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## Epidemiological Research on Ecstasy and Marijuana

**Objective:** The main objective of this study is to assess the interest in commonly abused and co-consumed illegal drugs, ecstasy and marijuana (also known as 3,4-methylenedioxyamphetamine (MDMA) and tetrahydrocannabinol (THC), respectively), utilizing google trends data. The primary goal of this study is to assess the interest in commonly abused and co-consumed illegal drugs, ecstasy and marijuana (also known as 3,4-methylenedioxyamphetamine (MDMA) and tetrahydrocannabinol (THC), respectively), utilizing google trends data.

**Materials and Methods:** A retrospective analysis was conducted based on google trends between 2004 and 2021, utilizing the keywords ecstasy and marijuana in Türkiye (T) and world (W). Relative Search Volumes (RSV) were assessed using the GraphPad statistical method.

**Results:** During the period of 2007-2021, the increasing trend in interest for ecstasy (T) and marijuana (W) persisted and was statistically significant (\* $p < 0.05$ ). However, the interest in marijuana (T) and ecstasy (W) statistically decreased in the third five-years period compared to the second five-years period (\* $p < 0.05$ ). Additionally, a positive linear relationship for these drugs was observed both in T and W ( $r = 0.2232$ ;  $p < 0.001$  and  $r = 0.4609$ ;  $p < 0.0001$ , respectively).

**Conclusion:** In utilizing this technology, insights can be drawn to prevent and address the worldwide public health issue of drug demand, supply, and addiction.

**Key Words:** Ecstasy, google trends, marijuana, MDMA, THC

### Ekstazi ve Esrar Üzerine Epidemiyolojik Araştırma

**Amaç:** Bu çalışmanın temel amacı, sıklıkla kötüye kullanılan ve birlikte tüketilen yasadışı uyuşturucular olan ekstazy ve marihuana (aynı zamanda sırasıyla 3,4-metilendioksümetamfetamin (MDMA) ve tetrahidrokanabinol (THC) olarak da bilinir) olan ilgiyi google trend verileri kullanarak değerlendirmektir.

**Gereç ve Yöntem:** 2004-2021 yılları arasında, Türkiye (T) ve dünyada (W) ekstazi ve esrar anahtar kelimeleri kullanılarak google trendse dayalı olarak geriye dönük bir analiz gerçekleştirildi. Göreceli Arama Hacimleri (RSV), GraphPad istatistiksel yöntemi kullanılarak değerlendirildi.

**Bulgular:** 2007-2021 döneminde, ekstazi (T) ve esrar (W) ilgisindeki artış eğilimi devam etmiş ve istatistiksel olarak anlamlı bulunmuştur (\* $p < 0.05$ ). Esrar (T) ve ekstazi (W) ise üçüncü beş yıllık dönemde ikinci beş yıllık döneme göre istatistiksel olarak azalmıştır (\* $p < 0.05$ ). Ayrıca, bu ilaçların T'de ve W'da pozitif doğrusal bir ilişkiye sahip olduğu belirlenmiştir (sırasıyla  $r = 0.2232$ ;  $p < 0.001$  and  $r = 0.4609$ ;  $p < 0.0001$ ).

**Sonuç:** Bu teknoloji ile dünya çapında bir halk sağlığı sorunu olan uyuşturucu talebini, arzını ve bağımlılığını önlemek için çıkarımlar yapılabilir.

**Anahtar Kelimeler:** Ekstazi, google trends, esrar, MDMA, THC

### Introduction

Psychoactive substances represent a prevalent and frequently favored category among contemporary youth, primarily for recreational purposes (1). Within this classification, MDMA colloquially known as ecstasy or molly, stands out as a prominent substance. Functioning as a psychoactive drug, MDMA elicits its effects by augmenting the activity of serotonin, dopamine, and norepinephrine neurotransmitters (2). Recognized for its classification within the amphetamine drug category and its manifestation of hallucinogenic effects (3,4), MDMA captures attention due to the varied sensations reported by users. The drug is characterized by a swift elevation in MDMA concentration in the bloodstream post-ingestion, initiating within 30 minutes and peaking approximately 2 hours later (5). However, this pleasurable experience concludes roughly 5 hours later with a subsequent decrease in serotonin levels (6).

In addition to MDMA, another class of substances, namely synthetic cannabinoids, has gained prominence. Marketed under common aliases such as marijuana, hemp, K2, spice (7), and synthetic cannabis (8), these substances were promoted as herbal incense or herbal smoking blends (9). Synthetic cannabinoids operate by binding to the same receptors as cannabinoids (THC) and cannabidiol (CBD) found in cannabis plants (10). The effects of Delta-9-THC, a key component, are mediated through partial agonist activity at the cannabinoid receptor CB1 in the central nervous system, as well as at the

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CB2 receptor expressed in immune system cells (11). Following metabolism, THC is primarily converted to 11-OH-THC in the body (12) and subsequently excreted in the feces and urine (13).

The internet, functioning as a medium that includes platforms like google, serves as a facilitator for the dissemination of user-shared experiences related to substance use through reports. This virtual space plays a significant role in the analysis of the temporal popularity of prominent search queries on google, accessible in different languages and geographic regions. The metric utilized for this analysis is termed as RSV, determined by the monthly scores provided by google trends. These scores are graphically represented, with the peak value of 100 representing the highest google search volume for one or more specified keywords (14). Today, analyses based on mathematical equations are gaining significance in the field of healthcare (15). Similarly, google trends studies rely on statistical data comparably.

The study aims to analyze interest fluctuations in ecstasy and marijuana between 2004 and 2021, explore their potential correlation in searches, identify substance abuse patterns, and assess public interest using google trends data.

#### Strengths and limitations of this study

**Strengths:** Google trends data is instrumental in identifying the increasing interest in drug abuse and addictive substances.

It serves as a valuable resource for enhancing public awareness and evaluating shifts in information-seeking behaviors related to highly addictive substances with medicinal applications, such as amphetamine and THC.

**Limitations:** Google trends data is only accessible at the state level, potentially compromising user privacy by providing personal data without their explicit knowledge. This limitation affects the comprehensiveness of search volume analysis.

Web-Searched Research Questions:

What are the subjective effects of ecstasy?

What is the mechanism of action for ecstasy?

How does marijuana impact casual users?

How does marijuana affect children when they first start using it?

How does marijuana influence a woman's body?

How does marijuana impact older adults?

What is the impact of regular medical marijuana use on patients' lives?

#### Materials and Methods

**Data Collection:** In this research, the 'all categories' option was selected as the search category, and the most prevalent drugs in the public were identified using the keyword 'drug misuse'. Utilizing google trends, the 'Subject' field was explored by

entering the most commonly used names in society, namely 'ecstasy' and 'marijuana', spanning from the earliest period (January 2004) to the present (November 2021). Searches were conducted for both T and W. The outcomes of this search, presented in comma-separated-values, were exported to an excel file for further analysis.

**Study Design:** The primary results of monthly google RSV for T and W since 2004 for 'ecstasy' and 'marijuana' were obtained and compared within four groups. The first period covers the years 2004-2006. The purpose of choosing this date range is that Turkiye's European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) membership was initiated in 2004 and accepted in 2007 (16). The other groups were formed by dividing them into five-year intervals between 2007 and 2021. In the second step of the study, the relationship between interest in 'ecstasy' and 'marijuana' was examined, since drug users also tend to other addictive substances.

Data is searched in English regarding the world scope and in Turkish for data limited to T (17). Translation of keywords has been confirmed using English-Turkish/Turkish-English translation using google translate.

**Statistical Analysis:** Customized tables (18) were utilized to determine the sample size. GraphPad Prism 6.00 (GraphPad Software, USA) was employed for data analysis. The normality of data was assessed using the Shapiro-Wilk normality test. Based on the results, the data from Turkiye did not exhibit a normal distribution. The Kruskal-Wallis test was employed, followed by the application of Dunn's post-hoc test. Spearman's rho correlation analysis was also conducted. Our data obtained worldwide demonstrated a normal distribution. The one-way ANOVA test was applied, followed by the utilization of Tukey's post-hoc test. Pearson correlation analysis was also used. Statistical significance was set at P values below 0.05.

#### Results

The investigation involved the querying of 'ecstasy' and 'marijuana' keywords on google trends spanning from January 2004 to December 2021, both within T and W. Beyond tracking the evolving interest in ecstasy and marijuana over the years, the study also delved into understanding the correlation between these two substances.

In Turkiye, Relative Search Volume (RSV) values for ecstasy exhibited variations across four distinct time brackets (2004-2006, 2007-2011, 2012-2016, and 2017-2021), registering values of 41.00 (16.00-94.00), 9.00 (3.00-75.00), 12.00 (7.00-100.0), and 14.00 (6.00-61.00), respectively. The initial period of 2004-2006 displayed a significantly higher RSV compared to subsequent periods (\*p<0.05). A subsequent rise was observed post-2007, with the 2007-2011 period showing a notable decline compared to the last two five-year spans (\*p<0.05; Table 1A and Figure 1A).

**Table 1.** (A) Comparison of the RSV score of ecstasy (T) between 2004-2021 in terms of four different periods (\*p<0.05). (B) Comparison of the RSV score of marijuana (T) between 2004-2021 in terms of four different (\*p<0.05). (C) Comparison of the RSV score of ecstasy (W) between 2004-2021 in terms of four different periods (\*p<0.05). (D) Comparison of the RSV score of marijuana (W) between 2004-2021 in terms of four different periods (\*p<0.05).

RSV scores in Turkiye					
(A)	periods	n	median (min-max)	p value	test statistic
Ecstasy	2004-2006 <sup>bcd</sup>	1095	41.00 (16.00-94.00)	*p<0.05	79.71
	2007-2011 <sup>acd</sup>	1095	9.00 (3.00-75.00)		
	2012-2016 <sup>ab</sup>	1095	12.00 (7.00-100.0)		
	2017-2021 <sup>ab</sup>	1095	14.00 (6.00-61.00)		
Marijuana	2004-2006 <sup>bcd</sup>	1095	55.50 (25-100)	*p<0.05	68.49
	2007-2011 <sup>ac</sup>	1095	35.50 (18.00-63.00)		
	2012-2016 <sup>abd</sup>	1095	41.00 (25.00-100.0)		
	2017-2021 <sup>ac</sup>	1095	32.00 (22.00-100.0)		
RSV scores World					
(C)	periods	n	mean ± std	p value	test statistic
Ecstasy	2004-2006 <sup>bd</sup>	1095	75.67 ± 11.49	*p<0.05	38.34
	2007-2011 <sup>acd</sup>	1095	59.37 ± 5.17		
	2012-2016 <sup>bd</sup>	1095	73.83 ± 9.75		
	2017-2021 <sup>abc</sup>	1095	65.60 ± 8.94		
Marijuana	2004-2006 <sup>b</sup>	1095	76.42 ± 12.22	*p<0.05	38.25
	2007-2011 <sup>acd</sup>	1095	62.40 ± 6.5		
	2012-2016 <sup>b</sup>	1095	77.95 ± 9.41		
	2017-2021 <sup>b</sup>	1095	79.55 ± 11.23		

a-d values with different letters within a row were significantly different (\*p<0.05)

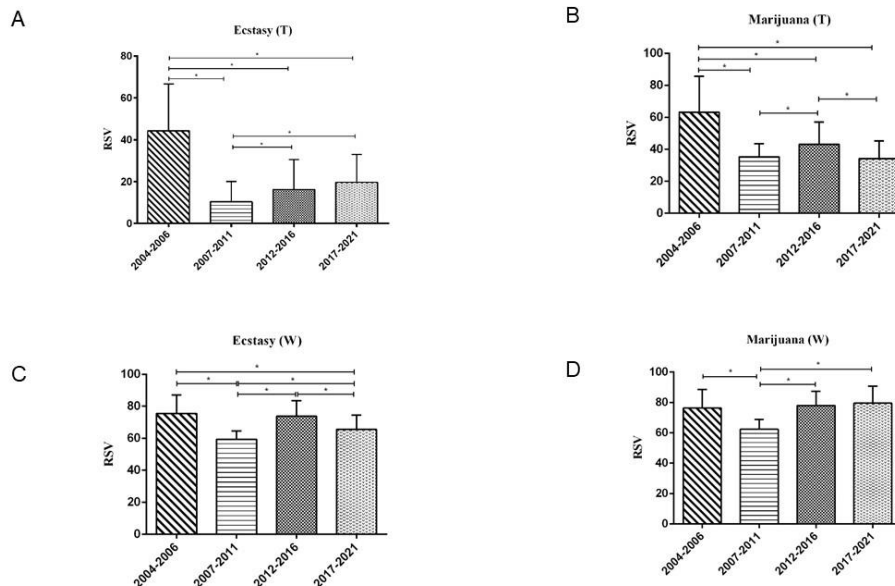
<sup>a</sup> p<0.05 compared to the 2004-2006 period

<sup>b</sup> p<0.05 compared to the 2007-2011 period

<sup>c</sup> p<0.05 compared to the 2012-2016 period

<sup>d</sup> p<0.05 compared to the 2017-2021 period

std: standard deviation



**Figure 1.** (A) Comparison of the RSV score of ecstasy (T) between 2004-2021 in terms of four different periods (\*p<0.05). (B) Comparison of the RSV score of marijuana (T) between 2004-2021 in terms of four different periods (\*p<0.05). (C) Comparison of the RSV score of ecstasy worldwide between 2004-2021 in terms of four different periods (p<0.05). (D) Comparison of the RSV score of marijuana worldwide between 2004-2021 in terms of four different periods (p<0.05).

For marijuana (T) RSV values, analysis covered the same time intervals (2004-2006, 2007-2011, 2012-2016, and 2017-2021), revealing values of 55.50 (25-100), 35.50 (18.00-63.00), 41.00 (25.00-100.0), and 32.00 (22.00-100.0), respectively. The period of 2012-2016 indicated an upswing compared to the initial and final five-year periods ( $p < 0.05$ ; Table 1B and Figure 1B).

On a W scale, the RSV values for ecstasy over four periods (2004-2006, 2007-2011, 2012-2016, and 2017-2021) were  $75.67 \pm 11.49$ ,  $59.37 \pm 5.17$ ,  $73.83 \pm 9.75$ , and  $65.60 \pm 8.94$ , respectively. RSV values between 2004-2006 and 2012-2016 significantly exceeded those of 2007-2011 and 2017-2021 ( $*p < 0.05$ ; Table 1C and Figure 1C).

Similarly, W RSV values for marijuana during the same four periods were  $76.42 \pm 12.22$ ,  $62.40 \pm 6.5$ ,  $77.95 \pm 9.41$ , and  $79.55 \pm 11.23$ , respectively. Although a notable decrease in RSV values occurred between 2007-2011 compared to 2004-2006 ( $*p < 0.05$ ), the last two time periods demonstrated a significant increase ( $*p < 0.05$ ; Table 1D and Figure 1D).

Correlation coefficients were computed for each keyword, employing Spearman's rho correlation analysis to establish the relationship between the interest in ecstasy (T) and marijuana (T). The findings revealed a significant positive correlation, albeit with a low strength ( $r = 0.2232$ ), between the levels of interest in ecstasy (T) and marijuana (T) ( $p < 0.001$ ). Consequently, the interest in ecstasy (T) and marijuana (T) exhibited a simultaneous increase with a modest degree of association. The variables were found to explain approximately 5% of the variance observed in each other (Table 2).

Pearson correlation analysis was employed to assess the relationship between interest in ecstasy (W) and marijuana (W). The worldwide interest in ecstasy and marijuana exhibited a moderate correlation ( $r = 0.4609$ ) and was significantly positive ( $p < 0.0001$ ). This indicates that there is a substantial connection between the levels of interest in ecstasy (W) and marijuana (W). The variance explained by the variables in relation to each other was calculated to be 21.24% (Table 3).

**Table 2.** Correlation between RSV values of ecstasy (T) and marijuana (T) between 2004-2021

	Ecstasy (T)	
	Spearman's $r_s$	p
<b>Marijuana (T)</b>	0.2232***	0.001

Data represents as Spearman's rho correlation coefficients ( $r_s$ ) and p values [\*\*\*Correlation is significant at the 0.001 level (two-tailed)]

**Table 3.** Correlation coefficient between RSV values of ecstasy (W) and marijuana (W) between 2004-2021

	Ecstasy (W)	
	Pearson's r	p
<b>Marijuana (W)</b>	0.4609****	0.0001

Data represents as Pearson's correlation coefficients (r) and p values [\*\*\*\*Correlation is significant at the 0.0001 level (two-tailed)].

## Discussion

Drug abuse and the use of addictive substances stand as prominent subjects within the realm of pharmaceutical toxicology. Medical toxicologists are frequently sought for consultations in treating individuals grappling with addiction to various substances, including alcohol, tobacco, heroin, lysergic acid, or others, across a spectrum of care settings (19). Notably, many highly addictive substances, such as amphetamine and THC, also possess legitimate medical applications. The illicit misuse of amphetamine, employed medicinally for attention deficit-hyperactivity disorder (ADHD), has become widespread in contemporary society (20). THC, the active component in marijuana, finds application as an anti-vomiting drug for cisplatin-induced vomiting (21).

MDMA ecstasy and cannabis, illicit substances prevalent in numerous countries, are frequently co-consumed. These substances take a forefront among addictive agents. An in vivo study observed that acute MDMA administration mitigated physical somatic withdrawal symptoms in THC-dependent mice (22). In the study, epidemiological evidence was presented to establish a correlation between drug use and supply. The findings elucidate a positive relationship between ecstasy and marijuana in both T and W since 2004. Recreational ecstasy/MDMA users commonly abuse cannabis, to mitigate the initial psychostimulant effects of MDMA and alleviate post-MDMA mood drops (23). Additionally, preclinical studies administering MDMA with THC aimed to provide neuroprotection and/or prevent toxicity, revealing that this combination induced hyperthermia while reducing hyperactivity (23). The escalation in MDMA and THC search volumes suggests their potential individual and combined usage.

Young individuals frequently combine legal and illegal drugs for recreational purposes. The United Nations European Drug Report highlights the co-use of marijuana and ecstasy among the young adult population (24). Despite marijuana being utilized to enhance psychotherapy effects in the 1970s, its contemporary usage has become illegal in various countries (25). Between 2005 and 2010, tranquilizer and sedative abuse constituted around 40% of all drug use in Europe (26). Opioid abuse is reported more frequently in men who use marijuana, tobacco, and alcohol (27). Ecstasy, having evolved into one of the psychostimulant

drugs for world recreational use, is particularly favored in nightlife settings (24). Hence, factors contributing to substance abuse can be assessed at individual, community, and societal levels, including peer norms (28).

Correlation analysis is crucial for understanding the relationship between public interest in ecstasy and marijuana, both in T and W. Factors such as police enforcement, anxiety regarding drug use, and potential health threats can negatively impact drug demand. The positive correlation between the RSV values of these drugs in T and W suggests that these two substances were collectively evaluated in search profiles as keywords. Türkiye's EMCDDA membership discussions and the initiation of trend data worldwide have been ongoing since 2004. Search data have progressively improved over time, leading to higher RSV values in the first two years. When evaluating this timeframe separately, the RSV values from the initial two five-year periods surpass those of the last five years. Our study reveals that, when examining the last five years

independently, the interest in marijuana searches surpassed that of ecstasy on a W scale, with a similar trend observed in T. While interpreting spikes in search volume may pose challenges, it undoubtedly elevates awareness of potential threat situations. This period might have been influenced by predictors such as police inspections, concerns, and health threats, which are crucial determinants of drug demand and supply.

As a valuable and easily accessible source of search data, google trends utilizes information accumulated over the years (29). This study, by presenting multi-year data on trends in illicit drug use, while not specifying a particular geographical location and lacking individual factor data, contributes to law enforcement's ability to respond effectively to drug production and distribution networks. Consequently, google trends, reflecting the intelligence and habits of a vast web search population and an internet-dependent society, facilitates the tracking of drug demand, supply, and addiction at a faster pace than traditional systems.

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