

**שם: שירז ורד**

**שם העבודה:**

## **Examining the associations between cannabis use, endocannabinoid system and brain health in older adults**

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### **Abstract**

#### **Background**

Due to changes in policies and perceptions, there has been an increase in cannabis use among middle- and older-aged adults. Yet, the implication of cannabis use on brain health is unknown. In addition, the endocannabinoid system, which modulates the effects of cannabis on the brain, may have important roles in brain aging. However, this hypothesis is based almost entirely on evidence from preclinical studies.

#### **Research question**

Is cannabis use and the endocannabinoid system associated with brain health?

#### **General aim**

To examine the association between cannabis use, endocannabinoid system and brain health among middle aged and old adults.

#### **Specific aims**

1. To examine the association of cannabis use with cognitive function (H1a) and MRI measures (H1b) among middle-aged and old adults.
2. To examine the association of the endocannabinoid system with cognitive function (H2b) and MRI measures (H2c) among middle-aged and old adults.
3. To examine whether the endocannabinoid system mediate the association of cannabis use (as well as age, education and physical activity) with brain health (cognitive function and MRI measures) among middle-aged and old adults. (H2a, H2b, H2c).

#### **Importance and innovation**

A plethora of evidence exists on the health implications of cannabis use in young adulthood and adolescence. In the current research, we propose to assess the implications of late-life use on the brain. Our findings may inform cannabis users and clinicians about the implications of cannabis use in this stage of life and may improve risk-assessment. Additionally, pre-clinical studies suggest that the endocannabinoid system may be implicated in brain aging, yet humans studies are scarce and

limited to small sample sizes and the exploration of few endocannabinoids. Here, we aim to identify specific endocannabinoid patterns that are related to accelerated brain aging while utilizing an agnostic approach that allows simultaneous measurement of multiple endocannabinoids rather than focusing on a few candidate compounds.