



## Chronic Marijuana Use Affects Human Islet Feature and Function

### AUTHORS

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### PURPOSE

Medical and recreational marijuana use is on the rise, and has been described in 27 of 100 nPOD T1D organ donors. Although standards for reporting of human islet characteristics have recently been established, and adapted by at least two major diabetes journals in 2019, lifestyle was not considered in the reporting recommendations. We hypothesized that chronic marijuana use in non-diabetic organ donors negatively impacts islet outcomes. To test this, characteristics and function of human islets isolated from pancreata of chronic marijuana users and non-user were examined.

### METHODS

Ten organ donors with a history of chronic marijuana use were matched for age, sex, and ethnicity to 19 individuals without documented use of marijuana. Characteristics and function of human islets from both donor groups were assessed *in vitro*, including immunofluorescent staining of cannabinoid receptors (CBRs). Islets were then transplanted into diabetic NOD SCID mice and the ability to reverse diabetes was assessed.

### SUMMARY OF RESULTS

There were no significant differences between groups in any of the established standards for reporting, including age, sex, BMI, cause of death, HbA1c levels, cold ischemia time, purity, viability, and glucose-stimulated insulin secretion (GSIS). Additionally, no differences were noted in ethnicity, blood glucose at admission, digested pancreas weight or time, and pre- or post-purification or culture IEQ yields.

Macroscopically, pancreata from marijuana users were darker in color and firmer on handling, compared to those from non-users. Compared to non-user islets, those from marijuana users appeared degranulated/mosaic and stained faintly with dithizone. Immunofluorescent staining showed that CBR1 expression was intensified in islets from chronic marijuana users compared to non-users. Moreover, statistically significant differences were found in the ability of transplanted islets to reverse diabetes in mice between the user and non-user groups ( $p=0.019$ ). Islets from 33% of marijuana-users reversed diabetes when transplanted into mice (3 out of 9). In contrast, islets isolated from non-user pancreata reversed diabetes in 79% of cases (15 out of 19). Finally, at four weeks post-transplantation, islets from chronic marijuana users displayed fewer insulin-positive cells compared to islets from non-user groups.



## CONCLUSIONS

Islets from chronic marijuana users more often fail to reverse diabetes upon transplantation into mice, suggesting that these cells are functionally inferior to those islets isolated from pancreata of marijuana-free donors.

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