the same reason, certain environments evoke or aggravate the symptoms, and other kinds of environment do not.

Because ADD is a condition that exists in equilibrium with a social and educational milieu, a special responsibility devolves upon the physicians and psychologists who diagnose the disorder. The disorder has a variable "threshold of expression," but the arbiters of where, precisely, that threshold lies are the doctors who make the diagnosis. Problems with attention and memory are among the most common complaints a normal individual will make, and most patients who complain of memory problems actually have deficits in attention. How does one decide whether those problems are simply normal variations of the human condition, or whether they are pathological? Is "pathological" the right word to use? How to be objective about it, not just relativistic. Physicians shouldn't take lightly a medical diagnosis that commits schools to additional expense, affords patients special privileges, and releases into a vulnerable population yet one more class of drugs with potential for harm.

The problem of ADD diagnosis is the formidable challenge of applying categorical thinking to a condition that is dimensional in nature. For the conventional diagnostician, the variability of its clinical presentation, the non-specific nature of its signs and symptoms and the unreliability of diagnostic instruments like ADD rating scales and the CPT are stumbling-blocks. To the fuzzy logician, variability, non-specificity, and unreliability are the necessary attributes of biological systems, and they have to be dealt with. In fact, most doctors who treat ADD

patients obey the rules of fuzzy logic without knowing it. They assign greater or lesser value to different inputs. The rating scale results of a custodial parent who knows the child well and is trying to help him succeed in school are assigned a higher value than the rating scale results of a hostile ex-husband whose priority is to make his ex-wife's life simply miserable, or of a teacher who doesn't believe in ADD. The results of cognitive testing are assigned more or less value for a graduate student who is having problems with her dissertation or an eight year old who can't sit still. In the former, for example, the CPT will almost always be perfectly normal, while performance on effortful attention tests will show deficits. The clinical complaints of an abrasive, volatile adult who insists that he is ADD and demands Adderall® are taken in a different vein from those of an earnest fellow who keeps losing jobs because he can't keep up with his paperwork.

This is how one falls into the ADD category. Buy a book or visit an internet site, and respond to questions like this:

- Do you fail to give close attention to details?
- Do you make careless mistakes at school or at work?
- Do you sometimes not listen when spoken to directly??
- Do you feel restless?
- Do you dislike work that requires sustained mental effort?
- Do you talk excessively?
- Do you lose things?
- Are you forgetful?
- Do you have difficulty doing fun things quietly?

The authors advise that if you respond "yes" to several of these questions, you probably "have ADD." In other words, if you think you have ADD, then you do. If it seems outlandish, it is only because it is. This is only a mild exaggeration of what comprises the "diagnostic" process for ADD, even in clinical trials.

Physicians use ADD rating scales more than any other instrument for the diagnosis of ADD in children, adolescents and adults. In our opinion, rating scales are a necessary part of the diagnostic process, but they are not sufficient. The advantage of rating scales is that they are a systematic way to ask about symptoms. The disadvantage is that they really just ask the patient (or the parent or teacher) the same question, over and over again, in slightly different ways. Rating scales are prone to what is known as a "halo effect." If you think you have ADD, or your kid, or your husband, you will mark every question "moderate" or "severe."

At the opposite extreme, a few clinicians take a pseudo-neurological approach to diagnosis. They use irrelevant technologies like quantitative EEG or SPECT imaging to diagnose the condition. After all, ADD is a brain-based disorder. This approach is as irrelevant as the old method of relying on neurological "soft signs." It is expensive, and there is no scientific basis whatever for relying on such tests to make the diagnosis, to confirm it or to "subtype" the condition.

Clinical psychologists often rely on psycho-educational tests – the usual test battery is an IQ test *cum* academic achievement tests. This is not a bad approach, but it is expensive. Unfortunately, such testing is not necessarily diagnostic. So, after incurring great expense, parents may learn that all that testing hasn't established whether their child has ADD or not. Giving a patient a test in a one-to-one session with a psychologist may or may not evoke the signs or symptoms of ADD.

This is *argumentum ad absurdum*, of course, and no respectable psychiatrist or psychologist advocates making the diagnosis of ADD simply on the basis of a rating scale, an EEG or a psychological test. But it conveys the quandary primary medical practitioners experience when confronted with a young patient – "Doctor, the teachers

say my son is hyperactive and needs Ritalin” – or an adult patient who announces that he has ADD and needs his prescription for amphetamine refilled.

RECOMMENDED APPROACHES

This from the Council on Scientific Affairs, American Medical Association, in 1998:

The overall approach to diagnosis may involve (1) a comprehensive interview with the child’s adult caregivers; (2) a mental status examination of the child; (3) a medical examination for general health and neurological status; (4) a cognitive assessment of ability and achievement; (5) use of ADHD-focused parent and teacher rating scales; and (6) school reports and other adjunctive evaluations if necessary (speech, language assessment, etc)....⁶

The economic impact of applying this method to a disorder that afflicts 5-10% of schoolchildren is well worth contemplating. Indeed, “diagnostic complexity” and “time constraints” were among the reasons cited by general practitioners for their “low level of interest” in ADHD management.⁷ The American Academy of Pediatrics suggests a less ambitious, but more realistic approach: rating scales from parents and teachers, exclusion of alternative diagnoses, and developmental testing, if necessary. Family practitioners are advised to use rating scales, to review the child’s school progress, to screen for vision or hearing impairment and co-morbid psychiatric conditions, and to use “objective measures of cognitive function.”⁸ Child psychiatrists are urged to interview the child and to utilize direct observations.⁹

Table 6.1. Recommendations for ADHD Diagnosis

ADHD DIAGNOSIS	AMA	AAP	AAFP	AACAP
Clinical History	Yes	Yes	Yes	Yes
MSE of the child	Yes	No	No	No
Developmental Testing	No	No	No	No
Cognitive Testing	Yes	No	Yes	No
ADHD Rating Scales	Yes	Yes	Yes	Yes
Direct Observations	No	No	No	Yes
School Reports	Yes	No	Yes	Yes
Exclusion of Alternative Diagnoses	No	Yes	Yes	Yes
Vision/Hearing Screen	No	No	Yes	No

1. CLINICAL HISTORY AND EXAMINATION.

The clinical presentation of ADD is variable but certain elements are essential. The core symptoms are inattention/distractibility, hyperactivity/impulsiveness and excitability/emotional instability. Because these are relatively non-specific symptoms, however, it is necessary to exclude other likely causes. The clinical history/examination is not only to elicit the signs and symptoms of ADD, but also to elicit signs of other conditions

6 Goldman LS, Genel M, Bezman RJ, Slanetz PJ. Diagnosis and treatment of attention-deficit/hyperactivity disorder in children and adolescents. Council on Scientific Affairs, American Medical Association. JAMA 1998; 279: 1100-7.

7 Shaw K, Wagner I, Eastwood H, Mitchell G. A qualitative study of Australian GPs' attitudes and practices in the diagnosis and management of attention-deficit/hyperactivity disorder (ADHD). Fam Pract 2003; 20: 129-34.

8 Smucker WD, Hedayat M. Evaluation and treatment of ADHD. Am Fam Physician 2001; 64: 817-29.

9 Dulcan M, Popper C. Concise Guide to Child and Adolescent Psychiatry. Washington: 1991.

that may have similar symptoms. We have found that two classes of patients are particularly likely to identify themselves as ADD: patients with bipolar disorder or obsessive-compulsive disorder. Cannabis users and young alcoholics like stimulants, too, because they can function better during the day.

The subjective experience, or perception, of inattention, lack of focus and distractibility is not diagnostic of ADD; rather, it is the appropriate occasion for a differential diagnosis. As we shall see time and again in this book, patients' perceptions of cognitive disability are often at variance with the results of cognitive testing. Beware of the patient who marches into your office and announces that he or she has ADD.

A good number of young patients with anxiety or depression also have ADD. They are, all three, very common disorders, so there will invariably be overlap. The purpose of the clinical evaluation is to determine which is the "primary handicapping condition." Treat that one first; the other symptoms may well resolve with just one treatment.

The diagnostic manuals insist that the signs and symptoms of ADD should have been apparent in early childhood, but many adult patients were simply underachievers who were never identified, or good kids who worked extra hard to overcome their disability. The symptoms of ADD may not become apparent until the patient has hit the wall, in high school, college, or graduate school, and his native coping strategies are no longer effective.

The physical/neurological/mental state examination, by itself, is not likely to reveal signs of ADD, because the patients are usually able to maintain their attention perfectly well in novel situations and one-to-one interactions. For the same reason, psychological testing may not indicate inattention or distractibility. ADD patients, children and adults, can do well enough in short bursts. It is the rare ADD patient who is overtly disorganized or disinhibited during a short interview. Young patients may have difficulty persevering in complex motor tasks, like tandem walk, or will be inappropriately playful in finger-to-nose, but these signs, like other neurological soft signs, are not diagnostic. I have always felt that the neurological examination is a terrific mental state exam. Since one is relating to the patient in a familiar way, he is put at ease. Since parts of the examination are thoroughly novel, one arouses the patient's interest or suspiciousness. Through it all, one is interacting with the patient, measuring his relatedness, his sensitivity to touch, his response to commands and his behavioral flexibility. But it is hardly ever diagnostic.

The real purpose of the examination is to exclude other likely diagnoses. A patient presenting with complaints of ADD is the occasion for a differential diagnosis that should include all of the psychiatric, medical, neurological, sensory and developmental problems that can cause mild cognitive impairment, behavioral or emotional dyscontrol.

2. RATING SCALES

The expert panels are as strong in support of rating scales as they are of the clinical history. It is fair to say that rating scales the *sine qua non* of ADHD diagnosis. ADHD Rating scales have been used for almost 50 years. If a pediatrician has the Vanderbilt Rating Scale in hand, he or she feels that the standard of care has been met.¹⁰ Many universities will qualify students for LD services if they have the Brown Rating Scale.¹¹

In fact, there is no reason *not* use rating scales to evaluate ADHD symptoms in children. There is even a standardized instrument, the Wender Utah Rating Scale, which captures childhood symptoms of ADHD in patients

10 Wolraich ML, Hannah JN, Pinnock TY, Baumgaertel A, Brown J. Comparison of diagnostic criteria for attention-deficit hyperactivity disorder in a county-wide sample. *J Am Acad Child Adolesc Psychiatry* 1996; 35: 319-24.

11 The Psychological Corporation. Brown ADD Scale. San Antonio Texas: Harcourt Brace and Company, 1996

who present as adults.¹² Rating scales are good for delineating symptoms and their perceived severity. Ideally, several informants should fill out a rating scale: parents and teachers, patient and spouse.

Like the DSM-4, rating scales are systematic but not objective. They are prone to “halo” effects – if the informant thinks a kid is hyper and needs Ritalin®, he or she is likely to score every item as “a severe problem” or “all the time.” On the other hand, if one likes the kid or is opposed to drug treatment, every item may be marked “not at all” or “never.” Agreement among different raters – even two parents -- is seldom very good¹³; the expert panels have never advised practitioners how to reconcile disparate ratings.

Rating scales are a necessary component of the diagnostic process, but they are not sufficient. And if you are going to do a comprehensive assessment, with attention to the problem of differential diagnosis, you ought to apply scales to assess depression, anxiety, obsessive-compulsive symptoms and other potential conditions as well. This is exactly the problem we encountered in the Neuropsychiatry Clinics, as the number of rating scales began to multiply; it is what led us to develop the Neuropsych Questionnaire (Chapter 24).

3. PSYCHOLOGICAL TESTING

My previous remarks notwithstanding, in the hands of an experienced examiner, conventional psychological tests can often capture the elements of inattention and impulsivity that characterize patients with the disorder. Psychological testing is also capable of identifying cognitive disabilities that may compound the problem of ADD and complicate management. An ADD patient with a borderline IQ score, a memory problem or a specific learning disability will necessarily require a more comprehensive treatment program.

A conventional IQ test, like the WISC or the WAIS, affords the examiner an opportunity to observe the patient’s relative strengths and weaknesses in different kinds of tasks. ADD patients may do poorly on auditory immediate memory tasks that tend to be rote and lacking in context, like Digit Span or Number-Letter Sequencing. Their deficits may show up in index scores like Working Memory and Processing Speed.

There are two problems with (neuro)psychological testing as a routine approach to ADD diagnosis. One is expense. In our neighborhood, comprehensive psychological evaluations for ADD can cost between \$800 and \$2000. After the evaluation is done, the patient has to seek out a physician to get a prescription for medication. The second problem is that the ordinary psychoeducational battery is only an *indirect* measure of ADD. Attention deficits, locomotor hyperactivity and cognitive impulsivity may or may not be evidenced when a child is in a small room, one-on-one with a single adult. In fact, the “freedom from distractibility” factor of the WISC-III was not found to be “a reliable or a valid index of attention or a diagnostic screening measure for identifying children with ADD.”¹⁴ For these reasons, most psychologists who evaluate large numbers of ADD children tend to complement their testing battery with computerized tests of attention. After all, what could be more objective for ADHD diagnosis than a direct measure of the child’s attentional ability?

The tests that are usually used for this purpose are usually variants of the Continuous Performance Test (CPT), an automated test of sustained attention. They come in various proprietary forms, but all require the subject to sit in front of a screen and to attend, for what feels like an inordinately long period of time, to an inordinately boring train of stimuli. As dull, boring tasks, they are *de facto* measures of sustained or vigilance attention, and paradigmatic, it is sad to say, of what most of us have to put up with every day at work and at school. In any event, they have been standardized (more or less), are cheap to administer, and take no more than

12 Ward MF, Wender PH, Reimherr FW. The Wender Utah Rating Scale: an aid in the retrospective diagnosis of childhood attention deficit hyperactivity disorder. *Am J Psychiatry* 1993; 150: 885-90

13 Wolraich ML, Lambert EW, Bickman L, Simmons T, Doffing MA, Worley KA. Assessing the impact of parent and teacher agreement on diagnosing attention-deficit hyperactivity disorder. *J Dev Behav Pediatr* 2004; 25: 41-7

14 Reinecke MA, Beebe DW, Stein MA. The third factor of the WISC-III: it’s (probably) not freedom from distractibility. *J Am Acad Child Adolesc Psychiatry* 1999; 38: 322-8.

30 minutes. Shorter versions of the CPT are less sensitive than the longer tests, but not by much, and patients find them to be less disagreeable. They can also be repeated more frequently.

One would expect precise measures of sustained attention, like the CPT, to be the “gold standard” for ADD diagnosis, but such is not the case. The correlation between CPT performance and parent or teacher rating scales is modest at best.^{15 16 17 18} The Conners CPT and the TOVA, two of the more commonly used CPT’s, are said to be equally sensitive (85%) in demonstrating attention dysfunction in children who have been diagnosed with ADD.^{19 20} The TOVA, however, generates unacceptably high false positive rates (30%) in normal controls and children with other psychiatric disorders (28%).^{21 22} Because the CPT is such a sensitive measure of CNS dysfunction, there are always multiple causes why someone’s performance on the test is impaired.²³

The visual CPT using letters as stimuli is the original test developed by Rosvold & Mirsky.²⁴ Auditory CPT’s are less easy to administer but more appropriate for children with suspected auditory attention difficulties. The results of visual and auditory CPT’s, however, do not necessarily correlate.²⁵ This is hardly surprising, because the CPT is notoriously unreliable.^{26 27}

The CPT is thought to be useful as an adjunct to clinical diagnosis, as its popularity attests. But it is not a “diagnostic” instrument, and, in the absence of acceptable levels of reliability, it may not even be appropriate for monitoring treatment effects.²⁸

4. COMPUTERIZED NEUROCOGNITIVE TEST BATTERIES

The CPT is also found in a number of computerized neurocognitive batteries, but in addition to the CPT, which is simply a measure of vigilance or sustained attention, they also measure other components of attention attention, memory, reaction time, information processing speed and executive control.

The rationale for using a more comprehensive neurocognitive screening battery is that ADHD is not simply a disorder of sustained attention. Indeed, impairment in sustained attention is common “to a certain extent” to all children with psychiatric disorders.²⁹ ADD is “a mild aberration of the regulatory apparatus of the brain, in particular the complex functional systems that are closely identified with the corpus striatum and the prefrontal

15 Forbes GB. Clinical utility of the Test of Variables of Attention (TOVA) in the diagnosis of attention-deficit/hyperactivity disorder. *Journal of Clinical Psychology* 1998; 54: 461-476

16 Raggio DJ, Pierce J. Use of the School Performance Rating Scale with children treated for attention deficit hyperactivity disorder. *Percept Mot Skills* 1999; 88: 957-60

17 Rielly NE, Cunningham CE, Richards JE, Elbard HJ, Mahoney WJ. Detecting Attention Deficit Hyperactivity Disorder in a communications clinic: diagnostic utility of the Gordon Diagnostic System. *Journal of Clinical and Experimental Neuropsychology* 1999; 21: 685-700

18 McGee RA, Clark SE, Symons DK. Does the Conners' Continuous Performance Test aid in ADHD diagnosis? *Journal of Abnormal Child Psychology* 2000; 28: 415-424

19 Conners CK. Issues in the study of adolescent ADD-H/hyperactivity. *Psychopharmacol Bull* 1985; 21: 243-50.

20 Greenberg LM, Waldman ID. Developmental normative data on the test of variables of attention (T.O.V.A.). *Journal of Child Psychology and Psychiatry* 1993; 34: 1019-1030.

21 Forbes GB. Clinical utility of the Test of Variables of Attention (TOVA) in the diagnosis of attention-deficit/hyperactivity disorder. *Journal of Clinical Psychology* 1998; 54: 461-476

22 Schatz AM, Ballantyne AO, Trauner DA. Sensitivity and specificity of a computerized test of attention in the diagnosis of Attention-Deficit/Hyperactivity Disorder. *Assessment* 2001; 8: 357-65

23 Riccio CA, Reynolds CR. Continuous performance tests are sensitive to ADHD in adults but lack specificity. A review and critique for differential diagnosis. *Annals of the New York Academy of Science* 2001; 931: 113-139.

24 Rosvold HE, Szwarcbart MK. Neural structures involved in delayed response performance. In: Warren JM, Abert K, eds. *The frontal granular cortex and behavior*. New York: McGraw-Hill, 1964: 1-15.

25 McGee RA, Clark SE, Symons DK. Does the Conners' Continuous Performance Test aid in ADHD diagnosis? *Journal of Abnormal Child Psychology* 2000; 28: 415-424

26 Conners CK. *Conners' CPT II for Windows*. 2000. North Tonowada, NY, Multi Health System

27 Greenberg L, Kindschi C. *Test of variables of attention*. Universal Attention Disorders, Edmonton, Canada . 1998

28 Riccio CA, Waldrop JJ, Reynolds CR, Lowe P. Effects of stimulants on the continuous performance test (CPT): implications for CPT use and interpretation. *Journal of Neuropsychiatry and Clinical Neuroscience* 2001; 13: 326-335.

29 Swaab-Barneveld H, de SL, Cohen-Kettenis P, Gielen A, Buitelaar J, Van EH. Visual sustained attention in a child psychiatric population. *Journal of the American Academy of Child and Adolescent Psychiatry* 2000; 39: 651-659.

cortex.” Neuropsychological studies of ADD children and adults reveal subtle but clear impairments in several complex functional systems: selective attention³⁰; memory^{31 32}; reaction time³³ and information processing speed³⁴; motor speed³⁵ and visuomotor ability³⁶; and executive control functions, like set-shifting³⁷, inhibitory control³⁸ and working memory.³⁹

What is also clear from the neuropsychological literature is that although many tests indicate impairment in ADD patients, no one test is sufficient to make the diagnosis on its own. Neuropsychologically, ADD patients are a diverse group; individuals may demonstrate deficits in one test, or in one cognitive domain, but not in another. For that reason, combinations of tests are more likely to yield useful information than any one single test.^{40 41 42 43} And for that reason, theories of the cognitive basis of ADD are likely to speak in terms of overarching principles like “dysregulation,” “behavioral inhibition” and “cognitive resource allocation”, rather than in terms of one specific cognitive domain.^{44 45}

When we studied the diagnostic properties of one such computerized neurocognitive test battery in 1063 adults and adolescents with ADD, compared to 1424 normal controls, we found no single test in the battery was sufficiently sensitive to stand alone as an ADD test. Combining scores from four tests – verbal memory, coding, the CPT and a working memory test – successfully identified the ADD patients 99% of the time.⁴⁶ The test battery was a good diagnostic tool, therefore, as long as the question was, is this patient ADD or normal? However, when we compared the ADD patients to patients with anxiety, depression or bipolar disorder, we discovered that none of the tests on the battery distinguished the ADD patients from the other three patient groups.⁴⁷ So, patients with ADHD may be cognitively impaired relative to normal controls, and these deficits are to be found in tests of

30 Brodeur DA, Pond M. The development of selective attention in children with attention deficit hyperactivity disorder. *J Abnorm Child Psychol* 2001; 29: 229-39

31 Muir-Broadus JE, Rosenstein LD, Medina DE, Soderberg C. Neuropsychological test performance of children with ADHD relative to test norms and parent behavioral ratings. *Arch Clin Neuropsychol* 2002; 17: 671-89

32 Roth RM, Wishart HA, Flashman LA, Riordan HJ, Huey L, Saykin AJ. Contribution of organizational strategy to verbal learning and memory in adults with attention-deficit/hyperactivity disorder. *Neuropsychology* 2004; 18: 78-84

33 Leth-Steensen C, Elbaz ZK, Douglas VI. Mean response times, variability, and skew in the responding of ADHD children: a response time distributional approach. *Acta Psychol (Amst)* 2000; 104: 167-90

34 Weiler MD, Bernstein JH, Bellinger DC, Waber DP. Processing speed in children with attention deficit/hyperactivity disorder, inattentive type. *Neuropsychol Dev Cogn C Child Neuropsychol* 2000; 6: 218-34.

35 Mitchell WG, Chavez JM, Baker SA, Guzman BL, Azen SP. Reaction time, impulsivity, and attention in hyperactive children and controls: a video game technique. *J Child Neurol* 1990; 5: 195-204

36 Kalff AC, Hendriksen JG, Kroes M, Vles JS, Steyaert J, Feron FJ, van Zeven TM, Jolles J. Neurocognitive performance of 5- and 6-year-old children who met criteria for attention deficit/hyperactivity disorder at 18 months follow-up: results from a prospective population study. *J Abnorm Child Psychol* 2002; 30: 589-98

37 Cepe Schachar R, Jadad AR, Gauld M, Boyle M, Booker L, Snider A, Kim M, Cunningham C. Attention-deficit hyperactivity disorder: critical appraisal of extended treatment studies. *Can J Psychiatry* 2002; 47: 337-48da NJ, Cepeda ML, Kramer AF. Task switching and attention deficit hyperactivity disorder. *J Abnorm Child Psychol* 2000; 28: 213-26.

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⁴⁶ The Identification of an ADHD Factor in a Broad-Spectrum Battery of Neurocognitive Tests

⁴⁷ A Cognitive Profile Indicative of ADHD is Found in Patients with Common Psychiatric Disorders

sustained and selective attention, memory, working memory, complex information processing and executive function.^{48 49 50 51 52} But, if the issue is to differentiate ADHD from the conditions that are most commonly in the differential diagnosis of a particular patient, the discriminant validity of cognitive testing is limited.⁵³ Thus, a paradox: a condition that is largely defined in cognitive terms is virtually indistinguishable, in terms of cognitive performance, from conditions like anxiety and depression, which are really quite different, and are not ordinarily thought of as cognitive disorders at all.

These data might be interpreted to mean that patients with anxiety, depression, etc., have co-morbid ADD, but an alternative explanation is this: that cognitive weaknesses are a relatively common event in a subgroup of patients with various psychiatric conditions. ADD tests, like the CPT and the computerized test batteries are likely just tapping into a system that may be dysfunctional from birth – in the case of ADD – or that may come awry during the evolution of certain psychiatric disorders.

4. CLINICAL COURSE

Even the most comprehensive evaluation will be subject to occasional error. A patient who has a typical history of ADD, no indication of alternative pathology, typical findings on psychological tests and a beneficial response to ADD meds probably has ADD; but he or she may have something else that you missed. One always hopes that the initial evaluation has really excluded problems like depression, bipolar disorder, anxiety disorders, obsessive-compulsive disorder, substance abuse, hypothyroidism, seizure disorders or neurodegenerative disease. If it hasn't, then the truth will out over time.

A METHOD FOR ADD DIAGNOSIS

In the face of the quantum indeterminacy of the universe and the frailty of our predictive powers, we hunker down, and we do the best we can. In the face of assigning neuropsychiatric diagnosis to a mass of schoolchildren whose numbers exceed all but the largest cities of the world, we try to make our observations as systematic and objective as they can possibly be. If we can't predict the future very well, at least we can prepare for it.

The principles of neuropsychiatric diagnosis, therefore, are not soundly based if they rely on some novel technology to penetrate the dark matter. In my career, I have encountered numerous demons that were supposed to generate perfect knowledge about the mental disorders. The level of catecholamine metabolites in the urine of the CSF were supposed to diagnose depression; failing that, it was persistent hypercortisolemia. Computerized EEG, SPECT and PET scanning were supposed to diagnose everything. Elaborate batteries of neuropsychological tests, administered with obsessive precision; multidisciplinary evaluations, that gathered experts from many fields; eager graduate students, observing a child and counting the frequency of the most trivial behaviors. Blood tests, hair samples, special diets, activity meters that you wear on your wrist when you're asleep.

48 *Eur Arch Psychiatry Clin Neurosci.* 2007 Mar;257(2):112-9. Neuropsychological assessment of adult patients with attention-deficit/hyperactivity disorder. Müller BW, Gimbel K, Keller-Pliessnig A, Sartory G, Gastpar M, Davids E.

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51 *Acta Psychiatr Scand.* 2004 Jul;110(1):45-54. Impaired spatial working memory in adults with attention-deficit/hyperactivity disorder: comparisons with performance in adults with borderline personality disorder and in control subjects. Dowson JH, McLean A, Bazanis E, Toone B, Young S, Robbins TW, Sahakian BJ.

52 [Biol Psychiatry.](#) 1998 Aug 15;44(4):260-8. Neuropsychological function in adults with attention-deficit hyperactivity disorder. [Seidman LJ](#), [Biederman J](#), [Weber W](#), [Hatch M](#), [Faraone SV](#)

53 [Clin Neuropsychol.](#) 2002 Feb;16(1):12-34. Neuropsychological characteristics of adults with ADHD: a comprehensive review of initial studies. [Woods SP](#), [Lovejoy DW](#), [Ball JD](#).

There is a new machine now that maps a child's eye movements as he takes an attention test and measures how much he fidgets with his feet during the test. The machine has been "approved" by a government agency, so it must be the real thing. But I don't believe it.

If the attainment of perfect knowledge is not possible, what we have to try to do is perfect the knowledge that we can attain. To that end, science yields to practical endeavor, and theoretical knowledge yields to common sense. The day-to-day practice of medicine is, at heart, a practical operation. The goal of the diagnostic process is to generate as much useful knowledge as you can in an efficient manner, to generate hypotheses about the nature of the problem, to test those hypotheses, and to be prepared to correct one's course of action as circumstances direct. It is not a question of tests, or machines, but a method. Efficiency and flexibility are the hallmarks of the method. As we have developed our method, the priority has been to liberate the physician from drudgery and routine, and to preserve for him or her ample opportunity for incisive inquiry, thoughtful deliberation and sage advice. The method is something we have developed in the clinics for ADD, but it is equally useful for virtually all of the neuropsychiatric disorders. In fact, we use the "test dose" paradigm in patients with many different conditions.

Taking it in order, we begin with the:

CLINICAL HISTORY AND EXAMINATION.

The clinical history, family history and rating scales are essential for clinical diagnosis but they are also the most time-consuming elements of the diagnostic process. A proper history and analysis of rating scale results usually takes a couple of hours. That is, a couple of hours of a doctor's time! Much of this data, however, can be obtained before the patient ever arrives at the physician's office, collected over the internet and feeding into an electronic record. This includes all of the referral information, from the patient or the referring doctor, and all of the pertinent demographic data, insurance information, permissions and releases. Most of the past medical history, social history and family history can be done in the same way. A substantial portion of the medical report, therefore, can be generated before the patient ever visits the clinic.

A medical assistant who greets the patient and takes his weight and blood pressure can also be trained to take at least the rudiments of a medical history. What remains for the physician is a review and elaboration of the history and the performance of an examination. The history and examination are not a ritual, but the occasion for incisive inquiry. They are an hypothesis-generating exercise.

RATING SCALES

We have had ample experience with rating scales over the years, and have just about done away with them. In Chapter 24, we describe a web-based symptom checklist we developed ourselves and call the "Neuropsych Questionnaire" (NPQ). It takes the place of all the rating scales we used to use. The long form has 200 questions and generates twenty general symptom scales; e.g., attention, memory, anxiety, depression etc. It takes about 15 minutes to complete, is saved to a database and can be printed out, fully scored, as soon as the patient is done with it. A shorter version, 45 questions long, takes about 5 minutes and is appropriate for follow up visits. The checklists are ideally completed by multiple parties, relatives and teachers, for example. If they haven't done it, you can call them up and send them to the website. Presto: correlative data.

The rationale for the NPQ is not to be a diagnostic instrument but simply a comprehensive review of the patient's symptoms, and their perceived intensity, in all of the different areas where neuropsychiatric symptoms occur.

PSYCHOLOGICAL TESTING

One can imagine, from the thrust of our writing so far, that we administer a comprehensive computerized test battery to every patient as part of the initial evaluation. In fact, we use several. In the past, we used proprietary test batteries that are commercially available, such as the NES2, MicroCog, the Conners CPT, the TOVA and CNS Vital Signs. More recently we have developed tests of our own, which are freely available on the Internet (www.ncneuropsych.com). One is an estimate of verbal and performance IQ and social acuity. Another is a test of academic proficiency. A third is a test battery that measures memory, processing speed, executive function and attention. The whole test battery takes less than an hour to administer, and a shorter version can be used for follow-up.

One important advantage of some computerized tests is catching fakes. University students in particular are interesting in obtaining stimulants and for obvious reasons. If his or her performance on a test battery is extremely low, one's index of suspicion should increase. The best computerized test batteries have built-in validity indicators.

THE "TEST-DOSE PARADIGM"

The dimensional inputs thus described have identified problems with executive control that are not the consequence of some other condition, and not faked, and that they are the likely cause of the patient's difficulties in the world. The action step thus prescribed is not to write a script, but to administer a "test dose." We do this as part of the ADD evaluation, but we also do it in patients with brain injury, MCI or early dementia, when stimulant treatment may possibly be helpful.

The test-dose paradigm takes advantage of the fact that stimulant drugs have an onset of action of about 45 minutes, and peak effects at 1-2 hours. These effects can be measured subjectively – *how does this medication make you feel* – and objectively, when the patient is re-administered a computerized test battery. Improved performance after a test-dose doesn't make the diagnosis, but it does increase one's confidence in deciding whether to prescribe a stimulant or not. Performing an EKG after a test-dose is a simple thing to do and can identify a substantial number of cardiac abnormalities that may complicate treatment with a stimulant. It is particularly useful in older patients who may be stimulant candidates for problems other than ADD.

The clinic nurse administers a dose of methylphenidate (0.30 mg/kg/dose) or amphetamine (0.15 mg/kg/dose). The patient is sent away to have some lunch, and then returns after an hour. Then the test battery is repeated, the patient's pulse and blood pressure are measured, an EKG is done, and inquiries are made about the patient's subjective response, the observations of family members who have accompanied him, and side effects. The comparative test scores are reviewed with the patient. This is also an opportunity to teach patients how the tests work, and how medications affect performance, so they can use Internet-based tests for follow-up testing on their own.

But don't people get better when they take the test a second time? The learning effect on computerized tests is actually quite small (about 2%), and ADD patients actually do worse when they take the test a second time. The following data is taken from a study of 127 ADD patients, age 7-55, who were given the "test dose" procedure as part of their initial evaluation. Seventy three patients were administered a single dose methylphenidate and 54, amphetamine salts. Domain scores are reported as standard scores (mean of 100, standard deviation of 15). In addition, a "Neurocognition Index" is also presented, an average score generated from the various domain scores. The differences are highly significant (two tailed t test) except for the memory domain score.

Figure 6.1a. Test Dose Data with Methylphenidate

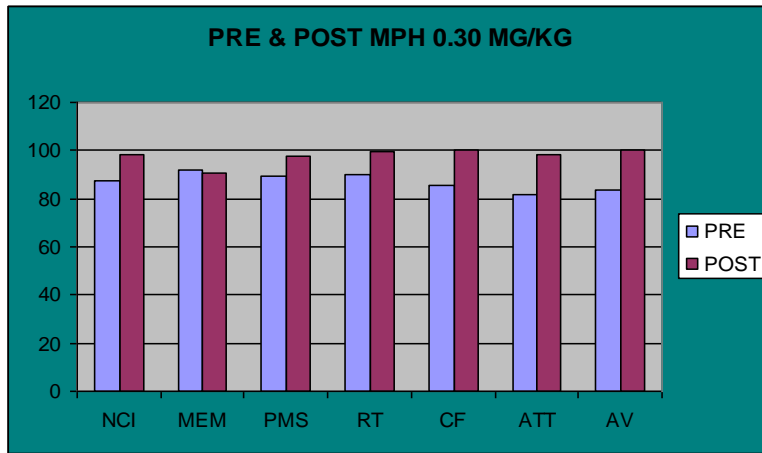
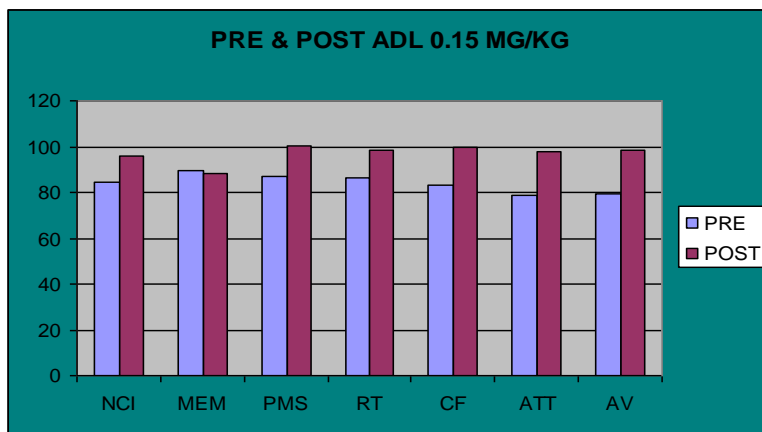
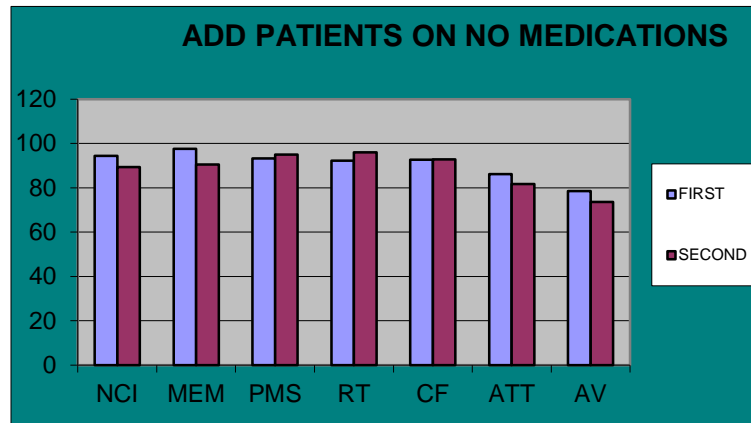


Table 6.1b. Test Dose Data with Amphetamine



The changes after a test dose, either with methylphenidate or amphetamine are clearly apparent. Multivariate analysis indicated equal effects for both drugs, and no effect relative to age or gender.

Nor can the changes be attributed simply to taking the test twice – a “learning effect.” For illustrative purposes, here is data from 24 ADHD patients, age 7-55, who took the Vital Signs battery on two occasions, off-drug both times. None of the differences are significant (two-tailed t test), and patients were as likely to do worse or better the second time.

Figure 6.2. CNS Vital Signs Scores in ADD Patients Tested Twice on No Medications

OBJECTIVE TREATMENT EVALUATION

The “test dose” paradigm” yields a great deal of data about the patient and his or her response to a psychostimulant drug. It is also a good way to educate patients about how drugs work, and how psychiatrists monitor drug treatment. It does not, however, indicate how well a patient will do clinically on a particular drug, or even which drug, or dose, is ideal for that patient.

It has been our custom to write two prescriptions for patients who do, in fact, have ADD, and who seem to do well after a test dose. One is for a two-week trial of long acting methylphenidate, and the second is for a two-week trial of long-acting amphetamine. We give the patient a likely dose range to try, and make arrangements to adjust doses and deal with problems by phone. We arrange for follow-up in one month, to determine which drug was preferable, and, if necessary, consider trials of alternative medications.

The same tests that are used in the test-dose paradigm are also available on the Internet, so serial evaluation of the patient’s cognitive status, on different doses of different medications, can be evaluated. The NPQ is also available for parents and teachers to report their observations. When we made those services available to patients, we thought it was a clever idea, but very few people have ever taken advantage of it. If stimulant medications work for an ADD patient, the effects are dramatic, and are reflected in meaningful changes in their everyday life; no need for a test.

Serial evaluation during patient visits is based on a short version of the NPQ and two very short measures of processing speed. If tests are delivered on a tablet, the patient can take them as he waits for the doctor. A central database compares results to previous visits.

SUMMARY

Poor performance on a neurocognitive battery does not prove that a patient has ADD, or that a stimulant drug is warranted. ADD is a clinical diagnosis, and physicians have to synthesize data from numerous sources to generate the appropriate action step. But it is appropriate to integrate neurocognitive data into the evaluation of any cognitive disorder, and also into the complicated process of treatment monitoring. It is really quite odd that anyone would treat a cognitive disorder without monitoring cognitive performance.

A positive response to a stimulant in the test dose paradigm does not prove that the patient “really has ADD,” or that the test dose drug is the one the patient ought to take long-term. But it does give you confidence in trying a couple of drug alternatives, and it teaches the patient (or parents) a little about how to evaluate drug effects

Similarly, a negative response to the test dose does not mean that the patient does *not* have ADD or that drug treatment is unwarranted. It does give pause, though; you may take the opportunity to reconsider your differential diagnosis before proceeding. The test dose paradigm is not an infallible procedure. But it does give the physician objective data upon which to base his or her clinical decisions. In the face of the quantum indeterminacy of the universe, and the fuzzy thinking that pervades our lives, a small increment of objective data is a welcome thing.