The Neurobiology of Drug Addiction: Neurophysiological and Behavioural Mechanisms Associated with Addiction

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The study was designed to investigate whether stressors could influence marijuana use/abuse in an animal model. Stressors are well known to be associated with drug-taking behaviour in humans. In animals, acute stress has been shown to increase self-administration or reward of addictive drugs such as morphine, cocaine, alcohol and amphetamine. Surprisingly, there are no such scientific studies of this phenomenon on marijuana or its psychoactive component, delta-9-tetrahydrocannabinol. It was therefore proposed that stressors could increase reward for marijuana use, which could ultimately lead to marijuana addiction.

An animal model of addiction, using the technique of place preference, was used to test this hypothesis. Positive place preference results were obtained with the known addictive drugs, cocaine and amphetamine, thus validating the technique. A given low dose of marijuana extract was first identified which produced neither rewarding nor aversive effects in the rat model. This dose was then used in combination with three parameters known to induce moderate to severe stress in rats, namely acute isolation stress, restraint stress and swimming stress. This technique was repeated using delta-9-tetrahydrocannabinol.

The results showed that the combination of a dilute marijuana extract with either isolation or restraint stress increased reward for marijuana. This effect was more significant for isolation stress. A low dose of delta-9-tetrahydrocannabinol also produced positive place preference. The results of the study strongly suggest that a dose of marijuana, which is not normally addictive, can become addictive if used in combination with certain acute stressors. This finding could have implications in humans in the Jamaican society, particularly with children, given the relatively high levels of societal stress, violence and drug-taking behaviour. The results may also be important in light of the controversies surrounding the use of marijuana.

These research findings have so far been presented at the Vancouver 2001 International Conference, held March 25-29, 2001; the 31st International Neuroscience Conference held in San Diego, November 10-15, 2001; and the 10th Annual Research Conference of the Faculty of Medical Sciences, held November 1, 2001.

Publications generated from the research include:

In 1986, a cohort of children born in Jamaica over a two-month period (September 1st - October 31st) was studied at the time of their birth. A sub-group of these children, those living in or attending school in Kingston and St. Andrew, had their school achievement, cognitive function, behaviour and self-esteem evaluated at age 11 years. These children are now being re-examined at age 15-16 years. The purpose of the second follow-up study is to identify the social, family, health and lifestyle factors which promote appropriate educational attainment, behaviour, self-esteem and emotional intelligence and engender resilience in Jamaican adolescents. The evaluation is also expected to help determine the factors responsible for producing the most stress in the lives of 16-year-olds.

In this ongoing research project, the children are identified using school records and a team of trained research nurses administers various anthropometric measurements, educational tests and questionnaires to them. Salivary samples are also taken from the children so that their levels of cortisol can be measured and stress levels determined. Parents are interviewed about their child’s development and teachers complete forms about the children’s behaviour within the school environment. School principals also complete questionnaires about school facilities.

Approximately 2,000 children are to be included in this follow-up study. Data collection began in October 2001 and will continue until August 2003. To date, 605 children in 42 schools have been evaluated and 167 parents and 272 teachers interviewed.

It is hoped that the findings from this project will assist in the development of national programmes for Jamaican adolescents. These should include the implementation of educational programmes for children with special needs and the development of training programmes for schools’ guidance counsellors to deal with the patterns of behaviour being exhibited by adolescents. The study should also allow for comparisons to be made with children in different countries in order to determine the strengths and weaknesses of our educational system.

The data collected in this phase of the project will be compared to data collected earlier on these children. This should help to determine the factors that contribute to positive or negative outcomes for adolescents and assist in the development of early intervention programmes.
Medical Sciences

Studies on Molecular Signal Transduction Mechanisms in Diabetes Mellitus

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The clinical profile of diabetes mellitus in the Caribbean encompasses the 30% insulin-dependent and the 70% non-insulin-dependent persons. In recent times, the prevalence of the disease in Jamaica has been 17.7%. Hyperglycaemia in non-insulin-dependent diabetes mellitus is the result of both resistance to insulin in muscle and other key insulin target tissues and decreased beta-cell insulin secretion. In addition to predisposing individuals to non-insulin-dependent diabetes mellitus, insulin resistance is a significant contributor to disease in the general population. Type 2 diabetes is a complex metabolic disorder characterised by elevated blood glucose levels and a marked increase in the risk of cardiovascular disease. Cardiovascular diseases (CVDs) are the major causes of mortality in persons with diabetes, and many factors, including hypertension, contribute to this high prevalence of CVD. Hypertension is approximately twice as frequent in patients with diabetes compared with patients without the disease.

S-nitrosoglutathione and S-nitroso-N-acetylpenicilamine, nitric oxide-donor drugs decompose in the body by a variety of mechanisms, to generate nitric oxide (NO) and are used in the treatment of cardiovascular disorders, particularly in the treatment of hypertension. In order to establish a diabetic model, we used streptozotocin that releases NO similarly to S-nitrosoglutathione and S-nitroso-N-acetylpenicilamine, except in larger amounts per unit weight of the drug administered. Using streptozotocin and the vitamin B3-derived compound nicotinamide, we established a diabetic state in adult rats. This diabetic state shares a number of features with non-insulin-dependent diabetes mellitus, and is characterised by stable moderate hyperglycaemia, glucose tolerance, altered glucose stimulated insulin secretion.

The findings of the study revealed that:

1. Mona rats treated with streptozotocin and nicotinamide have reduced insulin levels, of approximately less than 52% of the controls and;
2. Mona rats treated with streptozotocin and nicotinamide had reduced body weight and reduced total protein content compared with controls.

Preliminary results also revealed increased expression of glycoprotein PC-1 in the diabetic state as indicated from higher muscle PC-1 content in Mona rats treated with only 65 mg/kg of streptozotocin compared with rats treated with 65 mg/kg of streptozotocin and 180 mg/kg of nicotinamide.

These findings indicate that membrane glycoprotein PC-1 is a major factor in the aetiology of insulin resistance and is a potential new therapeutic target for antidiabetic therapy.

Further studies will involve the characterisation of protein kinase C (PKC), which has the effect of exacerbating insulin resistance and precipitating NIDDM and examine the signalling events that are involved in the activation of the insulin receptor substrate-1 (IRS-1) proteasome degradation pathway. This will assist in our understanding of the molecular mechanism and signal transduction pathways that insulin utilises to specifically regulate glucose uptake. The detailed understanding of these events will provide a conceptual framework for the development of new therapeutic targets to treat this chronic and debilitating disease process.
The aim of this research project is to use in vitro techniques and gene technology to identify and produce high yielding yam planting materials for farmers’ use. This approach allows for the production of disease-free planting materials, and has a high multiplicity rate. A one-meter yam vine, which is normally discarded, can give up to 100,000 plantlets in one year, once established in culture. The tubers produced from in vitro derived plantlets can be used as seed yams and/or ware tubers.

The use of tissue culture derived planting materials ensures disease-free materials, as the plants are viral indexed before multiplication in culture. The production of planting materials using in vitro techniques removes the need for cutting the harvested tuber in order to obtain planting stock, thus extending the shelf life of the product. This is particularly significant, as the cutting of tubers allows for fungal growth, which necessitates the use of fungicide in order to prevent excessive tuber loss.

Below is a list of some of the achievements of the project to date.

* The initiation, establishment and multiplication of the following yam cultivars (cv.) in culture: Dioscorea alata cv. Sweet yam, Dioscorea cayenensis cv. Roundleaf Yellow Yam and Dioscorea rotundata cv. Negro yam.
* The establishment and maintenance of a germplasm collection for near-extinct Jamaican yam varieties namely: Calabash, Mozella, Pum Pum, Chinese, Diamond, Akam, Dark Night, Moonshine, Bull Hoof, Yampie, Tau, Barbie and Hard yams.
* The acclimatization of in vitro derived yam plantlets for field trials.
* In vitro screening for high yielding yam varieties.
* The characterization of starches from twenty three Jamaican yam varieties namely: Roundleaf, Black Wiss, Negro, Lucea, Renta, St. Vincent (purple skin, white flesh), St. Vincent (pink skin, white flesh), Barbados, Mozella, Tau, Chinese, Short Neck Yampie, Long Neck Yampie, Akam, Calabash, Dark Night, Moonshine, Pum Pum, Guinea, Bitter, White, Hard and Sweet yams.
* The analysis of some biochemical transformations associated with the transfer of three varieties of yams (Sweet yam, Roundleaf Yellow Yam and Negro Yam) from the field to in vitro culture.
* Screening for gene(s) responsible for the breakage of dormancy (sprouting) during storage of yams.

Publications from this project include several articles in refereed journals and numerous conference papers.
Exploiting the Anti-Cholesterolemic, VLDL+LDL - Reducing and HDL-Increasing Properties of the Jamaican Wild Yams (Dioscorea Polygnoides and Rajania Cordata) for Sustainable Development

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This research project represents the second phase of an earlier project entitled, “Screening, Assessment and Identification of Anti-Nutritional Factors in Selected Common Caribbean Food Crops and Spices and A Study of the Effects of Their Consumption in Normal and Disease States”. It seeks to translate the findings from that project into benefits that are exploitable in the pharmaceutical/nutraceutical industries.

The wild yam in Jamaica is traditionally used to make “roots tonic” for the treatment of a wide range of diseases, but is also cooked and consumed. With the high prevalence of diabetes in the Caribbean Islands, affecting some 15-20% of the population (Richards, 1988; Ragoobirsingh et al., 1995), the Jamaican wild yam with its appreciable levels of Diosgenin (Asemota et al., 2002) needs to be exploited. Diosgenin has been shown to lower the indices of diabetes in rat models (Cayen and Dvornik, 1978, McAnuff et al., 2002). In a study designed to investigate plasma and liver lipid distributions in diabetic rats fed with sapogenin extract from the Jamaican wild yam, it was observed that the extract significantly lowered their blood cholesterol level in just three weeks. It also lowered their Very Low Density Lipoprotein and Low Density Lipoprotein (VLDL+LDL) and increased their High-Density Lipoprotein (HDL) levels.

The project has been designed to effect the translation of the above findings for use in humans for the purposes of sustainable development. The study will test the wild yam preparation using a guinea pig model, which closely mimics human physiology, for hypercholesterolemia as a prelude to human trials. The findings from the study should lead to the development of products from the Jamaican wild yam for use in the pharmaceutical/nutraceutical industries. The research will also facilitate the identification of the mechanism involved when the consumption of Jamaican wild yam lowers blood cholesterol and VLDL+LDL and increases HDL levels.

The findings should also show whether consumption of the Jamaican wild yam preparation has any toxic effect on the body, through an examination of its effects on the liver and kidneys. Additionally, the techniques used in this study may also be applied to tests on other plants for their potential for natural product development.

Several articles have been published in refereed journals, including Nutrition Research, Diabetologia Croatica, International Journal of Food Sciences and Nutrition. There have also been a number of conference presentations.
The increased cost of local sugar production and the fall in the price of sugar and its by-products on the world market has stimulated a search for new and innovative ways of revitalising and diversifying the local sugar industry. This has prompted investigations into a novel process of Xanthan gum production using a by-product of the sugar industry. Xanthan gum is a raw material produced through fermentation by the bacteria *Xanthomonas campestris*. It has unique properties which have allowed it to find numerous applications in the food, pharmaceutical and other industries as a thickener, stabiliser, emulsifier and suspending agent. It has widespread usage as an ingredient in several commonly-used products such as fertilisers, paints, dressings, juices, cake mixes, antacids, in cosmetic items such as toothpaste and hair care products. Its use extends even to the oil industry as an input in the process to recover oil in drilling operations.

However, the gum is currently imported at costs that are often prohibitive to local manufacturers and oil refining companies. With reduced prices, it could become extensively used in the petroleum industry in the Region and even in the wider international community, as vast quantities are required for the oil recovery process. Consequently, international research has been focusing on ways to reduce the cost of the production of Xanthan gum.

This research project has successfully utilised a by-product from the processing of sugar for the production of Xanthan gum. The low cost of the raw material has resulted in relatively low overall production costs, which will facilitate the supply of the product to local manufacturers at lower prices. The project is now working on maximising the product yield and quality of Xanthan gum to increase the efficiency of the production process and consequently its value to industry. Process optimisation, downstream processing and product purification are major activities that will be ongoing throughout the life of the project.

Results to date have been very encouraging and the focus is now on identifying and targeting potential partners in industry. A patent has been secured for this novel process, which will aid its transfer to industry by providing the rights to the process to the relevant parties.
Some of the benefits to be derived from the work in this project are:

- establishment and commissioning of new fermentation facilities at the Mona Campus, which will increase its ability both to teach and conduct research in fermentation technology;
- diversification of the local sugar industry through the utilisation of by-products from the processing of sugar cane in the production of Xanthan gum;
- supply of Xanthan gum to local manufacturers at reduced cost, which should increase local utilisation of the product;
- increased revenue for the University of the West Indies through the sale of patents or licensing agreements to commercial entities involved in Xanthan gum production; and
- development of Xanthan gum as a non-traditional export product.

This project was developed to meet the needs of the region through the utilisation of local raw materials. A Memorandum of Understanding has been signed between the Sugar Industry Authority (SIA) of Jamaica and the University of the West Indies, which should lead to the identification and provision of resources for the funding of a feasibility study. The identification of a suitable partner will ensure that the technology and its ensuing financial benefits remain in the region.
The purpose of this research project was to examine the daily activities of seniors and to determine how these activities contributed to their economic well-being as well as that of their families and communities. It also sought to identify the intergenerational supports of the young and old generations towards each other.

The project was carried out using a sample of the many income generating and community-based projects and programmes across the island, involving seniors. Information on activities within these projects was garnered through discussions, interviews and questionnaires.

The study revealed that seniors across the country are involved in several types of income generating projects, which include farming and animal and poultry rearing. Income generated from these activities is oftentimes used to assist others, especially young people, to cover costs such as tuition fees and sundry expenses. They also assist with community support activities such as feeding programmes, or make direct contributions to schools, whether individually or as part of a group.

The findings also revealed that seniors are very involved in family activities. Among the areas of involvement identified were the giving of advice and financial help, and 85% of respondents took part in after school care for children. Furthermore, despite some negative comments by seniors about the young people of today, the study revealed many intergenerational interactions and a relatively high tolerance and understanding between the two groups.

Several papers are being prepared for publishing. The findings are being used in case studies on successful ageing and to produce manuals of best practice. Additionally, the findings of such positive contributions of seniors to family challenge the prevailing view of older persons as economic burdens and will therefore be used in advocacy work.
The project sought to collect data on cancer mortality and the incidence of cancer in Jamaica and facilitate their analyses at the Jamaica Cancer Registry. Particular emphasis was placed on the common cancers found in both males and females.

During the project, published reports from the Registrar General's Department in St. Catherine were examined and deaths caused by cancer noted, using 1999 as the reference year. Mortality rates per 100,000 persons were calculated using the 1999 census figures for Jamaica, published by the Statistical Institute of Jamaica. The overall mortality from cancer was compared to deaths from all other causes and the mortality from specific cancers in both males and females was analysed to provide a list of the leading cancer mortality sites.

It has been observed that for 1999, cancers accounted for 17.7% of all recorded deaths in Jamaica. The age adjusted cancer mortality rate for the entire population was 140.5 per 1,000,000 (171.7 per 100,000 for males and 122 per 100,000 for females). In males, the leading cancers per 100,000 were those involving the prostate (53.9), lung (27.9) and stomach (15.2) while in females the leading cancers involved the breast (31.1), the uterine cervix (15.8) and the large bowel (10.0). The combined cancer mortality figures (males and females) revealed that cancer of the prostate (22.5), lung (16.3) and breast (16.0) were the leading sites.

The findings from this research project should be of interest to health care administrators who will be able to utilise the data to plan programmes of prevention and control especially for the leading cancers, thereby improving the overall health of the nation. As this is the first such analysis of cancer mortality, the data will also serve as a baseline against which the success of future cancer screening programmes, for example those of the breast, prostate and uterine cervix, can be judged. Furthermore, by comparing mortality statistics with cancer incidence data also published by the registry, cancer prevention and control programmes can be appropriately weighted in terms of budgetary expenditures for screening programmes, lifestyle adjustments and treatment protocols.

The manuscript entitled *Jamaica Cancer Mortality Statistics, 1999*, which emanated from the project, has been accepted for publication in *The West Indian Medical Journal*.
Identification and Characterisation of Insect Vector(s) of Lethal Yellowing (LY) Disease of Coconuts in Jamaica

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Lethal Yellowing (LY) disease is once again the single most important plant disease affecting the coconut industry in Jamaica (Been, B.O. 1999. *Position Paper on Lethal Yellowing Disease of Coconut*, Coconut Industry Board, Jamaica). This disease which is caused by a phytoplasma, has killed millions of coconut trees in the Caribbean over the past 40 years. Although much research work has been undertaken, the pathogen is yet to be obtained in pure culture *in vitro*.

The inability to culture phytoplasmas has slowed the progress of their identification, detection, characterisation and control (Schaff, S., Lee, I.M., and Davis, R.D. 1992. *Sensitive Detection and Identification of Mycoplasma-like Organisms in Plants by Polymerase Chain Reaction*, Biochemical and Biophysical Communications 186: 1503-1509). The deaths of Malayan Dwarf coconuts in western Jamaica in unusually high numbers in the 1980s indicated that the pathogen was capable of overcoming the resistance of that variety. In 1988, the incidence of LY disease increased significantly, and new outbreaks were reported in eastern Jamaica. Within six years, lethal yellowing disease destroyed all the Malayan Dwarf coconuts in Hart Hill (West Portland), Darlingford (East Portland) and Williamsfield (border of St Thomas and Portland). To date the vector of the phytoplasma responsible for the spread of LY disease in Jamaica is still not known and only the *Cixiidae Myndus crudus* in laboratory tests has been identified as an effective vector of LY in Florida (Howard, F. W. 1980. *Population Density of Myndus Crudus Van Duzee* (Homoptera:Cixiidae) in Relationship to Coconut Lethal Yellowing Distribution in Florida. *Principes* 24: 174-178).

This research project seeks to design strategies for managing the vector to effect control of the Lethal Yellowing disease in Jamaica. Molecular biology tools, such as nucleic acid hybridization, polymerase chain reaction (PCR), followed by restriction fragment length polymorphism analysis (RFLP), will be applied to the identification of potential phytoplasma vector species and the genetic diversity of phytoplasma associated with the Lethal Yellowing disease.

Preliminary results obtained using PCR and the primer pair P1/P7 indicate that the vector Myndus Crudus contains the phytoplasma associated with coconut lethal yellowing and therefore could be a potential vector for this disease in Jamaica. Further research work on Lethal Yellowing disease in coconut will include:

* molecular characterisation of insect fauna associated with the disease;
* identifying alternate host plant(s) acting as reservoirs for phytoplasma associated with the disease;
* determining the geographic distribution, host range and life history of insect vector(s) responsible for the disease; and
* undertaking transmission studies of phytoplasma from insect vector(s) to the host plants.

Malayan Dwarf Coconuts