INTRODUCTION
Cannabinoid presentations are on the agenda for the upcoming American Academy of Pain Management meeting in Reno, Nevada (Sept 26-29th, 2002). For details see http://www.aapainmanage.org/.

BASIC SCIENCE

RATIONALE. Recent studies have shown that several pharmacological actions induced by cannabinoids, including antinociception and reward, involve the participation of the endogenous opioid system. OBJECTIVES. The present study was designed to examine the possible involvement of the different opioid receptors in the anxiolytic-like responses induced by Delta(9)-tetrahydrocannabinol (THC). METHODS. The administration of a low dose of THC (0.3 mg/kg) produced clear anxiolytic-like responses in the light-dark box, as previously reported. The effects of the pretreatment with the CB(1) cannabinoid receptor antagonist, SR 141716A (0.5 mg/kg), or the micro-opioid receptor antagonist, beta-funaltrexamine (5 mg/kg), the delta-opioid receptor antagonist, naltrindole (2.5 mg/kg) and the kappa-opioid receptor antagonist, nor-binaltorphimine (2.5 mg/kg) were evaluated on anxiolytic-like responses induced by THC. RESULTS. SR 141716A completely blocked the anxiolytic-like response induced by THC, suggesting that this effect is mediated by CB(1) cannabinoid receptors. The micro-opioid receptor antagonist beta-funaltrexamine and the delta-opioid receptor antagonist naltrindole, but not the kappa-opioid receptor antagonist nor-binaltorphimine, abolished THC anxiolytic-like effects, suggesting an involvement of micro- and delta-opioid receptors in this behavioural response. CONCLUSIONS. These results demonstrate that the endogenous opioid system is involved in the regulation of anxiety-like behaviour by cannabinoids and provide new findings to clarify further the interaction between these two neuronal systems.


The aim of this work was to investigate the effects of single and repeated administration of the endogenous cannabinoid anandamide (20 mg/kg i.p.) on cytochrome P450-mediated biotransformation in the rat. In liver microsomes from chronically treated rats, an increase in cytochrome P450 content and in the activity and immunoreactivity of cytochrome P450 reductase was detected. Immunoblot analysis of the hepatic microsomal proteins revealed an increase in the relative level of cytochrome P450 2B1/2 and 3A2. The activity of monoxygenase enzymes linked to specific cytochrome P450 isoforms was significantly enhanced. This increase in the content and activity of the cytochrome P450 system was also seen in liver microsomes from acutely treated rats; however, these increases were smaller than those seen after prolonged treatment. After acute treatment, the brain cytochrome P450 and b(5) content was increased, whereas after chronic treatment, only that of b(5) was enhanced. Cytochrome P450 reductase activity and its relative abundance were increased only in the brains of chronically treated rats. The present findings demonstrate that anandamide administration increased the metabolic activity of the cytochrome P450 system in rat liver and brain.

NF-kappaB is a transcriptional regulator that plays a key role in immunity, inflammation and programmed cell death. We generated a PC12 cell line termed PC12kappaBluc that contains an integrated NF-kappaB-responsive reporter gene to directly measure NF-kappaB activity. The "classical" activators of NF-kappaB, phorbol 12-O-tetradecanoate-13-acetate and tumor necrosis factor alpha, strongly induced NF-kappaB activity in PC12kappaBluc cells. Activation of NF-kappaB could be attenuated by preincubating the cells with the cAMP analogue dbcAMP or via expression of the superrepressor IkappaBalphaS32A/S36A. PC12kappaBluc cells were subjected to several apoptotic paradigms, including treatment with 6-hydroxydopamine, H(2)O(2), K(2)Cr(2)O(7), MnCl(2), C(2)-ceramide or the cannabinoid receptor-1 agonist CP55,940. A simultaneous measurement of the NF-kappaB activity revealed that only administration of 6-hydroxydopamine or CP55,940 increased NF-kappaB activity. Using pharmacological and genetic strategies to attenuate NF-kappaB transcriptional activity, we demonstrate that the elevation of NF-kappaB activity by 6-hydroxydopamine and CP55,940 is not an integral part of the apoptotic signaling cascade in PC12 cells.


Over the past two decades a number of endogenous compounds that act as ligands for the cannabinoid receptors has been discovered. In analogy with the "endorphins" these compounds have been called "endocannabinoids". Endocannabinoids have been demonstrated in many mammalian tissues including humans and are widely distributed in the CNS, peripheral nerves, uterus, leukocytes, spleen and testicles. The uterus contains the highest levels of anandamide, the first discovered endocannabinoid, suggesting an important role for this substance in reproduction. Several studies have shown anandamide to be involved in the regulation of implantation and reduced activity of the enzyme that degrades anandamide has been associated with early pregnancy loss in humans. The bulk of the literature concerning endocannabinoids is based upon anandamide related studies; therefore, in this review we focus on the metabolism of anandamide and its role in reproduction.


C-3 Amido-indoles were found to selectively bind to the CB2 receptor. SAR studies led to optimized compounds with excellent in vivo potency against LPS induced TNF-alpha release in murine models of cytokine production.


OBJECTIVE: We have investigated the involvement of the endocannabinoid system in the delayed cardioprotection conferred by heat stress preconditioning in the isolated rat heart. METHODS: Rats were divided into eight groups (n=7 in each group), subjected to either heat stress (42 degrees C for 15 min, HS groups) or sham anaesthesia (Sham groups). Twenty-four hours later, their hearts were isolated, retrogradely perfused, and subjected to a 30-min occlusion of the left coronary artery followed by 120 min of reperfusion. Some hearts were perfused with either SR 141716 (a cannabinoid CB(1) receptor antagonist, 1 &mgr;M), SR 144528 (a CB(2) receptor antagonist, 1 &mgr;M) or L-NAME (a NOS inhibitor, 3 &mgr;M) 5 min before ischaemia and during the ischaemic period. RESULTS: The infarct size-reducing effect conferred by heat stress (35.7+/-.1.8% in Sham to 14.1+/-.0.6% in HS groups) was not altered by the perfusion of SR 141716 (11.2+/-.1.5%) but was abolished by both SR 144528 (36.6+/-.1.6%) and L-NAME (32.0+/-.4.4%). In hearts from non-heat-stressed rats, perfusion with SR 141716 (32.8+/-.1.6%), SR 144528 (33.4+/-.2.2%) and L-NAME (31.6+/-.2.9%) had no effect on infarct size. CONCLUSION:
These results suggest an involvement of endocannabinoids, acting through CB(2) receptors, and NO in the cardioprotection conferred by heat stress against myocardial ischaemia. The possible interaction between both mediators of the heat stress response remains to be determined.


1 There is considerable interest in elucidating potential endogenously derived agonists of the vanilloid receptor and the role of anandamide in this regard has received considerable attention. In the present study, we have used an electrophysiological technique to investigate the mechanism of activation of vanilloid receptors in an isolated vagal preparation. 2 Both capsaicin and anandamide depolarized de-sheathed whole vagal nerve preparations that was antagonized by the VR1 antagonist, capsazepine (P<0.05) whilst this response was unaltered by the cannabinoid (CB1) selective antagonist SR141716A or the CB2 selective antagonist, SR144528, thereby ruling out a role for cannabinoid receptors in this response. 3 The PKC activator, phorbol-12-myristate-13-acetate (PMA) augmented depolarization to both anandamide and capsaicin and this response was significantly inhibited with the PKC inhibitor, bisindolylmaleimide (BIM) (P<0.05). 4 The role of lipoxygenase products in the depolarization to anandamide was investigated in the presence of the lipoxygenase inhibitor, 5,8,11-Eicosatriynoic acid (ETI). Depolarization to anandamide and arachidonic acid was significantly inhibited in the presence of ET1 (P<0.05). However, in the absence of calcium depolarization to anandamide was not inhibited by ETI. 5 Using confocal microscopy we have demonstrated the presence of vanilloid receptors on both neuropeptide containing nerves and nerves that did not stain for sensory neuropeptides. 6 These results demonstrate that anandamide evokes depolarization of guinea-pig vagus nerve, following activation of vanilloid receptors, a component of which involves the generation of lipoxygenase products. Furthermore, these receptors are distributed in both neuropeptide and non-neuropeptide containing nerves. British Journal of Pharmacology (2002) 137, 39-48. doi:10.1038/sj.bjp.0704840


Anandamide (N-arachidonylethanolamine), an arachidonic acid derivative, is an endogenous ligand for both the brain-type (CB1-R) and spleen-type (CB2-R) cannabinoid receptors. To investigate the possible effects of anandamide on embryo implantation in the mouse, we used a co-culture system in which mouse embryos are cultured with a monolayer of uterine epithelial cells. Our results indicate that 14 nM anandamide significantly promotes the attachment and outgrowth of the blastocysts on the monolayer of uterine epithelial cells, and those effects could be blocked by CB1-R antagonists SR141716A, but not by SR144528, a CB2-R antagonist. It suggests that the effects of anandamide on embryo attachment and outgrowth are mediated by CB1-R. However, 56 nM anandamide is capable of inhibiting the blastocyst attachment and outgrowth, we, therefore, conclude that anandamide may play an essential role at the outset of implantation.


Acquisition and storage of aversive memories is one of the basic principles of central nervous systems throughout the animal kingdom. In the absence of reinforcement, the resulting behavioural response will gradually diminish to be finally extinct. Despite the importance of extinction, its cellular mechanisms are largely unknown. The cannabinoid receptor 1 (CB1) and endocannabinoids are present in memory-related brain areas and modulate memory. Here we show that the endogenous cannabinoid system has a central function in extinction of aversive memories. CB1-deficient mice showed strongly impaired short-term and long-term extinction in auditory fear-conditioning tests, with unaffected memory acquisition and consolidation. Treatment of wild-type mice with the CB1 antagonist SR141716A mimicked the phenotype of CB1-deficient mice, revealing that CB1 is required at the moment of memory extinction. Consistently, tone presentation during extinction trials resulted in elevated levels of endocannabinoids in the basolateral amygdala complex, a region known to control extinction of aversive memories. In the
basolateral amygdala, endocannabinoids and CB1 were crucially involved in long-term depression of GABA (gamma-aminobutyric acid)-mediated inhibitory currents. We propose that endocannabinoids facilitate extinction of aversive memories through their selective inhibitory effects on local inhibitory networks in the amygdala.


Cannabinoid receptors and their endogenous ligands, the endocannabinoids, have been detected in several blood immune cells, including monocytes/macrophages, basophils and lymphocytes. However, their presence in dendritic cells, which play a key role in the initiation and development of the immune response, has never been investigated. Here we have analyzed human dendritic cells for the presence of the endocannabinoids, anandamide and 2-arachidonoylglycerol (2-AG), the cannabinoid CB1 and CB2 receptors, and one of the enzymes mostly responsible for endocannabinoid hydrolysis, the fatty acid amide hydrolase (FAAH). By using a very sensitive liquid chromatography-atmospheric pressure chemical ionization-mass spectrometric (LC-APCI-MS) method, lipids extracted from immature dendritic cells were shown to contain 2-AG, anandamide and the anti-inflammatory anandamide congener, N-palmitoylethanolamine (PalEtn) (2.1 +/- 1.0, 0.14 +/- 0.02 and 8.2 +/- 3.9 pmol.10^-7 cells, respectively). The amounts of 2-AG, but not anandamide or PalEtn, were significantly increased following cell maturation induced by bacterial lipopolysaccharide (LPS) or the allergen Der p 1 (2.8- and 1.9-fold, respectively). By using both RT-PCR and Western immunoblotting, dendritic cells were also found to express measurable amounts of CB1 and CB2 receptors and of FAAH. Cell maturation did not consistently modify the expression of these proteins, although in some cell preparations a decrease of the levels of both CB1 and CB2 mRNA transcripts was observed after LPS stimulation. These findings demonstrate for the first time that the endogenous cannabinoid system is present in human dendritic cells and can be regulated by cell activation.


All of the therapeutic properties of marijuana (analgesic, antiemetic, appetite stimulant, antiglaucoma) have been duplicated by the tetrahydrocannabinol (THC) molecule or its synthetic derivatives. Today, the molecular mechanisms of action of these compounds have led to a general understanding of the pharmacological effects of marijuana and of its therapeutic properties. These mechanisms involve the specific binding of THC to the 7-transmembrane (7TM) domain G protein-linked receptor, a molecular switch which regulates signal transduction in the cell membrane. The natural ligand of the 7TM receptor is an eicosanoid, arachidonylethanolamide (AEA), generated in the membrane and derived from arachidonic acid. THC acts as a substitute ligand to the 7TM receptor site of AEA. THC would deregulate the physiological function of the 7TM receptor and of its ligand AEA. As a result, the therapeutic effects of the drug may not be separated from its adverse psychoactive and cardiovascular effects. The binding of THC to the 7TM receptor site of AEA induces allosteric changes in the receptor sites of neurotransmitter and opiates resulting in variable interactions and pharmacological responses. The pharmacokinetics of THC with its prolonged storage in fat and its slow release result in variable and delayed pharmacological response, which precludes precise dosing to achieve timely therapeutic effects. The experimental use of THC and of its synthetic analogues, agonists, and antagonists has provided novel information in the nature of molecular signaling in the cell membrane. As a result, the relationships between allosteric receptor responsiveness, molecular configuration of proteins, and physiological regulation of cellular and organ function may be further investigated.


OBJECTIVE: Previous reports have shown that the Delta(9)-tetrahydrocannabinol (Delta(9)TCH), the major psychoactive cannabinoid components of marijuana, is unable to inhibit thyroid hormonal activity. The aim of this study was to characterize the CB1 functional expression in the rat thyroid by a multi-methods approach. METHODS AND RESULTS: RT-PCR was used to detect the mRNA expression of the CB1 cannabinoid receptor (17.8±4.0% of the normalizing reference gene beta(2) microglobulin), as well as the expression of the endocannabinoid hydrolyzing enzyme, fatty acid amide hydrolase (46.9±4.3% of beta(2) microglobulin), in the rat thyroid gland. The CB1-encoded protein was detected in its glycosylated form (63 kDa) by Western blot, employing a polyclonal antibody, while CB1 immunohistochemical localization showed an intracellular positive staining in both follicular and parafollicular cells. In addition, a 30% decrease in serum levels of both 3,5,3' tri-iodothyronine (T(3)) and thyroxine (T(4)) was detected 4 h after the administration of the synthetic cannabinoid receptor agonist, WIN 55,212-2 (10 mg/kg i.p.). These effects were antagonized by pretreatment with the CB1 antagonist SR 141716A (3 mg/kg i.p.); thyrotrophin levels were unaffected by both treatments. CONCLUSION: These data indicate that functional CB1 receptors which are able to modulate the release of T(3) and T(4) are expressed in the rat thyroid, and suggest a possible role of cannabinoids in the regulation of rat thyroid hormonal activity.


Cannabinoids are involved in the control of pain at the spinal level through the cannabinoid receptor-1 (CB1) localized pre- and postsynaptically on primary afferent fibres and dorsal horn interneurones, respectively. Using immunocytochemistry, we show that in addition to its neuronal localization, CB1 is also expressed in numerous astrocytes in laminae I and II of the rat dorsal horn. This ubiquitous localization may account for the complex role played by cannabinoids in antinociception. CB1 receptors in astrocytes may be involved in the anti-hyperalgesic action of exogenous cannabinoids.


The design, synthesis and biological activities of potent pyrazole-based tricyclic CB(1) receptor antagonists (2) are described. The key synthetic step involves the ring closure of the lithiated alpha, gamma-keto ester adduct (4). The optimal nitroderivative (28) in this series exhibits a high CB(1) receptor affinity (pK(i)=7.2) as well as very potent antagonistic activity (pA(2)=8.8) in vitro. The regioselectivity of the pyrazole ring closure is shown to depend strongly on the aromatic substitution pattern of the applied arylhydrazine.


The substantia nigra pars reticulata (SNR) belongs to the brain regions with the highest density of CB(1) cannabinoid receptors. Anatomical studies indicate that the great majority of CB(1) receptors in the SNR are localized on terminals of GABAergic axons arriving from the caudate-putamen (striatonigral axons). The aim of the present experiments was to clarify the role of CB(1) receptors on terminals of striatonigral axons. Oblique sagittal slices, including the caudate-putamen and the substantia nigra, were prepared from brains of young mice. Electrical stimulation in the caudate-putamen elicited GABAergic inhibitory postsynaptic currents (IPSCs) in the SNR, which were studied by patch-clamp techniques. The long latency of IPSCs (14+/−1 ms) suggests that striatonigral axons were indeed activated within the caudate-putamen. The synthetic CB(1)/CB(2) cannabinoid receptor agonist WIN55212-2 (R(+)-2,3-dihydro-5-methyl-3-[(morpholinyl)methyl]pyrrolo[1,2,3-de]-1,4-b enzoxazin-yl]-1-naphthalenyl)methanone mesylate; 10(-5) M) decreased the amplitude of IPSCs by 93+/−1%. CP55940 ((-)cis-3-[2-hydroxy-4-(1,1-dimethylheptyl)phenyl]-trans-4-(3-hydroxypropyl)cyclohexanol; 10(-5) M), another CB(1)/CB(2) receptor agonist, also reduced IPSC amplitude, by 76+/−4%. The CB(1) cannabinoid receptor antagonist SR141716A (N-piperidino-5-(4-chlorophenyl)-1-(2,4-dichlorophenyl)-4-methyl-3-
pyrazole carboxamide; (10(-6) M) prevented the inhibition produced by WIN55212-2 (10(-5) M). Depolarization of SNR neurons led to suppression of IPSCs; this suppression was prevented by SR141716A (10(-6) M). Three observations indicate that the agonists inhibited neurotransmission presynaptically. (1) CP55940 (10(-5) M) enhanced the ratio of amplitudes of two IPSCs which were elicited by two electrical stimuli 100 ms apart (paired pulses). (2) WIN55212-2 (10(-5) M) did not change the amplitude of miniature IPSCs recorded in the presence of tetrodotoxin. (3) WIN55212-2 (10(-5) M) also had no effect on currents elicited in SNR neurons by ejection of the GABA(A) receptor agonist muscimol from a pipet. In summary, we have established a method which allows selective examination of GABAergic neurotransmission between striatonigral axons and SNR neurons. Using this method, the function of CB(1) cannabinoid receptors on terminals of striatonigral axons was unequivocally clarified. Activation of these receptors causes strong presynaptic inhibition of GABAergic neurotransmission between striatonigral axons and SNR neurons. This effect may be one explanation of the catalepsy observed in animals after cannabinoid administration. Endocannabinoids released from SNR neurons can modulate striatonigral neurotransmission by inhibiting GABA release from terminals of striatonigral axons.


The effect of cannabinoid on the tyrosine phosphorylation of focal adhesion kinase (FAK) and focal adhesion kinase-related non-kinase (FRNK) was investigated in differentiated mouse neuroblastoma N1E-115 cells. HU-210, a potent cannabinoid agonist, elicited a time-dependent enhancement of tyrosine phosphorylation of FRNK, but not FAK. Pretreatment of cells with antisense oligodeoxynucleotide targeting CB1 cannabinoid receptor abolished HU-210-induced FRNK tyrosine phosphorylation. In addition, pretreatment of cells with 8-Br-cAMP also blocked HU-210-induced FRNK tyrosine phosphorylation. These data demonstrated that HU-210 induces FRNK tyrosine phosphorylation by activating G(i)-coupled CB1 cannabinoid receptor in N1E-115 cells. This newly discovered, cannabinoid-induced FRNK tyrosine phosphorylation might be a novel mechanism for cannabinoid-induced functional changes.

CLINICAL SCIENCE


AIMS: The study was designed to investigate the acute effects of ingested tetrahydrocannabinol (THC) on auditory function. METHODS: Eight male subjects (aged 22-30 years), who had previous experience of cannabis use, took part in this study. They performed air conduction pure tone audiometry in both ears over 0.5-8 kHz. A simple test of frequency selectivity by detecting a 4-kHz tone under two masking noise conditions was also carried out in one ear. Three test sessions at weekly intervals were carried out, at the start of which they ingested a capsule containing either placebo, or 7.5 or 15 mg of THC. These were administered in a randomized cross-over, double-blind manner. Auditory testing as described above was carried out 2 hours after ingestion. Blood samples were also obtained at this time point and assayed for delta 9- and 11-OH-THC levels. RESULTS: No significant changes in threshold or frequency resolution were seen with the dosages employed in this study. CONCLUSIONS: This suggests that THC at the plasma levels attained in this study does not have profound effect on the processing of elementary stimuli by the auditory pathway.


There is a large amount of evidence to support the view that the psychoactive ingredient in cannabis, delta9-tetrahydrocannabinol (delta9-THC), and cannabinoids in general, can reduce muscle spasticity and pain under some circumstances. Cannabinoid (CB1) receptors in the CNS appear to mediate both of these effects and endogenous cannabinoids may fulfill these functions.
to some extent under normal circumstances. However, in the context of multiple sclerosis (MS), it is still questionable whether cannabinoids are superior to existing, conventional medications for the treatment of spasticity and pain. In the case of spasticity, there are too few controlled clinical trials to draw any reliable conclusion at this stage. In the case of pain, most of the available trials suggest that cannabinoids are not superior to existing treatments; however, few trials have examined chronic pain syndromes that are relevant to MS. Whether or not cannabinoids do have therapeutic potential in the treatment of MS, a further issue will be whether synthetic cannabinoids should be used in preference to cannabis itself. Smoking cannabis is associated with significant risks of lung cancer and other respiratory dysfunction. Furthermore, delta9-THC, as a broad-spectrum cannabinoid receptor agonist, will activate both CB1 and CB2 receptors. Synthetic cannabinoids, which target specific cannabinoid receptor subtypes in specific parts of the CNS, are likely to be of more therapeutic use than delta9-THC itself. If rapid absorption is necessary, such synthetic drugs could be delivered via aerosol formulations.


AIM: To assess the possible effects of tobacco and cannabis smoking on lung function in young adults between the ages of 18 and 26. SETTING AND PARTICIPANTS: A group of over 900 young adults derived from a birth cohort of 1037 subjects born in Dunedin, New Zealand in 1972/73 were studied at age 18, 21 and 26 years. MEASUREMENTS: Cannabis and tobacco smoking were documented at each age using a standardized interview. Lung function, as measured by the forced expiratory volume in one second/vital capacity (FEV1/VC) ratio, was obtained by simple spirometry. A fixed effects regression model was used to analyse the data to take account of confounding factors. FINDINGS: When the sample was stratified for cumulative use, there was evidence of a linear relationship between cannabis use and FEV1/VC (P < 0.05). In the absence of adjusting for other variables, increasing cannabis use over time was associated with a decline in FEV1/VC with time; the mean FEV1/VC among subjects using cannabis on 900 or more occasions was 7.2%, 2.6% and 5.0% less than non-users at ages 18, 21 and 26, respectively. After controlling for potential confounding factors (age, tobacco smoking and weight) the negative effect of cumulative cannabis use on mean FEV1/VC was only marginally significant (P < 0.09). Age (P < 0.001), cigarette smoking (P < 0.05) and weight (P < 0.001) were all significant predictors of FEV1/VC. Cannabis use and daily cigarette smoking acted additively to influence FEV1/VC. CONCLUSIONS: Longitudinal observations over 8 years in young adults revealed a dose-dependent relationship between cumulative cannabis consumption and decline in FEV1/VC. However, when confounders were accounted for the effect was reduced and was only marginally significant, but given the limited time frame over which observations were made, the trend suggests that continued cannabis smoking has the potential to result in clinically important impairment of lung function.


Background: Chronic pain is one of the most common reasons for therapeutic cannabis use. Objectives: To describe therapeutic cannabis use among patients with chronic pain. Methods: Patients with chronic pain who voluntarily indicated that they used cannabis therapeutically completed a questionnaire about the type of cannabis used, the mode of administration, the amount used and the frequency of use, and their perception of the effectiveness of cannabis on a set of pain-associated symptoms and side effects. The study was approved by the McGill University Health Centre Research Ethics Board. Results: Fifteen patients (10 male) were interviewed (median age 49.5 years, range 24 to 68 years). All patients smoked herbal cannabis for therapeutic reasons (median duration of use six years, range two weeks to 37 years). Seven patients only smoked at night-time (median dose eight puffs, range two to eight puffs), and eight patients used cannabis mainly during the day (median dose three puffs, range two to eight puffs); the median frequency of use was four times per day (range one to 16 times per day). Twelve patients reported improvement in pain and mood, while 11 reported improvement in sleep. Eight patients reported a 'high'; six denied a 'high'. Tolerance to cannabis was not reported. Conclusions: The results of this self-selected case series must be interpreted...
with caution. Small doses of smoked cannabis may improve pain, mood and sleep in some patients with chronic pain. Clinical trials are warranted to test these effects. Further prospective studies should examine the patterns and prevalence of cannabis use among chronic pain populations.


This article summarizes the results of research studies that indicate that the accepting, permissive approach to cannabis use is not justified. After theoretical introduction and a discussion of the forms currently available, we review research and epidemiological surveys demoting the effects of cannabis on various body systems. The deleterious effects associated with cannabis use and its derivatives are discussed.


BEHAVIOURAL SCIENCE


OBJECTIVES: This study examined whether adolescents’ recall of antidrug advertising is associated with a decreased probability of using illicit drugs and, given drug use, a reduced volume of use. METHODS: A behavioral economic model of influences on drug consumption was developed with survey data from a nationally representative sample of adolescents to determine the incremental impact of antidrug advertising. RESULTS: The findings provided evidence that recall of antidrug advertising was associated with a lower probability of marijuana and cocaine/crack use. Recall of such advertising was not associated with the decision of how much marijuana or cocaine/crack to use. Results suggest that individuals predisposed to try marijuana are also predisposed to try cocaine/crack. CONCLUSIONS: The present results provide support for the effectiveness of antidrug advertising programs.


AIMS: To (1) describe the South African Community Epidemiology Network on Drug Use (SACENDU), (2) describe trends and associated consequences of alcohol and other drug (AOD) use in South Africa for January 1997 to December 1999 and (3) outline selected policy implications identified by SACENDU participants. METHODS: A descriptive epidemiological study of AOD indicators based on data gathered from multiple sources, including specialist treatment centres, trauma units and quantitative studies of target groups such as school students and arrestees. Networks were established in five sentinel sites to facilitate the collection, interpretation and dissemination of data. RESULTS: Over time alcohol has been the most frequently reported primary substance of abuse across sites. Trauma and psychiatric data highlight the burden associated with alcohol abuse. Cannabis and Mandrax (methaqualone), alone or in combination, are the most frequently reported illicit drugs of abuse, generally comprising the largest proportions of drug-related arrests, drug-related psychiatric diagnoses and drug-positive trauma patients. From 1997 to 1999, a significant increase in indicators for cocaine/crack and heroin occurred in two sites. Ecstasy (MDMA) use, alone or in combination with other substances, is reported among young people. CONCLUSIONS: A broad range of globally abused substances is present in South Africa and the use and burden of illicit substances appears to be increasing. This points to the importance of ongoing monitoring of AOD trends. Through regular, systematic data collection the SACENDU project has made available more evidence-based information to direct AOD abuse policy and practice and has had an impact on research agendas.

The dollar value of an illicit drug market is an important statistic in drug policy analysis. It can be used to illustrate the scale of the trade in a drug; evaluate its impact on a local community or nation; provide an indication of the level of criminality related to a drug; and can inform discussions of future drug policy options. This paper calculates the first ever demand side estimates of the New Zealand cannabis black market. The estimates produced are calculated using cannabis consumption data from the Alcohol & Public Health Research Unit's (APHRU) 1998 National Drug Survey. The wholesale value of the market is estimated to be $81.3-104.6 million a year, and the retail value of the market is estimated to be $131.3-168.9 million a year. These demand side estimates are much lower than the existing supply side estimates of the market calculated using police seizures of cannabis plants. The retail figure is four times lower than the lowest national supply side estimate ($636 million) and seven times lower than the highest national supply side estimate ($1.27 billion). The demand side estimates suggest a much smaller cannabis economy to fuel organized criminal activity in New Zealand than previous estimates implied.