



Inter-individual variability in disease expression: the Tudor-Churchill spectrum

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Abstract

Henry VIII and Winston Churchill are clinically instructive when appreciating inter-individual variability in disease expression. Both were illustrious English leaders who as young men sustained multiple traumatic brain injuries, which may (or may not) have profoundly influenced their successes and failures of later years. Both men were admired and castigated; both struggled at various times with their bodies and their minds. Ultimately, one was initially a great man who descended as a flawed leader; the other was initially a flawed man who ascended as a great leader. Their similar yet contrasting case histories define the full spectrum (“Tudor-Churchill Spectrum”) of inter-individual variability in response to brain disease or injury. The Tudor-Churchill spectrum is the immense variability between individual patients and reminds us that every person is unique, deserving of individualized thought, personalized diagnosis and tailored treatment.

Keywords Dementia · Alzheimer’s disease · Brain trauma · Chronic traumatic encephalopathy · Concussion · Henry VIII · Winston Churchill

Introduction

Every patient is a unique human being. As the era of precision medicine and personalized treatment evolves, the utility of generalized diagnostic checklists must be balanced with an appreciation for individually expressed symptoms for diseases but especially within the context of neurologic disease. More than any other organ, the human brain as a consequence of its immense complexity defines our uniqueness not only from other species but more importantly from each other; not surprisingly, the manifestations of brain disease are correspondingly diverse, varying from person to person. An exemplary illustration of individualized symptom expression is the personality and behavioural change that sometimes accompanies traumatic brain injury. Henry VIII and Winston Churchill are

clinically instructive when appreciating inter-individual variability in disease expression.

Henry VIII and Winston Churchill were illustrious English leaders who as young men sustained multiple traumatic brain injuries, which may (or may not) have profoundly influenced their successes and failures of later years. Both men were admired and castigated; both had battles with their body and their spirit. Ultimately, one was initially a great man who descended as a flawed leader; the other was initially a flawed man who ascended as a great leader. Their similar yet contrasting case histories define the full spectrum (“Tudor-Churchill Spectrum”) of inter-individual variability in response to disease or injury.

Case history 1—Henry VIII (1491–1547)

Early Years: In the summer of 1499, the eminent Dutch intellectual Desiderius Erasmus described eight-year old Henry Tudor as someone who “has never neglected his studies”, “a universal genius”, and a “lively mentality which reaches for the stars” [1]. The young Henry Tudor had a mind avid for learning, excelling in virtually every subject. He thrived on a broad education in languages, music, poetry and sports; he was witty, charismatic and exhibited a keen appetite for art and athletics.

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By the time he ascended to the throne in 1509 at age 17, he was a much admired scholar and athlete. Indeed, in 1515, Sebastian Giustinian, the Venetian ambassador to England, described the young King Henry VIII as follows: “He is the handsomest potentate I ever set eyes on; this most serene man is not only of great valour, and most excellent in his personal endowments, but is likewise so gifted and adorned with mental accomplishments of every sort that we believe him to have few equals in the world. He speaks English, French and Latin; understands Italian well; is prudent and wise and free from every vice” [2]. Given Henry’s great gifts, England was high with hope for his reign.

Concussion Years: As a young king, Henry VIII experienced multiple concussions. Hunting, hawking, wrestling and jousting were obsessions for him. In his youth, he would frequently wrestle or joust multiple times in a single day, often being thrown heavily or struck several times within hours. In June 1520, Henry VIII wrestled Francis I of France. Details are few, but Henry was defeated when Francis using a wrestling technique known as the Breton trip, vigorously threw Henry to the ground, stunning him [3]. In March 1524, Henry was de-horsed during a jousting match after a lance struck him in the head through his open visor; despite being confused and suffering from a severe headache, he continued to joust throughout the day (and went on to suffer from chronic headaches after this accident) [4]. One year later, while attempting to pole-vault over a hedge, the pole broke with Henry falling heavily, striking his head and becoming unconscious, having to be dragged out of a watery ditch [5]. Then, on January 24, 1536, Henry VIII experienced his most significant concussion. While jousting, not only was he unseated but the fully armoured horse fell squarely upon his head leaving him unconscious for 2 hours [6]. Fearing death was imminent, preparations were being made to notify his successor when Henry unexpectedly regained consciousness. Thus, throughout his life Henry VIII had at least three or four major concussions and probably many other lesser ones.

Later Years and Legacy: Henry VIII’s reign had multiple notable achievements. He presided over sweeping changes that established the Royal Navy, brought Wales more fully into union with England, and ushered his nation into the Protestant Reformation. However, he is better known as a brutal oppressor who was easily frustrated often bursting into rage attacks, who ordered the execution of 57,000 people, and who had six wives, two of whom were beheaded. Between 1527 and 1536, Henry underwent profound personality changes transforming from an intelligent, vigorous monarch into an obese, moody, cruel and petty tyrant—it is the latter which epitomizes his historical record.

Henry VIII’s legacy is as England’s most infamous monarch. Towards the end of Henry’s reign, French Ambassador Castillon described him as “the most dangerous and cruel man in the world” [7]. The passage of time changed little. Three

hundred years later, the celebrated novelist Charles Dickens characterized Henry as “an intolerable ruffian, a disgrace to human nature, and a blot of blood and grease upon History” [8].

Case history 2—Winston Churchill (1874–1965)

Early Years: In the summer of 1884, the headmaster of St. George’s preparatory school in Ascot commented on the report card of ten-year-old Winston Churchill: “Conduct has been exceedingly bad; he is not to be trusted to do a single thing” [9]. This harsh assessment reflected the challenges faced by a fiercely independent boy rebelling against a rigid educational system; however, he was indeed a poor student performing well only in the very few subjects that interested him, particularly history (in which he did extremely well).

Churchill’s mediocre performance at school prevented him from attending university, leaving the military as his only career option. He took three attempts to pass the entrance exams for the Royal Military College, Sandhurst. Churchill’s poor mathematical skills precluded him from the artillery and engineers; he did not even qualify for the infantry, scoring just enough points to be admitted to the lowly cavalry. His father was disappointed in his son’s underachievement.

Concussion Years: Churchill experienced multiple concussions during his life. In 1889, as a 14-year old Harrow school-boy ascertaining how fast he could ride a tricycle, he swerved and crashed with such force that he was in the sickroom for a week with a concussion [10]. Four years later, while playing chase with his cousins he jumped from a bridge falling 30 feet to the ground, sustaining a head injury that left him unconscious for 3 days [11]. Fearing death was imminent, his father uncharacteristically curtailed a trip abroad to return to his bedside; Churchill convalesced for months before returning to normal. In 1895, as a cadet at the Royal Military College, Sandhurst, his horse “refused and swerved” on the steeplechase course, flinging him with such force that he was in bed for three days recovering [12]. In 1921, he was thrown from a camel as he visited the Sphinx with Lawrence of Arabia [13]. In 1922, while participating in a polo practice, he was somersaulted off of a pony landing heavily on his head—“every scrap of wind was knocked out of my body” leaving me in a state of “speechless consternation” requiring several days of recovery [14]. Beyond these multiple horse accidents, Churchill also sustained injuries whilst piloting an aircraft: having just taken off from Croydon Aerodrome, the aircraft stalled at 90 feet, plunging back to the ground leaving Churchill dazed and heavily bruised [15]. Finally, there are Churchill’s multiple automobile accidents in June 1914, February 1920, September 1921 and June 1926 [16–18]. However, his most significant motor vehicle accident was on December 13, 1931, when Churchill, forgetting that he was in America looked the wrong way when crossing a road and was

struck by a car travelling 35 mph [19]. Churchill was transferred to a hospital where he was diagnosed with a concussion and contusions of the forehead requiring sutures [20]. Thus, throughout his life, Churchill had at least three or four major concussions and probably many lesser ones.

Later Years and Legacy: Despite his slow start, Churchill had a meteoric mid-life rise in British politics establishing the Royal Navy Air Service and sequentially becoming Home Secretary (1910–1911), First Lord of the Admiralty (1911–1915), Secretary of State for War (1918–1920), Secretary of State for the Colonies (1921–1923) and Chancellor of the Exchequer (1924–1929). Then at age 65 (when most people retire), Churchill became prime minister, wielding bold, implacable leadership in the face of overwhelming odds and emerging as a freedom fighter who prevented Britain from being invaded, thereby helping to save Western liberal democracy. His successes continued post-war. In 1953 he was awarded The Nobel Prize in Literature “for his brilliant oratory in defending exalted human values”.

Winston Churchill’s legacy is as Britain’s most famous Prime Minister. Despite his unpredictable and enigmatic personality, he was an eloquent orator and an outstanding leader enthused with ambition and the courage to win at all costs. It is reported that in the late 1950s, an American schoolgirl posted a letter addressed simply to “The Greatest Man in the World”—the U.S. Postal Service forwarded it to the Royal Mail which delivered it to Churchill’s home address [21].

Discussion

Two leaders of Britain during troubled times, two men with surprisingly similar multi-concussion histories, two people with diametrically different life trajectories: Henry VIII and Winston Churchill bookend the spectrum of inter-individual variability in the manifestations of human response to injury or disease. Henry VIII’s autocratic monarchy descended into a reign dominated by his selfish, suspicious and savage character. Winston Churchill on the other hand ascended as a victorious wartime leader whose strength of character was central in defending Europe’s liberal democracy against autocratic fascism.

Henry VIII’s failings as a leader were mirrored by his own physical failings. Over the centuries, many attempts have been made to ascribe Henry’s decline into debauchery to a range of medical conditions, including syphilis, malaria, Cushing’s disease and a variety of other maladies [22, 23]. However, chronic traumatic encephalopathy (CTE) emerges as the most viable contender [4, 24]. The memory problems, depression, headaches, insomnia, obesity, grandiosity, unpredictability, emotional dysregulation, sociopathy, are all possible consequence of CTE secondary to repetitive head trauma [24]. And its impact may have been compounded by his other

multiple problems, particularly his chronically inflamed and infected leg ulcerations [25].

Like Henry VIII, Winston Churchill had multiple concussions and multiple health issues. Churchill had obesity, insomnia, grandiosity, emotionality, unpredictability, but never in a manner that were an impediment to success. Although much has been written about Churchill’s depression [26], others dispute this maintaining that Churchill’s referral to the Black Dog is over-interpreted and overstated [27]; also disputed is Churchill’s drinking history [28]. Churchill had multiple medical problems including bouts of pneumonia, appendicitis, hypertension, a myocardial infarction, atrial fibrillation and multiple ischaemic strokes. Yet despite this, he endured the incredible stress of leading wartime Britain. There is no evidence of chronic headache, no early dementia (except in the last years of life when multiple strokes yielded some cognitive impairment), no evidence of CTE or Alzheimer’s disease. Rather than spiralling into self-destructive despair, Churchill (at age 65 years) rose magnificently to the physically and mentally draining task of leading Britain and much of the free world during humankind’s bloodiest conflict. Although Churchill is still widely revered, in recent years his, comments on race and steadfast support of imperialist views have generated controversy, adding a dark side to his otherwise lionized legacy.

Although head injuries, such as those experienced by Henry VIII and Winston Churchill, have been a documented medical problem since ancient times, the realization that traumatic brain injury can adversely affect behaviour, personality and cognition has only been recognized more recently and is an area of ongoing research. Multiple brain regions are particularly susceptible to laterally sustained physical injury; for instance, the hippocampus, amygdala and mesial temporal structures are susceptible to both glutamate-mediated excitotoxicity and physical impact forces. These neuroanatomical regions, vulnerable to neurochemical and biomechanical injury, are key players in fear conditioning, contextual memory consolidation and retrieval of emotional memories [29]. Head injuries sustained through physical trauma applied either frontally or posteriorly to the cranium can affect the orbitofrontal cortex as well as causing frontal subcortical axonal injury via a coup-contrecoup process. Recovery from such brain injuries is variable with deficits in executive function (particularly working memory) persisting often for years. The mechanism of these ongoing behavioural deficits arises from reduced connectivity in working memory-relevant neurophysiological networks, including the default mode, central executive, dorsal attention and salience networks [30]. This persistent disconnection syndrome may persist for years with recovery being highly individualized, as well exemplified by Henry VIII and Churchill.

Clearly, concussions, such as those experienced by Henry VIII and Churchill, are to be avoided—the risk of long-term

sequelae is too great. As demonstrated by Henry VIII and multiple modern-day athletes, repeated head trauma can have devastating delayed effects [31]. However, accidents happen, and not all concussions are avoidable. The person who has sustained a concussion should hold out hope that on the Tudor-Churchill spectrum they lay towards the Churchill end. Such hope is good, especially in brain disease. The implications of the Tudor-Churchill spectrum are not confined to concussions. Individual symptoms and disease manifestations vary widely across the full spectrum of human disease including depression, asthma, myocardial infarction, diabetes mellitus and infections, as recently exemplified by widely different clinical presentations for the COVID-19 viral pneumonia. Paraphrasing Sir William Osler, we should avoid sweeping generalizations and care for the individual not the disease. The Tudor-Churchill spectrum is the model of inter-individual variability and reminds us that every person is unique, deserving of individualized thought, personalized diagnosis and tailored treatment, especially within the context of chronic brain disease.

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