ELSEVIER

Alzheimer's & Dementia 3 (2007) 137–142

Alzheimer's & Dementia

Perspectives

Historical note on Darwin's consideration of early-onset dementia in older persons, thirty-six years before Alzheimer's initial case report

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Abstract In February 1871, the great naturalist Charles Darwin received a letter from Dr. James-Crichton Browne, who was serving as Director of the largest lunatic asylum in England. Darwin had been introduced to Crichton-Browne 2 years earlier by Henry Maudsley, who believed that the young psychiatrist could provide Darwin with clinical examples of extreme emotional expression, to aid him in preparing to write *Expression of the Emotions in Man and Animals* (1872). This particular letter from Crichton-Browne contained the first and only reference to "premature dotage" or "senile decay" found anywhere in Darwin's entire corpus of correspondence, which amounted to more than 80,000 pages of handwritten letters to nearly 2,000 individuals throughout his lifetime. Moreover, this letter from Crichton-Browne, received by Darwin 36 years before the first case report of senile dementia by Professor Alois Alzheimer, explicitly noted that such premature dotage is the result of "brain wasting." Crichton-Browne believed that senile dementia was the result of a central nervous system disease, with the emotional lability observed in his patients linked inextricably to the disease process. This early hypothesis, of interest to Darwin in 1871, anticipated the groundbreaking neurohistopathologic research and case description by Alzheimer 36 years later, and has been confirmed by all clinical research in this field since 1907. This concordance between psychological symptoms and Alzheimer's disease continues to be an important area of study, leading to recent advances in our understanding of the genetics, neurobiology, and neurochemistry of psychiatric illness in older adults.

Keywords: Darwin; History; Alzheimer's disease; Senility; Dementia

1. Historical note

Charles Robert Darwin (1809–1882), the great English naturalist and father of evolutionary theory, the cornerstone of modern biology and the key framework by which we place advances in genetics and molecular biomedicine into context, remains arguably one of the most creative, meticulous, productive, and brilliant of scientists to advance human understanding within the past 200 years [1]. From his first published monograph, *The Voyage of the Beagle* (1839), to his last major work, *The Formation of Vegetable Mould Through the Action of Worms* (1881), Darwin published 22 major books on an unparalleled number of topics. In addition to his well-known seminal discoveries presented in *On the Origin of Species by Means of Natural Selection, or the Preservation of Races in the Struggle for Life* (1859), and in *The Descent of Man and Selection in Relation to Sex* (1871), Darwin published groundbreaking, painstakingly accurate, profusely documented works on topics including (but not limited to) the structure and distribution of coral reefs, the geology of volcanic islands, the fertilization of orchids by insects, and the evolutionary basis for emotional expression in mammals. This latter topic resulted in one of his more important monographs, published in 1872, *The Expression of the Emotions in Man and Animals* [2,3].

In accumulating the research evidence to prepare his book on the expression of emotion, Darwin corresponded

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1552-5260/07/$ – see front matter
doi:10.1016/j.jalz.2007.04.392

with dozens of academic scientists, medical practitioners, philosophers, clergy, and missionaries throughout the world. This rich correspondence allowed him to amass the evidence he needed to support his theories that emotional expression is largely an innate capacity that is similarly produced and interpreted cross-culturally, that is not dissimilar from what is observed mechanistically across the primate line, and that shares common features with a variety of other species throughout the class of mammals. Darwin sent inquiries, and received responses from his correspondents, with the aim of exploring the human expression of emotion from a developmental perspective across the entire lifespan. He had a special interest in the examination of emotional expression in patients who were committed to lunatic asylums, as he firmly believed that "the insane ought to be studied, as they are liable to the strongest passions, and give uncontrolled vent to them" (*The Expression of the Emotions in Man and Animals*, p. 20) [2]. As a result of his correspondence with the superintendent of one such institution, we know that Darwin was able to consider case reports and photographs of patients with major depression (melancholia), various psychoses (lunacy), epilepsy, hemiplegia (most likely secondary to focal cerebrovascular hemorrhages), and, one might assume, various forms of dementia. Hence, it is possible that Darwin made some direct statements that reveal his thoughts on dementia, or that he considered medical information pertaining to this subject that was made available to him in the preparation of his 1872 publication.

We searched for any indication that Darwin had either commented on, or considered, dementia in the elderly in *any* of his personal correspondence during his lifetime. During his fascinating life, Darwin corresponded with nearly 2,000 individuals, amounting to more than 14,500 surviving letters and over 80,000 pages of handwritten text. The Darwin Correspondence Project database was searched using the keywords "dementia," "senile," and "senility." The database contains transcriptions of all known letters exchanged by Darwin and his correspondents from the years 1822–1882, drawn from about 200 repositories around the world. However, it does not include comprehensive transcriptions of marginal notes made by Darwin on photographs and drawings.

No use of the word "dementia" was found throughout this corpus of transcribed letters. Several instances of the word "senility" were found, and all of these pertained to the occasional description of the aging and changing physical characteristics of ammonites, nautili, crustaceans, and various mammals and birds [4,5]. However, in response to a letter received by Alpheus Hyatt in November 1872 [4], Darwin provides some indication of his views of the physical concomitants of aging in humans, stating:

> A man in extreme old age differs much from a young man, & I presume every one would account for this by failing powers of growth. On the other hand the skulls of some mammals go on altering during maturity with advancing years—as do the horns of stags, the tail-feathers of some birds, the size of fishes &c; & all such differences I should attribute simply to the laws of growth, as long as full vigour was retained [6].

Apart from this comment on graceful aging, from a man who by 1872 was growing older himself, what did Charles Darwin have to say, in his entire corpus of collected correspondence, regarding the risk or behavioral correlates of early-onset dementia in older persons? The answer is quite simple: *very little*. There is a hint from Darwin's earlier writings (from one of his famous notebooks, rather than from his personal correspondence) to suggest that he had noticed a relationship between senility and emotional dysfunction [7]. In that notebook from 1838, Darwin wrote that "In Aunt B. the affections seem to have failed even more than the memory."[1] Although there is no other mention of the word "senile" in any of his correspondence during his younger and middle-aged years (through 1870), 33 years later, that early supposition that Darwin recorded in the M Notebook would be confirmed in a single letter sent by one of his many important correspondents, Dr. James Crichton-Browne [8] (see Appendix). Darwin had voiced his interest in collecting clinical data on the expression of emotions in humans with various illnesses, in preparation for his treatise on the subject, published in 1872. To this end, Darwin was introduced by Henry Maudsley to James Crichton-Browne (1840–1937) in spring 1869, when Crichton-Browne was 29 years old, the young Director of a large lunatic asylum and still in the early stages of his own illustrious career.

Crichton-Browne graduated from medical school in Edinburgh in 1862, and after several years working as an attending psychiatrist at various asylums, he was appointed in 1866, at the young age of 26, the Superintendent Medical Director of the West Riding Pauper Lunatic Asylum at Wakefield. Crichton-Browne held this important post for 9 years, and during this time he established the first pathology laboratory at a psychiatric institution. He attracted such notable figures to conduct research at the Asylum as David Ferrier and John Hughlings-Jackson [9,10]. Crichton-Browne was a leading psychiatrist and public speaker, and even a popular radio broadcaster, of his day; he used his influence to improve sanitation, lighting, and other basic health conditions for institutionalized patients in England [9,11]. In 1876, Crichton-Browne left the West Riding Asylum to take the prestigious position of Lord Chancellor's Visitor in Lunacy, edging out Henry Maudsley for the position, and he held this post for 46 years. Crichton-Browne's career is notable for many exceptional accomplishments, including the co-founding of the still top-tier

[1] Darwin's Aunt B. was Elizabeth Allen, who became his mother-in-law soon after this notebook was written. She was the wife of Josiah Wedgwood II, and Emma Darwin's mother. Charles married Emma Wedgwood in January 1839. However, because Josiah was also Charles's maternal uncle, Elizabeth Allen was also his aunt.

journal, *Brain*, with Ferrier, Hughlings-Jackson, and the director of another asylum, Sir John Bucknill [11].

As the young and very busy director of a large asylum, Crichton-Browne was introduced by Henry Maudsley to Charles Darwin. Darwin was eager to assemble clinical case-report data from patients with insanity, in his belief that mental illness provided a natural laboratory for the observation of raw, unbridled emotion. Believing that Crichton-Browne could assist in this regard, Maudsley encouraged the two to collaborate, and in spring 1869, Darwin and Crichton-Browne began an intense correspondence that amounted to over 40 letters exchanged between June 1869 and December 1875, i.e., 3 years after the publication of *Expression*. This exchange of ideas and clinical vignettes with Crichton-Browne is well-represented throughout Darwin's seminal book, and Darwin showed his gratitude by nominating Crichton-Browne for election to the Royal Society in 1883. Three years later, Crichton-Browne was knighted by Queen Victoria.

Crichton-Browne described a large number of patients, diagnoses, and observations on the expression of emotion to Darwin, and also sent Darwin many photographs, as Crichton-Browne had made portraits of his interesting patients at a photographic studio maintained at the asylum. One of his early letters to Darwin, dated February 16, 1871, appeared to be of particular interest, because Darwin referred to the contents of this particular letter several times in his "Introduction" to *Expression*. It is in this very letter, the transcription of which is provided in the Appendix, that we find Crichton-Browne's mention of a condition that many of his patients suffered from, that of "brain-wasting . . . or who are passing into premature dotage and senile decay." This portion of the letter to Darwin, with the relevant words underlined in red pencil by Darwin, is reproduced in Fig. 1. Crichton-Browne made mention of this condition because he believed that such patients were emotionally labile, such that "An ordinary greeting or simple question produces quivering of the features and a flow of tears" (see Appendix for complete transcript).

As shown in Fig. 1, Darwin used red pencil (which he often used) to underline the words "brain-wasting" and "senile decay." Two lines below, he also underlined "commonly weeping," indicating his interest in the relationship between such "premature dotage" and emotional lability. As noted above, we know that Darwin paid very close attention to the contents of this specific letter, insofar as he made reference to its contents, and more generally to Crichton-Browne's contributions to his research on the topic of the monograph, several times in writing his "Introduction" to *Expression* (pp. 1261–1275) [3]. In addition, this passage by Crichton-Browne (Fig. 1) was referred to directly in *Expression* (p. 1349), where Darwin noted that "for certain brain-diseases, as hemiplegia, brain-wasting, and senile decay, have a special tendency to induce weeping" [3].

Although we are uncertain whether Crichton-Browne was the first physician to draw a direct connection between

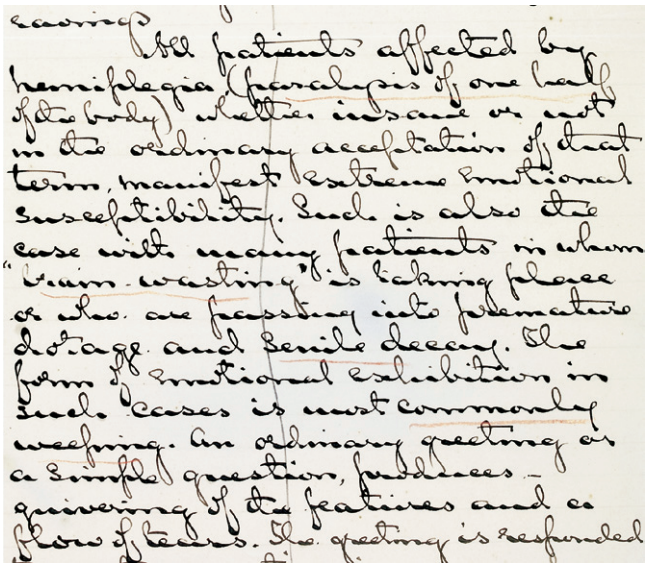

Fig. 1. Portion of page 2 of a letter from James Crichton-Browne to Charles Darwin, dated 16 February, 1871 (Cambridge University Library DAR 161:312; see Appendix for full transcription). In this portion of the letter, Crichton-Browne states: "All patients affected by hemiplegia (paralysis of one half of the body) whether insane or not in the ordinary acceptation of that term, manifest extreme emotional susceptibility. Such is also the case with many patients in whom 'brain-wasting' is taking place or who are passing into premature dotage and senile decay. The form of emotional exhibition in such cases is most commonly weeping. An ordinary greeting or a simple question, produces—quivering of the features and a flow of tears . . ." This photograph is reprinted with the permission of the Syndics of Cambridge University Library, Cambridge, England.

"premature dotage," "brain-wasting," "senile decay," and the emotional lability that may accompany such pathological aging, we are certain that he was a pioneer of his day in searching for the neurobiological substrates of conditions such as dementia (which, in the 19th century, was still being lumped together with "lunacy"), melancholia, and other psychiatric diseases. Older persons with dementia were quite often warehoused in asylums such as the one that Crichton-Browne directed, and in his letter, he stressed these two facts to the famed naturalist: 1) premature dotage is the result of a neuropathologic process ("brain-wasting"), and 2) this illness leads to increased emotional lability. This letter was received and considered by Darwin 36 years before Alzheimer characterized the core neuropathology of the disease (including the observation of neurofibrillary tangles using silver-impregnation staining) with light microscopy of postmortem tissue [12].

In his seminal case description of Auguste D., Alzheimer eloquently described the extreme emotional volatility that he observed in his famous patient [13], which included bouts of severe agitation, weeping, restlessness, panic, and terror [14]. Of course, the senile decay and dementia described by Alzheimer existed long before his initial case report, but what made this particular case so striking to Alzheimer was that his patient suffered the onset of dementia at the relatively young age of 51

years [14]. This unusual presentation drew Alzheimer's attention, resulting in his painstaking case description and postmortem histopathological analyses.

2. Discussion

Why did Crichton-Browne so confidently draw a correlation between "premature dotage" and emotional lability, and why did he mention this specific clinical condition to Darwin in his letter? He offered his observation that "many patients in whom brain-wasting is taking place" also "manifest extreme emotional susceptibility . . . and most commonly weeping," in an effort to provide the famed naturalist with added opportunities to observe and record extreme presentations of emotion. The fact that Crichton-Browne made this association is far from surprising, and in fact, we often rely on such behavioral observations in our current clinical practice to aid in our differential diagnosis for Alzheimer's disease. In fact, late-onset depression is quite often found in association with Alzheimer's disease at autopsy, and patients with greater lifetime episodes of depression appear to show greater hippocampal pathology on postmortem examination [15]. Moreover, both late-onset depression and Alzheimer's disease may result from common etiological substrates (e.g., vascular disease, or elevated homocysteine levels) [15–19]. Monoamine changes are frequently found in Alzheimer's patients, and such neurochemical disruption likely plays a central role in the expression of depressive symptomatology [15,18]. Symptoms of depression early in the course of disease may result from underlying comorbid etiological substrates [20], or from awareness of deficits, grief, and a pervasive sense of loss. In contrast, more severe psychiatric illness may often be observed in later stages of Alzheimer's disease (Braak and Braak stages V and VI) [21], because the core neuropathology affects tertiary association and frontal neocortices, along with the cortical-subcortical circuitry involving limbic structures [22,23].

Emotional lability is widely viewed as a common "soft sign" of Alzheimer's disease, and there is a well-established link between depression, as well as other psychological and neuropsychiatric syndromes (e.g., psychosis, or sleep disorders), and Alzheimer's disease [15]. In the earliest stages of the disease, one of the first symptoms to become evident for many patients is the onset of depression [24]. In fact, it was recently argued that although the prevailing clinical definitions of mild cognitive impairment exclude the presence of depression, it may be the case that those patients with persisting depressive symptoms are also at higher risk of progressing from mild cognitive impairment to Alzheimer's disease [25,26]. In his research on emotional expression in man and animals, Darwin was made aware of this linkage between emotional lability and dementia by one of the most progressive psychiatrists of his day, Sir James Crichton-Browne. In turn, Darwin's red-pencil marks, and his direct quote of Crichton-Browne's comments on this topic in *Expression*, provide evidence that he had considered and reflected on this link between "early dotage," "brain-wasting," and emotional lability in older persons, at least 36 years before Alzheimer's momentous work in Germany that culminated in the 1907 publication of his famous case report.

Acknowledgments

We express our sincere gratitude to Mr. Adam J. Perkins, Curator of Scientific Manuscripts, and to Mr. Godfrey Waller, Superintendent of the Manuscripts Reading Room, both at Cambridge University Library, for their very gracious and skilled assistance. We also thank the editors of the Darwin Correspondence Project for the use of their electronic resources and for valuable discussion, especially Dr. Paul White. We are also endebted to Randal Keynes for sharing his extensive knowledge of Darwin's family history. P.J.S. dedicates this article to his stepfather, Dr. Edward L. Etkind, for his unfailing support, wisdom, and encouragement. This article is also dedicated to the memory of Dr. Leon Thal, a passionate and brilliant leader in the global effort to discover a cure for Alzheimer's disease. Dr. Thal was a mentor and guide for so many of us, and he will be sorely missed.

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Appendix

Correspondence received by Charles Darwin, from Dr. James Crichton-Browne, Director of the West Riding Asylum (Wakefield, Yorkshire County, England), February 16, 1871. Transcript courtesy of the Darwin Correspondence Project. Transcription checked for accuracy against the original document by both authors.

West Riding Asylum, Wakefield

Feb 16th 1871.

My dear Sir,

I was greatly pleased to receive your letter of the 8th Inst. and to know that I have been of some little service to you in the important researches in which you have been engaged. It is no mere form of courtesy when I say that I value your approbation more than that of any one else now living. I have often been ashamed of the insignificance of the help which I have been able to afford you—and of the inadequacy of my answers to your searching questions. The fact is however that the duties of my position leave me very little time for congenial studies. The exigencies of the public service have already ruined my health & curtailed my capacities. They now threaten to shorten my life.

Pardon so much personal detail and accept my warm thanks for the promise of a copy of your new book which will be a genuine solace to me in this house of bondage. Along with this I send you hurried and disconnected answers to your questions. I have written them on foolscap as they were too long to embody in a letter. Let me know if they meet your wishes? I can furnish you with cases in illustration of every point. I trust to send you some interesting photographs in about a fortnight.

Do not hesitate to ask me any questions connected with my own specialty which require elucidation. It is a sincere pleasure & relief to me to work in your vein. Are you interested in morbid pigmentation. I have made what I consider some very curious observations on bronzing of the skin of Europeans in Addisons disease which are quite at your service if they bear upon your present investigations.

Maudsley writes excellently and brilliantly. What he requires is more extensive observations. Would you like to have a photograph of the ears of a late patient of mine which were covered, not with down, but with long strong bristles, or of the breast of a woman with two distinct milk-giving nipples?

With profound respect
Believe me
Yours most faithfully
J. Crichton Browne

Charles Darwin Esq

Enclosure to cover letter from Crichton-Browne:

1. Nothing is more characteristic of simple melancholia than a tendency to weep on the slightest occasion or on no occasion, and to weep disproportionately on the occurrence of any real cause of grief. One of the most frequent entries in our Case Books with reference to this class of patients is "Intensely emotional, cries when spoken to." I could any day point out to you in this Asylum a number of melancholics, who sit rocking themselves rhythmically backwards and forwards and who whenever you address them, stop this motion, purse up their eyes, pull down the corners of their lips more determinately and shed tears. The readiness and copiousness of the lachrymal secretion under such circumstances is sometimes remarkable. To illustrate the reasons given by melancholics for excessive manifestations of sorrow I may mention the case of a girl lately under my care—who wept a whole day and then confessed to me that

she was crying because she remembered she had once shaved off her eyebrows to promote their growth. My observations lead me to believe, that the ideas connected with emotional displays such as I have been describing in melancholics, are generally egotistic. Any remark connected with their own state, or anticipations, "a kind word" or an admonition is especially apt to plunge them into an unrestrained outburst of feeling. I believe I have read of some distinguished men (Poets?) who were very prone to tears—and I believe I have noted that in them it was the sentiment of *pity* that excited the weeping.

Acute maniacs have paroxysms of violent weeping "blubbering" in the midst of their ravings.

All patients affected by hemiplegia (paralysis of one half of the body) whether insane or not in the ordinary acceptation of that term, manifest extreme emotional susceptibility. Such is also the case with many patients in whom "brain-wasting" is taking place or who are passing into premature dotage and senile decay. The form of emotional exhibition in such cases is most commonly weeping. An ordinary greeting or a simple question, produces—quivering of the features and a flow of tears. The greeting is responded to, or the question is answered, directly enough in the midst of this exhibition of grief—and then perhaps, some painful notion suggests itself. It has seemed to me under such circumstances that the effort at expression was misdirected or too widely diffused that the consequent signs of grief suggested some painful impression, and that this was then referred to, as an explanation of the display of feeling. In many cases however this theory will not hold good, as no sorrowful or distressing idea comes up at all and the incongruity of the weeping seems never to be recognised. I have watched many cases in which the emotional manifestation continued into a state of complete fatuity, in which the power of speech had been altogether lost. Looking at the patient or addressing them would still induce movements of the features and an effusion of tears.

If desirable I can send quotations from standard authorities corroborating the proneness of hemiplegic patients to emotional manifestations. The fact is indeed well recognised by the whole medical profession.

2. There are undoubtedly many idiots and lunatics who laugh inordinately and without occasion[.] In my specialty we have a term Euphoria—insane joyousness—which is meant to designate the condition in which this occurs. Only yesterday (Feby 15) an idiot boy who cannot speak, described to me very graphically by signs, amidst explosions of laughter and with his face c[o]vered with the broadest smil[e]s how anoth[er] inmate of the Asylum had [given] him a black eye. [two and a half lines destroyed] amongst idiots an[d] [some text destroyed] are of course many [some text destroyed] give evidence of no emotion or [some text destroyed] who do not rise above reflex acts—, who are stolid or simpl[y] restless. There are others who constantl[y] moan & cry and evince painful mental states. There are others who are only destructive and passionate. But above these in the highest class of idiots and in imbeciles, the pleasurable emotions are I believe the most general. There are many idiots and imbeciles, who are constantly smiling and laughing, who are "pleas[ed] with a rattle, tickled by a straw [.]" I shall endeavour to procure and forward photographs of some of these '"good tempered idiots" as we call them who are now under my care. In some of them the expression of the face is a stereotyped smile. They are persistently joyous & benign[.] No ideas can possibly be connected with such an emotional state. Such creatures have [no] [se]nse of the ludicrous. They laugh [some text destroyed] because "it is their natu[re] [some text destroyed] They [some text destroyed] chuckle or [some text destroyed] a[some text destroyed] [some text destroyed] food as ple[as]ed [some text destroyed] they are stroked or patted [or] caressed, when bright colou[rs] are presented to them [some text destroyed] when they hear music. Some of them laug[h] more than usual when they walk or attempt any muscular exertion[.] In imbeciles and the weak minded where joyousness & laughter become connected with ideas, those appertaining to personal vanity are first found to be operative. Next come those associated with the approbation of others and the love of display.

Amongst *lunatics* as distinguished from idiots the placid or tremulous smile of the general paralytic is of course well known. In woman labouring under erotomania, nymphomania, or any disorder of the sexual propensities, I have observed that *hilarity* is predominant[.] I can supply a photograph very characteristic of the combination of mirthfulness and lu[st]. In certain chronic maniacs cachma[some text destroyed] are frequent, as [some text destroyed] acute maniacs. In these [some text destroyed] however pretend to [some text destroyed] in any psycholo[some text destroyed] who [some text destroyed].

3. In those lunatics in whom brisling of the hair is extreme, the disease is generally permanent or mortal. I have however seen cases in which there was a moderate degree of bristling & in which restoration of health and of the ordinary smoothness of the hair subsequently took place.

4. Large photographs of the insane are not to be purchased anywhere[.] I shall do my best to supply the desiderata.

J. Crichton Browne M.D. F.R.[S.] ¦ Wakefield