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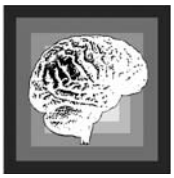

A brief review of the history of delirium as a mental disorder

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We review the most important concepts about delirium, from ancient times until the twentieth century. We also focus on the question of how these concepts have dealt with the particular problems posed by prognosis and outcome. Althought different terms have been used, a robust description of delirium has existed since antiquity – at some times as a symptom and at others as a syndrome. It is clear that, throughout the millennia, delirium has been – and still is – a highly lethal syndrome; a poor mental outcome for survivors was often noted. Not until the twentieth century was it thought that delirium was marked by a full recovery among survivors, and this was probably due to the desire for a clear distinction from dementia.

***Keywords**: delirium; historical concepts; history; outcome; prognosis*

Introduction

Despite the 'three millennia of delirium research' (Francis, 1995, 1999), delirium remains hard to define and difficult to study. Delirium is usually assumed to be an acute, fluctuating, transient and reversible condition caused by physical illness. Once the acute episode has remitted, the premorbid level of functioning is reached again, with personality reappearing intact. But

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experience and research shows that this is not always the case; delirium is often irreversible especially in the elderly and those with pre-existing dementia. While the two international classifications (ICD, DSM) can increase the concurred validity of a diagnosis between the professionals and facilitate the communication between them, both systems have been criticized regarding the definition of delirium. ICD and DSM define delirium as a disorder (even when the aetiology is known) but then characterize delirium as a syndrome (Lindesay, Macdonald and Starke, 1990). As the two systems do not define delirium according to outcome, it has been argued that (at least in survivors) delirium should be defined according to cognitive reversibility (Treloar and Macdonald, 1997*a*, 1997*b*).

This paper will review the most important of these concepts about delirium, from ancient times until the appearance of the two classification systems. Special attention will be paid to the question of how those concepts have dealt with the particular problems posed by prognosis and outcome.

Specifically, we will discuss how definitions of delirium have striven to:

(a) accommodate delirium within the current nosological system;
(b) assign diagnostic criteria that distinguish it from other mental disorders;
(c) classify it according to aetiologies;
(d) clarify the prognosis from the clinical manifestations.

We will review the recent literature; papers were selected after searching electronic databases (MEDLINE, EMBASE, IBSS), but mostly after manual searching of the references of previous papers and reviews. Throughout this review we will use the term 'Delirium' when the actual word was used, and 'delirium' when applying the modern equivalent.

The concept of delirium throughout the centuries

Ancient and medieval times

The word Delirium was first used in medical writing by Celsus in the first century AD (2.8; 3.16) to describe (either as a symptom or as a syndrome) mental disorders during fever or head trauma (Celsus 2.7). Additionally Celsus used the term phrenitis as an alternative to Delirium. Phrenitis had previously been introduced by Hippocrates in 500 BC (*Prognostikon* 4, in Lipourlis, 1983) to describe mental abnormalities caused by fever, poisoning or head trauma. It has been suggested that the current nomenclature about delirium is confusing because of the different names used to define and describe it (Lindesay *et al.*, 1990; Lipowski, 1990), and that the clinical meaning of the syndrome remained consistent through the centuries until the nineteenth century (Berrios, 1981; Lipowski, 1990), but it is worth noting that Hippocrates used about sixteen different words to refer to and name the

clinical syndrome which we now call delirium (Lipourlis, 1983), such as *ληρος* (leros), *μανια* (mania), *παραφροσυνη* (paraphrosyne), *παραληρος* (paraleros), *φρενιτις* (phrenitis), *ληθαργος* (lethargus), etc. It is difficult to find the exact meaning of these terms, e.g., the term *παραφροσυνη* (paraphrosyne) can be used as a meaning of madness but can also mean a decline in or a loss of consciousness. An apparent uniformity of nomenclature during antiquity may thus be due to the translation of many distinct words as 'Delirium' in English (Caraceni and Grassi, 2003).

The word delirium derives from the Latin *deliro-delirare* (*de-lira*, to go out of the furrow) – hence, to deviate from a straight line, to be crazy, deranged, out of one's wits, to be silly, to dote, to rave (Lewis, Short and Andrews, 1879). A second suggestion about the etymology of the word (cited in Schuurmans, Duursma and Shortridge-Baggett, 2001) is that it came from the Greek word *ληρος* (leros) which means silly talk, nonsense. Althought both words have a similar meaning (and phonetics), it is unlikely that delirium is derived from the Greek for two reasons. First, the etymological root of *ληρος* is possibly from the archaic '*la' (I shout), from which the Latin word *lamentum* (lament) also derives, and second, it is very rare – or even unknown – for the Greek letter 'η' to transform to the Latin 'i' and vice versa (Babiniotis, 1985).

Hippocrates (in Lipourlis, 1983) used the term phrenitis to describe an acute onset of behavioural problems, sleep disturbances and cognitive deficits which were usually associated with fever, while he used the term lethargus to describe inertia and dulling of the senses. He believed that lethargus can change to phrenitis and vice versa. According to Hippocrates gnashing during fever (for those who did not have this before illness) was a sign of the development of delirium and death. If delirium coexisted with gnashing, the death was almost certain (Prognostikon 3). Hippocrates identified another rather peculiar prognostic sign: older people with pain in the ear during fever were less prone to develop Delirium (Prognostikon 4), but we need to remember that only 10% of people lived more than 60 years at that time (Minois, 1989).

Celsus was probably the first to report occasional non-febrile causes: '*Raro sed aliquando tamex ex metu delirium nascitunatura*… (Rarely, but now and then, however, Delirium is the product of fright …)' (Celsus 3.18), but he suggested the same remedies as in other types of Delirium, except that for non-febrile Delirium wine could also be given. Celsus (3.18) said that not all deliria were reversible but in some cases, although the causes disappeared, patients continued to be insane (he used the word 'dementia' probably to mean insanity). However Soranus insisted that Delirium could never occur without fever and that insanity often started with it (Lipowski, 1990).

During the medieval period a remarkably accurate description of Delirium was given by the historian Procopius (*History of the Wars*, II.xxii–xxxiii) who described an epidemic of a possible bubonic disease in Constantinople in AD 542 (cited in Bury, 1958). He described hallucinations occasionally

preceding the disease. Some victims became violent with insomnia, excitement, shouting, rushing off in flight (perhaps resembling the modern concept of hyperactive delirium), while others drifted into coma, forgetting all those familiar to them, and seeming to sleep constantly, and they could die from lack of food or water if nobody cared for them (perhaps resembling hypoactive delirium). Procopius assumed that those who developed Delirium of either form were the lucky ones because, he believed, delirious people do not feel pain. Many medical authorities of medieval times such as Oribasious of Pergamon, Alexander of Tralles (Trallianos) and Paulus of Aegina (Aeginitis) reviewed and interpreted previous works by Hippocrates, Celsus, Galen, Sonarus and other medical predecessors.

In the mid-eighth century an Arab physician, Najab ub din Unhammad, listed nine classes of psychopathology, including the *Souda a Tabee* (febrile Delirium), according to Graham (1967). The *Souda a Tabee* was subdivided into *Souda* where patients showed impairment of memory, loss of contact with the environment and childish behaviour; but when *Souda* reached a chronic state, it became *Jannon* (agitated reaction) characterized by insomnia, restlessness and, at times, beast-like roars (Graham, 1967). Rhazes, a famous Persian physician, was in favour of a unified concept of delirium and described a condition named '*sirsen*' which corresponded to both lethargus and phrenitis and was due to fever or to excessive wine (Lipowski, 1990: 9).

The encyclopaedia of Bartholomeus Anglicus which was translated into English in 1495 had chapters on mental illness, reviewing all previous works. He introduced the word 'paraphrenesis' to distinguish Delirium caused by febrile illness (with a better prognosis) from Delirium 'phrenesis' caused by disease of the brain and its membranes, with a poorer prognosis (Bartholomeus Anglicus, *De proprietatibus*, 1535, quoted in Hunter and Macalpine, 1963: 1–4).

Throughout ancient and medieval times good descriptions of what we now call delirium existed, but with many different names. The principle subtypes of Delirium were described either as separate illnesses or as different forms of the same illness. Controversy existed about the outcome of Delirium, but general agreement was reached. With a few exceptions it was caused by febrile illnesses, and delirium was a grave clinical situation.

Sixteenth to eighteenth centuries

During the sixteenth century more writings appeared on phrenitis and Delirium. 'Paraphrenesis' reappeared as a term to distinguish delirium caused by fever, but it was also used by Guainerio to describe a pre-delirious phase (Lipowski, 1990: 10).

In the English medical literature the word 'delirium' was probably first used by Cosin (1592) in his book *Conspiracie for Pretended Reformation: viz. Presbyteriall Discipline*. This book was one of the earliest to put forward the defence of insanity. Delirium was defined as a 'weakenes of conceite and

consideration' and Lethargie as a 'notable forgetfulness of all things almost that heretofore an man hath knowen or of their names' (Cosin, 1592; quoted in Hunter and Macalpine, 1963: 44). Earlier, in 1547, Andrew Boorde distinguished delirium from fever, 'phrenyse' (phrenesis) from that toxic state caused from the use of hyoscyamus 'frantickenes' (Hunter and Macalpine, 1963: 13–15). The poor prognosis of delirium was recounted by Philip Barrought in 1593, who described 'phrenesis' as a 'continual madness' joined with acute fever and said that it was an incurable and deadly condition in most cases, and if it resolved it may be followed by a loss of memory and reasoning (see Lindesay, 1999; Lipowski, 1990: 11). One important contribution in the sixteenth century was the work of Ambroise Pare, a surgeon who wrote about delirium as a complication of surgical procedures. He described delirium as a transient condition that commonly followed fever and pain due to wounds, gangrene, and operations involving severe bleeding of the patient (see Lipowski, 1990: 11–12).

An interesting contribution to the concept of delirium was made by Thomas Willis. He explained delirium pathogenesis with his theory of animal spirits, departing from the traditional humoral theory. He accepted the theory current at the time that delirium and 'frenzy' (phrenesis) differed only in duration of their mental disturbance but he believed that delirium could also occur in conditions which were not accompanied by fever-like drunkenness or hysteria. He did not accept the idea that an inflammation of the diaphragm can cause 'paraphrenesis' (he had seen an autopsy of an abscess involving the diaphragm but the patient had not had delirium or paraphrenesis during life). He also stated that the prognosis of delirium depended on the nature of the febrile illness, the patient's age and previous health, and that while delirium may be resolved after the fever settled down, cases of protracted delirium might lead to 'a state of perpetual raving (madness), to melancholy, or to a state of foolishness and stupidity' (Eadie, 2003: 153). Another influential work in the seventeenth century was that of Richard Morton who suggested that delirium represents a waking dream – a theory which influenced developments in the next century (see Lipowski, 1990: 12).

By the beginning of the eighteenth century most medical writings distinguished Delirium on the one hand from phrensy or phrenesis on the other. The former was by then a general term for short-term madness or raving and the latter for a state caused mainly by fever or other physical illnesses. Phrensy or phrenesis was further divided into phrenesis and paraphrenesis. The former was associated with supposed brain inflammation, the latter with inflammation of other organs. However, paraphrenesis was also used to describe the prodromal stage of delirium. It was well recognized that delirium, although transient in most cases, was a serious clinical condition with bad prognosis, and that in some cases, despite the cessation of fever, mental dysfunction could continue and could be permanent. Further, a shift from the humoral explanation of delirium towards to a more 'chemical'

hypothesis – the inflammation of the 'animal spirits'– was taking place. Finally, parallels with dream states were emerging. These shifts in the meaning and notions of aetiology of delirium are reflected in two English medical dictionaries published at the beginning and in the middle of the eighteenth century. Quincy (1719) stated that mania or madness 'is a Delirium without fever' and that 'Delirium is the Dreams of waking Persons', while James (1745) stressed the relationship between Delirium and the disturbances of the sleeping-waking cycle (see Lipowski, 1990: 13; 1991).

In 1746 a treatise on delirium by Frings appeared which according to Lipowski (1990: 13–15; 1991) was the first one in English. There is controversy about this book: Frings claimed that he translated it from a Latin text and that he was for 'Some Time Physician to Don Francisco, Late Infant of Portugal'. Hunter and Macalpine (1963: 371–2) suggested that the name Frings was a pseudonym as nothing is otherwise known about the author, the Don Francisco of Portugal nor the Latin text. Whoever he (or she) was, Frings took against the 'Galenists' who used bleeding as a treatment for delirium despite the book being dedicated to Dr James Monro of Bethlem hospital, where bleeding was the usual practice. Frings used the term Deliriums to refer to mental disorder generally and included states with, without or after fever. He followed the current classification of 'phrensy' (phrenesis) and 'paraphrensy' (paraphrenesis) and he divided Deliriums in fever into two types, according to clinical manifestations: the 'ridiculous' when the patient was happy and cheerful, and the 'serious' when the patient was angry. He said that the latter had a bad prognosis (Lipowski, 1990: 13–15).

David Hartley in 1749 described hypnogogic and hypnopompic phenomena and visual hallucinations in delirium, and in 1794 Erasmus Darwin introduced disorientation and alteration of consciousness to distinguish delirium from 'madness' (see Hunter and Macalpine, 1963: 379–82, 547–51). He also named the febrile delirium with the Hippocratian word 'Paraphrosyne'.

Nineteenth century

In the nineteenth century the terms which described delirium developed even greater ambiguity. According to Berrios (1981) and Berrios and Porter (1995), this was partly for linguistic reasons especially in France where '*delire*' was used to refer both to specific errors of judgement (delusions) and to phrenesis. Thus there was a need for a term for organic delirium, so the term '*confusion mentale*' was introduced. Although Berrios has suggested that this did not influence British psychiatry, it has parallels with Darwin's views at the end of the previous century, who used the term Delirium to describe what would today be regarded a somatic hallucination.

> As when a patient is persuaded he has the itch, or venereal disease, of which he has no symptom and becomes mad from the pain this idea

> occasions. So that the object of madness is generally a delirious idea, and thence cannot be conquered by reason; because it continues to be excited by painful sensation, which is a stronger stimulus than volition. (Darwin, 1796; quoted in Hunter and Macalpine, 1963: 548)

The term 'confusion' as a synonym for delirium is in widespread use in all countries to this day.

During the nineteenth century, old terms such as phrenitis, phrensy, phrenesis, lethargy and paraphrensy or paraphrenesis gradually disappeared from medical language, and discussion turned mainly towards the psychopathology of delirium and its relations with dreams, and to disturbances of consciousness as a core feature of delirium.

At the beginning of the nineteenth century Sutton (1813) proposed the term Delirium tremens (because of the marked tremor of the hands) caused by excessive drinking or as a result of sensitivity to alcohol in certain people, and distinguished it from phrenesis. Greiner (1817) is credited with introducing the concept of the clouding of consciousness as the main feature of delirium. He believed that fever caused disturbances in the organ of consciousness in the brain, and that delirium's course, severity and clinical picture depended on the duration and degree of fever, as well on the patients' previous experiences and habits. He held that as fever fluctuates so does consciousness, and the patient may have lucid periods. He also believed that there was a close relation between dreams and delirium and that delirium represented a dream during the waking state. The association between delirium and clouding of consciousness was further explored by Hughlings Jackson in the 1860s (Hogan and Kaiboriboon, 2003; Lipowski, 1990: 23–5; 1991). In 1870 Hood reported cases of 'senile Delirium' and he stated that this was potentially reversible but could be fatal if not treated (see Lipowski, 1985: 290).

Berrios (1981) has suggested that during the second half of the nineteenth century the clouding of consciousness became the primary clinical criterion separating delirium from the rest of the insanities, but as late as 1879 von Krafft-Ebing stated that clouding of consciousness could exist in other mental disorders such as twilight states, stupor and ecstasy, while Kraepelin in 1915 wrote that clouding of consciousness could happen in transient hysterical states, catatonic stupor, melancholia and excitement (see Lipowski, 1990: 26).

In summary, the nineteenth century saw the introduction of two new concepts: clouding of consciousness and confusion, and an attempt was made to distinguish delirium caused by alcohol as a separate condition. Clinical symptoms rather than aetiology and prognosis became the focus of definitions (Lindesay, 1999).

Twentieth century

At the end of the nineteenth and the beginning of the twentieth centuries, although the influence of Kraepelin's work was enormous, his view that

the natural history of any mental illness must become part of its definition (Berrios, 1981) did not seem to affect definitions of delirium. This may be partly due to the agreement – unanimous at the time – that the outcome of delirium was either death or full recovery.

At the beginning of the century Pickett (1904) proposed a distinction between Delirium and confusion in elderly people, believing that Delirium always has an organic cause while confusion could be caused by other non-organic factors. A few years later Bonhoeffer described acute organic brain disorders as 'symptomatic psychoses' which included simple Delirium, hallucinosis, amentia, 'epileptic type' and symptomatic stupor, all of which were characterized by clouding of consciousness. He thought that 'delirium acutum' had a bad prognosis. Bonhoeffer suggested that the brain could react to exogenous noxae caused by physical illness and thus grouped these under 'acute exogenous reaction types' (Hoff and Berner, 1969; Neumarker, 1990, 2001). Eugen Bleuler held that it was not the type of noxae but their intensity and duration of influence that were significant in the development of these reactions, while Kraepelin argued that the distinctive features of the reaction types were not caused by the external damage itself but by their rapid development. Around the same time Adolf Meyer proposed a similar model of 'reaction types', of which the 'dysergastic reaction' represented acute organic disturbance, later explored by Wolf and Curran in 1935 (see Caraceni and Grassi, 2003: 3; Lipowski, 1990: 31).

Manfred Bleuler and Klaus Conrad disagreed about clouding of consciousness as a diagnostic criterion (Neumarker, 1990, 2001), but Kurt Schneider (1947, 1948: 37–40) in discussing the 'exogenous reaction' which he called '*körperlich begrundbare Psychosen* (physically related psychosis)' emphasized clouding of consciousness as a central diagnostic feature. He also accepted the possibility of chronicity and dementia.

Engel and Romano (1959) used EEG to investigate delirium and found that it was associated with a reduction of cerebral metabolic rate as indicated by an increase in slow wave activity. Lipowski, who worked and wrote extensively on delirium (e.g., Lipowski, 1990, 1991), is regarded as the father of modern research into this condition.

During the last part of the twentieth century, attempts were made to define mental disturbances, including delirium, by consensus, and two classification systems emerged: the DSM (*Diagnostic and Statistical Manual of Mental Disorders*) of the American Psychiatric Association and the ICD (International Classification of Diseases). A crucial factor in the development of ideas about delirium was demographic change, especially in developed countries, with an increasing proportion of hospital beds occupied by men and women in their seventies or eighties, often with multiple physical and cognitive problems (Jefferys, 1988).

Discussion and conclusions

In summary, it seems that despite the different terms that have been used, a robust description of delirium has existed since antiquity – at some times as a symptom and others as a syndrome. A further dichotomy was whether its definition depended on possible aetiology(ies) and its association with physical illness, or on clinical symptoms; each was thought more significant at different times and by different authorities. Given what we now know to be the protean manifestations of delirium, it is not surprising that definitions which were based on symptoms differed considerably. Philosophical theories about the body, the psyche and their relationship also influenced definitions of delirium since this is one of the few clinical conditions in which it is evident that a physical cause can produce mental problems. To this day, there has been universal agreement about the gravity of delirium and its bad prognosis, and also that if outcome was not death, full recovery was likely, although a few observers over the centuries suggested that delirium may lead to a more permanent mental disturbance even after its immediate cause was removed. It was not until the phenomenologicallly-focused nineteenth century that the pursuit of a syndrome took over from the attempt at a diagnosis with its prognostic and management implications. Not until the twentieth century was it thought that delirium was marked by a full recovery among survivors, and this was probably due to the desire for a clear distinction from dementia.

Most authorities agreed that delirium is connected with the presence of acute physical illnesses, especially inflammation and those causing fever.

We conclude that if delirium is anything it is a variety of syndromes with a variety of causes. Therefore, perhaps we will always have to study delirium by seeing it as a 'final common pathway' of symptomatology, and begin to explore cautious therapeutic interventions according to the aetiology of the delirium.

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