Duke University
Department of Psychology & Neuroscience,
Institute for Genome Sciences & Policy
2020 West Main Street, Suite 201, Box 104410
Durham, North Carolina 27708

EMBARGOED UNTIL: Wednesday, March 27th, at 3:00 PM U.S. Central Time (*JAMA Psychiatry*)

TITLE: *Polygenic risk and the development of heavy, persistent smoking and nicotine dependence: Evidence from a 4-decade longitudinal study*

A research team led by Dan Belsky, Avshalom Caspi, and Terrie Moffitt at Duke University reports that genetic risks for adult smoking problems may be treatable through programs to prevent teens from becoming regular smokers.

PUBLICATION SOURCE: JAMA Psychiatry, to appear online on March 27, 2013

THE FINDINGS:

- Smoking problems develop in 3 stages: *Initiation*, in which young people try cigarettes; *Conversion to regular smoking*, in which some individuals become habitual users; and *Progression to heavy smoking and nicotine dependence*, in which habitual use develops into addiction. In our study, we followed 1,000 individuals from birth through midlife to ask how 6 genetic markers discovered in to predict adult cigarette consumption influenced the development of smoking problems beginning in adolescence.
- Genetic risks did not predict which teens tried cigarettes.
- BUT, *for teens who did try cigarettes, being at high genetic risk increased the likelihood they would convert to daily smoking, progress to heavy smoking, become nicotine dependent, and struggle with cessation.*
- *For individuals who did not become regular, heavy smokers as teens, genetic risk was not associated with risk for persistent heavy smoking, nicotine dependence, or cessation failure later in life.*
- So-called "chippers," regular smokers who are able to smoke at parties or consume only one or two cigarettes per day without getting addicted, had the lowest genetic risk of any population group—their genetic risk was even lower than non-smokers.
- The genetic risk score captured information about risk for smoking problems that could not be obtained from individual's family histories of smoking.

WHY ARE THESE FINDINGS IMPORTANT?

- Despite public health efforts to promote smoking cessation, millions of Americans still smoke cigarettes. Our findings suggest that programs and policies to prevent teen smoking or to discourage teens who do smoke from becoming regular smokers may be an effective intervention with those at highest genetic risk for lifelong heavy smoking.
- Findings highlight the importance of a developmental approach to understand new genetic discoveries. We followed teens from the point they initiated smoking through mid-life to ask how new genetic discoveries cause individuals to become persistent heavy smokers. Our works shows that genetic risks act by accelerating the progression of smoking behavior in adolescence. This points to a priority target for intervention.

SUPPORTING DETAILS

Genetic Risk: We measured genetic risk using a polygenic (many gene) profile composed of 6 different genetic markers called single-nucleotide polymorphisms, or "SNPs." Each of these SNPs had already been discovered to be related to how many cigarettes a person smoked per day in genome-wide association studies (GWAS) of tens of thousands of adults. The GWAS research had asked whether each of millions of individual SNPs was more common in adults who smoked more cigarettes per day. The 6 SNPs in the genetic profile were reliably related to smoking in multiple GWAS meta-analyses.

Rapid Developmental Progression of Smoking Behavior: We measured early conversion to daily smoking and rapid progression to heavy smoking. Early conversion to daily smoking was defined as smoking at least 1 cigarette per day by age 15 years. Rapid progression to heavy smoking was defined as becoming a pack-a-day smoker by age 18 years.

Adult Smoking Problems: We measured persistent heavy smoking, nicotine dependence symptoms (using the Fagerstrom Test of Nicotine Dependence), and cessation failures in the third and fourth decades of life.

PARTICIPANTS:

Participants were members of the Dunedin Multidisciplinary Health and Development Study, which tracks the development of a birth cohort of 1,032 children born in 1972-1973 in Dunedin, New Zealand. This birth cohort's families represent the full range of socioeconomic status and health in the general population. Follow-ups have been carried out at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and most recently at age 38 years, when 95% of the living cohort members took part. We examined all of the cohort members with European ancestry who provided DNA samples (98%).

MEDIA CONTACTS:

Dan Belsky, *Center for the Study of Aging and Human* Development and *Institute for Genome Sciences and Policy, Duke University, Durham, NC;* tel: +1-919- 613-4534; e-mail: dbelsky@duke.edu

Avshalom Caspi*, Department of Psychology and Neuroscience, Duke University, Durham, NC;* tel: +1-919-475-1702; e-mail: avshalom.caspi@duke.edu

Terrie Moffitt, *Department of Psychology and Neuroscience, Duke University, Durham, NC;* tel: +1-919-475-2974; e-mail: terrie.moffitt@duke.edu

Timothy Baker, *Associate Director, Center for Tobacco Research and Intervention, University of Wisconsin-Madison, Madison WI;* tel: 608-262-7568; e-mail: tbb@ctri.wisc.edu

UNIVERSITIES INVOLVED:

(1) Duke University, Durham, NC, USA. (2) Gillings School of Public Health, University of North Carolina – Chapel Hill, Chapel Hill NC, USA. (3) University of Wisconsin – Madison, Madison WI, USA. (4) University of Otago – Dunedin, NZ. (5) Institute of Psychiatry, Kings College, London UK.

The study protocol was approved by the Otago Ethics Committee and university ethics review board. Parents and children gave informed consent for the research.

MAIN FUNDING SOURCES:

1. The U.S. National Institute on Aging 2. The U.S. Agency for Healthcare Research and Quality 3. The U.K. Medical Research Council 4. The New Zealand Health Research Council 5.The Jacobs Foundation

EXPERTS NOT INVOLVED IN THE RESEARCH WHO ARE WILLING TO BE CONTACTED FOR COMMENT:

Francesca Ducci MD PhD (Francesca.Ducci@kcl.ac.uk, +44-20 7848 0565); Jason Boardman PhD (boardman@colorado.edu, 303-492-2146); Karestan Koenen PhD (kck5@columbia.edu, 212-305-7482) Danielle Dick PhD (ddick@vcu.edu, 804-828-8756)