

Case studies of focal prefrontal lesions in Man

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1 Introduction

Against the nineteenth century backdrop of the tension between Franz Joseph Gall and Johann Spurzheim's *phrenology* versus Marie-Jean-Pierre Flourens' *equipotentiality*, Paul Broca and subsequently Carl Wernicke demonstrated cortical localization of expressive and receptive language functions and their descriptions were soon embraced by the larger medical and scientific community. As additional evidence of hemispheric specialization, John Hughlings Jackson described difficulty with "memory for persons, objects, and places" associated with posterior right hemisphere lesions which led him to introduce the term "imperception" (Finger, 1994). Interest in the frontal lobe was largely restricted to language characteristics associated with lesions of Broca's area as contrasted against those associated with more posterior lesions involving Wernicke's area.

Despite the advances of understanding brain function in the second half of the nineteenth century, the tension between the localizationist versus anti-localizationist camps continued to be present. Current interest in the frontal lobe extends far beyond expressive speech, and involves its role in executive functioning, perseveration, judgment, attention, emotional behavior, and motor programming and regulation, with regional specialization within the frontal system increasingly appreciated for unique contributions to complex human behavior. Thus, localization and antilocalization approaches are able to coexist within a functional system framework. In the present chapter, we will present important cases demonstrating the behavioral impairments associated with prefrontal lobe lesions that have greatly contributed to our understanding of neuropsychological functions of these regions. The prefrontal regions are those anterior and mesial to those subserving motor function (i.e. primary motor cortex and frontal eye fields) and expressive speech (i.e. Broca's area) (Benton, 1991).

Because lesions of these frontal lobe regions often result in recognizable and distinct frontal lobe syndromes, the entire frontal lobe is often regionalized into lateral (dorsolateral), mesial, and orbital frontal areas. Dorsolateral frontal syndrome (executive dysfunction syndrome) consists of difficulty generating hypotheses and flexibly maintaining or shifting sets, and may be assessed with neuropsychological tests including Card Sorting Test, generative fluency, poor organizational strategies, and motor programming deficits.

The mesial frontal/anterior cingulate syndrome is characterized by reduced spontaneous activity that ranges from *akineti mutism* to transient abulic hypokinesia (hypokinesia from “loss of will”). Patients are typically apathetic, do not speak spontaneously, will answer questions in monosyllables if at all, move little, eat and drink only if fed, show little or no emotion, and may be incontinent. If able to cooperate with neuropsychological testing, these patients may be able to perform adequately on many neuropsychological tests but have more difficulty on tests of response inhibition such as go/no-go tasks.

Orbital frontal syndrome, which is the primary topic of the cases presented in this chapter, is characterized by prominent personality changes. These changes may include emotional lability, impulsivity, irritability, becoming more outspoken and less worried, and occasionally showing imitation and utilization behaviors (enslavement to environmental cues). Orbital-frontal syndrome is caused by lesions of the orbital region (undersurface) of the frontal lobes. This area is also sometimes referred to as the limbic frontal lobe because of its extensive connectivity to limbic structures such as the amygdala.

Antecedents of current clinical interest in the frontal lobe lesions can be traced to the early nineteenth century during the heyday of phrenology, which postulated that cerebral specialization of complex human behaviors not only existed, but that they could be detected through examining the overlying skull, which reflected the size of the regions of behavioral specialization of underlying brain anatomy. It was also at this time that the pattern of convolutions began to become recognized as defining more or less consistent patterns of anatomy (e.g. Rolando, 1831), thereby allowing specific function to be more easily ascribed to underlying brain structure. By 1870, the gross morphology of the brain and its landmarks were well described (Benton, 1991). Gall and Spurzheim’s (1809) view of brain function was that the brain contained discrete mental faculties and functioned as an assemblage of “organs.” In contrast, Flourens proposed “mass action” of the brain in which a threshold of volume loss was necessary prior to the appearance of clinical symptoms.

Flourens derived support for his position by many reports of brain injuries without any associated functional impairment.

2 Phineas Gage

Against this backdrop of whether there existed a differentiation of function in the brain or whether the brain operated as a more holist unit emerges Phineas Gage, one of the most famous cases in behavioral neurology, neuropsychiatry, and neuropsychology. A review reveals how the initial report of Gage's injury was first used as evidence to support an antilocalizationist interpretation of brain–behavior relationships after a follow-up report 20 years later detailing Gage's behavioral deficits. In short, it is an early case study in the philosophy of science.

Gage's injury involved the projection of a large tamping iron, which was used to pack sand over an explosive charge to excavate rock during railway construction, through the left side of his skull. That this magnitude of injury did not immediately cause death was of great surprise, and the early characterization of this case focused upon Gage's surprising survival. The local newspaper report reflected the early belief that the injury caused no significant behavioral effect. "The most singular circumstance connected with this melancholy affair is, that he was alive at two o'clock this afternoon, and in full possession of his reason, and free from pain" *Free Soil Union* (Ludlow, Vermont) (Macmillan, 2000a). Using contemporary computational methods, the lesion likely involved bilateral anterior orbital frontal cortex, polar and anterior mesial frontal cortices, and the rostral anterior cingulate (Damasio *et al.*, 1994). The underlying white matter was more greatly involved in the left hemisphere. Gage developed epilepsy many years later, and died following status epilepticus in 1861 over 12 years following his accident.

John M. Harlow, MD was primarily responsible for Gage's medical care following the accident. Harlow's physiology professor at Jefferson Medical School was Robley Dunglison. Dunglison was not a "phrenologist," but considered the approach of phrenology as a potentially valid approach to characterize human brain function. Although Dunglison described phrenological theory in his 1832 text entitled *Human Physiology*, he also cautioned that "the views of Gall (Franz Joseph Gall) are by no means established. They require numerous and careful experiments, which is not easy for every one to institute" (Barker, 1995). This background likely provided the perspective needed to characterize the behavioral deficits when they were finally described in detail approximately 20 years later. It is likely that it was this exposure to phrenology that permitted Harlow to recognize and appreciate the fractionalization of behavior through this

unfortunate “experiment,” although Harlow did not report Gage’s behavioral changes in any detail until 20 years later (Harlow, 1868).

Harlow’s initial report emphasized Gage’s surprising physical recovery (Harlow, 1848, 1999). Despite this emphasis, however, there are several hints of significant behavioral change. Harlow stated that Gage “does not estimate size or money accurately, though he has memory as perfect as ever. He would not take \$1000 for a few pebbles which he took from an ancient river bed where he was at work.” He is also described as being “very childish,” exercising poor judgment (e.g. walking a long distance in cold and damp without an overcoat) and not following recommended activity levels during his recovery. Gage “appears to be in a way of recovering if he can be controlled,” and Harlow concludes by stating, “the mental manifestations of the patient, I reserve for a future communication.”

Because the behavioral changes were not explicitly described in Harlow’s 1848 report, Gage’s initial notoriety involved his remarkable recovery despite the significant damage to the brain, and this recovery was met with initial skepticism. Gage was subsequently examined by one of those skeptics, Henry Bigelow, MD from Harvard Medical School. As a historical aside, Bigelow was a pioneer in introducing ether anesthesia for surgery (Wheeler, 1997) as well as being a prominent antivivisectionist (Barker, 1995).

Bigelow wrote to Harlow requesting details of the case and subsequently arranged for Gage to travel to Boston and be examined (Macmillan, 2000a). Bigelow reported that Gage was “quite recovered in faculties of body and mind,” “A physician who holds in his hand a crowbar . . . will not readily believe that it has been driven . . . through the brain of a man who is still able to walk off . . . Being at first wholly skeptical, I have been personally convinced . . .” (Bigelow, 1850). Because Harlow always referred to the tamping iron by its proper name, Bigelow’s use of “crowbar” helps to trace the greater influence of Bigelow’s report compared to Harlow’s in subsequent citations of Gage, and there are multiple references to the “American crowbar case” (Barker, 1995).

In contrast to Harlow, who was exposed to phrenology during his training, Bigelow’s background was antilocalizationist and included F.A. Longet, the French physiologist who stated that “one healthy cerebral hemisphere may suffice for the exercise of intelligence . . . observations of severe wound of the brain: loss of cerebral substance affecting various regions of the cerebrum, with intact intelligence” (Barker, 1995). In Bigelow’s description of Gage, he states “it is well known that a considerable portion of the brain has been in some cases abstracted without impairing its functions. Atrophy of an entire cerebral hemisphere has also been recorded” (Bigelow, 1850). Thus, Bigelow’s description

of Gage as being “quite recovered in his faculties of body and mind” is consistent with this approach to understanding brain function.

The majority of references to the “crowbar” case cited Bigelow emphasizing complete mental recovery as evidence for the antilocalizationalist approach refuting phrenology, and this view of the case was widely reported in texts of that era (Barker, 1995). Of the 14 Gage citations in American medical journals prior to the 1868 report, 11 refer to Bigelow’s version and none describe a behavioral impairment alluded to in Harlow’s initial report (Barker, 1995).

Bigelow’s description of complete recovery was widely cited until 1868 when Harlow published another report on Gage, at which time the significant behavioral changes associated with the injury were detailed.

“His contractors, who regarded him as the most efficient and capable foreman in the employ previous to his injury, considered the change in his mind so marked that he could not give him his place again. The equilibrium, or balance, so to speak, between his intellectual faculties and animal propensities, seems to have been destroyed. He is fitful, irreverent, indulging at times in the grossest profanity (which was not previously his custom) . . . manifesting but little deference for his fellows, impatient of restraint or advice when it conflicts with his desires, at time pertinaciously obstinate, yet capricious and vacillating, devising many plans for future operation, which are no sooner arranged than they are abandoned in turn for others appearing more feasible.”

Indeed, Gage “was no longer Gage.”

Harlow’s (1868) descriptions of Gage were quickly incorporated into American texts, but less quickly in Europe (Barker, 1995). David Ferrier reported in the mid 1870s that Gage had no change in intellectual function. However, after reading a reprint of Harlow’s 1868 paper sent to him by H. P. Bowditch, a physiology professor at Harvard, Ferrier wired for copies of the now famous woodcuts illustrating Gage’s injury. These were subsequently used in his Goulstonian lectures on cerebral localization in which focal mapping of cerebral function was used as an example of how frontal lobe injury could be associated with personality changes in the absence of sensory or motor deficits (Neylan, 1999). The importance of Gage is evident in the continuing citation of this case involving multiple recent articles and books (Damasio *et al.*, 1994; Macmillan, 2000a, 2000b; Haas, 2001; Mataro *et al.*, 2001; Fleischman, 2002; Ratiu & Talos, 2004; Wagar & Thagard, 2004).

In Ferrier’s reply to Bowditch, he states initially that “I think your proposal to imitate the lesion with the brain in situ would be a most desirable experiment” and later commented “I hope—Bigelow notwithstanding—that Putnam and you will really carry out your proposed investigation. I can do no experimental work now. . . . All that is done away with as I cannot work under the accursed

antivivisection laws” (Barker, 1995). Thus, Bigelow’s antivivisectionist activism likely contributed additional tension to the localization versus antilocalizationist debate on Gage’s recovery.

Interestingly, Ferrier’s observations about how the same data can be interpreted in vastly different lights continue to be applicable today.

“In investigation the reports on diseases and injuries of the brain I am constantly being amazed at the inexactitude and distortion to which they are subjected by men who have some pet theory to support. The facts suffer so frightfully that I feel obliged always to go to the fountain-head—dirty and muddy though this frequently turns out.”

3 Patient K. M.

The beneficial effect of extensive frontal lobe resection on cognition and behavior is detailed in the case of K. M., a 27-year-old man who underwent bilateral frontal lobe resection for poorly controlled posttraumatic epilepsy (Hebb & Penfield, 1940; Hebb, 1945). This is an important case, not only for understanding the contribution of the prefrontal region to cognition and behavior, but also because it demonstrates an important distinction between an active or irritative lesion associated with an ongoing seizure focus compared to that associated with a destructive lesion, as well as how there may be negative behavioral effects of abnormal tissue on normal tissue such that pathological tissue may interfere with normal brain function. As noted by Hebb (1945), “the small and diffuse region of partial necrosis can have a greater effect in the production of symptoms than a larger area of complete destruction and clean cut removal of tissue.”

K. M. sustained a skull fracture with significant brain injury when he was 16 years old, resulting in damage to both frontal lobes. After his injury, he developed severe posttraumatic epilepsy with significant behavioral changes. The significant behavioral changes included poor judgment (e.g. going outside in winter without proper clothing) or forgetting to perform an errand for which he originally set out to perform (e.g. mailing a letter). In this context, he appeared behaviorally very similar to Gage. More importantly, however, was a significant change in K. M.’s temperament in which he became violent, stubborn and destructive, a problem made more significant by his large physical size and strength. He even appeared to enjoy scaring his neighbors, acting as though he was in one of his violent moods even when he was not.

Because of the medical intractability of K. M.’s seizures, he underwent epilepsy surgery by Dr. Wilder Penfield at the Montreal Neurological Institute removing “one third of the mass of the frontal lobes” bilaterally. K. M. was tested

with the Stanford-Binet and McGill revision of the Army Beta tests both pre- and postoperatively. When tested 2 months after surgery, K. M.'s Stanford-Binet IQ increased from 83 to 94. It is unclear if this improvement occurred at least in part as a function of the different forms of the Stanford-Binet being used for pre- and postoperative assessments (Form L preoperatively and Form M postoperatively). Form M did not contain a vocabulary test (Sattler, 1974), and higher scores tended to be associated with Form M in subsequent postoperative evaluations. Nevertheless, it is clear from these data that no significant decline in overall function was present. In addition to the changes on the Stanford-Binet, a postoperative improvement on the McGill revision of the Army Beta test was described from 63 to 71. Although it is likely that practice effects contributed to the improvement from pre- to postoperative scores since Army Beta contained many of the subtests that Wechsler incorporated into the WAIS (Boake, 2002) and the performance tests tend to be more affected by practice than verbal subtests (Lezak *et al.*, 2004), as with the Stanford-Binet, these data indicate the absence of a significant cognitive decline following surgery. Good postoperative performances were also described for Kohs blocks, backward digit span, and category sorting. Thus, surgical resection of the frontal lobes in K. M. did not apparently produce any significant neuropsychological impairment.

A significant postoperative behavioral improvement in personality and temperament was described. "The patient has now a pleasant personality. He is no longer facetious or vulgar . . . but is considerate of the other patients and has acquired a pleasant sense of humor." The negative behaviors developed after K. M.'s brain injury. Six years after the operation, K. M. was described as being "one of the more popular persons in the village." Thus, even in the absence of formal diagnostic evaluation, there is evidence of significant behavioral improvement following surgery with a return to premorbid behavioral tendencies. In fact, he was described years later by his relatives as being his "old self" (Hebb, 1945).

As real-world evidence of both his behavioral normalization as well as the absence of developing significant neuropsychological impairment is his military service that was performed following the surgery, K. M. enlisted in the army without apparent difficulty for either cognitive or behavior reasons. He continued to serve without incident until he had a seizure following significant physical exertion, at which time he was medically discharged from the service. K. M. had no difficulty finding work, although a labor shortage associated with World War II may have contributed in part to that ease. He was able to manage his money without significant difficulty and, although not "saving" money for the future, always had money on hand when it was needed. Of course, not planning for the distant future financially is characteristic of many individuals without bilateral prefrontal injury, and is hardly diagnostic.

An important contribution of this case is the demonstration that extensive frontal resection is not necessarily associated with a loss of psychometric intelligence. "For the effect of lesions of the frontal lobe on human intelligence, it seems that one will have to look elsewhere than to clinical observation or ratings by intelligence tests such as are now available." Further, normal performances were noted on several tests that are presently commonly associated with "frontal lobe function" including backward digit span and category sorting.

More important, however, is that K.M.'s lesion (s) was very different from that of Gage; K.M. had significant preexisting damage to the region that was resected, and further, this area was associated with significant and active seizure focus. The negative effect associated with the epileptogenic region (i.e. nociferous cortex) is described explicitly. "It becomes evident that human behavior and mental activity may be more greatly impaired by the positive action of an abnormal area of brain than by the negative effect of its complete absence." As later noted by Hebb, "the question . . . of whether (frontal lobe) behavioral defects are the result of the surgical removal or whether they are due to the presence of pathological changes in the remaining part of the brain" continues to be appropriate for clinical correlates of brain function, even in the present days of sophisticated neuroimaging.

4 More recent "classics": patient E.V.R.

E.V.R. was a 35-year-old man and a successful accountant and comptroller before developing personality changes, which led to the discovery of a large orbital frontal meningioma compressing both frontal lobes (Eslinger & Damasio, 1985). After successful surgical resection, the lesion was described as involving both orbital and lower mesial frontal cortices. Although E.V.R. returned to work after 3 months, his performance and overall behavior changed dramatically. He quit his job to invest in a building partnership with a previous coworker who had been fired, and subsequently lost his entire savings. E.V.R. was then fired from multiple jobs, generally due to being late for work and being disorganized. Nevertheless, E.V.R.'s basic skills, manners, and temper were appropriate. His wife of many years left him, and E.V.R. moved in with his parents. He remarried, was again divorced, and subsequently was considering marriage to a woman 14 years his senior (a "semiprominent socialite") who he was trying to convince to support the establishment of a "luxury travel business" to drive "wealthy people" on vacation around the country in a motor home.

Much of his behavior was ritualistic and compulsive, with some days consumed entirely by shaving and hair-washing. Purchasing small items required

in-depth consideration of brands, prices, and the best method of purchase. He refused to part with dead houseplants, old phone books, six broken fans, five broken television sets, three bags of empty orange juice concentrate cans, 15 cigarette lighters, and countless stacks of old newspapers.

Despite these behavioral changes, neuropsychological testing was normal. Two years after surgery, E. V. R.'s WAIS verbal IQ was 120, performance IQ was 108, and Wechsler Memory Scale MQ was 140. All MMPI scales were in the normal range. One evaluation concluded that "adjustment problems are not the result of organic problems or neurological dysfunction . . . instead they reflect emotional and psychological adjustment problems and therefore are amenable to psychotherapy." In a separate neuropsychological assessment, E. V. R. obtained all six categories on the Wisconsin Card Sorting Test in only 70 sorts, and had normal memory performance using the Brown-Peterson interference procedure, an approach that has been reported to be sensitive to frontal lobe lesions (Stuss & Levine, 2002).

E. V. R. has maintained an interest in world events and could discuss complex social issues as well as the economy and financial matters. In contrast to his personal behavior in which he continually made errors in judgment, his social judgment for problems presented to him during testing was good. For example, when given a vignette about a psychiatrist refusing to provide treatment to a patient after the psychiatrist found out that the patient was forced to engage in cannibalism to stay alive, E. V. R. replied, "The psychiatrist's duty is to treat a patient for whatever his mental ills may be, not to judge whether he should have or shouldn't have treatment."

5 More recent "classics": imitation, utilization, and environmental dependency

The contrast between the ability to make good abstract judgments to verbal scenarios and his poor real-time judgments in his personal life is the most valuable contribution of this case. This dissociation contrasts with patients with "acquired sociopathy" in which the approach to real-life social problems and hypothetical social problems tend to be the same (see next section). As the authors note: "He had learned and used normal patterns of social behavior before his brain lesion, and although he could recall such patterns when he was questioned about their applicability, *real life situations failed to evoke them.*"

The issue of behavior being elicited by real-life situations was described in two papers in which behavioral response was directly dependent upon the

environment (Lhermitte, 1986; Lhermitte *et al.*, 1986). Imitation behavior occurs when a patient imitates the imitation of the examiner's gestures without being instructed to do so and is considered to be a form of utilization behavior in which objects in the environment elicit behavioral response. Both are symptoms of the same behavioral disorder.

The inferior portion of frontal lobes (unilateral or bilateral) tends to be associated with imitation or utilization behavior. Types of behavior that may elicit imitation include sudden hand clapping or saluting, thumbing one's nose, folding a piece of paper, or simply tapping the leg with various rhythms. Patients with imitation or utilization behavior tend to have additional neuropsychological impairment in both memory and intelligence, poor performance on the Wisconsin Card Sorting Test, and not surprisingly, motor perseveration on Luria figures.

Patients demonstrating imitation behavior believe it to be volitional and report that they thought the examiner had meant for them to imitate. In that sense, imitation behavior differs from echolalia or echopraxia. As discussed by the authors, the parietal lobes process a constant stream of incoming sensory information forming a constant link between the subject and external world. Frontal lobe impairment removes inhibitory influences such that the behavioral dependence is affected more by the quality of the external stimulus field and less by internal factors.

Two cases are described in detail who demonstrated behaviors that were not only dependent on the physical environment, but also reflected more complex social factors such as the socioeconomic background of the patients and their gender. Lhermitte introduced the term "environmental dependency" to describe the behaviors. The first case was a 51-year-old male engineer with a high socioeconomic background who developed a left frontal oligodendroglioma that was resected, and then treated with chemotherapy and radiation therapy. The second patient was a 52-year-old woman with an astrocytoma of the basal left frontal lobe that was resected, which was followed by radiation therapy. She came from an average background and had been employed doing domestic work.

Both of these patients were exposed to a variety of social situations, and at times, responded very differently to the identical setting. For example, when entering a room with a buffet table and approximately 20 people present, the male patient helped himself to food and orange juice while the female patient unstacked chairs, arranged glasses on the serving table, and offered to serve food to Lhermitte (including port!). The male patient from a higher socioeconomic background acted like a guest, whereas the female patient who had been employed providing domestic help acted like a hostess.

A similar pattern was seen when the patients sat down next to a table that contained a variety of items including makeup and handguns. After sitting down next to a table, the male patient first frowned when seeing the makeup items until he saw the handguns, which he picked up and examined. The female patient, in contrast, immediately picked up the makeup products and began to apply them to her face.

In an apartment, the male started examining the paintings that were hanging on the wall as if he were in an art gallery after the author quietly uttered the word "museum." The female patient started to walk though the apartment after hearing "museum," but she did not study the paintings systematically; instead she paid a great deal of attention to the curios on the table. In both these and other examples, behavior was elicited through cues in the environment (environmental dependency), which was modulated by the patient's personality and prior experiences. The patients thought that they had reacted in a naturally volitional way toward the environment. This call to action can even be observed to a less degree in healthy subjects as observed by behavior when a bowl of popcorn or potato chips is placed on a table.

Lhermitte described environmental dependency syndrome as a physical adherence to external stimuli resulting from a loss of autonomy from the environment. There is a reciprocal relationship between the frontal and parietal regions. In the healthy brain, the prefrontal lobe has an inhibitory influence on more basic behaviors that arise from sensory stimulation in the environment. In addition, the prefrontal regions (particularly the dorsolateral region) allows the elaboration of goal-directed and adaptive behavior, based upon both environmental contingencies as well as the subject's internal state from limbic information received through the paralimbic orbital frontal region. When the prefrontal region is damaged, the normal interaction is disturbed and the behaviors triggered by sensory stimulation in the partial lobes are "released" without inhibitory control. In this case, sensory stimulation (visual or tactile) may result in utilization of imitation behavior.

6 Early prefrontal injury

All of the cases described above sustained their injuries as adults. A small series of two patients (called only A and B in the report) who sustained prefrontal injuries before 16 months of age illustrate how age of injury affects behavioral outcome.

Patient A was a 20-year-old woman who was run over by a vehicle when she was 15 months and apparently recovered fully within days. MRI performed as an

adult indicated bilateral frontal lobe involvement involving polar and ventromedial areas. Patient B was a 23-year-old man who had a right frontal lobe tumor resected when he was 3 months of age. As an adult, MRI revealed unilateral right frontal injury of the medial and dorsal pole.

The first patient's behavioral difficulties did not emerge until she was 3 years old when she did not respond normally to punishment. In adolescence, she was disruptive, verbally and physically abusive, and would steal from family and from stores. She became pregnant at 18 years old, but after birth, she displayed no sensitivity to her baby's needs. She was unable to hold down a job due to lack of dependability and gross work infractions.

The second patient was not as disruptive at school, but generally lacked normal motivation. He, too, could not hold down a job, and fathered a child but failed to fulfill any paternal obligation. He engaged in petty planned thievery and would threaten and occasionally physically assault others. He also lied frequently, often with no known motivation.

According to the authors, the magnitude of these behaviors is more severe than in comparably lesioned adults. In contrast to adults such as E. V. R., these patients did not retrieve the complex socially relevant knowledge when queried, presumably because it was never acquired. In addition, unlike adult patients sustaining similar injuries, these two subjects displayed antisocial behavior such as violence against others and repeatedly stealing items (i.e. "acquired sociopathy"), although much of the behavior did not seem to be goal-directed, appearing more impulsive in character.

7 Concluding remarks

The cases reported in this chapter were selected based upon their historical importance, their relevance to demonstrating different behavioral effects based upon specific lesion characteristics, as well as their demonstration of some inhibitory control over behaviors elicited by environmental cues or imitation. Although the story of Phineas Gage is often cited, it is typically not described in great detail. In addition, the fact that Gage's behavioral outcome was used for approximately 20 years as evidence that significant frontal lobe damage could be present without pronounced behavioral change is almost without exception not included.

There is often times a tendency to treat all lesions as equivalently disruptive to cognition and behavior. K.M. demonstrated a much improved behavioral outcome following surgical resection of an existing lesion despite the fact that

the surgical lesion involved a much greater volume of brain tissue compared to the original epileptogenic lesion. In present nomenclature, the disruptive effect of the “active” lesion is termed “nociferous.”

The cases of K. M. and E. V. R. demonstrate an absence of neuropsychological impairment following extensive frontal lobe damage, despite multiple assessments using comprehensive batteries with tests commonly used to assess frontal lobe function. Interesting here was the dissociation between the ability of E. V. R. to provide “correct” answers to social and ethical situations when presented to him in the laboratory setting and his ability to implement “correct” behaviors in the real world. In particular, E. V. R.’s desire to make a living by driving “rich people” around in a mobile home is an example that certain types of poor social skills are unlikely to be fully captured by formal tests or questionnaires.

Lhermitte’s report of imitation and utilization behavior, and his case reports of two patients with environmental dependency syndrome, depicts a different facet of frontal inhibitory control over behavior since it provides details of a nonemotional response to environmental cues rather than an alteration of behavior in which either poor judgment is seen or a “coarsening” of personality develops. The reciprocal relationship between the frontal and parietal regions illustrates the constant dynamic interaction between various brain regions and systems, and helps to illustrate how normal frontal lobe function exerts selective control of response to both simple items in the environment as well as orchestrated, complex, and individually specific response to different social contexts. The contribution of frontal lobe function to human behavior ranges from the personality changes of Phineas Gage to the blurring of “free will” associated with environmental dependency disorder, illustrating why much of our understanding of frontal lobe function has been derived from carefully described case studies.

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