

# EFFECT OF MARIJUANA USE ON THYROID FUNCTION AND AUTOIMMUNITY

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## INTRODUCTION

- Medicinal Cannabis use has been legalized in twenty four states thus far.
- Hillard and Lomax have shown that acute administration of the tetrahydrocannabinol (THC) in mice reduces the levels of T4 and TSH by as much as 90% for up to 6 hours. When THC is taken chronically, however, the thyroid depressant effect is lost, which may indicate the development of tolerance (1, 2).
- In human subjects there are two conflicting reports on the chronic effect of marijuana use on thyroid function, but acute effects of marijuana have not been studied. (3)
- Furthermore, several studies have shown that cannabis has immune modulatory effects in other autoimmune conditions, but to our knowledge no data is available on the effect of cannabis on autoimmune thyroiditis.
- We conducted a two year cross sectional analysis of National Health and Nutrition Examination Survey (NHANES) data (2009-2010 and 2011-2012) collected by the Center for Disease Control and Prevention (CDC).

## METHODS

- Two periods of NHANES data (2009-2010, 2011-2012) on self reported marijuana use, thyroid function tests, and  $\alpha$ -TBGA and  $\alpha$ -TPOA levels were merged for this analysis.
- Questions were self-administered using the ACASI, assessing life time marijuana use, timing and frequency of use.
- We categorized subjects into two groups: 1) recent marijuana users (used within 30 days of testing) and 2) past users (more than 30 days of testing) or non-users.

## METHODS

- Frequency and timing of absolute marijuana usage were compared with thyroid hormone and antibody levels using Spearman correlation analysis.
- We categorized each thyroid parameter as normal and abnormal, using the NHANES cut offs.
- Data were placed into 2x2 tables, and Fischer exact test was then used to compare levels of thyroid hormones (normal and abnormal) and antibody positivity between the two groups of recent users versus past users or non-users. All tests were done using p value 0.05 as the level of significance.

## RESULTS

- A total of 4851 subjects who responded to NHANES questionnaire regarding marijuana use from two NHANES data sets were analyzed.
- A total of 53% of the subjects reported lifetime cannabis use with 18 % reporting recent use in the last 30 days.
- There were weak but statistically significant inverse correlations between recent marijuana use and thyroid antibody levels:  $\alpha$ -TBGA and  $\alpha$ -TPOA ( $r = -0.07$ ,  $p = 0.003$  and  $r = -0.05$ ,  $P = 0.02$ , respectively), while free T3 showed a significant positive correlation ( $r = 0.05$ ,  $P = 0.04$ ) (table 2)

Variable	N	Mean	SD	Median	Minimum	Maximum
Thyroglobulin antibodies (IU/mL)	1696	4.205	49.847	0.60	0.60	1672
Triiodothyronine (T3), free (pg/mL)	1712	3.328	0.735	3.30	2.10	28.84
Thyroxine, free (ng/dL)	1715	0.816	0.142	0.80	0.26	2.30
Thyroid stimulating hormone (uIU/mL)	1714	1.793	3.054	1.38	0.03	99.56
Thyroid peroxidase antibodies (IU/mL)	1699	18.044	85.046	0.60	0.18	942.00

## RESULTS

- Using the 2x2 tables and based on the NHANES cutoff of 4IU/mL for positive TBGA, recent marijuana users showed a significantly lower rate of rate of positive TBGA (2.8 % in recent users versus 6.1 % in non users /chronic users) compared to non-users or past users. (Table 3)

Variables	Thyroglobulin antibodies (IU/mL)	Triiodothyronine (T3), free (pg/mL)	Thyroxine, free (ng/dL)	Thyroid stimulating hormone (uIU/mL)	Thyroid peroxidase antibodies (IU/mL)
Marijuana use (n)	$r = 0.05662$ (1536) $P = 0.0265$	$r = 0.0527$ (1553) $P = 0.0402$	$r = 0.024$ (1554) $P = 0.27$	$r = 0.03330$ (1553) $P = 0.1896$	$r = -0.07503$ (1541) $P = 0.0032^*$

Table 3. Fischer exact test to compare levels of anti-thyroglobulin antibody between marijuana user and non-users/past-users.

Marijuana use	Anti-thyroglobulin antibody (IU/mL)		
	Normal (negative)	Abnormal (positive)	Total
Never or more than 30 days Number (percentage)	1328 (93.92%)	86 (6.08%)	1414 (83.3%)
Within past 30 days Number (percentage)	274 (97.16%)	8 (2.84%)*	282 (16.6%)
All subjects Number (percentage)	1602 (94.46%)	94 (5.54%)	1696 (100%)

## DISCUSSION

- Subjects who reported recent marijuana use have a lower prevalence of thyroid autoimmunity.
- We also found a trend of higher T3 levels in acute users.
- No significant differences in other thyroid parameter were noted.

## DISCUSSION

- Our data suggests that marijuana use may have immune modulatory effects on the thyroid gland.
- It is well known that endocannabinoid receptor-2 (CB2) activation is linked to suppression of immunity and has been implicated in several autoimmune disorders including multiple sclerosis, rheumatoid arthritis, colitis and hepatitis and recently in uveitis .
- However, involvement of CB2 in thyroid autoimmunity has not been reported in human or animals yet.
- The mechanism by which CB2 activation leads to inhibition of the humoral immune response may be through direct effects on immune cells as well as by changing the expression of various cytokines. Studies have suggested that exogenous cannabinoids elicit a shift in the cytokine expression profile from the Th1 pro inflammatory to anti-inflammatory Th2. (4)
- In conclusion, our data suggests that THC may have a role in modulating thyroid autoimmunity with clinical implications for a possible protective association between THC and Hashimoto's Thyroiditis, or Autoimmune Acquired Hypothyroidism. Clinical trials evaluating the effects of acute and chronic marijuana administration on thyroid autoimmunity and function are necessary.

## REFERENCES

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