

December 31, 2011

To The Editor in Chief,
Pharmacologyonline (Newsletter),

I do think remarkable, after our Letter of December 25 (that we really appreciate for the splendid on-line, prompt publication as Note N-99, of same Volume 3), to present throughout your exquisite competence and courtesy, to our very intelligent, bright and clever passionate Readers, the succession of my recent two Science's Letters, that had been refused by those Editors, inviting myself to "another outlet". I mean, just another proof of the scientific usefulness, as real need of our still unic online S.I.F. Journal:

December 31, 2011 6.15
To The Editors,
Science Magazine

I cannot be silent and so ashamed on our Organization. Nevertheless, I do think, as an old, still active AAAS member, that you should at least make available as Collateral Science Material the Letters and/or the arguments of the Letter contributions throughout the Web.

While, about the MS# 1218517 (Web Submission ID: 184148), I will have immediately published both the Premise and the Text "in another outlet", about the previous MS# 1215782 (Web Submission ID: 180589) I send now today the attachment above (Pharmacologyonline 3: 991-992 (2011) Newsletter, and if you will insist do not read this my offended reply, I really still hope you will decide to insert its new scientific as well social arguments, in one related Science' upcoming "News Focus".

Very truly, sincerely Yours,
Luigi Rossini, M.D., Ph.D., AAAS Member# 1573340250.

-----Messaggio originale-----

From: Science Editors
Sent: Friday, December 30, 2011 5:30 AM
To: rossiniluigi@hotmail.it
Subject: Your Letter to Science

MS# 1218517

Dear Dr. Luigi,

Thank you for sending a Letter-to-the-Editor to Science. We have read over your contribution, but will not be able to publish it in the magazine. We are letting you know as a courtesy in case you wanted to seek another outlet for your letter.

Please do not reply to this email, as it will not be read by Science. Unfortunately the volume of submissions precludes specific discussions about individual submitted letters.

Sincerely,
The Editors
Science Magazine

December 21, 2011, 8.09

Dear author:

Thank you for using Science's Web submission site. It will take approximately one or two business days to process the receipt of your submission. If you are notified that one or more of your uploaded files is unreadable, you will need to return to the site to replace the unreadable files. In order to return to the site, you will need to have the following information:

First Author's Last Name: Luigi

Corresponding Author's Email Address: rossiniluigi@hotmail.it

Web Submission ID: 184148

Questions about your submission may be addressed to us at science_editors@aaas.org

Sincerely,
The Editors

December 22, 2011 19.29

To The Editors
Science Letter

Dear Science Editor,

Premise:

On October 21, 2011 I submitted a "Letter" (web ID 180589) to discuss and comment on

Andrew Grove's Editorial "Rethinking clinical trials" (Science Volume 333, 23 September 2011) as well as to contribute our recent one-year experience. The Editors, who were also sent my recent US curriculum and the full text of our last seven published papers as Supporting Online Material, replied on November 19, 2011 at 5.30 am as follows: "MS#1215782 Dear Dr. Rossini, Thank you for sending a Letter-to-the-Editor to Science. We have read over your contribution, but will not be able to publish it in the magazine. We are letting you know as a courtesy in case you wanted to seek another outlet for your letter. Please do not reply to this email, as it will not be read by Science. Unfortunately the volume of submissions precludes specific discussions about individual submitted letters. Sincerely, The Editors Science Magazine". Dr Dan Bradu, the co-author of most contributions, and I, as well as other colleagues were very surprised. I therefore decided not to renew my subscription to the AAAS after 50 years running. The Letter will be presented, without modifications, at the 4th Int Conference on Drug Discovery & Therapy, Dubai, U.A.E., February 12-15, 2012, coorganized by one of my mentors, the Nobel laureate Dr Ferid Murad. However, I believe that it needs a scientific review after careful examination of the full texts of the supporting notes, involving around 137 Countries, and that it deserves an extended, proper presentation in one of Science's upcoming "News Focus".

While awaiting your reply, which I hope will be favorable, I am now submitting a new Letter to comment on and add my original data to those of Dominici et al (1), and Grillner (2), having been a Visiting Professor in Dr Carlo Terzuolo's Neurophysiology Lab, Physiology Dept, University of Minnesota, in the Sixties. There, among many others, I met Drs Rodolfo Llinas and Richard Poppele, and Francesco Lacquaniti thereafter, whose methods I applied to a different field (non invasive metabolic and electric features in the crayfish stretch receptors in vitro. See, for an example, CA Terzuolo, B Chance, E Handelman, L Rossini and P Schmeltzer, *Biochim. Biophys. Acta*, 126 (1966) 361-372).

I hope you will consider both submitted contributions. I am at your disposal for any clarification and any change that may be deemed useful, and hope to be allowed to collaborate as a still active AAAS member.

And now, below, the very short Letter:

Locomotor Primitives and Their Evolution Modules

The report by Dominici et al (1) and the related Perspective by Grillner (2) agree on the premises and the evolutionary features of the locomotor complex specific adaptation that emerged some

560 million years ago, possibly evolving from similar central pattern generator neurocircuitries which have been analyzed with modeling and advanced time and space multiple EMG detections. However, the different phases of the common control CPG-system may be integrated by those generally operating in swimming activities. Indeed in the 1950s, i.e. much earlier than the references reported by the authors (see also Kiehn, 2006 (3)) some relevant but unusual pictures emerged (4) from application to rodents—rats, but mostly ordinary guinea pigs—at different stages of development of Sherrington's and Pavlov's methods, focusing on thermal sensitivity. Spinal lesions that deinhibit somatic (and visceral) natal preterm temporarily coordinated motor patterns of reactivities, that can be later re-acquired by the adult animal by selective thermal conditioning, as well pharmacological media, had already been sufficiently characterized. Single leg/foot vs unilateral swimming local features, and preparative anticipating behaviors predominantly or only to cold vs warm (around 19°C vs 38°C medium ranges, 1-to-2°C domesticated selective) had been set free, even in subthalamic, cerebellarly interfering, and hypothermic preparations, visuomotor, olfactory, and, after being firmly established, originating trigeminal mediations excluded. These aspects have not yet been analyzed in humans, perhaps having only been communicated in Italian (only one collateral note having recently appeared (5)). Nevertheless, projects, as prospectives and hopes, claim to be amplified and verified (i.e. (6)).

References

1. N. Dominici *et al.*, *Science* **334**, 997 (2011).
2. S. Grillner, *Science* **334**, 912 (2011).
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6. L. Rossini, *Pharmacologyonline Newsletter*, **1**, 754 (2010).

October 21, 2011 7,47

To The Editors,

Science Letter,

Rethinking Clinical Trials

The Editorial of 23rd September (1), overlapping with the PolicyForum in the same issue (2), recalls the Special Section of 10th October 2008 (3), discussed in (4). The complex question is clearly international, global, and needs to be viewed in those equally essential perspectives, i.e. (5), given the ability of *e-commerce* – as of course *e-health* - of storing and processing communication, i.e. of dealing with data, as recently discussed (6). Exhaustive collection and use of the available information remains a key element; however these data cannot be limited to pre-marketing data where clinical, including human, pharmaco-toxicological experimental-translational biomedical research is concerned, as the present patient advocate author acknowledges and as the U.S. Office of Technology Assessment (OTA) has laid down in its *ad hoc* documents, as everyone knows, since 1976. WHO-ITA/ITA-OMS, a denomination approved by the World Health General Assembly for a body involving the sixth founding member of the WHO Pharmacovigilance Programme, and the initiator of the world *e-network* of exchange of national reports of side-events and suspicious or confirmed adverse drug reactions (SADRs) in real-life use of medications, has recently made available a first series (7) of its collected and processed data. These data are released on the 40th anniversary of the founding of the International Data Bank, to date the only such international Bank, whose seat is at the Uppsala Collaborative Centre (UMC). The analysis, initially focusing on the 201,928 reports received from the associated Countries with regard to the 73 diagnostic contrast media in use, especially iodinated radiographic agents (ATC V08A, subclasses -A, -B, -C e -D) and paramagnetic enhancers for NMR imaging (Subclass ATC V08C-A), showed broadly inhomogeneous profiles of the products categorized as ATC classes and subclasses, and even as “biosimilars”, highlighting striking differences when they were subdivided into the WHO system-organ class disorders (SOC-D-SADRs profiles). These conclusions add to the data already reported by the authors (8), and to the knowledge acquired from chemico-physical data, translational pre-clinical experiments and pre-marketing standardized clinical trial regulations.

The model study carried out on these data, which was sent to the WHO Headquarters, the European Medicinal Agency (EMA), the UMC, and the 141 Pharmacovigilance offices of the

current 137 Collaborating Countries, corresponds at least partly to the ideas, notions and proposals reviewed in the Editorial (1). The first objective autoclassification data based on the model and on a Matlab program (described in the 4th contribution of our current series (7)) will be able to be developed and extended also by the currently distributed *Teaching Resources* (9).

References

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