Clinical pictures of unknown origin in neurology: past, present and future usefulness of artificial intelligence

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Although, in the course of the last 50 years, the achievements in the medical field have been astonishing, at the beginning of the third millennium a number of clinical pictures are still left without a precise nosographic origin.

In the past, the delay in scientific communication was the main explanation presented for the lack of understanding of clinical pictures of unknown nosographic origin. The history of medicine provides excellent examples of this dispersion of human capital, even if the history of clinical neurology presents “exceptions” (the pictures that we now call de la Tourette’s syndrome and Parkinson’s disease) that indicate that major clinical syndromes could be clearly detected and relatively rapidly diffused even in the 19th century.

Contrary to the past, the delay in scientific communication no longer seems an obstacle to the sharing of medical knowledge. Nevertheless, the problem of the in-depth comprehension of clinical pictures of unknown nosographic origin still remains dominant, mainly because of the limited spread of ample and flexible online accessible databases of unknown nosographic origin clinical syndromes. The need for interactive electronic archives and other artificial intelligence resources in order to promote progress in clinical knowledge is discussed in this paper.

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Key words: Artificial intelligence; de la Tourette’s syndrome; History of medicine; Medical electronics; Neural networks; Parkinson’s disease.

Background

At the beginning of the third millennium a number of clinical pictures are still left without a precise nosographic origin. Although, in the course of the last 50 years, achievements in the medical and health care fields have been astonishing, a great amount of work is still needed to clarify the pathophysiological bases of many clinical syndromes.

Starting from the cognitive and operational processes that have led distinguished physicians of the past to describe

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In 1884, that is, a year before the classical description included in his (now) well-known paper published in the *Archives de Neurologie*, Georges Gilles de la Tourette reported several movement disorders which he retained similar to each other, and different from true chorea. Although already in 1825 J.M.G. Itard was probably the first who described a phenotype with involuntary movements and peculiar vocalizations, in 1885 de la Tourette described 9 patients suffering from a striking syndrome of motor and verbal tics, characterized by involuntary movements, echolalia, coprolalia and uncontrollable sounds. de la Tourette’s syndrome is nowadays universally recognized as a common genetic disorder with a wide spectrum of neurobehavioral problems, and the eponym clearly identifies the first author who fully described this clinical picture presenting with, besides the tics, features of attention deficit-hyperactivity disorder, obsessive compulsive disorders and other comorbid behavioral problems.

Even if the diffusion of clinical knowledge in the neurological field has been in the past probably faster than in other clinical areas – and perhaps not by chance modern informatic databases of genetic alterations in neurology appear among the best examples of what is so far available for the clinicians and the researchers of the international scientific community – there is no doubt that the lack of rapid and capillary communication pathways constituted a major obstacle to the adequate spreading of clinical knowledge throughout the international medical community. The 19th century scientific information was vehiculated only on paper, and the absence of quicker media prevented the timely expansion of new and updated knowledge, such as that elaborated by de la Tourette. In fact, although the classical paper of de la Tourette was published in a journal diffused at that time, the first description available in Italian of the de la Tourette’s syndrome is only dated some decades later.

It is worth pointing out that in the 1885 paper de la Tourette summarized the syndrome through three key concepts, namely motor and verbal tics, involuntary movements and uncontrollable sounds, whereas in recent textbooks the eponym identifies the syndrome through the following diagnostic criteria: the presence of multiple motor and phonic tics; the occurrence of such tics many times over a period of more than one year; the change in time of the anatomic location, number, frequency, complexity, type and severity of the tics; the onset before the age of 21 years; the incapacity to explain the involuntary movements and noises with other clinical conditions. In brief, the diagnosis of de la Tourette’s syndrome has been refined, but the first signs described in the past still overlap with current diagnostic features.

To remain within the neurological context, James Parkinson’s work is today acknowledged and well known. “The patient can rarely form any recollection of the precise period of its commencement. The first symptoms perceived are a slight sense of weakness with a proneness to trembling in some particular part; sometimes in the head, but most commonly in one of the hands and arms … The propensity to lean forward becomes invincible… As the debility increases and the influence of the will over the muscles fades away, the tremulous agitation becomes more vehement”. This is only a part of the effective description of the disease that Parkinson named, in his 1817 medical publication, the “shaking palsy”. This clinical report is now considered a classic in pathology case reports, even if relevant “a posteriori errors” are detectable in the description, for example with regard to Parkinson’s idea that “the senses and intellects were uninjured”. Parkinson’s essay described 6 case histories of patients affected by the disease, and also included the author’s definition of the disorder, a definition in general still valid today. As in the former case, the 1817 Parkinson definition included three key concepts, which were weakness, tremor, disorder of posture and gait; recent textbooks describe the clinical picture as a syndrome consisting of a variable combination of tremor, rigidity, bradykinesia and a characteristic disturbance of posture and gait. In this case too, dissemination of the definition of this syndrome took time to gain real widespread recognition across Europe, even if, already at the end of the 19th century, it appeared on the Treatise on Nervous and Mental Diseases of Charcot, the major neurology text of the period. The limited diffusion of this clinical picture could possibly also be ascribed to the fact that the description was reported in a volume, and not on a journal paper.

It may be noted that the description of a very limited number of cases (6 in Parkinson’s essay, 9 in Gilles de la Tourette’s paper) was to revolution the history of clinical medicine, not immediately, however, but with the passing of decades, since the transmission of clinical knowledge less than 200 years ago was laborious and much slower than today, even in the case of rapidity “exceptions”, such as the neurological pictures here discussed. The question may be posed, as regards today, whether the description of a clinical picture detected in a limited number of individuals, elaborated by someone operating in the 2005 global village, would be considered a major disease of the future. To what extent such a future is near or far is likely to depend, among other things, upon the large availability of on-line accessible, continuously updated databases of case reports of unknown nosographic origin.

**The present and the future**

Contrary to the past, today lack of speedy communication no longer seems to constitute an obstacle to the shar-
The understanding of medical knowledge. Paper journals have wide diffusion and the publication of new case reports can rapidly determine the verification of international researchers with regard to the correctness of the description, to its frequency and to its analogies with other clinical conditions. With reference to this, a first problem is that a large – and not always a “less important” – proportion of observations and studies is not published. However, since clinical records on paper stored in physical libraries are certainly no longer the unique template of collected medical knowledge, the virtually infinite potentialities of electronic communication allow real-time circulation of true, or putative, discoveries and developments.10,11

Nonetheless, the problem of the in-depth understanding of clinical pictures of unknown nosographic origin still remains. Why? In the specific area of such syndromes, even if the potentialities of electronic devices may overcome physical obstacles to knowledge communication, the current relatively limited diffusion and use of ample, flexible and accessible online databases of unknown origin clinical syndromes is, in our view, a major explanation for the lack of understanding of the pathophysiological background of a number of clinical pictures, even in 2005.12

This is possibly due to the fact that clinical pictures of unknown origin, even if accurately studied with regard to their pathophysiological mechanisms, are considered orphan syndromes from a therapeutic point of view, since the pharmaceutical market has limited interest in them. One of the problems is also constituted by the limitations discernable in the diffused sharing of pathophysiological and clinical data collected on a limited number of cases. Individual clinical centers, in fact, can only collect a limited number of cases. However, if they could share their data in a structured and ample format with other centers, and store the information in flexible, easily accessible and shared electronic archives, the probability of reaching an understanding would be increased. Furthermore, the availability of such an instrument as a database of case reports of unknown nosographic origin would be useful for the process of transforming information into knowledge, as confirmed by current clinical cognitive views.13

On the basis of the latter consideration, currently electronic archives are becoming available, and, taking the example of OMIM (“Online Mendelian Inheritance in Man”), out of approximately 3100 Mendelian phenotypes described in it, about 1700 have now an identified molecular base. OMIM is a database cataloguing human genes and genetic disorders developed for the World Wide Web by the National Center for Biotechnology Information. This archive contains textual information, reference and also links to MEDLINE. However, as has been said, approximately 45% of phenotypes contained in OMIM still await their molecular base. Lights and shadows therefore remain in the virtual international scientific community, and the present neurological scenario confirms this view. In fact, a wealth of knowledge has already been achieved in many different and unusual pictures referable to movement disorders, but the available electronic databases in general are still not “intelligent enough” if compared to current standards set in other research settings. Unknown nosographic origin pictures continue to be a great medical challenge that collocates itself in the intriguing and complex cognitive context that constitutes the third of the three described below.

In clinical cases in which the physician is skilled and/or the clinical condition is familiar, the identification of the clinical presentation of the condition/disease is immediate, through the swift recognition of the characteristics of “similar” patients previously observed. In this first scenario the abilities required of the physician refer to his/her cultural and operational preparation, and to a satisfactory organization of his/her cognitive network of memorized knowledge (“semantic network”).

In the case in which the physician is less skilled and/or the clinical case is unusual, the diagnostic reasoning has to be based upon the hypothetical-deductive pattern, through the formulation of various diagnostic hypotheses and the search for additional data which may be present or absent. In this second scenario the abilities required of the physician refer to the perception of relevant and pertinent diagnostic data, and to the aggregation of the data obtained in defined nosographic models.

The third scenario includes the clinical presentation of cases of unknown nosographic origin. In this case the human intelligence may be effectively enhanced by the artificial intelligence.14 In fact, in such a scenario, the artificial intelligence, coupled with mining techniques, may be retained to play a very important role in the cognitive process. Assuming that some sorts of data will be codified and/or presented in the same way by different clinical groups, or that this may be achieved by neural networks and mining techniques, the role of the artificial intelligence would be that of finding possible relations or correlations among the data collected from all over the world and determining analogies among apparently uncorrelated case reports.15 With specific regard to rare disorders, a list of websites is reported in the appendix.

Conclusions

Starting from the past of clinical medicine we have reached the present and the future of artificial intelligence. In a comprehensive view, the development of medical knowledge should be seen as a continuous spectrum; the “neurological” examples (de la Tourette’s syndrome and Parkinson’s disease) that emerge from the
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past still appear valid in the present and their didactic value projects itself in the future of “neural” networks. The common denominator of our journey through time is represented by human cognitive patterns.

With regard to these, in the past their role was decisive in identifying what are now well established clinical pictures. In the future, for the comprehension and identification of clinical pictures of unknown nosographic origin, the role of ample and flexible electronic archives, within the framework of a historical-cognitive approach such as that proposed in this paper, is clearly indicated.

Riassunto

Per quanto negli ultimi 50 anni le nuove acquisizioni in ambito medico siano state eccezionali, ancora oggi, all’inizio del terzo millennio, molti quadri clinici restano senza una precisa classificazione nosografica.

Nel passato il ritardo nella comunicazione scientifica rappresentava la spiegazione principale per il deficit di comprensione di quadri clinici di origine nosografica sconosciuta. La storia della medicina fornisce molti casi di dispersione di capitale umano, per quanto la storia della neurologia presenti interessanti “eccezioni” (i quadri che oggi chiamiamo “sindrome di Gilles de la Tourette” e “morbido di Parkinson”) che indicano che grandi sindromi cliniche potevano essere chiaramente descritte e relativamente velocemente diffuse già nel diciannovesimo secolo.

Contrariamente a quanto avvenuto nel passato, il ritardo nella comunicazione scientifica non sembra oggi più essere un ostacolo essenziale alla condivisione delle conoscenze mediche. Ciononostante, il problema della comprensione approfondita di quadri clinici di origine sconosciuta rimane ancora dominante, soprattutto a causa della limitata diffusione di archivi elettronici ampi e flessibili di sindromi cliniche di origine sconosciuta.

Nell’articolo viene discussa la necessità presente e futura di archivi elettronici interattivi e di altri fonti di intelligenza artificiale al fine di promuovere il progresso delle conoscenze cliniche.

Parole chiave: Informatica medica; Intelligenza artificiale; Morbo di Parkinson; Reti neurali; Sindrome di Gilles de la Tourette; Storia della medicina.

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Appendix

- http://www.orpha.net/ (accessed on April 22nd, 2005)
- http://omni.ac.uk/browse/mesh/D004194.html (accessed on April 22nd, 2005)

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