Nearly Identical Sequence in the SARS-CoV-2 RNA and Schizophrenia-associated Gene: Are COVID-19 and Schizophrenia Genetically Associated?

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July 7, 2020

Abstract

The unfortunate global outbreak of COVID-19 has had many implications in different aspects of public health, particularly mental and psychological wellbeing. Psychosis, or more specifically, schizophrenia, is a mental disorder of perplexing etiology, that has been said to occur partly due to genetic predisposition. Now amid the COVID-19 pandemic, new evidence suggests that there might be a genetic link between schizophrenia and SARS-CoV-2, the cause of COVID-19, that could have implications in the area of schizophrenia research.

Genetic Correlation Between COVID-19 and Schizophrenia

The initial measures taken by the majority of countries in the beginning of the COVID-19 pandemic, including the tried-and-true method of quarantine and the more recently developed strategy of social or physical distancing, were mostly effective in terms of prevention. However, they brought about several other complications for patients with underlying mental conditions such as psychosis; especially schizophrenia. There is now evidence suggesting that a small fraction of patients can actually develop psychosis a result of exposure to the novel coronavirus (Brown et al., 2020).

A mental disorder of multifactorial etiology, schizophrenia is an acknowledged cause of disability around the world. It encompasses an extensive array of altered mental functions, e.g., cognitive and behavioral impairment, that impose a great amount of expenses both to the patient and the healthcare system. Schizophrenia is said to be strongly associated with a number of genetic variations, as it shows an inheritance pattern in nearly 80 percent of the cases (Moudi et al., 2020).

"Netrin G1" or "NTNG1" is a gene located on the first chromosome, that is thought to contribute to the pathogenesis of schizophrenia. The transcriptional product of NTNG1 is ultimately processed into a protein, that plays an important role in the axon guidance during neuronal development. Interestingly, there might be a peculiar link between NTNG1 and the genetic material of SARS-CoV-2, since there are two specific sequences on both ends that share a great similarity to each other (Lehrer & Rheinstein, 2020).

SARS-CoV-2 is an enveloped virus, with a single-stranded RNA molecule as its genetic material. The overwhelmingly rapid spread of COVID-19 may potentially imply that the virus might have adapted to its human host sometime in the past. This could be true, since there is a 117-base pair sequence on the ORF1b gene of the novel coronavirus, that was also detected on NTNG1 in the human genome with a 94.6 percent similarity.

ORF1 is a vital gene with the longest sequence in the RNA of coronaviruses. The gene encodes several non-structural proteins (NSP), that as enzymes, are actively involved in the replication of the virus in the host cell. ORF1 consists of two immediately adjacent parts called ORF1a and ORF1b. Of the 16 NSPs being encoded by the ORF1 complex, five (NSP12 to NSP16) are located on the second segment or ORF1b (Hu et al., 2017). The recently discovered sequence, nearly identical to the one in NTNG1, stretches from NSP14 to NSP15. The former codes for an exoribonuclease, which corrects potential errors that might have occurred during the duplication of the viral genetic material. NSP15, on the other hand, is translated into a protein that is responsible for degradation of residual viral RNA, so that the virus can evade the antiviral defenses of the host cell (Lehrer & Rheinstein, 2020).

The human parallel sequence in the SARS-CoV-2 RNA is quite close to the sequence encoding the viral spike or S protein, which binds to the angiotensin-converting enzyme 2 (ACE2) on the surface of the host cell, prior to the internalization of the virus by the cell. The two sequences are only separated by a 904-base pair interval and NSP16 (Lehrer & Rheinstein, 2020).

Of lesser significance is the discovery of identical sequences in the SARS-CoV-2 RNA and the genome of chimpanzee. Similarly, three short sequences of different lengths, between 24 to 31 base pairs, have been identified on the chromosomes 1, 3 and 10 of chimpanzee, that share a varying similarity of 80 to 100 percent with specific sequences in the SARS-CoV-2 genome. However, no identical sequences were found in orangutan or bonobo (Lehrer & Rheinstein, 2020).

Nearly 8 percent of human DNA is made of "HERV" or "human endogenous retroviruses". These viral sequences have become integrated to our DNA throughout the course of human evolution, and are no longer recognized as foreign material. Some HERVs are responsible for the physiological tolerance between the fetal and maternal side of the placenta (Kurth & Bannert, 2010).

Conclusion

Despite the fact that SARS-CoV-2 is not a retrovirus, it is not totally unusual to come across a peculiar sequence in our DNA, that would be matched with that of another species. It would be too soon to judge about the possible link between COVID-19 and schizophrenia, as the findings are of preliminary nature. However, the existence of such a link could have important implications in prevention and treatment of COVID-19, especially in patients with schizophrenia.

Keywords : schizophrenia; NTNG1; SARS-CoV-2; ORF1; COVID-19

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