INTRODUCTION
Starting May 1st 2002, the CCIC executive is pleased to introduce a monthly newsletter to all CCIC members and affiliates. The purpose of this document is to disseminate current research abstracts in the field of basic, clinical and behavioural cannabinoid studies. As we are all aware, this is an exciting and rapidly growing field of therapeutics and it is important that we remain abreast of published research, in our own and in other related fields.

The content of this newsletter is derived from weekly Medline searches for papers related to cannabis and cannabinoids (keywords cannab*, marijuana, marihuana). Abstracts (where available) from the previous month are reproduced from the Medline reports. News items which occasionally appear in Medline are not reproduced; other excellent resources for monitoring cannabis related press coverage can be found online. Links to some of these sites can be found at the CCIC website (www.ccicht.ca).

We welcome your input and ideas as this newsletter develops. Please contact the newsletter editor with additional items that you may want to include.

BASIC SCIENCES
NOTES: INTRODUCTION:: Anandamide (ANA) is an endogenous ligand for the cannabinoid receptors Cb1 and Cb2 that is able to synergistically stimulate the proliferation of hematopoietic growth factor-dependent blood cells in serum-free culture. To elucidate the mechanisms by which ANA enhances the proliferative responses of hematopoietic cells, we investigated the ANA-mediated effects on proliferation, cell cycling, apoptosis and intracellular signaling of erythropoietin-stimulated 32D/EPO cells. MATERIALS AND METHODS:: 32D/EPO cells were cultured serum free to determine the effects of EPO and anandamide on these cells. Proliferation was analyzed by tritiated thymidine incorporation. Apoptosis as well as cell cycle analysis was carried out by flow cytometry. MAPKinase activation was determined by Western blotting, using phospho-specific MAPK antibodies. RESULTS:: Simultaneous addition of erythropoietin (EPO) and ANA enhanced DNA synthesis and increased 32D/EPO cell numbers in serum-free culture. Interestingly, ANA did not alter the G1/S transition but it accelerated each of the successive cell cycle phases of EPO-stimulated 32D/EPO cells. Percentages of apoptotic 32D/EPO cells were equally low in cultures supplemented with EPO alone or a combination of EPO and ANA. Both cultures showed enhanced activation of two mitogen-activated protein kinases, namely, extracellular factor responsive kinases 1 and 2 (ERK1/2), as well as the MAPK-target gene protein c-Fos. This fully correlated with the synergistic stimulation of proliferation of 32D/EPO cells by EPO and ANA. ANA had no effect on EPO-induced STAT-5 activation of 32D/EPO cells. Experiments with the Cb2 receptor-specific antagonist SR144528 demonstrated that the synergistic stimulation of proliferation by ANA was partially Cb2 receptor-mediated. CONCLUSION:: These data suggest that the positive effects of ANA on the erythropoietin-induced proliferation of 32D/EPO cells are mediated by receptor-dependent as well as receptor-
independent mechanisms, both of which involve activation of the mitogen-activated protein kinases, ERK1/2.


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**NOTES:** The CB(1) cannabinoid receptor is widely distributed in the central nervous system. The substantia nigra pars reticulata (SNR) belongs to the brain regions with the highest density of CB(1) receptors. According to anatomical studies, most of the CB(1) receptors in the SNR are localized on terminals of striatonigral GABAergic neurons. The aim of the present study was to clarify the function of these receptors. Electrophysiological properties of SNR neurons were studied in brain slices with the patch-clamp technique. Inhibitory postsynaptic currents (IPSCs) were elicited in parasagittal slices by electrical stimulation in the internal capsule. The mixed CB(1)/CB(2) cannabinoid receptor agonist WIN55212-2 (1 &mgr;M and 10 &mgr;M) concentration dependently decreased the amplitude of IPSCs. CP55940, another mixed CB(1)/CB(2) cannabinoid receptor agonist, also lowered IPSC amplitude. Superfused alone, the CB(1)-selective antagonist SR141716A (1 &mgr;M) increased the amplitude of IPSCs. In interaction experiments, SR141716A (1 &mgr;M) prevented the inhibition produced by WIN55212-2 (1 &mgr;M). WIN55212-2 (1 &mgr;M) had no effect on GABAergic currents elicited by ejection of muscimol (1 mM) to the surface of the slices. WIN55212-2 (10 &mgr;M) did not influence the frequency and amplitude of spontaneously occurring IPSCs (sIPSCs) and the firing rate of SNR neurons. The results show that activation of CB(1) cannabinoid receptors inhibits GABAergic neurotransmission in the SNR. The likely mechanism is presynaptic inhibition of GABA release, since cannabinoids had no effects on currents evoked by direct stimulation of GABA(A) receptors by muscimol and on the amplitude of sIPSCs. The enhancement of IPSCs by the cannabinoid antagonist probably reflects continuous inhibition of GABAergic neurotransmission by an endogenous cannabinoid. SNR neurons receive GABAergic input from three sources: from the corpus striatum, the globus pallidus and from neighbouring SNR neurons. The observed inhibition of GABAergic neurotransmission was probably due to depression of the transmission between striatonigral axons and SNR neurons. No direct actions of cannabinoids on SNR neurons were observed in addition to this synaptic effect.


**NOTES:** Endocannabinoids are retrograde messengers that are released from central neurons by depolarization-induced elevation of intracellular Ca2+ concentration [Ca2+]i or by activation of a group I metabotropic glutamate receptor (mGluR). We studied the interaction between these two pathways for endocannabinoid production in rat hippocampal neurons. We made a paired whole-cell recording from cultured hippocampal neurons with inhibitory synaptic connections. Activation of group I mGluRs, mainly mGluR5, by the specific agonist (RS)-3,5-dihydroxyphenylglycine (DHPG), suppressed inhibitory postsynaptic currents (IPSCs) in about half of the neuron pairs. A cannabinoid agonist, WIN55,212-2, suppressed IPSCs in all DHPG-sensitive pairs but not in most of DHPG-insensitive pairs. The effects of both DHPG and WIN55,212-2 were abolished by the cannabinoid antagonists, AM281 and SR141716A, indicating that activation of group I mGluR releases endocannabinoids and suppress inhibitory neurotransmitter release through activation of presynaptic cannabinoid receptors. Depolarization of the postsynaptic neurons caused a transient suppression of IPSCs, a phenomenon termed depolarization-induced suppression of inhibition (DSI) that was also abolished by cannabinoid antagonists. Importantly, DSI was enhanced significantly when group I mGluRs were activated simultaneously by DHPG. This enhancement was much more prominent than expected from the simple summation of depolarization-induced and group I mGluR-induced endocannabinoid release. DHPG caused no change in depolarization-induced Ca2+ transients, indicating that the enhanced DSI by DHPG was not due to the augmentation of Ca2+ influx. Enhancement of DSI
by DHPG was also observed in hippocampal slices. These results suggest that two pathways work in a cooperative manner to release endocannabinoids via a common intracellular cascade.


NOTES: Activation of cannabinoid receptors causes inhibition of spasticity, in a mouse model of multiple sclerosis, and of persistent pain, in the rat formalin test. The endocannabinoid anandamide inhibits spasticity and persistent pain. It not only binds to cannabinoid receptors but is also a full agonist at vanilloid receptors of type 1 (VR1). We found here that vanilloid VR1 receptor agonists (capsaicin and N-N’-(3-methoxy-4-aminoethoxy-benzyl)-(4-tert-butyl-benzyl)-urea [SDZ-249-665]) exhibit a small, albeit significant, inhibition of spasticity that can be attenuated by the vanilloid VR1 receptor antagonist, capsazepine. Arvanil, a structural "hybrid" between capsaicin and anandamide, was a potent inhibitor of spasticity at doses (e.g. 0.01 mg/kg i.v.) where capsaicin and cannabinoid CB(1) receptor agonists were ineffective. The anti-spastic effect of arvanil was unchanged in cannabinoid CB(1) receptor gene-deficient mice or in wildtype mice in the presence of both cannabinoid and vanilloid receptor antagonists. Likewise, arvanil (0.1-0.25 mg/kg) exhibited a potent analgesic effect in the formalin test, which was not reversed by cannabinoid and vanilloid receptor antagonists. These findings suggest that activation by arvanil of sites of action different from cannabinoid CB(1)/CB(2) receptors and vanilloid VR1 receptors leads to anti-spastic/analgesic effects that might be exploited therapeutically.


NOTES: This study investigates the effect of microinjections of capsaicin in the periaqueductal grey matter of rats on nociceptive behaviour and the possible interactions with NMDA and mGlu receptors. Intra-periaqueductal grey microinjection of capsaicin (1-3-6 nmol/rat) increased the latency of the nociceptive reaction in the plantar test. This effect was prevented by pretreatment with capsazepine (6 nmol/rat), which had no effect per se on the latency of the nociceptive reaction. 7-(Hydroxyimino)cyclopropa[b]chromen-1alpha-carboxylate ethyl ester (CPCCOEt, 50 nmol/rat) and 2-Methyl-6-(phenylethynyl)pyridine (MPEP, 50 nmol/rat), antagonists of mGlu(1) and mGlu(5) receptors, respectively, completely blocked the effect of capsaicin. Similarly, pretreatment with DL-2-Amino-5-phosphonovaleric acid (DL-AP5, 5 nmol/rat) and riluzole (4 nmol/rat), an NMDA receptor antagonist and a voltage-dependent Na(+) channels blocker which inhibits glutamate release, respectively, completely antagonized the effect of capsaicin. However, pretreatment with (2S)-alpha-Ethylglutamic acid (30 nmol/rat) and (RS)-alpha-Methylserine-O-phosphate (MSOP, 30 nmol/rat), antagonists of group II and group III mGlu receptors, respectively, had no effects on capsaicin-induced analgesia. Similarly, pretreatment with N-(piperidin-1-yl)-5-(4-chlophenyl)-1-(2,4-dichlorophenyl)-4-methyl-1H-pyr azole-3-carboxamide (SR 141716A, 5 pmol/rat), a selective cannabinoid CB(1) receptor antagonist, did not affect the capsaicin-induced antinociception. In conclusion, this study shows that capsaicin might produce antinociception at the periaqueductal grey level by increasing glutamate release, which activates postsynaptic group I mGlu and NMDA receptors.


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NOTES: The role of cannabinoid (CB) receptors in the regulation of gastric acid secretion was investigated in the rat by means of functional experiments and by immunohistochemistry. In anaesthetized rats with lumen-perfused stomach, the non selective CB-receptor agonist WIN 55,212-2 (0.30 - 4.00 &mgr;mol/kg, i.v.) and the selective CB(1)-receptor agonist HU-210
(0.03 - 1.50 μg·mol kg(-1), i.v.), dose-dependently decreased the acid secretion induced by both pentagastrin (30 nmol kg(-1) h(-1)) and 2-deoxy-D-glucose (1.25 mmol kg(-1), i.v.). By contrast, neither WIN 55,212-2 (1 - 4 μg·mol kg(-1), i.v.) nor HU-210 (0.03 - 1.50 μg·mol kg(-1), i.v.) did modify histamine-induced acid secretion (20 μg·mol kg(-1) h(-1)). The selective CB(2)-receptor agonist JWH-015 (3 - 10 μg·mol kg(-1), i.v.) was ineffective. The gastric antisecretory effects of WIN 55,212-2 and HU-210 on pentagastrin-induced acid secretion were prevented by the selective CB(1)-receptor antagonist SR141716A (0.65 μg·mol kg(-1), i.v.) and unaffected by the selective CB(2)-receptor antagonist SR144528 (0.65 - 2 μg·mol kg(-1), i.v.), followed by continuous infusion of 10 mg kg(-1) h(-1)) significantly reduced, but not abolished, the maximal inhibitory effect of HU-210 (0.3 μg·mol kg(-1), i.v.) on pentagastrin-induced acid secretion; by contrast, pretreatment with atropine (1 mg kg(-1), i.v.) did not modify the antisecretory effect of HU-210. Immunoreactivity to the CB(1) receptor was co-localized with that of the cholinergic marker choline acetyltransferase in neural elements innervating smooth muscle, mucosa and submucosal blood vessels of rat stomach fundus, corpus and antrum. In contrast, CB(2) receptor-like immunoreactivity was not observed. These results indicate that gastric antisecretory effects of cannabinoids in the rat are mediated by suppression of vagal drive to the stomach through activation of CB(1) receptors, located on pre- and postganglionic cholinergic pathways. However, the ineffectiveness of atropine in reducing the effect of HU-210 suggests that the release of non cholinergic excitatory neurotransmitters may be regulated by CB(1) receptors.

**Pre- and postsynaptic localizations of the CB1 cannabinoid receptor in the dorsal horn of the rat spinal cord.** Salio, C., Fischer, J., Franzoni, M.F. and Conrath, M. Neuroscience.2002;110(4):755-64.

**NOTES:** Several lines of evidence show that endogenous and exogenous cannabinoids modulate pain transmission at the spinal level through specific cannabinoid-1 (CB1) receptors. Since anatomical data concerning spinal CB1 receptors are rather contradictory, we studied the cellular and subcellular localizations of the CB1 receptors by immunocytochemistry. Results show a dual pre- and postsynaptic localization of CB1 receptors. Presynaptic receptors are evidenced by the labeling of (1) heterogeneous dorsal root ganglion neurons and (2) axons of Lissauer's tract. Postsynaptic receptors are shown by the labeling of numerous interneurons in the outer part of lamina II. Double immunolabelings show that lamina II outer CB1 neurons, probably islet cells, may also contain GABA or nitric oxide synthase. Numerous CB1-containing neurons in lamina X are also immunostained with anti-nitric oxide synthase (NOS) antibody. Under the electron microscope, CB1 immunoreactivity is exclusively localized postsynaptically in both somatic and dendritic compartments. The absence of labeling on primary afferent axon terminals is discussed and compared to the absence of labeling on terminals or vesicle-containing dendrites of islet cells, where a presynaptic localization was expected according to data of the literature.


**NOTES:** Expression of the cannabinoid 1 (CB1) receptor and its regulation were studied in the different nociceptive and non-nociceptive sub-populations of cultured primary sensory neurones of adult rats. Bandairaea simplicifolia isolec tin B4 (IB4) binding and calcitonin gene-related peptide (CGRP) immunostaining were used to distinguish between the glial cell-derived neurotrophic factor (GDNF)- and nerve growth factor (NGF)-responsive nociceptive and the non-nociceptive primary sensory neurones while a specific CB1 receptor antibody was used to study the expression of the CB1 receptor protein. About half of the total number of primary sensory neurones (47±3.2%) cultured for 1 day in the presence of both neurotrophic factors (50 ng/ml each) showed CB1 receptor-like immunostaining, whereas 21.8±3.3% and 32.7±5.6% of the neurones showed CGRP-like immunopositivity and IB4 binding, respectively. A proportion of the CB1 receptor-like immunopositive neurones was immunostained for CGRP (31.7±5.5%) and IB4 (48.2±7.5), with a minimal (1%) co-expression of CGRP and IB4 binding. About a fifth of the CB1 receptor-like immunopositive neurones did not show either CGRP-like immunostaining or IB4 binding. To find out whether CB1 receptor expression in nociceptive primary sensory neurones is regulated by GDNF or NGF, cultures were grown in the presence or absence of the
neurotrophic factors for 7 days. Vanilloid receptor 1 (VR1) immunostaining was used as a control marker to monitor the effect of the neurotrophins. In cultures maintained in the presence of both factors (50 ng/ml each) 51±2.6% and 42.4±1.2% of the cells showed CB1 receptor-like and VR1-like immunostaining, respectively. In cultures grown for 7 days in the absence of either of the neurotrophic factors the relative number of VR1-like immunopositive cells decreased to 13.4±2.7%, whereas the relative number of CB1 receptor-like immunopositive neurones was unchanged (50.6±1.1%). Our data suggest that the CB1 receptor is expressed in all of the three major sub-populations of primary sensory neurones and that the CB1 receptor expression is not regulated by either NGF or GDNF.


NOTES: Cb2 is a novel protooncogene encoding the peripheral cannabinoid receptor. Previous studies demonstrated that 2 distinct noncoding first exons exist: exon-1A and exon-1B, which both splice to protein-coding exon-2. We demonstrate that in retrovirally induced murine myeloid leukemia cells with proviral insertion in Cb2, exon-1B/exon-2 Cb2 messenger RNA levels have been increased, resulting in high receptor numbers. In myeloid leukemia cells without virus insertion in this locus, low levels of only exon-1A/exon-2 Cb2 transcripts were present and receptors could not be detected. To elucidate the function of Cb2 in myeloid leukemia cells, a set of in vitro experiments was carried out using 32D/G-CSF-R (granulocyte colony-stimulating factor receptor) cells transfected with exon-1B/exon-2 Cb2 complementary DNA and a myeloid cell line carrying a virus insertion in Cb2 (ie, NFS 78). We demonstrate that a major function of the Cb2 receptor is stimulation of migration as determined in a transwell assay. Exposure of Cb2-expressing cells to different cannabinoids showed that the true ligand for Cb2 is 2-arachidonoylglycerol (2-AG), which may act as chemotactrant and as a chemokinetic agent. Furthermore, we observed a significant synergistic activity between 2-AG and interleukin-3 or G-CSF, suggesting cross-talk between the different receptor systems. Radioactive-ligand binding studies revealed significant numbers of Cb2 receptors in normal spleen. Transwell experiments carried out with normal mouse spleen cells showed 2-AG-induced migration of B220-, CD19-, immunoglobulin M-, and immunoglobulin D-expressing B lymphocytes. Our study demonstrates that a major function of Cb2 receptor expressed on myeloid leukemia cells or normal splenocytes is stimulation of migration.

CLINICAL SCIENCES


NOTES: Pain is the leading symptom of most diseases. Humans have always tried to overcome pain using physical and chemical means, and it is believed that opioids and salicylates present in natural products have been used since prehistoric times. The development of the sciences, in particular chemistry and medicine, in the 19th century led to the discovery of the active ingredients of poppy and willow bark (morphine and salicylic acid). Shortly after, synthetic chemistry provided substitutes produced from coal tar (ie, acetyaminophen, aspirin, phenazone, and pethidine). These represent the two main types of analgesics commonly used to treat mild and serious pain: the opioids (pethidine) and the antipyretic analgesics, which may be further divided into the aspirin-derived (acidic) nonsteroidal anti-inflammatory drugs (eg, ibuprofen) and the phenazone and acetylaminophen-like (nonacidic) antipyretic analgesics (which have little anti-inflammatory activity). Chemical modifications and broad-spectrum screening provided medicine with thousands of pharmacologic analogs that broadened the therapeutic spectrum but did not supplant the original compounds developed in the 19th and early 20th century. Recently, molecular biology and genomics have led to the development of new target-selective chemical entities for use in pain relief. These include selective cyclooxygenase (COX)-2 inhibitors, substance P, blockers or agonists of cannabinoid and vanilloid receptors, inhibitors of tetrodotoxin-resistant Na channels, and many more. Most of these selective compounds did not succeed in everyday pain treatment. Some look promising, including the COX-2 selective inhibitors, but doubts remain about the superiority of these new compounds in everyday use. This is particularly the case with the generation of selective COX-2 inhibitors currently in clinical use.

NOTES: Objective: The existence of cannabis-induced psychosis (CP) remains controversial, partly because of methodological problems. We hypothesize that acute schizophrenia (AS) and CP can have distinct demographic, premorbid and clinical features. Method: We compared 26 patients with CP to 35 with AS, after their cannabis-consumption status was confirmed by repeated urine screens. Patients with CP were assessed after at least 1 week but not more than 1 month of abstinence. Symptoms were evaluated with the Present State Examination (PSE).

Results: In group CP, male gender, expansive mood and ideation, derealization/depersonalization, visual hallucinations, and disturbances of sensorium were more frequent than in group AS. Premorbid schizoid personality traits were more frequently associated to AS and antisocial personality traits to CP.

Conclusion: The continuous heavy use of cannabis can induce a psychotic disorder distinct from AS. These two clinical entities share some features but they differ in others.

BEHAVIOURAL STUDIES


NOTES: Under controlled laboratory conditions, eight adult subjects smoked placebo and three different potencies of marijuana cigarettes ranging in Delta(9) THC content. Immediately following smoking, subjects were exposed to a laboratory task that provided concurrently available response options. One option systematically decreased in reinforcement frequency throughout the session, and thus required a reallocation of behavior to the non-decreasing option to maximize monetary earnings. After smoking the two highest doses (1.77% and 3.58% Delta(9) THC) subjects earned fewer reinforcers and allocated a higher proportion of responding to the decreasing option, compared with placebo and the lowest dose. The difference in reinforcers earned could not be accounted for by a change in response rates. Quantitative and graphical analyses revealed that the higher doses produced considerable periods of time spent on the decreasing option despite earning few reinforcers. The data are discussed with regard to marijuana effects on dopamine/cannabinoid systems and adaptive behavior change.


NOTES: The focal point of this paper is the transition from drug use to drug dependence. We present new evidence on risk for starting to use marijuana, cocaine, and alcohol, as well as risks for progression from first drug use to the onset of drug dependence, separately for each of these drugs. Data from the National Comorbidity Survey (NCS) were analyzed. The NCS had a representative sample of the United States population ages 15-54 years (n = 8,098). Survival analysis techniques were used to provide age- and time-specific risk estimates of initiating use of marijuana, cocaine, and alcohol, as well as of becoming dependent on each drug. With respect to risk of initiating use, estimated peak values for alcohol and marijuana were found at age 18, about two years earlier than the later peak in risk of initiating cocaine use. With respect to risk of meeting criteria for the clinical dependence syndrome, estimated peak values for alcohol and marijuana were found at age 17-18. Peak values for cocaine dependence were found at age 23-25. Once use began, cocaine dependence emerged early and more explosively, with an estimated 5-6% of cocaine users becoming cocaine dependent in the first year of use. Most of the observed cases of cocaine dependence met criteria for dependence within three years after initial cocaine use. Whereas some 15-16% of cocaine users had developed cocaine dependence within 10 years of first cocaine use, the corresponding values were about 8% for marijuana users, and 12-13% for alcohol users. The most novel findings of this study document a noteworthy risk for quickly developing cocaine dependence after initial cocaine use, with about one in 16 to 20 cocaine users becoming dependent within the first year of cocaine use. For marijuana and alcohol, there is a more insidious onset of the drug dependence syndrome.

NOTES: Aims: This study assessed the prevalence of substance use among Iranian patients with nephrologic disease (chronic renal failure) who were admitted in different nephrologic wards at Shiraz general hospitals. Design: Cross-sectional survey using structured interview and also using DSM-IV criteria for substance dependency. Setting: General hospitals in Shiraz city (patients with nephrologic disease admitted in different nephrologic wards). Participants: 64 (32 men and 32 women) patients selected randomly. Findings: Data were gathered by a structured interview from 64 patients admitted in nephrologic wards of general hospitals in 2001. The mean age was 49.39 years (SD = 19.62) ranging from 18 to 80 years. 26 (40.6%) of the subjects (65.6% of the men and 15.6% of the women) reported the use of substance(s) once or more in their lives. The majority, 23 (35.9%) used tobacco, 9 (14.1%) used opium and 2 (3.1%) used alcohol. None had used cannabis, heroin, cocaine or LSD. 20 (31.3%) of the subjects (50% of the men and 12.5% of the women) were currently substance dependent, using DSM-IV criteria. The majority, 18 (28.1%) were nicotine dependent, and 6 (9.4%) were opium dependent. There was a nonsignificant relationship between income or occupation or education and prevalence of substance use. The reported reasons for initial use of substance(s), in order of frequency, were enjoyment, modeling and release of tension, and also for current users were, habit, enjoyment and need. Conclusions: Substance use especially cigarettes, opium and alcohol was found to be high among patients. There was no report of cannabis, heroin, cocaine or LSD use. Cultural attitudes toward substance use were found to affect the type and amount of use. These findings can be considered when planning preventive or therapeutic programs.

NOTES: This study examined the moderating effects of impulsivity and affect lability on relations between marijuana use frequency and use consequences. From a sample of 592 undergraduates, 300 marijuana users completed a survey that assessed marijuana problems and the hypothesized risk and vulnerability factors. Affective variables were significantly associated with increased marijuana problems above and beyond the effects of gender and lifetime use frequency. A hypothesized vulnerability mechanism, whereby impulsivity strengthened the relationship between use frequency and marijuana problems, was observed. The findings support the hypothesis that affect dysregulation enhances risk for marijuana problems among young adults who use marijuana.

NOTES: OBJECTIVE: The effect of delinquency subtype on the development of substance dependence symptoms was examined. It was proposed that early-onset delinquents possess characteristics that increase their likelihood of developing substance dependence problems earlier and more rapidly than late-onset delinquents and nondelinquents. METHOD: The development of alcohol, nicotine, and cannabis dependence symptoms (DSM-III-R) was examined over a 6-year period of adolescence (age 11-17) among 36 early-onset delinquent, 86 late-onset delinquent, and 25 nondelinquent boys from a large epidemiological twin sample. Multilevel/random coefficients models were used to compare groups on the rate of growth in number of symptoms over time. RESULTS: As expected, early-onset delinquents showed an earlier onset and a faster rate of increase in the number of cannabis and nicotine dependence symptoms than late-onset delinquents and controls. Both delinquent groups had a more rapid increase in alcohol dependence symptoms than controls. CONCLUSIONS: The data showed that early-onset delinquency is associated with earlier onset of substance use disorder symptoms and more rapid acceleration of problems with drugs than late-onset delinquency. Treatments for boys with early-onset delinquency should account for their increased risk for drug use problems in adolescence and the potential effects of those problems on the course of antisocial behavior.

CONFERENCE NEWS
International Cannabinoid Research Society (ICRS) meeting Monterey, California July 10-14th 2002. For details see www.CannabinoidSociety.org