"Youth 2.0 project": Multi-professional Intervention to Protect Adolescents from NPS and Other Drug Use

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Introduction: The COVID 19 pandemic has significantly affected the consumption of drugs determining a substantial increase in psychiatric discomfort and mental illness, especially among youth. Our study focuses the attention on Terni, a city in the center of Italy, actually defined by journalists as "the black heart of drug dealing in Umbria": in fact, according to the Central Directorate for Drug Services report, in this city more than half of the drug related deaths of Umbria are registered; in addition, more than 60% out of hashish, cocaine and heroin detected in Umbria are seized in Terni. To cope with these emerging challenges, the "Youth 2.0" Project in Terni, a city in the center of Italy heavy affected by the drug problem, aimed to provide a personalized tailored interventions for young people aged between 14-24 years old suffering from mental illness, psychiatric disorders, psychological distress and a wide range of substance/non-substance related forms of addictions in specific semi residential centers. The project, which involved schools-based intervention, group meetings and family meetings, clinical screenings among others, was implemented with the support of the families, law enforcement agencies, the Usl Umbria 2 Addiction Department and Child Neurodevelopmental Disorder Centre. The aim of our study is to evaluate the impact of such project on the intake of illegal substances among this cohort.
Methods: Retrospective analysis of the clinical data collected by Usl Umbria 2 Addiction Department concerning adolescents between 14 and 24 years old and comparison between those involved/not involved in the "Youth 2.0" Project during 2019-2022.
Results: A general increase in substance addictions rate (smoking, alcohol, drugs) was recorded. The consumption of illegal substances (in particular cannabinoids) grew of almost 10% (from 58% in 2019 to 64% in 2022). In addition, novel trends of substance misuse were also identified. Whereas heroin and cocaine were the most widespread substances, NPS, expecially cannabinoids, remained the preferred drug of choice in the population under 20 years of age. For what concern Youth 2.0 project, we noticed a significant decrease in cannabinoids use among adolescents in charge at the Usl Umbria 2 Addiction Department (from 3.9% in 2019 to 2.9% in 2022) with a parallel exponential growth (from 1.3% in 2019 to 5.2% in 2022) in adolescents monitored with Youth 2.0 Project.
Conclusions: Findings confirms the crucial importance of identifying and promoting appropriate intervention strategies in collaboration with various stakeholders (families, schools, police, clinical staff) to reduce the substance intake among young people. Considering also the function of self-care medication that some adolescents attribute to cannabinoids, these preliminary data lead us to assume that the "Youth 2.0 Project" provided a valid alternative to drug consumption especially for what concerns cannabinoids and derivatives.

doi: 10.1016/j.etdah.2023.100116

Synthetic Cannabinoid and Methadone Co-administration in Prolonging the QTc Interval

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Introduction: Synthetic cannabinoid receptor agonists (SCRAs) are frequently used with other psychoactive substances. We aimed to investigate the poly-pharmacology of SCRA-related deaths and mechanism of SCRA toxicity.
Methods: NPSAD analysis - Cases with post-mortem detections of SCRA(s) and/or methadone were extracted from the National Programme on Substance Abuse Deaths (NPSAD). In vitro pharmacology - Guinea pig hearts were perfused in standard Krebs solution at constant pressure. The ECG was recorded, with the beat-to-beat ventricular cycle length variability quantified. Methadone and the SCRA 5F-ADB were applied alone and in combination.
Results: NPSAD analysis - In SCRA-related deaths, methadone was the most commonly co-detected pharmaceutical medication (n=68/254 cases). The median methadone concentration in methadone-only deaths (0.66mg/L) was significantly higher than in deaths attributable to methadone-SCRA co-administration (0.47mg/L; $p<0.05$). In vitro pharmacology - Low dose (10¬μM) methadone elongated the QTc interval (13.8msec¬±2.6). Co-application of 5F-ADB further increased the QTc interval, in a dose-dependent manner (0.3-30nM), by a maximum of 60.9msec¬±7.4. 5F-ADB alone had no effect.
Conclusions: The SCRA 5F-ADB significantly reduces the toxicity threshold of methadone, likely via QT elongation. SCRA-related fatality may therefore be linked to co-administration with compounds that induce long QT syndrome. Careful consideration is needed when prescribing medications to people who use SCRAs.

doi: 10.1016/j.etdah.2023.100117

Potential Effects of Selected Synthetic Cannabinoids on Neuronal Senescence: Impact on Proliferation and Beta-Galactosidase Activity in SH-SY5Y Cells

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Introduction: Synthetic cannabinoids (SC) display a pharmacological mechanism similar to that of Δ9-tetrahydrocannabinol (THC), the key active principle of cannabis. SC are full agonists with higher potency at the CB1 and CB2 receptors, contrasting with THC's partial agonism. Cannabis use precipitates certain aspects of senescence/ageing, so it is plausible that SC act alike. Thus, for the present study the impact of SC exposure on in vitro neuronal cells proliferation and beta-galactosidase activity (a marker of senescence) was determined, to investigate their putative pro-senescence effects.
Methods: Human neuroblastoma SH-SY5Y cells were exposed to 1μM, 1nM and 1pM AMB-FUBINACA and ADB-FUBINACA for 24, 48, 72 and 96h, after which the sulforhodamine B assay (an indirect measure of cell proliferation) was conducted. To determine CB1R and CB2R involvement, the assays were repeated after cells' pre-incubation for 20 min in the presence of the selective antagonists, SR141716A and SR144528, respectively, at 0.5μM. Beta-galactosidase activity was measured in cells exposed to 1μM and 1nM AMB-FUBINACA for 22 passages (P24-46, 68 days), using the Enzo Life Sciences Cellular Secescence Activity Assay kit.
Results: At 96h, SH-SY5Y proliferation was increased after exposure to test concentrations of both SC ($p<0.05$); the use of CB1 antagonist reverted proliferation for AMB-FUBINACA, while CB2 antagonist reversed effects for both SC ($p<0.05$). Preliminary results show increased beta-galactosidase activity at passage 46 in SC-treated cells ($p<0.05$).
Conclusions: These results show a possible influence of SC on senescence-associated markers, proving the need to test additional neuronal ageing markers.

doi: 10.1016/j.etdah.2023.100118