An Editorial-Approach Perspective on some of Our Preliminary Data Regarding the Neuropsychiatric and Gastrointestinal Manifestations in Covid-19

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Abstract

Considering the previous experience of our group in studying both the neuropsychiatric disorders, as well as the gastrointestinal ones, and the interaction between these type of manifestations, and also having in mind the current COVID-19 pandemics, in the current short editorial we will focus our attention on describing very briefly some of our preliminary data regarding the neuropsychiatric and gastrointestinal manifestations in COVID-19.

Keywords: Covid-19, neuropsychiatric, gastrointestinal.

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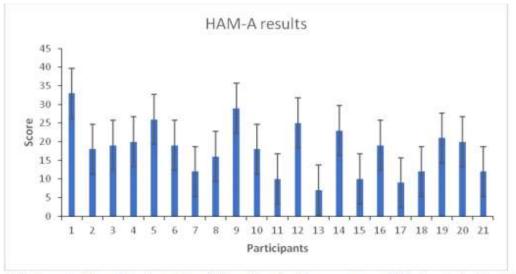
Introduction

Thus, considering the ever-growing importance in understanding the mecanistics behind the current COVID-19 pandemics, and our previous experience in studying both the neuropsychiatric disorders, as well as the gastrointestinal ones, and the interaction between these types of manifestations we concentrate our attention here on some of our preliminary data regarding the neuropsychiatric and gastrointestinal manifestations in COVID-19.

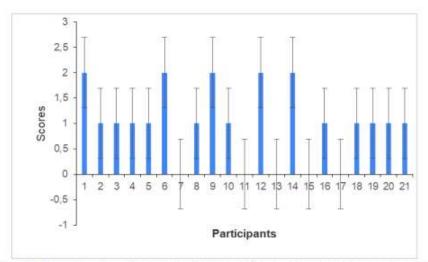
We previously showed on numerous occasions that the brain-gut axis and the so-called "second-brain" from the gut are very well correlated to most of the neuropsychiatric disorders [1-10].

Thus, in one of first preliminary attempts to better understand or to speculate on the neuropsychiatric and gastrointestinal manifestations associated with COVID-19, we used a group of volunteers, on which we studied if there were any "correlations between anxiety levels, gastrointestinal manifestations and social isolation following the lockdown due to this specific coronavirus outbreak in Romanian students"[11].

Our data back then in the spring showed that there were particular anxiety-related manifestation associated with the lockdown situation, and even more, these were correlated with a specific series of gastrointestinal manifestations (Figure 1- as taken from our original manuscript) [11]:



IAM-A results. The results of a number of 21 participants with a mean score of 18 and a standard deviation



Gastrointestinal symptoms. Score given by participants regarding gastrointestinal symptoms, lowest score being 0 (absent symptoms) and highest 2 (moderate symptoms).

Figure 1. Anxiety and gastrointestinal related manifestation in our selected volunteers during the pandemics lockdown.

Similar aspect were actually also previously demonstrated in areas or countries such as China, Hong Kong or Jordan [12-14].

Following that, the attention of our group focused on a specific scale (VAS-IBS scale) for studying the most important functional digestive disorder, which is considered to be the Irritable Bowel Syndrome (IBS), by also using a number of volunteers that were infected with COVID-19 and establishing the correlations that might exist between the viral pathology and their subsequent digestive manifestations [15 - in press].

Although our specific data was not published yet, we can certainly say that COVID-19 infection resulted in a significant alteration of constipation, abdominal pain, bloating, vomiting processes and the related emotional status, as measured by the specific VAS-IBS scale [15 - in press].

In fact, previous authors described IBS-like manifestations in COVID-19 infection [16, 17].

It also seems that mechanistically, some manifestations resemble the pathology of IBD, Reiter's syndrome or Guillain-Barre syndrome [18-20].

It is also worth mentioning in this context, that in a computational and modern mathematical approach our group also did some preliminary and speculative studies on "Forecasting the Spreading of COVID-19 across Nine Countries from Europe, Asia, and the American Continents Using the ARIMA Models" [21] and predicting in the summer of 2020 the epidemiological evolution of COVID-19 spreading in countries such as Ukraine, Romania, the Republic of Moldova, Serbia, Bulgaria, Hungary, USA, Brazil, and India [21].

Also, in the same context, we were also interested in "Testing the Accuracy of the ARIMA Models in Forecasting the Spreading of COVID-19 and the Associated Mortality Rate" [22], by following the complex mathematical and computational models that could further explain and predict some epidemiological aspects of this pandemic situation (for example we also did focus on the total number of patients hospitalized in ICU), especially since for example this specific ARIMA technique was also previously used in the last years for malaria, tuberculosis influenza, brucellosis and other important similar disorders [23-29].

In addition, in a more therapeutical-related approach, our group described and focused in the summer of 2020 on the relevance of vitamin B3 in the context of COVID-19 [30], considering also the possible implications of the oxidative stress status in this SARS-CoV-2 infection [31].

Conclusions

Thus, as suggested from this preliminary data, we can further speculate that there is indeed a possible neuropsychiatric and gastrointestinal background/correlation in COVID-19 pathological manifestations.

References

[1. Balmus, I.-M.; Lefter, R.; Ciobica, A.; Cojocaru, S.; Guenne, S.; Timofte, D.; Stanciu, C.; Trifan, A.; Hritcu, L. Preliminary Biochemical Description of Brain Oxidative Stress Status in Irritable Bowel Syndrome Contention-Stress Rat Model. Medicina 2019, 55 (12), 776. doi:10.3390/medicina55120776.

[2. Ioana-Miruna Balmus, Ovidiu Ilie-Dumitru, Alin Ciobica, Roxana-Oana Cojocariu, Carol Stanciu, Anca Trifan, Mirela Cimpeanu, Cristian Cimpeanu, Lucian Gorgan, Irritable Bowel Syndrome between Molecular Approach and Clinical Expertise—Searching for Gap Fillers in the Oxidative Stress Way of Thinking Medicina 2020, 56(1), 38; https://doi.org/10.3390/medicina56010038.

[3. Balmus Ioana-Miruna, Ciobica Alin, Cojocariu Roxana, Alina Costina Luca, Gorgan Lucian, Irritable Bowel Syndrome and the Neurological Deficiencies: Is There A Relationship? The Possible Relevance of the Oxidative Stress Status, Medicina 2020, 56(4), 175; https://doi.org/10.3390/medicina56040175.

[4. RADU LEFTER, ALIN CIOBICA, DANIEL TIMOFTE, DANIELA ABABEI, ROMEO DOBRIN, ANDREI LUCA, ANCA TRIFAN, CAROL STANCIU, CATALIN SFARTI, A new biological approach in generating an irritable bowel syndrome rat model -focusing on depression in sucrose splash test and body weight change, Romanian Biotechnological Letters, 2020, Vol. 25, Nr. 3, 1554-1562.

[5. Roxana Cojocariu, Ioana Miruna Balmus, Radu Lefter, Luminita Hritcu, Dana Ababei, Alin Ciobica, Simona Copaci, Lucian Copolovici, Dana Copolovici, Ștefana Jurcoane, Beneficial effects of Camelina sativa oil on behavioural (memory, anxiety, depression and social-related) manifestations and oxidative stress parameters in a mice model of irritable bowel syndrome, Romanian Biotechnological Letters, 2020, Vol. 25, Nr. 3, 1532-1540.

[6. Roxana Oana Cojocariu, Ioana Miruna Balmus, Radu Lefter, Daniela Carmen Ababei, Alin Ciobica, Luminita Hritcu, Fatimazahra Kamal, Bogdan Doroftei, Behavioral and oxidative stress changes in mice subjected to combinations of multiple stressors relevant for irritable bowel syndrome, Brain Sciences, 2020, 10(11), 865; <u>https://doi.org/10.3390/brainsci10110865</u>.

[7. Ioana – Miruna Balmus, Cojocariu Roxana – Oana, Alin Ciobica, Stefan Strungaru, Roxana Strungaru – Jijie, Alina Cantemir, Catalina Galatanu, Lucian Gorgan, Preliminary Study on the Tears Oxidative Stress Status and Sleep Disturbances in Irritable Bowel Syndrome Patients, Oxidative Medicine and Cellular Longevity, vol. 2020, Article ID 4690713, 2020, IF 4,8, <u>https://doi.org/10.1155/2020/4690713</u>.

[8. Alin Ciobica, Padurariu Manuela, Alexandrina Curpan, Iulia Antioch, Roxana Chirita, Cristinel Stefanescu, Alina-Costina Luca and Mihoko Tomida, Mini-review on the connections between the neuropsychiatric and dental disorders: current perspectives and the possible relevance of oxidative stress and other factors, Oxidative Medicine and Cellular Longevity, Volume 2020, Article ID 6702314, <u>https://doi.org/10.1155/2020/6702314</u>, 2020.

[9. Ovidiu Ilie-Dumitru, Alin Ciobica, Jack McKenna, Bogdan Doroftei, Ioannis Mavroudis, Minireview on the relations between gut microflora and Parkinson's disease – further biochemical (oxidative stress), inflammatory and neurological particularities, Oxidative Medicine and Cellular Longevity, Volume 2020, Article ID 4518023, <u>https://doi.org/10.1155/2020/4518023</u>, 2020.

[10. Radu Lefter, Alin Ciobica, Iulia Antioch, Daniela Ababei, Luminita Hritcu, Alina-Costina Luca, Oxytocin differentiated effects according to the administration route in a prenatal valproic acid-induced rat model of autism, Medicina 2020, 56(6), 267

[11. Alexandrina Curpan, Alexandra Săvucă, Luminița Hritcu, Alin Ciobîcă, Daniel Timofte, Peiu Sorin Nicolae, Correlations between anxiety levels, gastrointestinal manifestations and social isolation following the lockdown due to coronavirus outbreak in Romanian students, Bulletin of Integrative Psychiatry, 2020, 3, 86, 63-69, DOI link : 10.36219/BPI.2020.3.07.

[12. Wong TW, Gao Y, Tam WWS. Anxiety among university students during the SARS epidemic in Hong Kong. Stress Heal. 2007; 23:31–5.

[13. Zhang Y, Ma ZF. Impact of the COVID-19 pandemic on mental health and quality of life among local residents in Liaoning Province, China: A cross-sectional study. Int J Environ Res Public Health. 2020; 17(7).

[14. Sallam M, Dababseh D, Yaseen A, Al-Haidar A, Ababneh NA, Bakri FG, et al. Conspiracy beliefs are associated with lower knowledge and higher anxiety levels regarding covid-19 among students at the university of Jordan. Int J Environ Res Public Health. 2020; 17(14):1–15

[15. Ovidiu Ilie et al., Studying some possible irritable bowel syndrome manifestations in COVID-19 patients, in press, 2020.

[16. Zhou D, Dai S-M, Tong Q. COVID-19: a recommendation to examine the effect of hydroxychloroquine in preventing infection and progression. J Antimicrob Chemother 2020.

[17. Bescos R, Ashworth A, Cutler C, Brookes ZL, Belfield L, Rodiles A, et al. Effects of Chlorhexidine mouthwash on the oral microbiome. Sci Rep 2020;10:5254.

[18. Taxonera C, Sagastagoitia I, Alba C, Mañas N, Olivares D, Rey E. 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. Aliment Pharmacol Ther 2020;52:276-283.

[19. Ono K, Kishimoto M, Shimasaki T, Uchida H, Kurai D, Deshpande GA, et al. Reactive arthritis after COVID-19 infection. RMD Open 2020;6:e001350.

[20. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, et al. Guillain–Barré Syndrome Associated with SARS-CoV-2. N Engl J Med 2020;382:2574–6.

[21. Earnest, A.; Chen, M.I.; Ng, D.; Sin, L.Y. Using autoregressive integrated moving average (ARIMA) models to

predict and monitor the number of beds occupied during a SARS outbreak in a tertiary hospital in Singapore.

BMC Health Serv. Res. 2005, 5, 36. [CrossRef] [PubMed]

9. Gaudart, J.; Touré, O.; Dessay, N.; Dicko, A.L.; Ranque, S.; Forest, L.; Demongeot, J.; Doumbo, O.K. Modelling

malaria incidence with environmental dependency in a locality of Sudanese savannah area, Mali. Malar. J.

2009, 8, 61. [CrossRef] [PubMed]

10. Liu, Q.; Liu, X.; Jiang, B.; Yang, W. Forecasting incidence of hemorrhagic fever with renal syndrome in China

using ARIMA model. BMC Infect. Dis. 2011, 11, 218. [CrossRef]

11. Nsoesie, E.; Beckman, R.; Shashaani, S.; Nagaraj, K.; Marathe, M. A simulation optimization approach to

epidemic forecasting. PLoS ONE 2013, 8, e67164. [CrossRef]

12. Zheng, Y.-L.; Zhang, L.; Zhang, X.-L.; Wang, K.; Zheng, Y.-J. Forecast model analysis for the morbidity of

tuberculosis in Xinjiang, China. PLoS ONE 2015, 10, e0116832. [CrossRef] [PubMed]

13. He, Z.; Tao, H. Epidemiology and ARIMA model of positive-rate of influenza viruses among children in

Wuhan, China: A nine-year retrospective study. Int. J. Infect. Dis. 2018, 74, 61–70. [CrossRef] [PubMed]

14. Cao, L.; Liu, H.; Li, J.; Yin, X.; Duan, Y.; Wang, J. Relationship of meteorological factors and human brucellosis

in Hebei province, China. Sci. Total Environ. 2020, 703, 135491

22. Ilie, O.-D.; Ciobica, A.; Doroftei, B. Testing the Accuracy of the ARIMA Models in Forecasting the Spreading of COVID-19 and the Associated Mortality Rate. Medicina 2020, 56, 566.

23. Earnest, A.; Chen, M.I.; Ng, D.; Sin, L.Y. Using autoregressive integrated moving average (ARIMA) models to predict and monitor the number of beds occupied during a SARS outbreak in a tertiary hospital in Singapore.

BMC Health Serv. Res. 2005, 5, 36.

24. Gaudart, J.; Touré, O.; Dessay, N.; Dicko, A.L.; Ranque, S.; Forest, L.; Demongeot, J.; Doumbo, O.K. Modelling malaria incidence with environmental dependency in a locality of Sudanese savannah area, Mali. Malar. J 2009, 8, 61.

25. Liu, Q.; Liu, X.; Jiang, B.; Yang, W. Forecasting incidence of hemorrhagic fever with renal syndrome in China using ARIMA model. BMC Infect. Dis. 2011, 11, 218.

26. Nsoesie, E.; Beckman, R.; Shashaani, S.; Nagaraj, K.; Marathe, M. A simulation optimization approach to epidemic forecasting. PLoS ONE 2013, 8, e67164.

27. Zheng, Y.-L.; Zhang, L.; Zhang, X.-L.; Wang, K.; Zheng, Y.-J. Forecast model analysis for the morbidity of tuberculosis in Xinjiang, China. PLoS ONE 2015, 10, e0116832.

28. He, Z.; Tao, H. Epidemiology and ARIMA model of positive-rate of influenza viruses among children in Wuhan, China: A nine-year retrospective study. Int. J. Infect. Dis. 2018, 74, 61–70.

29. Cao, L.; Liu, H.; Li, J.; Yin, X.; Duan, Y.; Wang, J. Relationship of meteorological factors and human brucellosis in Hebei province, China. Sci. Total Environ. 2020, 703, 135491

30. Bogdan Doroftei, Ovidiu-Dumitru Ilie, Roxana-Oana Cojocariu, Alin Ciobica, Radu Maftei, Delia Grab, Emil Anton; Jack McKenna, Nitasha Dhunna; Gabriela Simionescu, Minireview Exploring the Biological Cycle of Vitamin B3 and Its Influence on Oxidative Stress: Further Molecular and Clinical Aspects, Molecules, 2020, 25(15), 3323; https://doi.org/10.3390/molecules25153323

31. Cecchini R, Cecchini AL. SARS-CoV-2 infection pathogenesis is related to oxidative stress as a response to aggression. Med Hypotheses. 2020;143:110102. doi:10.1016/j.mehy.2020.11010.