

Responding to: Toward Understanding the Biology of Crime in Trinidad and Tobago

The Editor,

Sir,

I have read with great interest the article by Derek Emmanuel “Toward Understanding the Biology of Crime in Trinidad and Tobago”, available at doi: 10.7727/wimj.2013.297. I too have observed the escalation of crime in Trinidad and Tobago and concur with Emmanuel’s hypothesis with regard to the existence of a biological connection. I believe that social science has evolved beyond the point of summarily attributing criminal behaviour to environmental factors or fractured familial relationships. In support of Emmanuel’s position on the “biological underpinnings of criminal behaviour” and holistic clinical and social intervention to mitigate crime, I would like to amplify his statements and introduce my own perspectives by exploring historical legal case histories, scientific experiments at the molecular level (DNA coding level) and posing a hubristic view of the future. Hopefully this will spark some debate.

The following questions that may amplify Emmanuel’s biological underpinnings of criminal behaviour:

- What genes come into play to trigger the hunter-behaviour?
- Did modern humans inherit these genes from our African ancestors?
- Can MRI scans be used to trace this kind of behaviour to changes in the frontal lobe, which controls decision-making, or to the amygdala, which controls human emotion?
- How does the criminal justice system view this behaviour in light of current genetic technological advances which shake the free-will foundation of the modern legal system?
- What is the jurisprudence record on adjudicating such criminal behaviour today?
- Can embryo/genome editing save the day by removing or silencing criminal behaviour genes from modern day humans before they become symptomatic?

To put things in perspective and explore these questions, let us cite a landmark case as reported by Forzano and colleagues (5):

Abdelmalek Bayout, an Algerian citizen who moved to Italy in 1993, admitted in 2007 to stabbing and killing Walter Perez. Perez had insulted Bayout over the Kohl eye makeup (lead based mascara worn by some men) the Algerian was wearing. Bayout, a Muslim, claims he wore the makeup for religious reasons. The convicted man was affected by schizophrenia and was actively psychotic at the time of the

crime, having discontinued his psychotropic medication. The lower court judge partially agreed with the defence attorney that Bayout’s “psychiatric illness” was a mitigating factor and sentenced him to nine years and two months in prison – around three years less than Bayout would have received had he been deemed to be of sound mind.

Bayout’s defence attorney appealed this decision to a higher court and the appellate judge asked forensic scientists for a new independent psychiatric report to decide whether he should commute the sentence further as, in his words, “*there is increasing evidence that some genes together with a particular environmental insult may predispose people to certain behaviour*”. For the new report, a molecular neuroscientist at Italy’s University of Pisa, and a cognitive neuroscientist at the University of Padova, conducted a series of tests on Bayout. They found abnormalities in brain-imaging scans and in four genes that have been linked to violent behaviour including the gene encoding the neurotransmitter metabolizing enzyme monoamine oxidase A (MAOA), COMT, SCL6A4 and DRD4 genes. Table 1 has an explanation of these genes.

The defence team used a 2002 study (6) to show that low levels of MAOA expression is associated with aggressiveness and criminal conduct of young boys reared in abusive environments. The appellate judge decided to further reduce Bayout sentence by one year because he carried a few genetic variants thought to be associated with a predisposition to aggressiveness (7).

To answer the question of transgenerational inheritance of genes, many consortia of investigators around the world have elucidated the genomes of modern humans as well as Neanderthals and our ancient ancestors and have made comparisons of the genomes. In 2010, DNA evidence showed that after modern humans left Africa about 60 000 years ago, they bred for a short period of time with archaic humans, and, as a result, some populations today have more archaic genes than others. One thing should be reiterated: all living humans are members of the extant species *H sapiens* and by definition, all must equally be modern humans. The majority of our genes (> 90%) derives from our common African heritage (8–10).

One may think that the Italian case settles the argument that a person has no control over their choices because of their genes and this rationale could lead to the acceptance of genetic determinism in criminal cases. Looking at the historical record, the 1994 Stephen Mobley case in the United States of America (USA) was the first case in the world in which the defence asked to have their client tested for MAOA deficiency. Researchers have reported as many as 200 cases in the US in the last five years where lawyers have attempted to use genetic evidence and as many as 20 cases in the United Kingdom (UK)

Table 1: Genes linked to violent and criminal behaviour.

Gene	Functionality	Variant dysfunction	Cytogenetic location
<i>MAOA</i>	Gene encode mitochondrial enzymes which catalyze the oxidative deamination of amines, such as dopamine, norepinephrine, and serotonin.	Brunner syndrome; problematic impulsive behavior (such as arson, hypersexuality and violence), sleep disorders and mood swings. Referred to as the “warrior gene”.	Xp11.3
COMT	Catechol-O-methyltransferase catalyzes the neurotransmitters dopamine, epinephrine, and norepinephrine.	Risk factor for schizophrenia, bipolar disorder, panic disorder, anxiety, obsessive-compulsive disorder (OCD), eating disorders, and attention deficit hyperactivity disorder (ADHD), due to inefficient processing of information in the prefrontal cortex.	22q11.21
SCL6A4	Solute Carrier Family 6 (Neurotransmitter Transporter), Member 4.	Serotonin transporters are linked to neuroticism, sexual behaviour, alcoholism, clinical depression, hypertension and OCD.	17q11.2
DRD4	This gene encodes the D4 subtype of the dopamine receptor.	Mutations have been associated with psychiatric conditions including schizophrenia, bipolar disorder, autonomic nervous system dysfunction, ADHD, and the personality trait of novelty seeking.	11p15.5
DRD2	Discoidin Domain Receptor Tyrosine Kinase 2. This gene encodes the D2 subtype of the dopamine receptor.	Myoclonus dystonia and schizophrenia.	11q23.3
HLA-DRB9	Major histocompatibility complex, class II, DRβ9 (pseudogene).	Schizophrenia and other unidentified diseases.	6p22.1
SDCCAG8	Serologically Defined Colon Cancer Antigen 8.	Bardet-Biedl syndrome 16, Schizophrenia and bipolar disorder.	1q43
C10orf32	Chromosome 10 Open Reading Frame 32 is a Protein Coding gene.	Schizophrenia, blood pressure, aneurysm, Parkinson’s disease and coronary artery disease.	10q24.32
miR137	MicroRNA-137 has been implicated to act as a tumour suppressor in several cancer types.	Schizophrenia and mental retardation.	1p21.3
(CACNA1C)	Calcium Channel, Voltage-Dependent, L Type, Alpha 1C Subunit.	Schizophrenia, bipolar disorder, autism, Timothy syndrome, and Brugada syndrome.	12p13.33
(MAU2)	Sister Chromatid Cohesion Factor homolog.	Bipolar disorder and high-density lipoprotein.	19p13.11
ITIH3/4	Inter-alpha-trypsin inhibitor heavy chain H3 is a protein that is encoded by the <i>ITIH3</i> gene.	Schizophrenia, bipolar disorder, mental retardation and adiponectin	3p21.1
MMP16	Matrix metalloproteinase 16	Schizophrenia	8q21.3.

Source: Author’s construct (2015) Data obtained from the Human Gene Database.

Note: nearest gene is given in parentheses

in the last five years (11). These defence tactics have been unsuccessful so far, however, a few have influenced sentencing. Worldwide, sentencing guidelines for judges authorize punishment mitigations for offenders suffering from a reduced mental capacity. We contend that Bayout should have been subjected to compulsory hospitalization in a psychiatric institution where he could receive holistic treatment along the lines suggested by Emmanuel rather than incarceration.

To set the record straight, an earlier legal case of criminal behaviour was reported some 2500 years ago. Plato reported that a man was banished from a city because he was the third generation in his family to be found guilty of committing a crime. Obviously, his status as a third generation criminal was considered important evidence against him. Banishment

was interpreted to mean that no further generations of this criminal family would be born in that city. Maybe this was the first recorded legal finding and sentencing based on genetics. It is interesting how this number three appears in our history – three strikes in baseball and you are out or in the US criminal justice system, three strikes and you go to jail, or three strikes under eugenics law and you become sterilized or 3 consecutive wickets in cricket and you have a hat-trick. I think that Plato started something here.

The Bayout case cited in Italy supports the impulsive aggression that Emmanuel describes in his Viewpoint piece and further gives credence to his findings of violent criminal behaviour as part of the psychopathological symptoms of these maladjusted citizens of Trinidad and Tobago. The field of Epi-

genetics (12) may hold the answers to Emmanuel's holistic crime plan that incorporates clinical as well as social intervention strategies. Environmental and social stress at the molecular level is where we can see the resultant changes to DNA – epigenicity and polymorphisms. In humans, the gene NR3C1, which is linked to stress response, can undergo epigenetic modification due to childhood abuse, which in turn can affect a person's ability to deal with stress in their lives.

Rats have a similar gene and in rat models, maternal care (grooming pups) influences hypothalamic-pituitary-adrenal function through epigenetic programming (DNA methylation). It has been established that pups that were stressed because they were raised by negligent mothers, have extra methyl groups in their DNA, in a region that controls expression of NR3C1 – the equivalent gene in rats. Such methylation can reduce NR3C1 gene expression. In humans the NR3C1 gene encodes a protein expressed in neurons called glucocorticoids. Lower expression of NR3C1 increases stress and is associated with psychotic behaviour and severe forms of depression. This model has been observed in humans when suicide victims who were abused as children had the same methylation in their DNA repressing the NR3C1 gene (13–15).

The question now becomes, how can the new revolution in genetics save the day? We recall the debate in the sixties when journalists were decrying the advent of “test-tube babies” and “designer babies” which further triggered the rebirth of eugenics. However, critics were silenced when the first baby was created outside the mother's body. Today, *in vitro* fertilization (IVF) is an unremarkable occurrence and has paved the way for pre-implantation genetic diagnosis (PGD). Back then, futurists were already talking about the ability to alter the genes we pass to our children and another ethical debate kicked into high gear. In a historic decision, the UK became the first country to legalize a gene therapy technique (three-person *in vitro* fertilization) which could help women to avoid passing genetic defects onto their children (16).

Tools in the genome engineering arsenal include the molecular scissors clustered regularly interspaced short palindromic repeats, (CRISPR), chosen as the Method of the Year in 2011, and this system has been hailed as a revolution for this field. Another tool is transcription activator-like effector nucleases, (TALENs) developed in 2010 which also allows embryo editing. The third method is zinc-finger nucleases, (ZFNs) developed in 1990 and referred to as the “molecular cut-and-paste” tool. The last tool in the arsenal was developed this year and is called binding to designed library, extracting and sequencing, (BunDLE-seq). This is a quality assurance tool that quantitatively measures transcription factor binding to thousands of 200-bp sequences in a single experimental assay.

These tools are already used in the laboratory to edit the genome in animal embryos by changing, inserting, deleting defective genetic sequences, or adding desirable traits. Today, more than 200 life-sciences companies, research institutions, non-profit organizations, patient-advocacy groups and in-

vestors are focussed on developing and commercializing therapeutics, including those involving genome and embryo editing. The objective of these groups is to demonstrate that it is possible to produce children free of specific genes involved in inherited disease. If it is possible to correct the DNA in a woman's egg, or a man's sperm, those cells could be used in an *in vitro* fertilization (IVF) clinic to produce an embryo and then a child. It is also possible to directly edit the DNA of an early-stage IVF embryo using CRISPR. In January, US President Obama announced the Precision Medicine Initiative as a bold new research effort to revolutionize how we improve health and treat disease. Although he may have been thinking of Pharmacogenomics, we believe that embryo editing may find a place in this initiative.

In 2005, Lewis posed the futuristic questions: can we conceive of a situation where a drop of blood determines if you will be incarcerated for crimes not yet committed? Furthermore, what if the gene variants of criminal behaviour are identified and edited before becoming symptomatic, thereby negating any violence (18). We can reassure Lewis and Emmanuel that we have arrived at that day when technology has the wherewithal and has accomplished that task (18–19) in the new genetic revolution amid heated ethical debate. Noblest James Watson was attributed with saying, circa 1980: *We used to think our fate was in our stars. Now we know, in large measure, our fate is in our genes.* Many years earlier, Shakespeare, speaking through Cassius, already knew that our fate was not in our stars: *Men at times are masters of their fates: the fault, dear Brutus, is not in our stars, but in ourselves.*

I started this Letter with questions and so will end with a few questions:

- By silencing and editing these aggressive genes, where will the military find the next Chris Kyle from a normalized population?
- Where will we find another Mayweather or Pacquiao to entertain us?
- Will genetic engineering turn to the dark side and create our superheroes?

Keywords: Embryo editing, epigenicity, transgenerational inheritance, warrior gene.

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