EPP0646

Nanopore sequencing as a novel approach to transcend into the deep universe of schizophrenia

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doi: 10.1192/j.eurpsy.2023.944

Introduction: Schizophrenia (SCZ) is a chronic neuropsychiatric disorder possessing a multifactorial nature and dual facets of symptoms with a core underlying genetic mechanism that is still obscure. Lately, genomic studies revealed numerous single nucleotide polymorphisms (SNPs) that are non-coding and influence ribonucleic acid (RNA) expression, particularly its splicing.

Objectives: Considering that next-generation sequencing (NGS) protocols focus upon long-read sequencing as opposed to conventional RNA sequencing methodologies once with the advent of Oxford Nanopore Technologies' (ONT) MinION, we primarily aimed to gather and review all evidence into how this approach may deepen and further offer insight into SCZ still undiscovered domain.

Methods: The relevant literature searches were performed using distinct combinations of keywords including "schizophrenia" alongside „Nanopore", "MinION", and "Oxford Nanopore Technologies" on four databases (PubMed/Medline, ISI Web of Knowledge, Scopus, and ScienceDirect). We implied the entries to strictly "research articles" written in English as inclusion criteria.

Results: By restricting the returned results starting with the year when the platform was officially launched, a total of n = 69 studies were displayed between the pre-established interval (2014 – 2022). If taken per database, n = 2 were identified in PubMed/Medline, n = 7 in ISI Web of Knowledge, n = 4 in Scopus, and n = 56 in ScienceDirect. In chronological order, n = 0 were published in 2014, n = 3 in 2015, n = 7 in 2016, n = 7 in 2017, n = 9 in 2018, n = 3 in 2019, n = 7 in 2020, n = 19 in 2021 and n = 14 in 2022. Finally, per the strategy applied, n = 49 were returned for "schizophrenia" + "Nanopore" from which n = 2 in PubMed/Medline, n = 5 in ISI Web of Knowledge, n = 4 in Scopus, and n = 38 in ScienceDirect. For "schizophrenia" + "MinION, there was a cumulative number of n = 5, from which we had n = 0 in PubMed/Medline, n = 0 in ISI Web of Knowledge, n = 0 in Scopus, and n = 5 in ScienceDirect. Finally, for "schizophrenia" + "Oxford Nanopore Technologies" were displayed n = 15, and the situation was n = 0 in PubMed/Medline, n = 2 in ISI Web of Knowledge, n = 0 in Scopus, and n = 13 in ScienceDirect.

Conclusions: We presently assist to a fulminant ascension in the literature, with applicability in other fields. Perhaps as cornerstone stands a recent publication in which the authors reveal the risk of the Calcium Voltage-Gated Channel Subunit Alpha1 C (*CACNA1C*) gene involved, being identified thirty-eight novel exons and two hundred and forty-one novel transcripts following RNA purification from six regions (cerebellum, striatum, and dorsolateral prefrontal cortex) among which targeted were cingulate, occipital and parietal cortexes.

Disclosure of Interest: None Declared

EPP0647

The suitability of zebrafish (danio rerio) as an optimal organism to further investigate the associated schizophrenia-like phenotype

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doi: 10.1192/j.eurpsy.2023.945

Introduction: Zebrafish (*Danio rerio*) has evolved over the years as a preferred organism due to its vast repertoire in research fields that mimic a targeted phenotype, particularly behavioral typologies and specific attributes comparable to murine models and relatively high homology with humans. Considering this consideration, different pharmacological treatments have been tested and proven that under different concentrations may trigger schizophrenia (SCZ)-like symptoms.

Objectives: Starting from the actual stage of knowledge according to which agents used as N-methyl-D-aspartate (NMDA) inhibitors (MK-801, ketamine, and phencyclidine) alongside psychedelic (mescaline, lysergic acid diethylamide), psychoactive substances (amphetamine), and non- and essential amino acids (proline and methionine), we aimed to reunite and review all existing evidence. This approach may offer an updated and critical overview regarding the possible future directions surrounding these compounds regarding the pharmaco-dynamics/kinetics.

Methods: To ensure the coverage of all relevant literature, we performed searches in four databases (PubMed/Medline, ISI Web of Knowledge, Scopus, and ScienceDirect) per combinations of keywords: "schizophrenia" with "MK-801", "ketamine", "phencyclidine", "mescaline", "lysergic acid diethylamide", "amphetamine", "proline", "methionine", and "zebrafish". Eligible studies had to be "research article(s)" written in English.

Results: A total of n = 246 studies were returned during the established interval (2010 – 2022). Precisely, n = 16 were identified in PubMed/Medline, n = 16 in ISI Web of Knowledge, n = 17 in Scopus, and n = 197 in ScienceDirect per database. If taken per year, n = 13 were published in 2010, n = 12 in 2011, n = 15 in 2012, n = 24 in 2013, n = 21 in 2014, n = 21 in 2015, n = 32 in 2016, n = 8 in 2017, n = 12 in 2018, n = 9 in 2019, n = 17 in 2020, n = 34 in 2021, and n = 28 in 2022. Depending on the combination of keywords, we had the following situation: n = 65 for "schizophrenia+MK-801+zebrafish", n = 42 for "schizophrenia+ketamine+zebrafish", n = 21 for "schizophrenia+phencyclidine+zebrafish", n = 4 for "schizophrenia+mescaline+zebrafish", n = 5 for "schizophrenia+lysergic acid diethylamide+zebrafish", n = 36 for "schizophrenia+amphetamine+zebrafish", n = 37 for "schizophrenia+proline+zebrafish", n = 36 for "schizophrenia+methionine+zebrafish".

Conclusions: There can be seen an uprising trend in the current literature of studies focused on the administration of MK-801, ketamine, amphetamine, proline, methionine, and phencyclidine aiming to trigger SCZ-like symptoms as opposed to mescaline and lysergic acid diethylamide. Most of the data is contradicting, with