methods: Differentiated SH-SY5Y cells (dopaminergic phenotype) were used as the in vitro model. The compounds cytotoxicity (0-25 µM) was evaluated, 24h after exposure, by the neutral red uptake and resazurin reduction assays, to select non-cytotoxic concentrations. To evaluate the potential neuroprotective effects against iron (III)-induced cytotoxicity, the cells were exposed to ferric nitrilotriacetate (FeNTA, 500 and 1000 µM, 24h), a ferric (Fe3+) iron aggressor, in the presence and absence of compounds. Also, the cells were exposed to MPP+ (500 and 1000 µM), a neurotoxin that induces an in vitro PD model, with or without simultaneous exposure to the tested compounds, and their potential protective effects evaluated 24h after exposure. Moreover, the compounds effects on the activity of P-glycoprotein (P-gp), an efflux transporter impacting several neurodegenerative diseases [5], were assessed through the rhodamine 123 accumulation assay. **Results:** The dual-acting agents demonstrated to be safe towards differentiated SH-SY5Y cells, and with minor effects on P-gp activity, therefore presenting a small potential for pharmacokinetic interactions. Noteworthy, several of the tested derivatives showed a significant protection against MPP+- and FeNTA-induced cytotoxicity, 24h after exposure to the aggressors, highlighting their promising neuroprotective effects. **Conclusions:** In conclusion, the new dual-acting agents tested demonstrated their potential use as a new therapeutic disease-modifying strategy for PD.

Keywords: Parkinson's disease; catechol O-methyltransferase (COMT); dopamine; ferroptosis; hydroxypyridin-4-ones

References:

[1] Oertel, WH. Recent advances in treating Parkinson's disease. F1000Research 6: 260-260, 2017.

[2] Raza C, Anjum R, Noor Ul Ain S. Parkinson's disease: Mechanisms, translational models and management strategies. Life Sciences 226: 77-90, 2019.

[3] Moreau C, Duce JA, Rascol O, Devedjian JC, Berg D, Dexter D, Cabantchik ZL, Bush AI, Devos D. Iron as a therapeutic target for Parkinson's disease. Mov Disord 33: 568-574, 2018.

[4] Dong J, Yanhua C, Song L, Weidong L. Current Pharmaceutical Treatments and Alternative Therapies of Parkinson's Disease. Curr Neuropharmacol 14: 339-355, 2016.

[5] Gil-Martins E, Barbosa DJ, Silva V, Remião F, Silva R. Dysfunction of ABC transporters at the blood-brain barrier: Role in neurological disorders. Pharmacology & Therapeutics 213: 107554, 2020.

POSTER 130

The impactof cannabinoids in Schizophrenia: a systematic review

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Resumo

Introduction: The association between the use of Cannabis and the development of schizophrenia has been a heavily researched and debated topic for over three decades. Due to the high morbidity and mortality of schizophrenia, and to the extensive, widespread use of cannabinoids, it is important to clarify if Cannabis abuse is in fact a component cause or even a direct trigger of the onset of this disease. **Objectives:** The present work aimed at conducting a systematic review of the available literature to determine the likelihood of an association between the consumption of cannabinoids and the incidence of schizophrenia. **Methods:** A thorough research of scientific publications was performed on multiple databases, including PubMed, Scielo, Science.gov, BMC, Cochrane, Google Scholar, and other relevant sources. A total of 6,328 published articles were found through specific combinations of keywords related to Cannabis/cannabinoids and schizophrenia. After application of exclusion criteria (e.g., duplicates; studies in idioms other than English, Portuguese and Spanish; conference abstracts; letters to the Editor; reviews; meta-analysis; articles not fully available; animal, in vitro or in situ studies; studies on the treatment of schizophrenia or cannabis-related complications; studies on schizophrenia remission; postmortem studies; questionnaires), 58 studies were included in this systematic review. **Results:** Most of the studies (52 out of 58) described a close association between Cannabis consumption and the onset of schizophrenia, or at least an increased risk of development of the disease. Some of the studies (4) further

showed a dose-response relationship. An association for vulnerable individuals was only described in 14 publications. Six studies associated Cannabis use with an earlier onset of schizophrenia when compared to schizophrenic patients who had no consumption history. Only 6 studies were unable to find any correlation.**Conclusions:** Data from this systematic review collectively support an involvement of Cannabis abuse in the onset of schizophrenia, which substantiates the need to raise public awareness about the consumption of cannabinoids. Nevertheless, further studies are essential to determine the precise role of Cannabis use on the development of this type of psychotic disorders, and the potential factors (genetic or environmental) influencing this association.

Keywords: cannabis use disorder; synthetic cannabinoids; phytocannabinoids; tetrahydrocannabinol (THC); Mental health

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POSTER 131
Acidúrica malónica

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Resumo

Introdução: A acidúrica malónica (AM) é uma doença hereditária autossómica recessiva do metabolismo, diagnosticada no rastreio neonatal. Deve-se a uma deficiência da malonil Co-A descarboxilase, com acumulação de ácido malónico, sendo uma patologia muito. Consequentemente, existe inibição de várias vias metabólicas como o ciclo de Krebs, a neoglicogénese e a oxidação de ácidos gordos de cadeia longa.**Objetivos:** Os objetivos deste trabalho têm como fundamento explicar o que é a AM, perceber como é feito o diagnóstico e apresentar dois estudos científicos.**Material e Métodos:** O método usado consistiu no rastreio de recém-nascidos para doenças metabólicas hereditárias, e na realização de análises bioquímicas e ao gene MLYCD (malonil coenzima A) para o diagnostico da doença.Foi analisado um caso real e obtiveram-se os seguintes resultados: criança coreana de 3 meses de idade diagnosticada com AM admitida no hospital para diagnóstico de uma cardiomegalia. O rastreio para doenças metabólicas hereditárias mostrou um resultado normal mas a análise ao gene MLYCD assim como as análises bioquímicas confirmaram o diagnóstico de AM. O paciente apresentava níveis elevados de malonilcarnitina(C3DC), elevada excreção urinária de malonato e foi identificada uma nova mutação no codão de iniciação do gene MLYCD. Em 2020, com 5 anos, e com uma dieta adaptada, apresentava uma significativa melhoria da função cardíaca. **Conclusões:** Apesar do rastreio neonatal poder detetar a maioria dos casos, os médicos devem estar cientes de que os sintomas podem aparecer anteriormente, porém um resultado negativo não exclui a doença. A implementação precoce de uma dieta restrita em gorduras de cadeia longa e rica em hidratos de carbono e triglicerídeos de cadeia média, em combinação com medicamentos cardíacos melhora o resultado da doença cardíaca, mas não evita as deficiências no desenvolvimento neurológico e anormalidades. Então aconselha-se implementar uma vigilância do SNC como padrão.

Palavras-chave: acidúria malónica; MLYCD; erros inatos do metabolismo; beta-oxidação; cardiomiopatia

Referências:

[1] Sarah Snanoudj, Stephanie Torre, Bénédicte Sudrié-Arnaud, Lenaig Abily-Donval, Alice Goldenberg, Gajja S. Salomons Stéphane Marret Soumeya Bekri Abdellah Tebani, Heterogeneous Clinical Scenario in a Consanguineous Family of Malonic Aciduria. International Journal of Molecular Sciences, 2021.

[2] Cristel Chapel-Crespo Dimitar Gavrilov, Mary Sowa Jessica Myers Debra-Lynn Day-Salvatore Haley Lynn Debra Regier Danielle Starin Maija Steenari Kees Schoonderwoerd Jose E. Abdenur, Clinical, biochemical and molecular characteristics of malonyl-CoA decarboxylase deficiency and long-term follow-up of nine patients, pag 113-121, volume 18, 2019.