Chapter 11 – Changes in Behavior

Section 1

Jeffrey Victoroff, MD
Associate Professor of Clinical Neurology
USC Keck School of Medicine
Redondo Beach, CA

Dale Moquist, MD
Memorial Family Practice Residency Program
Houston, TX

Rosabel Young, MD
Assistant Professor and Director, Movement Disorders Program
King-Drew Medical Center
Los Angeles, CA

Part I: The 15-Minute Neurobehavioral Evaluation

It is 3:30 on Friday afternoon. The front desk buzzes your nurse, announcing the arrival, without an appointment, of a 35-year-old woman accompanying her 83-year-old father. Four other patients are waiting for examining rooms. You are with a four-year-old girl whose asthma is worsening.

“What’s the problem?” you overhear your nurse ask the receptionist, her tone conveying the slightest hint of skepticism. “Oh,” she says. “I see,” she says. “For how long?” she asks. She sighs. Hearing that sigh, you know you’re going to be seeing them.

This section will attempt to outline the 15-minute neurobehavioral assessment. Today’s pace of practice has accelerated from the epoch of luxurious 45-minute health promotion discussions to an unsettling “Beat the Clock” of frenetic juggling of priorities, hoping, in that circus act, not to drop any patient’s ball. A high proportion of primary care visits involve behavioral problems, requiring us to quickly and confidently distinguish between medical/neurological causes and primary psychiatric conditions. So it is essential that we devise realistic strategies for walking into the examining room in total ignorance of the diagnosis and walking out 15 minutes later with a plan. Naturally, we need flexibility. Some things simply demand more time, perhaps not as much for diagnosis as for negotiating the exchange of human information in ways that strengthen the bond between healer and patient. But the burden, increasingly and perhaps absurdly, is now on primary care physicians to attempt to offer an attending’s experienced care with an intern’s time schedule. Hence, we will be practical. Since the pleasure in practice is often proportional to the sense of mastery, we hope this plan for rapid neurobehavioral evaluation will make that Friday afternoon a better day, granting the reward of confidence in our practical approach.
We will organize the Neurobehavior Evaluation in ways that aid triage, by following the conventional sequence of history, examination, and laboratory evaluation. However, we recognize that there is actually a continuous evolution of diagnostic hypotheses, a solution to a jigsaw puzzle of biological cause and behavioral effect with every interlocking piece contributing to the next step in the strategy, rather than a linear observation of clinical facts. Given this, we will present the Neurobehavior Evaluation as a series of decisions that progressively narrow the focus of etiology and intervention. This chapter will focus on the following issues for adults:

- **Delirium (confusional state)**
- **Dementia**
- Discrete problems of thinking (e.g., amnesia, aphasia, apraxia)
- Psychiatric syndromes having identifiable neurobehavioral/medical causes (See Table 11.1-1).

**Table 11.1-1: Adult Neurobehavioral Syndromes**

**Delirium (a.k.a. Confusional state)** = altered mental status in an apparently awake or somewhat lethargic person (but not sleeping or comatose), usually acute or subacute in onset, with impairment in level of responsiveness or attentiveness to the environment. Example: hepatic encephalopathy.

**Key points:**
- Awake or lethargic
- Acute or subacute
- Impaired attention

**Dementia** = acquired impairment in cognition sufficient to interfere with the conduct of waking life, not due to impaired arousal, usually with subacute or chronic presentation, usually impairing multiple aspects of thinking. Example: dementia of the Alzheimer type.

**Key points:**
- Impacts on awake activities
- Subacute or chronic
- Intact attention

**Discrete problems of thinking:**
- Amnesia = impaired learning
- Aphasia = impaired language
- Agnosia = impaired recognition of sensory stimuli
- Apraxia = impaired functional motor skills with intact strength and coordination

**Executive function impairment** = e.g., altered planning, self-monitoring, idea analysis, or idea generation

**Psychiatric syndromes that have identifiable neurobehavioral/medical causes:**
- Depression
- Mania
Psychosis

Anxiety

You enter the room. The elderly man sits, slightly slumped in a vinyl chair. He looks up slowly when you enter, not quite making eye contact.

We adopt the “every picture tells a story” stance in neurobehavioral assessment (Table 11.1-1). From the first glance, you already know that this man has enough lower extremity motor function to make it to the examining room, and enough interactiveness with his daughter to be guided there with neither the support of a wheelchair nor the swaddling of restraints. This already favors a fairly well functioning spinal cord and brainstem for both motor processes and arousal and decreases the odds of a large stroke, subarachnoid hemorrhage (SAH), or meningitis. You know he has enough intact peripheral sensory organ function and enough intact transfer of sensation to sensory cortex to note your entry into the room, so it’s likely that much of the visual pathway from eye to occipital lobe is working. You know that the sensory information of your coming, by parallel processing, has also successfully reached his brainstem arousal system and parts of the limbic/emotional response system that provide motivation to respond to your presence. You know that there is working give-and-take of electrochemical discourse between these systems and the frontal cortex that is necessary to organize a motor response to your entrance. And you know that this man can manage the transfer of commands from prefrontal cortex (for planning) to primary motor cortex (for doing) and from motor cortex passing all the way down to anterior motor horn cells to activate a symphony of muscle contraction to lift his head to give you that half-glance. So you know that at least some of the cortical-to-cortical connections and the long cortex-to-spinal cord connections work fine. And, if you happened to notice that his eyes moved together, roughly in your direction, then you know that the cortical eye fields can still send signals to the brainstem, which can still coordinate the third and sixth cranial nerves for purposeful conjugate gaze. In a second, you already know a lot about this man’s brain.

But he does not observe the niceties of social intercourse. Is he lethargic? Deaf? Depressed? Assuming that his vital signs are reasonably reassuring, the second step after the first glance is history.

What are the priorities? Tables 11.1-2, 11.1-3, and 11.1-4 outline key elements of our assessment, suggesting a few high priority items in the history and examination. The rapid neurobehavioral assessment is a matter of triage; not a lock-step progression, but a hierarchical test of the acuity of the condition ruling out emergency, then urgency, then more benign or chronic states. As in pediatrics, our history taking now becomes a delicate balancing of information you may get from the caregiver, who can be an ally with varying sophistication and agendas, and from the patient, whose very responses to historical questions instantly become part of the exam.

Tables 11.1-2, 11.1-3, 11.1-4

Key Elements Of The Rapid Neurobehavioral Evaluation
Table 11.1-2—History of the Present Illness and Past Medical History

History of Present Illness
How much? How quickly? What’s changed?
Items of special concern:
T: Recent trauma?
H: Headache?
I: Incontinence?
S: Sleep disturbance?
I: Irritability?
S: Sensory change, including numbness, or special senses such as vision and hearing?
M: Motor changes such as slowing or tremor?
A: Appetite loss?
D: Delusions?
D: Depression?

Past Medical History
Items of special concern:
1. Lifetime mental health interventions
2. Lifetime drug/alcohol history, especially anticonvulsants or psychotropics
3. Lifetime traumatic brain injury, stroke, TIA, MI, tumor, renal, or kidney disease

Table 11.1-3—Examination

Mental status vital signs: responsiveness, orientation, agitation Aphasia screen:
1. Say “dog”
2. “What part of my shoe is this?”
4. 5. “Please raise your right hand. Okay, put your left hand on your right shoulder. Good, now first put your right hand on your left knee, then your left hand on your right ear.”
6. “What’s the difference between a car and a boat?”

Working memory and mental control:
1. Recall “tuna, Paris, strength” after 3–5 m
2. Month’s backwards

Self-reported mood, delusions, hallucinations

Features of the physical and elementary neurological examination of special relevance to the assessment of behavior
Table 11.1-4—Decisions in the Laboratory Evaluation

**Electrolytes** (any major change can cause delirium; low sodium particularly lowers the seizure threshold)

**Blood count** (e.g., megaloblastic anemia hints at B₁₂ deficiency; hematocrit < 24 may contribute to delirium)

**Liver function tests** (e.g., for hepatic encephalopathy)

**Ca, Ph, Mg** (deficits lower the seizure threshold; parathyroid disease produces dementia)

**Thyroid function tests** (to rule out the most common endocrine dementia)

**B₁₂** (to rule out subacute combined degeneration)

**Serum VDRL** (helps rule out neurosyphilis; positives generally require CSF exam)

**EKG** (cardiac dysfunction may compromise brain perfusion or hint at metabolic disorders)

**Neuroimaging** (rule out, e.g., strokes, tumors, hydrocephalus)

**Lumbar puncture** (in acute delirium to r/o infection or subarachnoid blood; in dementia usually only when syphilis serology is +)

**EEG** (when seizures, metabolic encephalopathy, herpes, or Creutzfeldt-Jakob are suspected)

The Chief Complaint and History of Present Illness

“What seems to be the problem?” you might say. The answers come from the daughter. The patient doesn’t look up. That in itself is quite telling.

**Key points:**

- How much?
- How long?
- What’s changed?

These are the three questions you want immediate answers to in assessing altered mental status (AMS). While we present them in a certain order, there is no strict sequence to getting this information; it’s really a matter of assembling a gestalt.

These are the three questions you want immediate answers to in assessing altered mental status (AMS). While we present them in a certain order, there is no strict sequence to getting this information; it’s really a matter of assembling a gestalt.

**How Much Has Behavior Changed?**

Has the patient gone from a vigorous, sociable retirement to a tragically contracted, nearly “vegetative” state? From a sensory deprived developmentally delayed nearly mute resident of a group home to a not-feeding-himself sensory deprived developmentally delayed nearly mute resident of a group home? The magnitude of the shift from baseline in the overall interactiveness and independence level is the first cue to acuity. However, it tells us less about brain locale than we might wish. The first scenario from retirement to catastrophe suggests a global dysfunction that is sometimes assumed to be due to diffuse or multifocal brain injury. But this picture of profound “global” decline might be produced by even a modest interruption in the millimeter-range brainstem...
arousal systems—such as that caused by systemic infection, a slower than expected metabolism of digoxin or metoclopramide, or a tiny critically-placed stroke (e.g., in brainstem or thalamus).

The second scenario is more the house-of-cards effect, where, in a patient whose behavior depends on a tenuous balance of marginally functioning systems, even a slight shift in one system may produce marked decline. Another example might be an emphysematous patient with mild CHF who has just dropped his PO2 from 65–55. Perhaps the most important thing about “how much”, is that it hints a bit at the plan. Large amplitude changes are much more likely to warrant prompt work-up, but even a slight drop in independence may compel dramatic rearrangement in the care giving duties.

How Long Has This Problem Taken to Develop?

Has the patient been dwindling for three years? Or is this a case of, “he was good when he went to bed last night, but this morning we found...” Rapid onset is usually assumed to imply some sudden physiological shift, such as acute infection, toxic ingestion, stroke, subarachnoid hemorrhage (SAH), or seizure. And, very roughly speaking, the more rapid the change, the more urgent the need for diagnosis and intervention. This is particularly true now that we can provide improved intervention during the first several hours after a “brain attack” (acute nonhemorrhagic stroke), and many brain attacks present only with behavioral symptoms. However, neurologic conditions are notoriously susceptible to threshold effects, so that even a chronic problem may present acutely. For example, a slow growing brain tumor may be symptomless until the edema reaches a critical threshold, then numbness, weakness, or lethargy can appear in minutes. Again, the main advantage of knowing “how long” is a matter of the urgency of the plan: Stat labs? Scan? Hospitalize? All of these may be appropriate in acute confusional states of unknown cause. On the other hand, if vital signs are benign and the level of consciousness has been the same for three weeks, urgent laboratory tests and hospitalization are less likely to be required this Friday evening. Table 11.1-5 lists conditions organized in terms of rapidity of onset.

Table 11.1-5: Rate of behavioral change and causes*

*In rough order of frequency. Note that some conditions span different rates of onset, but are more likely to appear in one category than in another

Very Rapid onset, seconds to minutes

- Acute intoxication
- TIA, stroke
- Syncope
- Seizure
- Subarachnoid hemorrhage
- Epidural hematoma
- Critical decompensation of mass (herniation, hemorrhage)
- Panic attack
- Intermittent explosive disorder (episodic dyscontrol)

Rapid onset, hours to days
Toxic/metabolic encephalopathies, including withdrawals
Bacterial or viral infection
Stroke
Subdural hematoma
Increased intracranial pressure

Subacute onset, days to 1 month
Toxic/metabolic encephalopathies
Brain tumor
HIV-associated syndromes (e.g., AIDS-dementia complex, CNS lymphoma, CNS toxoplasmosis)
Fungal meningitis
Tuberculous meningitis
Carcinomatous meningitis
Increased intracranial pressure
Subdural hematoma
Neuroleptic malignant syndrome
Major depressive episode
Post-partum depression
Stroke

Insidious onset, months to years
Neurodegenerative diseases (e.g., Alzheimer’s, Parkinson’s)
Cerebrovascular dementia
Toxic/metabolic encephalopathies
Brain tumor
HIV-associated syndromes
Neurosyphilis
Normal Pressure Hydrocephalus
Subdural hematoma
Major depressive episode, Dysthymia

Fluctuating course
TIAs
Seizures
Syncope
Cardiac arrhythmias, esp. intermittent atrial fibrillation
Dementia with Lewy bodies
Neurocysticercosis

As rapidly as we would like to narrow our focus on the acute versus chronic, we
shouldn’t be misled by two types of chronological confounds. First, and most frequent, is the “false acute” history. Especially in dementias, it is common for a family member to suddenly notice a behavior change that has really been developing for years but suddenly becomes obvious because a minor illness has robbed the patient’s tenuous cognitive reserve. This has sometimes been called a beclouded dementia, but the essential idea is simply that a new mental or physical stress brings out the previously hidden symptoms of dementia in a patient who has been getting by on the edge of normal functioning. For instance, a person with mild Alzheimer’s disease or hypothyroidism may not have exhibited obvious dementia until they get the flu, or their CHF decompenses, or they are given an antihistamine or anticholinergic agent. The same thing can happen when a novel life challenge pushes the patient beyond their reserve: “He was perfectly fine,” you are told, “until we took him to that new symphony hall for his birthday, and he just got all turned around in the parking garage.” A visiting relative, a trip to Las Vegas, a driver’s license renewal exam, any such novelty may stress a brain that functions well in a routine life, uncovering a chronic cognitive impairment.

Second, there is the less frequent “false chronic” history, when family members suggest that the new problem is long-term, since today’s condition doesn’t seem much different from the last year. This is most common among those with prior behavior problems in whom change is harder to detect—a developmentally delayed child or adult who becomes subtly toxic on their anticonvulsant, or a schizophrenic who develops a tumor-induced aphasia in the last three weeks about whom it’s remarked, “Oh, he’s always said things that were hard to follow.”

What’s Changed?

Note, even though we will eventually address the CNS locale, this is not the neurology attending’s medical-student-tormenting question, “Where’s the lesion?” This is the simple question, “What’s different?” The following questions may facilitate a focused review of systems, recalled with the useful mnemonic: THIS IS MADD! (See Tables 11.1-2, 11.1-3, 11.1-4).

The advantage of reviewing these issues is self-evident; we are searching for the bounds of the problem, and any hint we can get of etiology or localization. For instance, asking about recent trauma, even if it was assumed to spare the head (“Well, he did get into the fender bender two months ago.”) may actually uncover previously unsuspected traumatic brain injury. Headaches that have increased in frequency or severity from the patient’s formerly infrequent and mild headaches might hint at hydrocephalus, a space-occupying lesion, escalating hypertension, or metabolic disorders such as hypoglycemic episodes. Poor sleep not only occurs in many mood and thought disorders, but may hint at sleep apnea, a frequently missed cause of otherwise unexplained mildly impaired cognition, especially in middle-aged men.

The daughter’s answer, “Yes, he’s really slowed down,” may not seem to help in identifying the problem, but it actually can be quite useful because this is not the usual answer in a hemispheric stroke or tumor, which would be a little more likely to produce a hemiparesis the daughter would note, and it is more consistent with diffuse or multifocal processes such as toxic, metabolic, infectious, or neurodegenerative disorders. Unfortunately, general slowness might also be due to increased intracranial pressure that diffuses the effect of a focal mass, or due to focal disorders of the basal ganglia producing a
Parkinson’s-like slowing (bradykinesia).

Of course, the answer, “You know, he keeps falling to the left,” or any such hint of asymmetry leads to the “Ah hah!” that rapidly focuses our inquiry on focal processes such as stroke or mass lesion or trauma. However, we must also beware of the phenomenon of “red-herring localization”: a diabetic may experience a drop in glucose level—a systemic problem—and present with right-sided weakness and aphasia because of some unpredictable asymmetric reserve capacity of his cortical neurons. A hyperlipidemic patient with mild basilar artery stenosis, altogether neurologically asymptomatic until today, may have a visual hallucination. This may occur because one visual field is briefly blinded due to global cerebral hypoperfusion that disproportionately affects the area served by the stenotic vessel, but it’s actually caused by transient cardiac arrhythmia—best treated as a heart more than brain problem.

So, the first goal is simply to get an accurate fix on “what about this man’s behavior inspired this Friday clinic visit?” The net result of the “how much”; “how long”; and “what”, questions might simply be: “A 35-year-old woman states that her 83-year-old father is ‘just different’, really slowed down, and has been for a month.” Such a seemingly indeterminate characterization is potentially loaded with diagnostic information. Some conclusions are obvious: it’s less likely to be SAH because we don’t hear about sudden change or head pain. It’s less likely to be a bacterial or viral meningitis, which are also usually more precipitous. However, despite the “one-month” history, we must still consider problems that you’d ordinarily expect to cause a sudden change, such as a stroke or traumatic brain injury, but escape detection because they’ve also impaired the patient’s ability to complain. “He never said anything,” an informant accurately reports about a history of head trauma, because after standing up under the open kitchen cabinet door and bumping his or her head three months ago, the patient shrugged it off as just another of life’s little traumas as their subdural hematoma was forming due to the increased bleeding tendency caused by the Coumadin they take for their atrial fibrillation, and today the resulting amnesia prevents their even recalling the trauma. “No, he/she hasn’t complained of weakness or numbness,” the informant accurately reports because the patient’s stroke two weeks ago not only damaged the right frontal lobe causing a mild left hemiparesis, but also the right parietal cortex, causing anosognosia - denial of their own hemiparesis. Obviously, still open to consideration in this case are toxic or metabolic disorders, systemic infections, chronic CNS infections, or neurodegenerative diseases.

The present history, of course, could be considerably elaborated if we are rigorous and go into recent travel, exposures to others with illness, exposure to chemicals, nutritional changes, etc. But, in the parsimony of our 15-minute assessment, the most commonly missed pertinent parts of the history and the two general medical questions we must really ask are, 1) “Any infectious symptoms (UTI’s or URI’s)?”, 2) “What drugs or medicines has he been taking?” This last question has probably yielded more specific neurobehavioral diagnoses than any, and notoriously uncovers iatrogenic disorders. Stimulants, depressants, drugs with CNS toxicities, and illicit drugs including alcohol account for 35 percent to 60 percent of cases of new-onset confusional syndromes.

Table 11.1-6 lists some drug causes of altered mental status (AMS). In addition, particularly in cases of suspected dementia, we may need to work a little to establish the onset.
“I understand your Dad has been different for the last month, but, in the last few years, was he just the same fellow as he was twenty years ago?” “Pretty much,” she answers, “although he hasn’t been gardening so much in the last few years.”

This change in activities might be due to arthritis, weather, or a myriad of other reasons, but such an innocuous answer might also be the first hint we get that the present illness may actually have been long in coming on. We might proceed to ask a very open-ended question that sometimes gets to the depth of the problem:

“What worries you most about this?” She ponders a moment. “He’s just...not my Dad.” Absently, she drags her sleeve across her eye.

There is obviously no exact formula, no turn of phrase or tone of voice that will reliably elicit key answers, and every family physician will creatively find their own way. But answers such as this, vague as they may seem, can alert us. This is not a minor matter; the daughter senses that Mr. Johnson is in serious trouble.

Table 11.1-6: Drug Causes of Altered Mental Status

**Sedative hypnotics and opioid analgesics** such as benzodiazepines, neuroleptics (e.g., haloperidol (Haldol®), prochlorperazine (Compazine®), metoclopramide (Reglan®), promethazine (Phenergan®), meperidine (Demerol®), pentazocine (Talwin®), other opiates.

**Antihistamines**, particularly diphenhydramine (Benadryl®).

**Anticholinergic agents** such as benztropine mesylate (Cogentin®), trihexyphenidyl (Artane®), and tricyclic antidepressants.

**Histamine blockers**, especially cimetidine (Tagamet®).

**Cardiovascular agents**, including beta blockers, amiodarone (Cordarone®), calcium channel blockers, digitalis preparations, doxazosin, disopyramide phosphate (Norpace®), methyldopate HCl (Aldomet®).

**Selective serotonin reuptake inhibitors (SSRIs)** such as fluoxetine (Prozac®), sertraline (Zoloft®), paroxetine (Paxil®).

**Anti-inflammatory drugs** such as corticosteroids and nonsteroidal anti-inflammatory agents (including aspirin).

**Drugs with stimulant or sympathomimetic properties** such as aminophylline, theophylline, ephedrine, phenylephrine and phenylpropanolamine and herbal ephedra.

**Muscle relaxants** such as baclofen (Lioresal®), or carisoprodol (in Soma®).

**Antimicrobials** such as sulfamethoxazole, aminoglycosides, tetracycline, ticarcillin.

**Antineoplastic drugs** including aminoglutethimide, asparaginase, 5-Flourouracil, methotrexate, vinca alkaloids.

Cholesterol-lowering agents

**Drugs of abuse** including alcohol, nicotine, cocaine, amphetamines, caffeine, hallucinogens, phencyclidine, barbiturates, opiates, inhalants

Past Medical History

Perhaps the easiest question to ask, and occasionally worth repeating, from
the HPI, is: “Has anything like this ever happened before?” High proportions of patients seen for neurobehavior assessment have chronic problems with recurrent episodes of AMS, from major depression to transient ischemic attacks (TIAs). Although it may sound redundant, repeating this question occasionally elicits answers such as, “Oh, you mean like that time back in Iowa when they had to do that thing to his brain?”

Otherwise, areas for special attention in the past medical history include:

1. Any lifetime mental health interventions
2. Any use of drugs, prescribed or not (A useful helpful question is, “Did he ever in his life take medicine for seizures, or his mood?”)
3. Any history of head trauma (Including youthful boxing, or incarceration, which may only suggest increased risk for unreported head trauma but also possibly hints at temperament, addictive traits or intermittent explosive behavior.)
4. Any vascular disease (increased risk of TIAs and stroke)
5. Any solid tumor (increased risk of brain metastasis or paraneoplastic syndromes)
6. Any renal or liver disease (risk of encephalopathy)
7. Any HIV risk factors (including blood transfusions in the early 1980s)

Mr. Johnson denies any of the index medical problems. He only recalls taking occasional acetaminophen. His daughter wisely dumps the contents of his medicine cabinet on the examining table. There are full bottles of a calcium channel blocker, a diuretic, with prescription from another physician two years ago, and an over-the-counter cough suppressant-decongestant-antihistamine syrup, and a half-empty container of bismuth subsalicylate (Pepto-Bismol®) and another of acetaminophen.

The Neurobehavioral Examination

It has been estimated that 70 percent of medical diagnoses are made on the basis of history. The additional information, culled from a few minutes of informal observation in peripheral vision, may add a great deal, particularly in behavioral disorders. But, let us assume you have 5 minutes left to undertake the formal neurobehavioral examination. Again, it is understood that some factors, level of consciousness, cooperation, and language barriers, may frustrate any such artificially imposed schedule, and that a full assessment really takes longer. Nonetheless, we offer the following only in the interests of suggesting ways to efficiently negotiate the largest branches of the decision tree (see Tables 11.1-2, 11.1-3, 11.1-4).

It is conventional to describe this examination in terms of cognitive domains, e.g., attention, mood, language, memory, but in practice, every moment provides opportunities to examine multiple domains. For instance, we extend our hand to greet the patient. Their response in the next two seconds may partly reveal level of consciousness, social appropriateness, affect, vision, presence of dominant sided bradykinesia or dysmetria or paresis. In addition, as we attempt to strategize, our first goal is not so much to systematically assess cognitive domains as to rapidly get a sense for the acuity of the situation. We need to establish, if possible in the first few minutes, whether or not we are
dealing with an acute confusional state (delirium) that is more likely to require immediate action. (Note: the terms “delirium” and “confusional state” are used interchangeably. Neither one is ideal because each has misleading connotations from colloquial use. “Delirium” popularly connotes a striking behavior change, but it actually means a broad spectrum of AMS including very subtle changes. “Confusion” is rather vague, since popular use applies it to everything from error to psychosis. In the neurobehavioral evaluation, by a delirium, we specifically mean AMS with diminished attention, assayed in terms of coherence and responsiveness). So we need to assess the “vital signs of behavior,” the keys to severity, acuity, and need for prompt intervention.

The Vital Signs of Behavior

The Vital Signs of Behavior

Level of responsiveness

Orientation

Degree of agitation

We approach the 83-year-old man and extend our hand, introducing ourselves. He looks at the hand, looks up at us, mutely smiles, and accurately reaches to offer a firm handshake.

This is not normal. Social adepts will watch your hand in their peripheral vision as you begin reaching toward them, beginning their own arm movement before you have even fully extended yours, and will say something pleasantly appropriate. So we already suspect AMS. But at least his level of responsiveness is sufficient to respond to this cue, if too slowly, and there is no overt anger, suspiciousness, sadness, or agitation. Not to belabor the point, but our examination is really conducted in this way, painting a pointillist portrait by inference from every fleck of behavior.

Level of responsiveness simply refers to what the patient does in response to what we do, and whether that is normal. At lower response levels, this is the basis of the Glasgow Coma Scale (GCS). Coma is addressed elsewhere in this volume, but overlaps with this neurobehavioral examination since delirium is on a continuum with coma (while dementia isn’t) and delirious patients may lose a point or two on the GCS for failing to move or verbalize appropriately. In delirious patients, level of responsiveness might be quickly assessed by the rate and appropriateness of responses to soft voice, then, if necessary, loud voice, then, if necessary, some form of touching to trigger an alerting response. If the patient appears awake, but does not respond until we touch them, we still cannot assume encephalopathy is present, since deafness, uncooperativeness, paralysis, or (quite rare) catatonia may produce the same lack of response. Language barriers or aphasia, however, do not really compromise this test, since the examiner’s voice itself should surely elicit an alerting response. (Imagine yourself ill in a foreign hospital). Mr. Johnson superficially seems to have a normal level of responsiveness.

"Would you please look up for a moment?” may be among the best first questions we can ask. Ability to follow a one-step midline body command tests the most basic level of comprehension, something we learned to do at 18 months old. Even a quadriplegic patient on a respirator or a locked-in patient with no motor control below the brainstem can look up. Patients who have been mistakenly assumed to be aphasic, stuporous, or ‘vegetative’ will be extremely
grateful that you ask this initial question, giving them a chance to demonstrate their intact cognition. In addition, it tests hearing, an essential prerequisite for the validity of the entire examination. We ask this question. After a pause, Mr. Johnson looks up at his daughter a bit quizzically. It might have been an appropriate response, but other patients promptly look up at the ceiling. The response delay and direction makes us wonder about a slight deficit in Mr. Johnson’s level of responsiveness. We reserve judgment.

Orientation, so called, is a reasonable place to proceed with the direct verbal questioning of the patient. Again, these “who, where, when” questions actually assess multiple domains, including alertness, recent memory, and general knowledge, but we are asking in order to see whether the patient has been able to maintain sensory receptiveness, conscious awareness, and a coherent stream of ideas for the last several hours or so. The “why are you here?” question often provides telling information about not only alertness, but also insight, judgment, thought content, mood, personality, and degree of irritability.

By the time we’ve checked orientation, which may have taken less than a minute in many cases, it is quite likely that we will have a fair idea of whether the patient is delirious and whether they are so agitated as to require a higher level of vigilance, if not sedation or restraint. As a rough rule, if the patient can hear, seems to be trying to cooperate, speaks your language, and isn’t aphasic, they will give prompt (if wrong) answers to these questions, proving that they have an acceptable level of responsiveness. If they do not do so, it is very likely that they are in a confusional or encephalopathic state, upping the ante for prompt intervention.

Perhaps the most difficult exception to this rule is the differential diagnosis of receptive (Wernicke’s) aphasia versus confusion. Both problems lead to abnormal verbal responses. The Wernicke’s patient is somewhat more likely to produce jargon, and nonsensical speech, with clear enunciation, while the delirious patient is more likely to produce grammatically correct, if inappropriate, statements, with some degree of slurring and/or decreased arousal or wandering attention. Another exception is severe mood disorder, e.g., the profoundly depressed patient with psychomotor retardation (who in fact is encephalopathic as shown by global hypometabolism on brain PET scans), or severe thought disorder (psychosis), e.g., in schizophrenia, and also seen in severe depression or mania. Both of these may mimic a medical and/or neurologic confusional state.

If we reach the conclusion that level of responsiveness is depressed, it increases the likelihood of certain diagnoses, such as toxic or metabolic encephalopathy (including drug withdrawal), neuroinfection or systemic infection (especially with fever), hypoxia, increased intracranial pressure (IICP) with or without mass, large stroke, epilepsy-associated phenomena, or CNS vasculitis. Since the mortality rate for delirium is quite high, (15 percent–65 percent of admissions), a suspicion of any of these problems again obliges us to consider jumping ahead: stat labs? Scan? Hospitalize?

On the other hand, if the patient evinces a satisfactory level of responsiveness, it shifts the diagnostic balance somewhat more in favor of small stroke, tumor without mass effect, neurodegenerative disease, or “primary” psychiatric disease. (For the purposes of this discussion, we will accept the conventional dichotomy between “primary” [“idiopathic”] and “secondary” [due to medical/neurologic conditions] psychiatric disorders, understanding that it is a rather arbitrary rule of thumb created by our slowness to unravel the pathophysiology of a subset of brain-based behavioral disturbances).
So far, 70 seconds into the examination, we have shaken our patient’s hand and he has responded to one command and five questions. “John Johnson. It’s Tuesday, isn’t it?” “Where are we?” “Oh, I don’t keep up with that kind of thing.” “Why are you here?” “Well, I’m here, aren’t I?” He chuckles, punching you lightly on the arm, “and so are you!”

There is no slurring, but the responses come out like the pouring of lumpy soup: a bit slow, then suddenly too fast. His eyes are a bit wider than you’d ordinarily expect, searching, and a little red, as if sleep has eluded him. The uncertainty of the day of the week in itself is not abnormal. He seemed to understand the questions and produce fluent speech, making aphasia less likely. But the emptiness of the other responses indicates definite cognitive disturbance. In addition, while level of responsiveness is fairly good, the odd pacing of his verbal output leaves us uncertain: is this just cognitive impairment (as in dementias like Alzheimer’s), or is there also a confusional state (delirium), with impaired attention to the world around him?

After the Mental Status Vital Signs – Focusing the Examination

Ideally, at this point we would perform a complete assessment of affect, mood, thought content, thought process, attention, memory, language, calculations, abstraction, right/left orientation, judgment, insight, praxis, and constructions. We will not. Instead, the press of time often favors focusing the examination on issues we’ve become particularly concerned about and deferring other parts of the examination until later. How do we focus? We’ve already substantially narrowed the differential diagnosis based on the rate of onset, degree of change from baseline, type of dysfunction, and presence or absence of a confusional syndrome. This guides the next few minutes of the examination. For instance, an insidious onset causing a mild change without confusion frees us to test complex cognitive functions; we are thinking of neurodegenerative diseases, slow-growing tumors, and the like. Any overt depression or psychosis obliges us to give extra attention to affect and thought processes; whether primary or secondary, we are thinking of psychiatric distress. A rapid onset, large change with confusion suggests that we’d perhaps serve the patient better by rushing to the neurologic examination and laboratory evaluation; we are concerned about an acute and possibly emergently treatable encephalopathy.

If time permits (meaning the apparent absence of an acute confusional state), we can proceed to screen for "higher cortical functions."

[Note: Cognitive functions that seem to us to be more phylogenetically advanced than arousal, less directly tied to autonomic response than emotions, and separate from psychotic thought processes are sometimes called “higher cortical functions.” This phrase usually refers to processes such as memory, praxis, or self-monitoring. These were called “higher cortical functions” because of early theories that such functions were mediated by the late-evolving heteromodal association cortex, that is, cortex such as the inferior parietal lobule or prefrontal lobe that integrates multiple subcortical pathways, and it has sometimes been assumed that impairment of those behaviors only occurs following damage to those cortical areas. However, clinical experience shows that subcortical injuries may produce indistinguishable syndromes. For this reason, a more accurate phrase might be “cortical/subcortical cross-modal integrative cognitive functions.” But that’s a mouthful.]
Many clinicians use the 30 point Mini-Mental State Examination (MMSE) in these circumstances (Folstein et al, 1975 see Appendix A). On the one hand, we must recognize the limits of using the MMSE or any uniform cognitive screening instrument. The MMSE was not intended to provide a diagnosis. An Alzheimer’s patient can score 0 or 30. An aphasic patient can score 0 and be completely alert, achieving the same score as a patient in deep coma. A severely psychotic patient may score 30 while a cognitively intact but uncooperative patient may score 5. On the other hand, such a uniform set of queries has four advantages: 1) it touches on a number of cognitive domains and takes just five minutes in a cooperative patient; 2) it is widely used and the normative value of a near-perfect score has been well established; 3) specific items sometimes reveal specific problems; and 4) although definitive health outcomes research is needed on this subject, the presence of decline on successive tests may reveal an otherwise occult dementia, so we suggest doing the MMSE as a routine part of health screening for adults over 55.

Whether or not we perform the MMSE, at this point in almost every evaluation a high priority is to test that the remainder of interaction with the patient involves meaningful communication. We should quickly screen for aphasia.

The One-minute Aphasia Screen

1. “This may sound a little silly, but could you please say ‘dog’?”
2. “Thanks, now, what part of my shoe is this?” (Indicate the heel).
3. 4. 5. “Good. Please raise your right hand. Okay, put your left hand on your right shoulder. Good, now first put your right hand on your left knee, then your left hand on your right ear.”

1. “This may sound a little silly, but could you please say ‘dog’?”—Simple repetition tests hearing, Wernicke’s area, the arcuate fasciculus (white matter tract from temporal to prefrontal cortex), Broca’s area, the transfer of impulses from Broca’s area to the motor speech cortex, and the transfer from motor cortex down to brainstem neurons controlling the muscles of articulation.

2. “Thanks, now, what part of my shoe is this?” (Indicate the heel). Naming is not well localized in the brain, but asking for the name of a medium-frequency target (e.g., heel, sleeve, cuff) is a good general screen for dominant hemisphere function. High-frequency words like ‘pen’ are so well ingrained that they may be named despite an aphasia; low-frequency objects like ‘stem’ or ‘lapel’ may be too education-dependent to fairly test language.

3. 4, 5. “Good. Please raise your right hand. Okay, put your left hand on you right shoulder. Good, now first put your right hand on your left knee, then your left hand on your right ear.” Having established basic functionality of the left hemisphere, we return to receptive language. By quickly marching up through levels of complexity, from a one-step unilateral command to a two-step cross-body appendicular (extremity) command, we can rapidly get a rough estimate of degree of comprehension. Alert adults can usually manage a three-step sequence. Pointing at one, then two, then three things around the room is an alternative and tells more about environmental awareness but less about comprehension. Note again that it is challenging to distinguish
between Wernicke’s aphasia and confusion, but confused patients are more likely to have wandering or fluctuating attention. In addition, apraxia can manifest as failure to follow cross-body commands, but the apraxic patient can usually still point to things about the room.

6. “Thank you. Now, I know this may sound a little funny, but what’s the difference between a car and a boat?” The exact question we ask to stimulate fluent conversation is not as important as its evocative effect. We don’t want to ask something that can be answered with “Yes”, or with a monosyllabic answer like “Sure.” We want to hear the patient assemble a fluent string of words, regardless of content, correctly sequencing subject, predicate, and object. So, “Tell me the things you’d buy for a picnic?” is better than, “Do you think the Cubs have a shot this year?” Though our goal is to test for a productive (Broca’s) aphasia, odd answers may also help us discover interesting things about the patient’s ideas. (See Tables 11.1-2, 11.1-3, 11.1-4)

Mr. Johnson shrugs and cooperates, speaks fluently, and follows two-step, but not three-step, commands. He is easily distracted as the nurse walks by the door, and twice, you have to repeat questions. “Well, a car is, like, for out here, but boats you gotta’, you know, get to someplace with ‘em.”

As fluent as this is in a grammatical sense, it is sorely lacking in depth and meaning. This aphasia screen may have required a minute or two, depending on whether we’ve been able to draw conclusions from casual observations of the patient’s verbal interactions even before any formal testing. Reading, writing, or repetition of nonsense phrases all might be useful to test, but we have already assessed most language functions and the memory capacities required to answer orientation questions.

For the purposes of our rapid evaluation, it is rarely urgent to specify the type of aphasia. It is enough, in most cases, to note that language performance is abnormal, assume that the dominant hemisphere is probably affected, then look for an etiology. However, if we wish to go into slightly greater depth, and understanding that the classic syndromes do not typically appear in pure form, nor are they strictly localizable, several rough rules of thumb help to characterize brain/language relationships:

**Broca’s aphasia** = productive aphasia: impaired rate and fluency of speech output; stereotyped speech (“I am; I am”); poor generation of word lists; poor writing; and poor repetition, classically due to posterior-inferior frontal lobe dysfunction.

**Wernicke’s aphasia** = receptive aphasia: impaired comprehension, often affecting both spoken and written material; poor repetition; sometimes “word salad”, paraphasic errors, or nonsense words despite some recognizable grammar (e.g., “We aren’t what to going that the fordun is, is it?”), classically due to posterior-superior temporal lobe or adjacent parietal lobe dysfunction.

**Transcortical motor aphasia** is similar to Broca’s but repetition is relatively spared, classically due to subcortical prefrontal lobe lesions.

**Transcortical sensory aphasia** is similar to Wernicke’s but repetition is relatively spared, classically due to subcortical parietal lobe lesions.

**Conduction aphasia** is relatively worse repetition than production or comprehension, classically due to interruption in the arcuate fasciculus, the subcortical tract running between Wernicke’s and Broca’s regions.
Mixed aphasia combines features of productive and receptive impairment, either due to patchy dominant hemisphere cortical dysfunction or subcortical lesions that affect both motor and sensory tracts. When severe, this is a global aphasia.

Next we should test two facets of thought that are necessary for a coherent stream of consciousness and to assure that what we say to the patient is at least briefly retained: working memory and mental control.

Working memory, a type of short-term memory, refers to the temporary storage of information that is available for review or mental manipulation. Intact working memory depends not only on the medial temporal lobe memory system but also on the activity of several mid-prefrontal lobe regions. (See Tables 11.1-2, 11.1-3, 11.1-4).

It is beyond the purpose of this chapter to cover the neurobiology of memory, but recent advances are so intriguing that a very brief review might interest the reader: short term memory seems to be based on temporary changes in patterns of synaptic responsiveness. Longer-term memory seems to depend on new protein synthesis and resulting lasting structural changes in synapses. The electrochemical phenomenon of long-term potentiation (LTP), by which a series of stimuli leads to a change in subsequent neural response, may be the physiological underpinning of learning.

Learning probably involves:

1. The **medial temporal lobe memory system** (entorhinal cortex, hippocampus, parahippocampal gyrus and amygdala) and

2. The **prefrontal lobe working memory system**.

The **medial temporal lobe memory system** allows us to incorporate information into a lasting memory trace. This system is activated by the excitatory amino acid neurotransmitter glutamate, but it also requires the presence of acetylcholine (the profound lack of which correlates with memory loss in dementia of the Alzheimer type). The amygdala seems to have a special role, contributing emotional weighting to the memory process. The **working memory system** is a sort of memory buffer in which stimuli and ideas may be manipulated, both during learning and recollection. Recent evidence from functional MRI experiments suggests that especially complex memories require more superior and dorsolateral prefrontal cortical activation.

A simple test of working memory is to ask the patient to repeat and remember three words. Three visual objects are often used, ("apple, table, penny"), but the presence of a table in the room gives the patient a cue, and very common visual things may be stored more easily than abstract concepts. One strategy might be to use one visual object not currently in sight, one somewhat less easily visual word, and one abstract word, e.g., "tuna, Paris, strength." Make sure the patient repeats all three, (registration or immediate memory), to confirm that they’ve activated the prefrontal lobe working memory store.

Our 83-year-old patient repeats the words accurately, if bemusedly, after two attempts.
the other one.” Clearly something was retained, and, because he had repeated “Paris” at the registration stage, we know that his phonemic substitution (terrace, rhyming with Paris) is not just from hearing loss.

We may then give the patient hints about the words, (e.g., either category cues, “one of them was a city,” or the more generous multiple choice cues, “was the city Rome, Paris, or London?”), to see what it takes to jog their memory. In theory, if the patient doesn’t remember any of the words, even with cues, it suggests a severe amnesia, a learning problem, often involving medial temporal cortex. However, if they benefit from cues, it indicates that learning is intact, but that there is a retrieval problem, sometimes due to a subcortical dysfunction such as Parkinson’s disease. In practice, no such localization distinction should be assumed on the basis of our brief test; we are just getting a sense for the severity of the memory problem. Nor can we assume that memory impairment uncovered by this quick test identifies a particular condition. Digitalis toxicity, Alzheimer’s disease, or anxiety may lead to the same results. But at least we have a better idea of the patient’s ability to maintain a brief lock on a mental reservoir. Mr. Johnson chooses from the multiple-choice list, “Paris, of course! Didn’t I say that?” We conclude that cues help him a bit, but his memory is definitely impaired. What’s more, he may even be having trouble monitoring his own behavior from just seconds earlier, which may be another sign of possible prefrontal dysfunction and a hint of inattention (beyond a short-term memory deficit), somewhat suggesting that there might be confusion rather than simple dementia.

Mental control, sometimes called “executive function”, is the ability to adaptively manipulate information in working memory. This capacity is also referred to with the overlapping concepts of “executive” or “frontal lobe” function; although the prefrontal cortex is only part of the multiregional system invoked. Spelling a word backwards, counting backwards by 7’s or 3’s, naming every third letter of the alphabet, or reciting the months of the year in reverse all require more than just memory. There are the additional elements of 1) undertaking and maintaining focus on a task in the midst of external or internal distractions - requiring brainstem arousal, midline frontal lobe and limbic motivational systems, and prefrontal attentional systems—as well as, 2) correctly planning and sequencing the production of the answer—requiring working dorsolateral prefrontal lobes.

We ask Mr. Johnson to recite the months backward. “Sure. January, February...” he starts rapidly forward. We remind him of the task. “Oh, December...ah... September, November, December! And I want my shoes!” He grins.

As his daughter has intuited, Mr. Johnson is in trouble. Not only does he show signs of disorientation, memory impairment, and mental dyscontrol, but he has also made a couple of odd comments that were not direct responses to our questions. This is a tough case. We still don’t know for certain whether this is a dementia or a new onset confusional state, since he has not demonstrated overt lethargy. But his fluctuating rate of speech, slight response delays, distractibility, apparent immediate forgetfulness of his own statements and spontaneous behavioral detours make us concerned about mild confusion.

If we were less concerned about quickly assessing Mr. Johnson, or had more time, or noted odd interactions or movements that still required explanation, we might screen for several classic syndromes of cross-modal integrative cognitive function:
Ideomotor apraxia: The patient fails to do on command motor acts that they apparently have the strength and coordination to perform. We ask the patient “Show me how you would hammer a nail” or “salute” or “comb your hair” or “how does a boxer hold his hands?” or “blow a kiss” and we see a slow, awkward, befuddled attempt to comply. Dysfunction of the dominant hemisphere with or without paresis or aphasia can produce this apraxia. The rare neurodegenerative condition corticobasal–ganglionic degeneration may also produce this.

Ideational apraxia: The patient fails to generate or mime a sequence of actions that one would commonly need to perform to complete some common activity of daily living. We ask the patient “Show me how you would prepare a bowl of cereal” or “write, seal, stamp and mail a letter” and the patient fails to some degree. This problem occurs in both dementia’s and confusional syndromes.

Constructional apraxia: difficulty copying two or three-dimensional figures. It is sometimes assumed that this indicates right cortical dysfunction. In fact, almost any CNS dysfunction may interfere with copying a figure, from infarcts that affect motor function to impairments anywhere in the visual system. However, setting aside localizing value, constructional difficulty may be quite sensitive to confusional states or dementias, where drawing is often disorganized, as opposed to psychosis or mood disorder, where drawing is usually preserved.

Angular gyrus syndrome: a surprisingly well-localized tetrad of impairments, including difficulties with right/left discrimination, identifying fingers, performing calculations, and writing, classically due to dysfunction at the intersection of the posterior temporal lobe and the inferior parietal lobe.

Neglect: primarily seen as lack of attention to one side of the environment, most often after right parietal injury, producing inattention to the left hemi-world. The patient may shave half of their face or eat the food on half of their tray.

Anosognosia: impairment in recognizing the presence of an illness, including motor or sensory problems, often accompanied by neglect. For instance, the patient may deny having left hemiparesis, saying “Nothing’s wrong with me,” as she lifts her plegic left arm, “but could you get this dog out of my bed?” This is common with right hemisphere strokes, especially those involving both frontal and parietal lobes.

Prosopagnosia: failure to recognize faces. This may take the form of inability to recognize relatives, or difficulty identifying pictures of celebrities. It is most often due to bitemporal–occipital lesions.

All of these syndromes are most frequently reported after strokes, since these unfortunate experiments of nature often selectively damage isolated brain regions. However, any process that can affect the relevant parts of the brain may present with these complex cognitive syndromes. Tumors, traumatic brain injury, or neuroinfections may all produce these impairments.

We still need a quick screen for psychiatric symptoms such as depression, psychosis, and anxiety. Mania is possible, but less common and usually apparent from the early moments of the visit in the rapid speech and hyperactivity of the patient. In Mr. Johnson’s case, we’ve already gotten an impression of his apparent lack of extreme depression, agitation, or fearfulness in the face of a clear impairment of cognition. Nonetheless, a couple specific questions are worthwhile as a loose seine to catch mood or thought disorders.