INTRODUCTION

Here is the latest summary of research abstracts. Note that registration for the 2205 ICRS meeting is March 15th, 2005 (http://cannabinoidsociety.org).

BASIC SCIENCE


Inhibitory interneurons terminating on Purkinje cell dendrites contribute to cannabinoid-mediated cerebellar plasticity, consistent with the intense expression of cannabinoid CB1 receptor protein in the cerebellar molecular layer. CB1 labelling in the molecular layer has been attributed to parallel fibers originating from granule cells, climbing fibers originating in the inferior olive, and inhibitory interneurons in the deep molecular layer (basket cells). However, the cellular distribution of CB1 in the cerebellar molecular layer has remained poorly understood. We used double fluorescence labelling to test for co-localization of nuclei with CB1 receptor protein. Labelling was intense surrounding nuclei in the deep and superficial molecular layer; consistent with basket cell and stellate cell inhibitory interneurons that regulate depolarization-induced suppression of inhibition (DSI) of Purkinje cells.


CB1 is the most abundant metabotropic receptor of the brain, being found in areas classically involved in learning and memory and present at higher density at presynaptic terminals. Different sets of evidence support the idea that endogenous ligands (endocannabinoids) to the CB1 receptors act as modulators of neurotransmission. In hippocampus, endocannabinoids seem to act as retrograde messengers mediating down-regulation of GABA release. Previous reports have described a cognitive impairment effect of cannabinoid agonists, or facilitation by antagonists. The scope of the present study is to investigate the effect of intrahippocampal administration of the CB1-selective antagonist, AM251, in two behavioral tasks. One hundred and twelve male Wistar rats with bilateral cannulae implanted in the CA1 region of the dorsal hippocampus were trained in a step-down inhibitory avoidance task (IA, footshock, 0.5mA) or an open field habituation task (OF). Immediately, after training, animals received an infusion of 0.55, 5.5, and 55.5ng/side of AM251 (Tocris), or its vehicle (DMSO/saline), via these cannulae. Our results show that AM251 disrupted memory consolidation of the IA task, but not the OF task, an effect that seems to be purely mnemonic since the drug showed no motor performance effects. Only the intermediate dose (5.5ng/side) of AM251 was effective in IA and the absence of effect with the larger dose may be the consequence of non-specific binding. The fact that OF was not affected raises the possibility that this endogenous system requires some degree of aversiveness to be recruited. We propose that increased levels of endogenous cannabinoids in the hippocampus, following a training session, contribute to facilitate memory consolidation, a process that may have been disrupted with AM251.

Cannabinoids are the constituents of the marijuana plants. The central effects of exogenous cannabinoids are implicated in enhancing mood, altering emotional states, and interfering in the formation of short-term memory. Cannabinoid receptors are G protein-coupled receptors with seven transmembrane domains that are expressed on the cell surface with their binding domain exposed to the extracellular space. To date, two cannabinoid receptors have been cloned, CB1 and CB2. Recent evidence suggests that a third CB3 receptor is out there, waiting to be cloned. The endocannabinoids may represent the first members of a new classes of neuromodulators, that are not stored in cell vesicles, but rather synthesised by the cell on demand. The endogenous cannabinoid system could play a central role in several neuropsychiatric disorders and is also involved in other conditions such as pain, spasticity and neuroprotection. Implication of cannabinoid system in the pathogenesis and development of schizophrenia is also discussed.


BACKGROUND: The endocannabinoid system has been implicated in the modulation of emotional processes. METHODS: These experiments aimed to investigate the effects of the cannabinoid CB1 receptor antagonist rimonabant (SR141716) in animal models measuring aspects of emotional reactivity and depression. RESULTS: Rimonabant had weak anxiolytic-like activity in the elevated plus-maze and failed to affect flight and risk assessment activities in the mouse defense test battery (MDTB). It produced clear anxiolytic-like effects in the Vogel conflict test (.3-3 mg/kg intraperitoneal [i.p.]) and on defensive aggression in the MDTB (1 and 10 mg/kg, i.p.). The effects of rimonabant in the MDTB paralleled those observed with CB1 receptor knockout mice in this procedure. In the forced-swimming test in rats and the tonic immobility paradigm in gerbils, rimonabant (3 and 10 mg/kg per os [p.o.]) produced antidepressant-like effects that were comparable to those observed with the reference antidepressant, fluoxetine. In the chronic mild stress model in mice, repeated administration of rimonabant (10 mg/kg, p.o.) for 5 weeks improved the deleterious effects produced by stress. CONCLUSIONS: These findings point further to a role for the endocannabinoid system in the modulation of emotional processes and suggest that it may be primarily involved in the adaptive responses to unavoidable stressful stimuli.


The wake-promoting neuropeptides orexins (hypocretins) play a crucial role in controlling neuronal excitability and synaptic transmission in the CNS. In this study, using whole-cell patch-clamp recordings in an acute dorsal raphe nucleus (DRN) slice preparation, we report that orexin B (OxB) depresses the evoked glutamate-mediated synaptic currents in DRN 5-HT neurons. The OxB-induced depression is accompanied by an increase in the paired-pulse ratio and the coefficient of variance, suggesting a presynaptic site of action. OxB also reduces the frequency but not the amplitude of miniature EPSCs, indicating that depression of glutamatergic transmission is mediated by a decrease in glutamate release. Surprisingly, the OxB-induced inhibition of glutamatergic transmission is abolished by postsynaptic inhibition of G-protein signaling with GDPbetaS, suggesting that this effect is signaled by postsynaptic orexin receptors and expressed presynaptically, presumably through a retrograde messenger. Interestingly, the OxB-induced depression of glutamate release is mimicked and occluded by the cannabinoid receptor agonist WIN 55,212-2, and is abolished by the CB1 cannabinoid receptor antagonist AM 251. These results imply that the OxB-induced depression of glutamatergic transmission to DRN 5-HT neurons is mediated by retrograde endocannabinoid release. Examination of downstream signaling pathways involved in this response indicates that the effect of OxB requires the activation of phospholipase C and DAG lipase enzymatic pathways but not a rise in postsynaptic intracellular calcium. Therefore, our findings reveal a previously unsuspected mechanism by
which postsynaptic orexin receptors can modulate glutamatergic synaptic transmission to DRN 5-HT neurons.


CB2 cannabinoid receptor-selective agonists are promising candidates for the treatment of pain. CB2 receptor activation inhibits acute, inflammatory, and neuropathic pain responses but does not cause central nervous system (CNS) effects, consistent with the lack of CB2 receptors in the normal CNS. To date, there has been virtually no information regarding the mechanism of CB2 receptor-mediated inhibition of pain responses. Here, we test the hypothesis that CB2 receptor activation stimulates release from keratinocytes of the endogenous opioid beta-endorphin, which then acts at opioid receptors on primary afferent neurons to inhibit nociception. The antinociceptive effects of the CB2 receptor-selective agonist AM1241 were prevented in rats when naloxone or antiserum to beta-endorphin was injected in the hindpaw where the noxious thermal stimulus was applied, suggesting that beta-endorphin is necessary for CB2 receptor-mediated antinociception. Further, AM1241 did not inhibit nociception in micro-opioid receptor-deficient mice. Hindpaw injection of beta-endorphin was sufficient to produce antinociception. AM1241 stimulated beta-endorphin release from rat skin tissue and from cultured human keratinocytes. This stimulation was prevented by AM630, a CB2 cannabinoid receptor-selective antagonist and was not observed in skin from CB2 cannabinoid receptor-deficient mice. These data suggest that CB2 receptor activation stimulates release from keratinocytes of beta-endorphin, which acts at local neuronal micro-opioid receptors to inhibit nociception. Supporting this possibility, CB2 immunolabeling was detected on beta-endorphin-containing keratinocytes in stratum granulosum throughout the epidermis of the hindpaw. This mechanism allows for the local release of beta-endorphin, where CB2 receptors are present, leading to anatomical specificity of opioid effects.


The cannabinoid CB(1) receptor allows endocannabinoids to act as intercellular and retrograde messengers in the central nervous system. Endocannabinoid actions have been implicated in both synaptic plasticity and neuroprotection. Here, cannabinergic activation of extracellular signal regulated-kinase (ERK) and focal adhesion kinase (FAK) occurred correspondingly in long-term hippocampal slice cultures. The stable endocannabinoid analogue R-methanandamide activated ERK1/ERK2 subtypes of mitogen-activated protein kinase (MAPK) through the upstream activator MAPK kinase (MEK). R-methanandamide also promoted FAK signaling, but in a MEK-independent manner. Both events of ERK and FAK activation were selectively blocked by N-(morpholin-4-yl)-1-(2,4-dichlorophenyl)-5-(4-iodophenyl)-4-methyl-1H-pyrazole-3-carboxamide (AM281), a cannabinoid CB(1) receptor antagonist, and the blockage was associated with a gradual decline in synaptic markers. Interestingly, the integrin antagonist Gly-Arg-Gly-Asp-Ser-Pro also caused the disruption of R-methanandamide-mediated ERK and FAK responses and upset the integrity of excitatory synapses. These results suggest that the endocannabinoid system supports synaptic maintenance through linkages with MAPK pathways and integrin-related FAK signaling.


Dopamine and endogenous cannabinoids display complex interactions in the basal ganglia. One possible level of interaction is between CB1 cannabinoid and D2 dopamine receptors. Here we demonstrate that CB1 signaling is profoundly altered by a regulated association of CB1 and D2 receptors. This provides the first evidence that CB1/D2 receptor complexes exist, are dynamic, and are agonist regulated with highest complex levels detected when both receptors are stimulated with sub-saturating concentrations of agonist. The consequence of this interaction is a differential preference for signaling through a 'non-preferred'
G-protein. In this case D2 receptor activation, simultaneously with CB1 receptor stimulation, results in the receptor complex coupling to Galphas protein in preference to the expected Galphai/o proteins. The result of this interaction is an increase in the second messenger cAMP, reversing an initial synergistic inhibition of adenylyl cyclase activity seen at sub-threshold concentrations of cannabinoid agonist. Additionally, a pertussis toxin insensitive component in the activation of ERK 1/2 kinases by the cannabinoid agonist CP55,940 is revealed in cells stably expressing both CB1 and D2 receptors. Thus, concurrent receptor stimulation promotes a hetero-oligomeric receptor complex and an apparent shift of CB1 signaling from a pertussis toxin sensitive inhibition to a partly pertussis toxin insensitive stimulation of adenylyl cyclase and ERK 1/2 phosphorylation.


For the purpose of purification and structural characterization, the CB1 cannabinoid receptors are expressed in methylotrophic yeast Pichia pastoris. The expression plasmid was constructed in which the CB1 gene is under the control of the highly inducible promoter of P. pastoris alcohol oxidase I gene. To facilitate easy detection and purification, a FLAG tag was introduced at the N-terminal, a c-myc epitope and a hexahistidine tag were introduced at the C-terminal of the CB1. In membrane preparations of CB1 gene transformed yeast cells, Western blot analysis detected the expression of CB1 proteins. Radioligand binding assays demonstrated that the tagged CB1 receptors expressed in P. pastoris have a pharmacological profile similar to that of the untagged CB1 receptors expressed in mammalian systems. Furthermore, the tagged CB1 receptors were purified by anti-FLAG M2 affinity chromatography and the identity of the purified CB1 receptor proteins was confirmed by Western blot analysis. MALDI/TOF mass spectrometry analysis of the peptides extracted from tryptic digestions of purified CB1 preparations detected 17 peptide fragments derived from the CB1, thus further confirming the identity of the purified receptor. In conclusion, these data demonstrated for the first time that epitope tagged, functional CB1 cannabinoid receptors can be expressed in P. pastoris for purification and mass spectrometry characterization.


BACKGROUND: TRPV1 is a ligand-gated ion channel whose activation by capsaicin increases intracellular Ca(2+) ([Ca(2+)]i). TRPV1 and cannabinoid CB1 receptor activation are capable of eliciting analgesia. In this study, using recombinant human (h) and rat (r) TRPV1 receptors expressed in HEK293 cells, we have performed a comparison of both TRPV1 species at 22 and 37 degrees C and compared endo- and exocannabinoid activity at both receptors. METHODS: [Ca(2+)]i was measured in Fura-2-loaded HEK293hTRPV1 and HEK293rTRPV1 cells. To assess native CB1 receptor activity, [(35)S]GTPgammaS binding to membranes prepared from rat cerebellum was measured. RESULTS: Both capsaicin (pEC50 rat approximately 6.9 and pEC50 human approximately 6.8 at 37 degrees C) and anandamide (pEC50 rat approximately 5.3 and pEC50 human approximately 5.8 at 37 degrees C) produced a concentration-dependent increase in [Ca(2+)]i in rat and human systems and at 22 and 37 degrees C. In HEK293rTRPV1 cells, anandamide appeared to be a partial agonist. Capsazepine demonstrated competitive antagonism at both human and rat TRPV1 receptors and at both temperatures studied. Capsazepine effects were not temperature dependent: pKB at rTRPV1 was 5.98 at 22 degrees C and 6.02 at 37 degrees C, and pKB at hTRPV1 was 6.76 at 22 degrees C and 6.75 at 37 degrees C. However, there was a consistent 6-fold increase in capsazepine potency for hTRPV1 relative to rTRPV1. The exocannabinoid Delta(9)-tetrahydrocannabinol failed to increase [Ca(2+)]i, although its solvent ethanol was an effective TRPV1 activator. In the [(35)S]GTPgammaS binding assay using rat cerebellar membranes, anandamide (pEC50 approximately 5.8) and Delta(9)-tetrahydrocannabinol (pEC50 approximately 7.1), but not capsaicin, stimulated binding. Delta(9)-tetrahydrocannabinol was a partial agonist. pEC50 values for anandamide at rTRPV1 and hCB1 were similar. CONCLUSIONS: There were small differences in the pharmacology of rat and human TRPV1 receptors. Whilst capsaicin activated
TRPV1 and Delta(9)-tetrahydrocannabinol activated CB1, anandamide is an endogenous agonist for both receptor systems.


Genetic contributions to the etiology of substance abuse and dependence are topics of major interest. Acute and chronic cannabis use can produce drug-induced psychosis resembling schizophrenia and worsen positive symptoms of schizophrenia. The endocannabinoid system is one of the most important neural signaling pathways implicated in substance abuse and dependence. The fatty acid amide hydrolase (FAAH) is a primary catabolic enzyme of endocannabinoids. To clarify a possible involvement of FAAH in the etiology of methamphetamine dependence/psychosis or schizophrenia, we examined the genetic association of a nonsynonymous polymorphism of the FAAH gene (Pro129Thr) by a case-control study. We found no significant association in allele and genotype frequencies of the polymorphism with either disorder. Because the Pro129Thr polymorphism reduces enzyme instability, it is unlikely that dysfunction of FAAH and enhanced endocannabinoid system induce susceptibility to either methamphetamine dependence/psychosis or schizophrenia.


Bioscouring of hemp (Cannabis Sativa L) using pectate lyase (EC 4.2.2.2), Scourzyme L, was performed at 55 degrees C and pH 8.5 in a nonagitated system. The enzyme concentration, treatment time and substrate concentration were varied to obtain the kinetic constants, K(m) and V(m). Greater enzyme concentration and a longer treatment improved the removal of the low methoxy pectin component as indicated by UV spectroscopy. Removal of pectate caused no crystalline transformation in the fibres, except for a slight decline in the crystallinity order index analysed by Fourier Transform infrared spectroscopy and wide angle X-ray diffraction. This corresponded well with the single fibre bundle tensile mechanical properties test. Smooth surfaces and separated fibres observed using SEM images were evidence of successful treatment, supported by weight loss at low temperature of a pectic substance. After treatment, the pectin substance was no longer observed during thermogravimetry. An increase in surface area and pore size after scouring were further evidence of modification.SEM micrograph of Scourzyme-treated hemp fibres.

endocannabinoids and ethanol potentiate each other’s inhibitory effects on alpha7-nACh receptor function through distinct regions of the receptor.


Cerebral vascular smooth muscle cells express the CB1 cannabinoid receptor and CB1 receptor agonists produce vasodilation of cerebral arteries. The purpose of this study was to determine whether vasoconstriction of rat middle cerebral artery (MCA) results in the local formation of endocannabinoids (eCBs) which, via activation of CB1 receptors, oppose the vasoconstriction in a feedback manner. The thromboxane A2 (TXA2) mimic, U-46619, significantly increased N- arachidonylethanolamine (AEA) and 2-arachidonylglycerol (2-AG) content of isolated MCA, while 5-hydroxytryptamine (5-HT) decreased AEA and 2-AG content. If eCBs play a feedback role in the regulation of MCA tone, then CB1 receptor antagonists should enhance the constriction of MCA produced by U-46619 but not 5-HT. U-46619 caused concentration-dependent constrictions of endothelium-denuded MCA. Two CB1 receptor antagonists, SR141716 and AM251, decreased the EC50 value for U-46619 to constrict endothelium-denuded MCA without affecting Emax. A low concentration of CB1 receptor agonist Win 55212-2 (30 nM) produced vasodilation of MCAs constricted with low but not saturating concentrations of U-46619. SR141716 had no effect on the 5-HT concentration-contraction relationship. These data suggest that TXA2 receptor activation increases MCA eCB content which, via activation of CB1 receptors, reduces the constriction produced by moderate concentrations of the TXA2 agonist. Although 5-HT-induced vasoconstriction is reduced by exogenous CB1 receptor agonist, activation of 5-HT receptors does not increase eCB content. These results suggest that MCA production of eCBs is not regulated by constriction per se, but likely via a signaling pathway that is specific for TXA2 receptors and not 5-HT receptors.


Cannabinoids like anandamide are involved in pain transmission. In this study we evaluated the effects of administrating N-(4-hydroxyphenyl)-5Z,8Z,11Z,14Z-eicosatetraenamide (AM404), an inhibitor of anandamide reuptake and monitoring the expression of c-fos, a marker of activated neurons in an experimental model of neuropathic pain (sciatic nerve tying). Fos expression was monitored 14 days after tying of sciatic nerve and 2 h after non-noxious stimulation. We showed that non-noxious stimulation increased Fos-positivity in the dorsal superficial laminae of the lumbar spinal cord of tied animals but not in the control animals. AM404 significantly reduced Fos induction in tied animals. Co-administration of cannabionoid CB(1) receptor, cannabinoid CB(2) receptor and transient receptor potential vanilloid type 1 (TRPV-1) antagonists reduced the effect of AM404 and this reduction was higher using cannabinoid CB(1) receptor antagonist. These results suggest that AM404 could be a useful drug to reduce neuropathic pain and that cannabinoid CB(1) receptor, cannabinoid CB(2) receptor and vanilloid TRPV-1 receptor are involved.


Chemical investigation of the pollen grain collected from male plants of Cannabis sativa L. resulted in the isolation for the first time of two flavonol glycosides from the methanol extract, and the identification of 16 cannabinoids in the hexane extract. The two glycosides were identified as kaempferol 3-O-sophoroside and quercetin 3-O-sophoroside by spectroscopic methods including high-field two-dimensional NMR experiments. The characterisation of each cannabinoid was performed by GC-FID and GC-MS analyses and by comparison with both available reference cannabinoids and reported data. The identified cannabinoids were delta9-tetrahydrocannabinol, cannabidivarin, cannabicitran, delta9-tetrahydrocannabivarin, cannabicyclol, cannabidiol, cannabichromene, delta9-tetrahydrocannabinol, cannabigerol, cannabinol, dihydrocannabinol,
cannabielsoin, 6a, 7, 10a-trihydroxytetrahydrocannabinol, 9, 10-epoxycannabidiol, 10-O-ethylcannabidiol, and 7, 8-dehydro-10-O-ethylcannabidiol.


We evaluated the ability of cannabidiol (CBD) to impair the migration of tumor cells stimulated by conditioned medium. CBD caused concentration-dependent inhibition of the migration of U87 glioma cells, quantified in a Boyden chamber. Since these cells express both cannabinoid CB1 and CB2 receptors in the membrane, we also evaluated their engagement in the antimigratory effect of CBD. The inhibition of cell was not antagonized either by the selective cannabinoid receptor antagonists SR141716 (CB1) and SR144528 (CB2) or by pretreatment with pertussis toxin, indicating no involvement of classical cannabinoid receptors and/or receptors coupled to Gi/o proteins. These results reinforce the evidence of antitumoral properties of CBD, demonstrating its ability to limit tumor invasion, although the mechanism of its pharmacological effects remains to be clarified.

CLINICAL SCIENCE


OBJECTIVE: To determine possible effects of prolonged marijuana use on the cerebrovascular system during a month of monitored abstinence and to assess how the intensity of current use might have influenced cerebrovascular perfusion in these marijuana users. METHOD: The authors recorded blood flow velocity in the anterior and middle cerebral arteries using transcranial Doppler sonography in three groups of marijuana users who differed in the intensity of recent use (light: n = 11; moderate: n = 23; and heavy: n = 20) and in control subjects (n = 18) to assess the nature and duration of any potential abnormalities. Blood flow velocity was recorded within 3 days of admission and 28 to 30 days of monitored abstinence on an inpatient research unit in order to evaluate subacute effects of the drug and any abstinence-generated changes. RESULTS: Pulsatility index, a measure of cerebrovascular resistance, and systolic velocity were significantly increased in the marijuana users vs control subjects. These increases persisted in the heavy marijuana users after a month of monitored abstinence. CONCLUSIONS: Chronic marijuana use is associated with increased cerebrovascular resistance through changes mediated, in part, in blood vessels or in the brain parenchyma. These findings might provide a partial explanation for the cognitive deficits observed in a similar group of marijuana users.


BACKGROUND: Cannabis use is a major problem in inner cities and has been causally implicated in psychosis. Very few of the available hospital-based studies of the implications of cannabis usage have involved psychiatric intensive care units (PICU); but PICU receive many of the most challenging and resource-hungry-and incompletely understood-patients in the mental health system. AIMS: To study the clinical impact of cannabis abuse in a PICU, and to compare the use of atypical and typical antipsychotics in this setting. METHOD: 115 patients admitted to a PICU consented to take part in an open label naturalistic study. BPRS, TCI-240, weight, length of admission and routine bloods were evaluated in all participants. RESULTS: There was a high rate
of cannabis abuse (71.3%) in the PICU population. Patients who abused cannabis spent longer in PICU because their psychoses were more severe. They were younger at first hospital admission. Cannabis also had metabolic implications, with higher blood glucose levels at admission and greater weight increase. Atypical antipsychotics were effective in treating psychosis inpatients positive to cannabis at admission. CONCLUSION: Our findings suggest that cannabis abusers had a more severe psychotic illness, especially in schizophrenia. There are additional complications in terms of weight gain for cannabis users.


Toxic shock syndrome is a rare but potentially fatal toxin-mediated febrile illness. We report a case of toxic shock syndrome complicated by life-threatening organ dysfunction with high toxin-1 and staphylococcus enterotoxin type A levels that were successfully reduced by early introduction of plasma exchanges. The report shows the time course of the concentrations of anandamide and 2-arachidonyl glyceride and confirms that early introduction of plasma exchange can result in a rapid reduction of circulating toxins and mediators in the treatment of life-threatening multiple organ dysfunction.


INTRODUCTION: Cannabis is the most widely used illegal drug in Israel, and unlike most of the other illegal drugs, it is common among segments of the population with higher demographic characteristics. CASE REPORT: A healthy 20 year old male patient, with two previous admissions with atrial fibrillation, was admitted to the emergency room with paroxysmal atrial fibrillation. The patient presented evidence of cannabis abuse, and no other pathologic cause for atrial fibrillation. Sinus rhythm was restored and the patient was discharged. DISCUSSION: Cannabis abuse is responsible for a wide range of pathologies, including cognitive impairment, a rise in the prevalence of lung, head and neck tumors, atrial and ventricular arrhythmias, and an increase in the risk of ischemic cardiovascular events. CONCLUSIONS: Cannabis abuse can induce atrial fibrillation in predisposed patients. Good practice may consider the inclusion of cannabis abuse tests in young patients admitted due to atrial fibrillation, and definite medical advice to stop the drug abuse.


This case report describes a 22-year-old woman with severe arterial ischemia leading to claudication and ulceration of the feet, presumably due to long-term abuse of amphetamine derivatives, such as "speed" or "ecstasy," and cannabis. Known causes for peripheral occlusive disease, such as atherosclerosis, vasculitis, or collagen vascular disease, were excluded. Laboratory test results did not show evidence of risk factors for thromboembolic diseases. Conventional angiography and magnetic resonance-angiography showed occlusions of medium- and small-sized arteries of both calves and feet. In the past, vasculitis-like arteriopathy was attributed to the abuse of amphetamines as well as of cannabis. However, amphetamines have been reported to be associated with necrotizing vasculitis mainly of cerebral arteries. Therefore, the abuse of methamphetamine or "ecstasy" also appears to play a role in the development of peripheral arterial occlusions and seems to have broad similarities with Buerger's disease.


BACKGROUND: Results of previous research examining long-term residual effects of marijuana use on cognition are conflicting. A major methodological limitation of prior studies is the
inability to determine whether differences between users and non-users are due to differences in genetic vulnerability preceding drug use or due to the effects of the drug. METHOD: Fifty-four monozygotic male twin pairs, discordant for regular marijuana use in which neither twin used any other illicit drug regularly, were recruited from the Vietnam Era Twin Registry. A minimum of 1 year had passed since the marijuana-using twins had last used the drug, and a mean of almost 20 years had passed since the last time marijuana had been used regularly. Twins were administered a comprehensive neuropsychological test battery to assess general intelligence, executive functioning, attention, memory and motor skills. Differences in performance between marijuana-using twins and their non-using co-twins were compared using a multivariate analysis of specific cognitive domains and univariate analyses of individual test scores. Dose response relationships were explored within the marijuana-using group. RESULTS: Marijuana-using twins significantly differed from their non-using co-twins on the general intelligence domain; however, within that domain only the performance of the block design subtest of the Wechsler Adult Intelligence Scale--Revised reached a level of statistical significance. CONCLUSIONS: Out of the numerous measures that were administered, only one significant difference was noted between marijuana-using twins and their non-using co-twins on cognitive functioning. The results indicate an absence of marked long-term residual effects of marijuana use on cognitive abilities.


Drug misuse represents a risk factor for cerebrovascular disease, especially among young people. Despite the fact that cannabis is the most widely used illicit drug, there are only a few reports associating its use with cerebrovascular disease. We describe a patient who suffered three ischaemic strokes immediately after cannabis consumption. Other stroke aetiologies were ruled out, and neuroimaging revealed infarcts in different arterial areas as well as evidence of non-atherosclerotic arterial disease, which suggests an underlying vasculopathy of uncertain (toxic or inflammatory) origin. Cannabis use may be associated with ischaemic stroke in young patients, but its mechanism is unclear.


Objective: Although a number of studies have examined the respiratory impact of marijuana smoking, such studies have generally used convenience samples of marijuana and tobacco users. The current study examined respiratory effects of marijuana and tobacco use in a nationally representative sample while controlling for age, gender, and current asthma. Design: Analysis of the nationally representative third National Health and Nutrition Examination Survey (NHANES III). Setting: U.S. households. Participants: A total of 6,728 adults age 20 to 59 who completed the drug, tobacco, and health sections of the NHANES III questionnaire in 1988 and 1994. Current marijuana use was defined as self-reported 100+ lifetime use and at least 1 day of use in the past month. Measurements and Main Results: Self-reported respiratory symptoms included chronic bronchitis, frequent phlegm, shortness of breath, frequent wheezing, chest sounds without a cold, and pneumonia. A medical exam also provided an overall chest finding and a measure of reduced pulmonary functioning. Marijuana use was associated with respiratory symptoms of chronic bronchitis (P=.02), coughing on most days (P=.001), phlegm production (P=.0005), wheezing (P<.0001), and chest sounds without a cold (P=.02). Conclusion: The impact of marijuana smoking on respiratory health has some significant similarities to that of tobacco smoking. Efforts to prevent and reduce marijuana use, such as advising patients to quit and providing referrals for support and assistance, may have substantial public health benefits associated with decreased respiratory health problems.


RATIONALE: Illicit drug use can increase driver crash risk due to loss of control over vehicle trajectory. This study asks, does recreational use of +/-3,4-Methylenedioxymethamphetamine (MDMA; ecstasy) and tetrahydrocannabinol (THC; marijuana) impair cognitive processes that help direct our safe movement through the world? OBJECTIVE:
This study assesses the residual effects of combined MDMA/THC use, and of THC use alone, upon perceived trajectory of travel. METHODS: Perception of self-motion, or heading, from optical flow patterns was assessed using stimuli comprising random dot ground planes presented at three different densities and eight heading angles (1, 2, 4 and 8 degrees to the left or right). On each trial, subjects reported if direction of travel was to the left or the right. RESULTS: Results showed impairments in both drug groups, with the MDMA/THC group performing the worst. CONCLUSIONS: The finding that these psychoactive agents adversely affect heading perception, even in recently abstinent users, raises potential concerns about MDMA use and driving ability.


BEHAVIOURAL SCIENCE


INTRODUCTION: Cannabis use is strongly associated with the use and abuse/dependence of other illicit drugs. Gateway and common liabilities models have been employed to explain this relationship. We sought to examine this association using a combination of the discordant twin design and modeling methods. METHOD: We assess the relationship between early cannabis use and the subsequent use and abuse/dependence of other illicit drugs in a population-based sample of male and female twin pairs using four analyses: (i) analysis of the association between early cannabis use and other illicit drug use and abuse/dependence in the entire sample of twins, (ii) assessment of the influence of early cannabis use in twin 1 on twin 2's use or abuse/dependence of other illicit drugs, (iii) use of twin pairs discordant for early cannabis use in a discordant twin design and (iv) a model-fitting procedure. RESULTS: We found: (i) a strong association between early cannabis use and use and abuse/dependence of other illicit drugs in the sample, (ii) twin 1's early cannabis use is significantly associated with the twin 2's other illicit drug use, (iii) the role of correlated genetic factors with some evidence for a causal influence, and (iv) the correlated liabilities model fits the data well. CONCLUSIONS: Early cannabis use is strongly associated with other illicit drug use and abuse/dependence. The relationship arises largely due to correlated genetic and environmental influences with persisting evidence for some causal influences.


Objective: To compare public health and legal policies to reduce the harm associated with cannabis use in Canada and Australia, given similarities between both countries. Method: A review of the epidemiological and health policy literature. Results: Although both countries have adopted harm minimization, a continued heavy reliance on legislative and punitive approaches in both Canada and Australia has failed to arrest the increase in cannabis use, especially among young people. A Senate inquiry in Canada has recommended the liberalization of laws on the possession and use of cannabis, while tightening legislation against operating vehicles or machinery while intoxicated. Conclusions: Existing policies are not evidence-based and lead to adverse outcomes such as criminalization of otherwise law-abiding citizens and diversion of resources from more effective policing or health service initiatives.

Cannabis consumption is on the rise in the French-speaking Community of Belgium, especially among teenagers. The physical and mental harms related to that drug prompted us to search for factors associated with cannabis consumption. The aim of this paper is thus to identify a series of potential predictors of teenager's cannabis use and particularly the influence of peer and family integration. The data analyzed were taken from the 1998 data bank "Health Behavior in School-Aged Children", an international quantitative cross-national study, which takes place every four years. The variables investigated were peer and family integration and the habit of drug consumption (tobacco, alcohol or a narcotic other than cannabis) as potential determinants of the experimentation, current usage of cannabis (at least once a month) and regular usage (at least once a week). Apart from the socio-demographic variables, these predictors were investigated by univariate and multivariate analysis (logistic regression). The analyses covered 744 students in Catholic high schools. Results showed that 30.2% of students had tried to smoke cannabis and 50% of them continued to smoke it at least during the previous month. Age, number of income in the family, strong peer group integration [OR 7.7; CI 95% (3.5;17.3)] and drug-consumption habit [for example, tobacco use: OR 7.4; CI 95% (4.8;11.32)] were associated with cannabis experimentation. Age, gender, nationality, average family integration [OR 2.13; CI 95% (1.1;4.1)] and other drugs use as addiction to nicotine [OR 9.5; CI 95% (5.6;16.3)] determined the current consumption of the substance. Preventive action should aim at improving the teenager's integration into the family circle in order to prevent the trial and consumption of cannabis. In addition, prevention should include the consumption of (addictive) substances in general.


The study characterized self-reported driving behaviour, attitudes towards driving and assumptions about the effects of cannabis on driving, among two different volunteer groups: 63 regular cannabis users (RCUs; cannabis use>monthly) and 46 undergraduate student users, all from the West Midlands. More detailed information was provided by structured interviews with an additional sample of 23 regular users from southern England. Within each group, many respondents had driven whilst under the influence of cannabis (regular users, 82%; students, 40%; interviewees, 100%). Majorities among the regular users and interviewees continued to do so at least monthly. Most users believed that cannabis impaired driving only slightly. More stops by the police for drug-driving than for drink-driving were reported, but these rarely resulted in conviction and were not deterrent. Hence, cannabis users are very willing to drive after using the drug (often combined with alcohol), and even while intoxicated. They consider its effects on driving to be minimal; indeed, many consider it to promote better driving. Attitudes towards drink-driving were much more negative. Finally, most interviewees said that roadside drug testing would be the only efficacious deterrent to drug-driving.


Semiparametric group-based mixture modeling was used with data from an adolescent school sample (N = 1205) for three purposes. First, five trajectory groups were identified to characterize different patterns of change in the frequency of marijuana use across four waves of assessment during adolescence. These trajectory groups were labeled Abstainers, Experimental Users, Decreasers, Increasers, and High Chronics. Second, trajectory group comparisons were made across eight adolescent risk factors to determine distinctive predictors of the trajectory groups. Findings indicated, for example, that the High Chronic group, relative to the other trajectory groups, had higher levels of delinquency, lower academic performance, more drug using friends, and more stressful life events. Third, adolescent trajectory group comparisons were made across 10 risk behaviors in young adulthood (average subject age = 23.5 years) and the occurrence of psychiatric and substance abuse disorders. Findings indicated some consistency across adolescence to young adulthood with regard to risk factors, and specificity with regard to
the prediction of disorders. Adolescent trajectory group membership was significantly associated in young adulthood with cannabis and alcohol disorders but not with major depressive disorders or anxiety disorders.

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