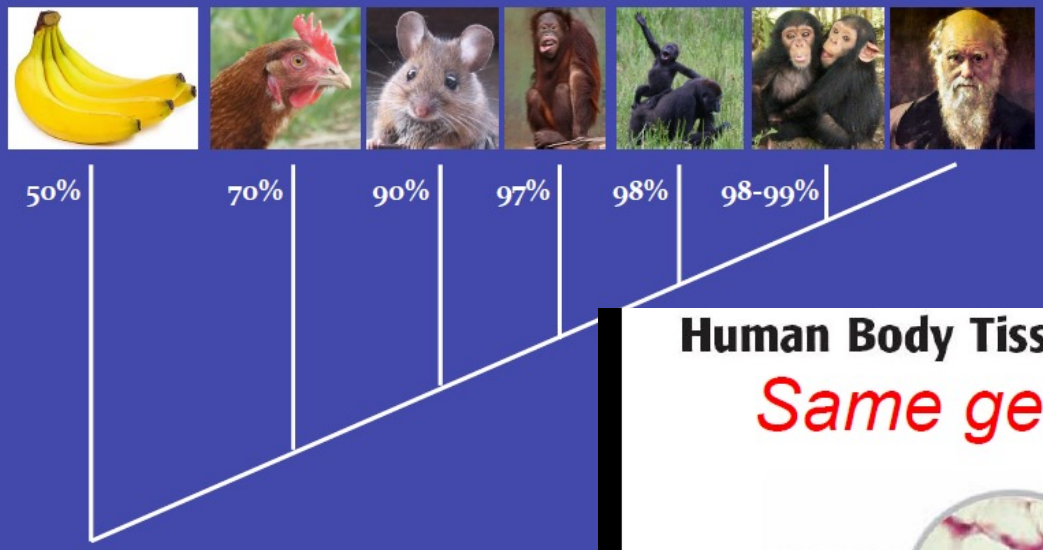
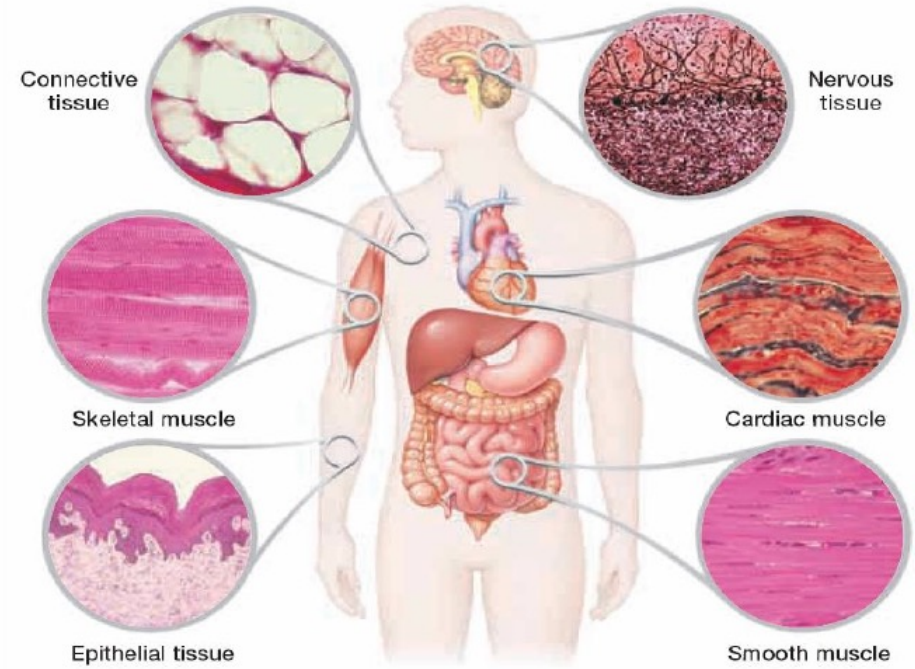
Do we really share 50% of our genome with a banana?

Different species, not so different genome



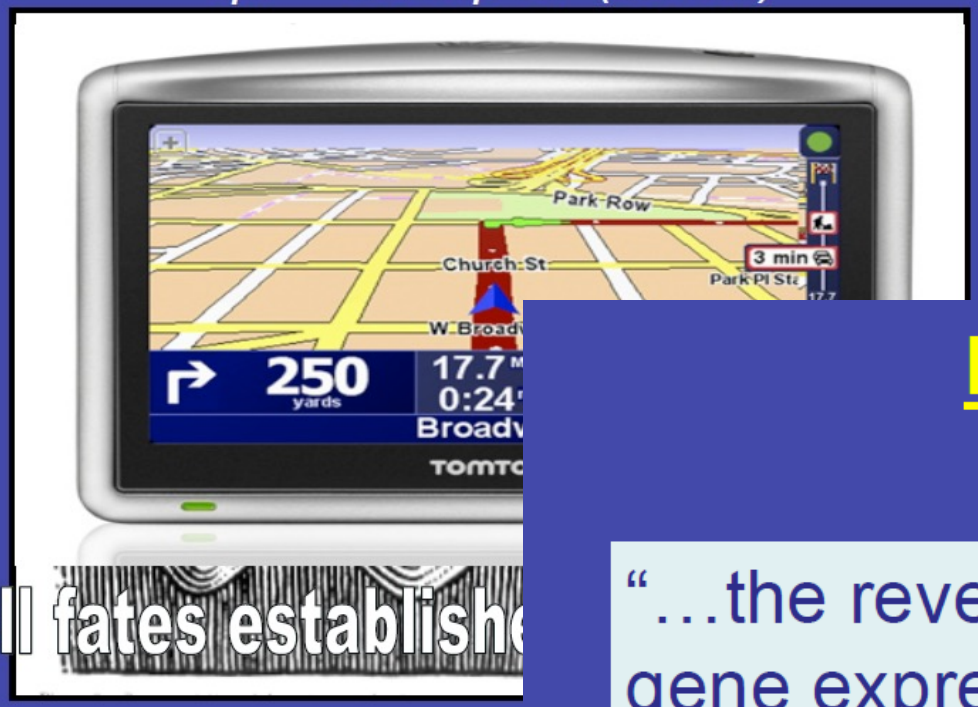
Human Body Tissues

Same genome, different cells



Conrad H Waddington's Epigenetic Landscape (1942)

epi = "on top of" (Greek)



Epigenetics

"…the reversible regulation of gene expression mediated principally through changes in DNA methylation and chromatin structure, occurring independently of the DNA sequence…"

Henikoff & Matzke - 1997

Proc Natl Ac

Epigene

Fraga MF, E

C, Carlsson

Epigenetics U

Your DNAmet does not lie!!!

- Do you smoke? Have you really stopped ?
- Can you digest dairy?
- Are you really as young as you say?
- Do you drink alcohol?
- Do you really go to the gym?

EWAS data: Epigenome wide association study of DNA met

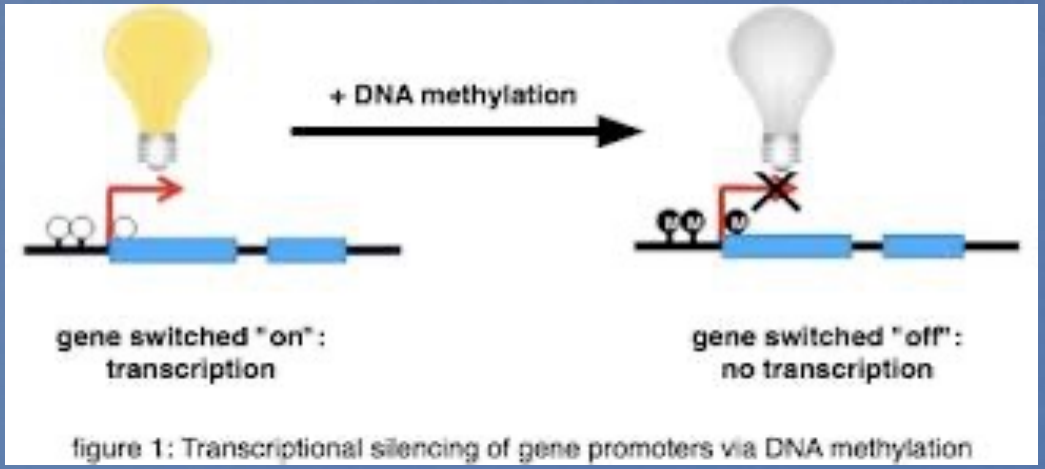


figure 1: Transcriptional silencing of gene promoters via DNA methylation

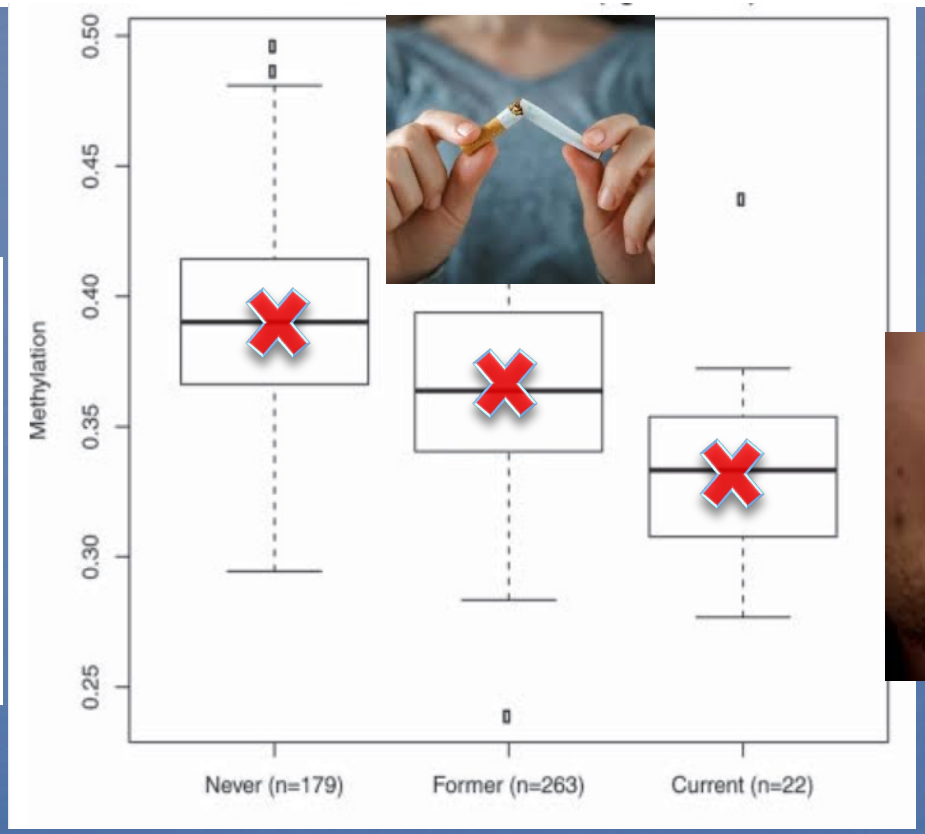
DNAmet smoking score

RESEARCH PAPER

Epigenetics 9:10, 1382–1396; October 2014; © 2014 Taylor & Francis Group, LLC

Cigarette smoking reduces DNA methylation levels at multiple genomic loci but the effect is partially reversible upon cessation

Loukia G Tsaprouni[1,2,†], Tsun-Po Yang[1,3,†], Jordana Bell[4], Katherine J Dick[5,6], Stavroula Kanoni[7], James Nisbet[1], Ana Viñuela[4], Elin Grundberg[8], Christopher P Nelson[5,6], Eshwar Meduri[1,4], Alfonso Buil[9], Francois Cambien[10], Christian Hengstenberg[11], Jeanette Erdmann[12], Heribert Schunkert[13], Alison H Goodall[5,6], Willem H Ouwehand[1,14], Emmanouil Dermitzakis[9], Tim D Spector[4], Nilesh J Samani[5,6], and Panos Deloukas[1,7,15,*]



Molecular Psychiatry (2018) 23, 422–433
www.nature.com/mp

OPEN

ORIGINAL ARTICLE

A DNA methylation biomarker of alcohol consumption

C Liu[1,2,3,55], RE Marioni[4,5,6,55], ÅK Hedman[7,55], L Pfeiffer[8,9,55], P-C Tsai[10,55], LM Reynolds[11,55], AC Just[12,55], Q Duan[13,55], CG Boer[14,55], T Tanaka[15,55], CE Elks[16], S Aslibekyan[17], JA Brody[18], B Kühnel[8,9], C Herder[19,20], LM Almli[21], D Zhi[22], Y Wang[23], T Huan[1,2], C Yao[1,2], MM Mendelson[1,2], R Joehanes[1,2,24], L Liang[25], S-A Love[23], W Guan[26], S Shah[6,27], AF McRae[6,27], A Kretschmer[8,9], H Prokisch[28,29], K Strauch[30,31], A Peters[8,9,32], PM Visscher[4,6,27], NR Wray[6,27], X Guo[33], KL Wiggins[18], AK Smith[21], EB Binder[34], KJ Ressler[35], MR Irvin[17], DM Absher[36], D Hernandez[37], L Ferrucci[15], S Bandinelli[38], K Lohman[11], J Ding[39], L Trevisi[40], S Gustafsson[7], JH Sandling[41,42], L Stolk[14], AG Uitterlinden[14,43], I Yet[10], JE Castillo-Fernandez[10], TD Spector[10], JD Schwartz[44], P Vokonas[45], L Lind[46], Y Li[47], M Fornage[48], DK Arnett[49], NJ Wareham[16], N Sotoodehnia[18], KK Ong[16], JBJ van Meurs[14], KN Conneely[50], AA Baccarelli[51], IJ Deary[4,52], JT Bell[10], KE North[23,56], Y Liu[11,56], M Waldenberger[8,9,56], SJ London[53,56], E Ingelsson[7,54,56] and D Levy[1,2,56]

"144 CpGs was highly predictive for discriminating current heavy alcohol drinkers from non-drinkers (AUC40.90) in all replication cohorts.

As a biomarker, these selected CpGs performed better than commonly clinical variables and biomar- kers in discriminating current heavy alcohol drinking.

The biomarker analysis and ancestry-stratified meta-analysis showed : 1) a number of DNA methylation sites displayed consistent alcohol-related effects in whole-blood samples of people of EA and AA but 2) some specific to EA"

Does cannabis leave a signature on our DNA?

Received: 18 December 2019 | Revised: 30 April 2020 | Accepted: 15 June 2020

DOI: 10.1002/ajmg.b.32813

ORIGINAL ARTICLE

American Journal of Medical Genetics Part B Neuropsychiatric Genetics | WILEY

Epigenome-wide analysis uncovers a blood-based DNA methylation biomarker of lifetime cannabis use

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Funding information
National Institute of Environmental Health Sciences, Grant/Award Numbers: ZO1 ES-044005, ZO1 ES-049032, ZO1 ES-049033; RTI International, Grant/Award Number: Fellow Program

Abstract

Cannabis use is highly prevalent and is associated with adverse and beneficial effects. To better understand the full spectrum of health consequences, biomarkers that accurately classify cannabis use are needed. DNA methylation (DNAm) is an excellent candidate, yet no blood-based epigenome-wide association studies (EWAS) in humans exist. We conducted an EWAS of lifetime cannabis use (ever vs. never) using blood-based DNAm data from a case–cohort study within Sister Study, a prospective cohort of women at risk of developing breast cancer (Discovery N = 1,730 [855 ever users]; Replication N = 853 [392 ever users]). We identified and replicated an association with lifetime cannabis use at cg15973234 (CEMIP): combined $p = 3.3 \times 10^{-8}$. We found no overlap between published blood-based cis-meQTLs of cg15973234 and reported lifetime cannabis use-associated single nucleotide polymorphism (SNPs; $p < .05$), suggesting that the observed DNAm difference was driven by cannabis exposure. We also developed a multi-CpG classifier of lifetime cannabis use using penalized regression of top EWAS CpGs. The resulting 50-CpG classifier produced an area under the curve (AUC) = 0.74 (95% CI [0.72, 0.76], $p = 2.00 \times 10^{-5}$) in the discovery sample and AUC = 0.54 ([0.51, 0.57], $p = 2.87 \times 10^{-2}$) in the replication sample. Our EWAS findings provide evidence that blood-based DNAm is associated with lifetime cannabis use.

KEYWORDS

biomarker, cannabis, DNA methylation, epigenome-wide association study, EWAS, marijuana

Does cannabis leave a signature on our DNA?

Osborne et al. *Translational Psychiatry* (2020)10:114
https://doi.org/10.1038/s41398-020-0800-3

Translational Psychiatry

ARTICLE Open Access

Genome-wide DNA methylation analysis of heavy cannabis exposure in a New Zealand longitudinal cohort

Amy J. Osborne[1], John F. Pearson[2], Alexandra J. Noble[1], Neil J. Gemmell[3], L. John Horwood[4], Joseph M. Boden[4], Miles C. Benton[5], Donia P. Macartney-Coxson[5] and Martin A. Kennedy[2]

Abstract

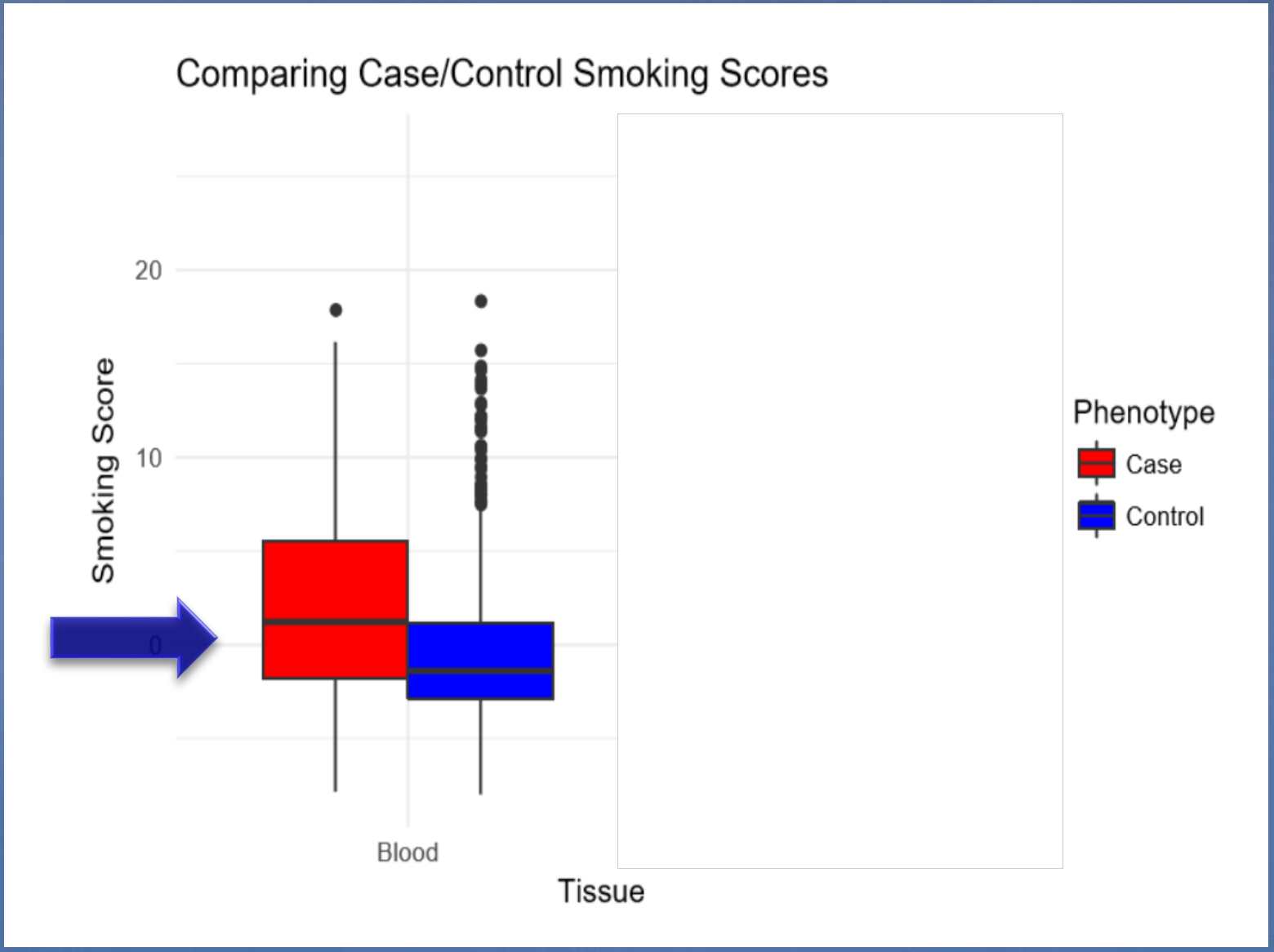
Cannabis use is of increasing public health interest globally. Here we examined the effect of heavy cannabis use, with and without tobacco, on genome-wide DNA methylation in a longitudinal birth cohort (Christchurch Health and Development Study, CHDS). A total of 48 heavy cannabis users were selected from the CHDS cohort, on the basis of their adult exposure to cannabis and tobacco, and DNA methylation assessed from whole blood samples, collected at approximately age 28. Methylation in heavy cannabis users was assessed, relative to non-users ($n = 48$ controls) via the Illumina Infinium® MethylationEPIC BeadChip. We found the most differentially methylated sites in cannabis with tobacco users were in the *AHRR* and *F2RL3* genes, replicating previous studies on the effects of tobacco. Cannabis-only users had no evidence of differential methylation in these genes, or at any other loci at the epigenome-wide significance level ($P < 10^{-7}$). However, there were 521 sites differentially methylated at $P < 0.001$ which were enriched for genes involved in neuronal signalling (glutamatergic synapse and long-term potentiation) and cardiomyopathy. Further, the most differentially methylated loci were associated with genes with reported roles in brain function (e.g. *TMEM190*, *MUC3L*, *CDC20* and *SP9*). We conclude that the effects of cannabis use on the mature human blood methylome differ from, and are less pronounced than, the effects of tobacco use, and that larger sample sizes are required to investigate this further.

Introduction

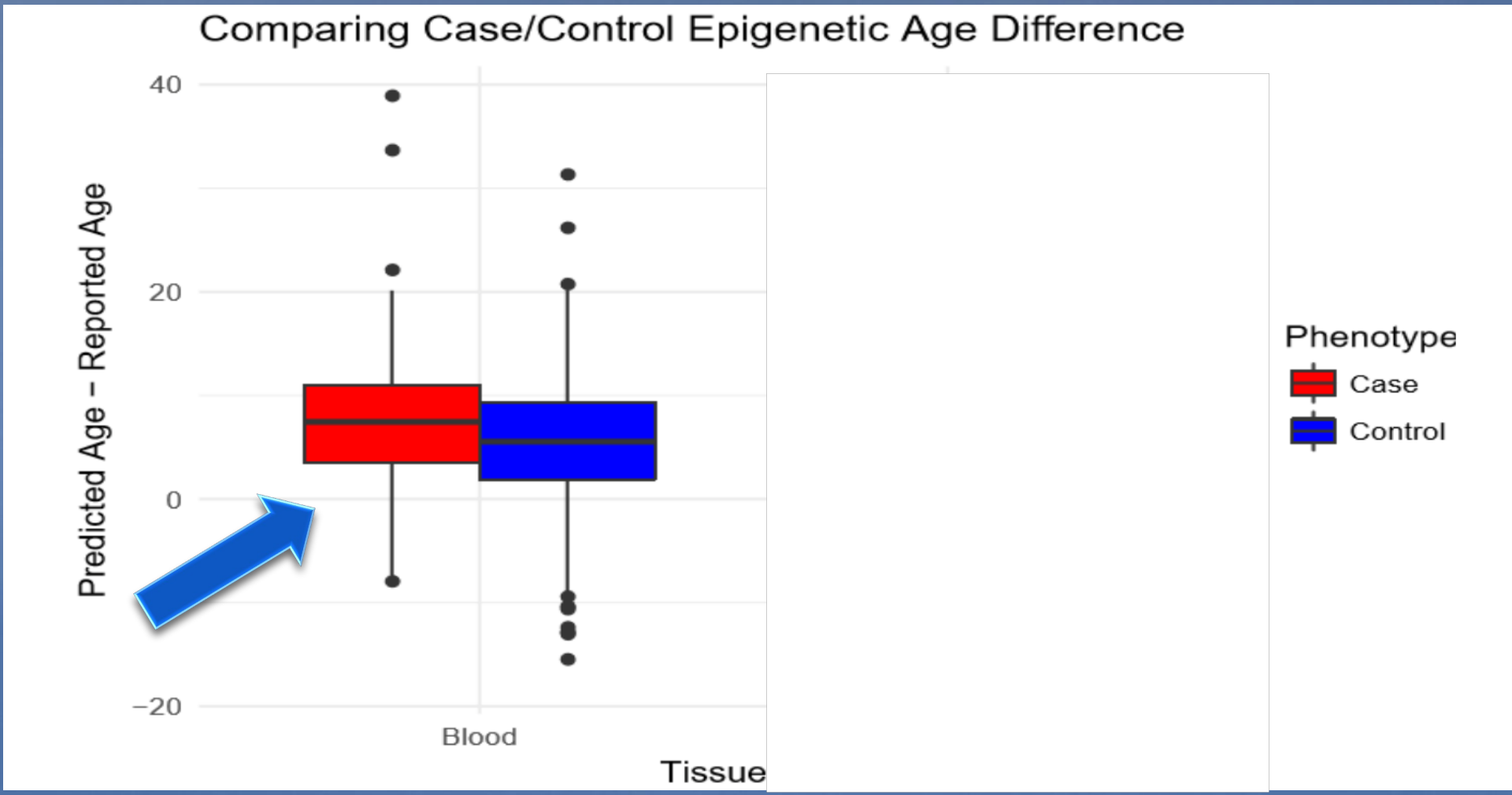
Cannabis use is an important global public health issue, number of areas, including mental health (psychosis[7–9], schizophrenia[10,11], depression[12,13]) and illicit drug abuse[14].

Do you really know how old you are?

EWAS smoking score: the EUGEI example

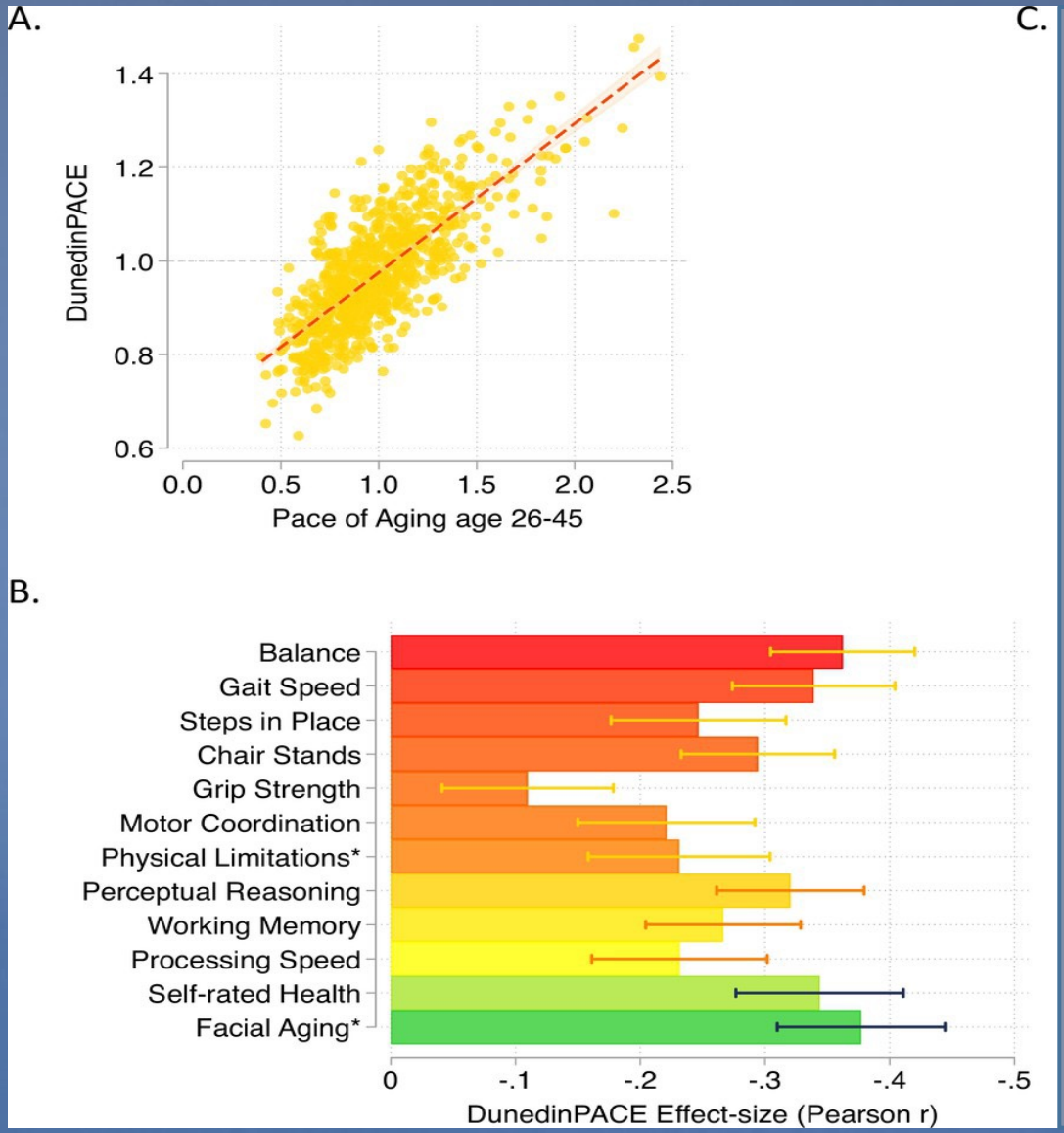


EUGEI-EWAS: DNA-met age score

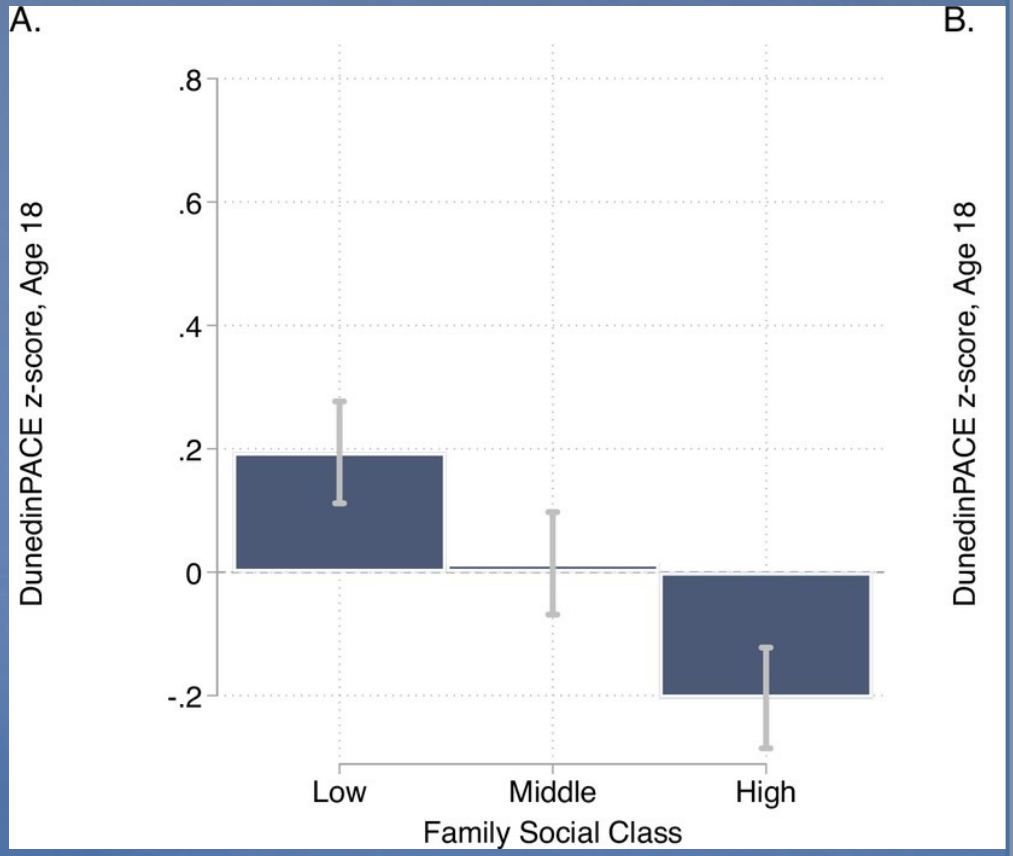


DunedinPACE score:

DunedinPACE is a novel blood biomarker of the pace of aging.



DunedinPACE levels by strata of childhood socioeconomic status (SES) and victimization in the E-Risk Study.



Social adversity and epigenetic aging: a multi-cohort study on socioeconomic differences in peripheral blood DNA methylation

Giovanni Fiorito[1,2], Silvia Polidoro[1], Pierre-Antoine Dugué[3,4], Mika Kivimaki[5], Erica Ponzi[6], Giuseppe Matullo[1,2], Simonetta Guarrera[1,2], Manuela B. Assumma[1,2], Panagiotis Georgiadis[7], Soterios A. Kyrtopoulos[7], Vittorio Krogh[8], Domenico Palli[9], Salvatore Panico[10], Carlotta Sacerdote[11], Rosario Tumino[12], Marc Chadeau-Hyam[13], Silvia Stringhini[14], Gianluca Severi[1,15], Allison M. Hodge[3,4], Graham G. Giles[3,4], Riccardo Marioni[16], Richard Karlsson Linnér[17], Aisling M. O'Halloran[18], Rose A. Kenny[18], Richard Layte[18], Laura Baglietto[19], Oliver Robinson[13], Cathal McCrory[18], Roger L. Milne[3,4] & Paolo Vineis[1,13]

- Low socioeconomic status (SES) is associated with earlier onset of age-related chronic conditions and reduced life-expectancy, but the underlying biomolecular mechanisms remain unclear. Evidence of DNA-methylation differences by SES suggests a possible association of SES with epigenetic age acceleration (AA).

- The associations were only partially modulated by the unhealthy lifestyle habits of individuals with lower SES. Individuals who experienced life-course SES improvement had intermediate AA compared to extreme SES categories, suggesting reversibility of the effect and supporting the relative importance of the early childhood social

www.nature.com/scientificreports

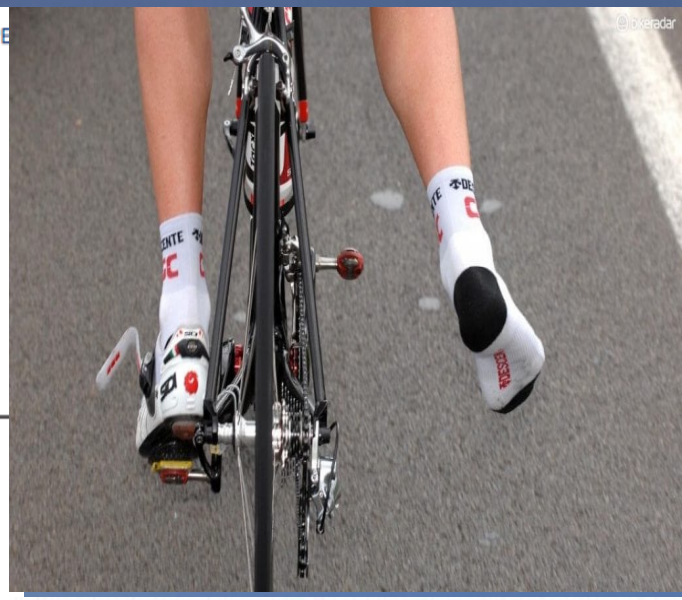
DNAmet and Exercise

RESEARCH PAPE

Epigenetics 9:12, 1557–1569; December 2014; Published with license by Taylor & Francis Group, LLC

An integrative analysis reveals coordinated reprogramming of the epigenome and the transcriptome in human skeletal muscle after training

Maléne E Lindholm[1,*,†], Francesco Marabita[2,*,†], David Gomez-Cabrero[2], Helene Rundqvist[3], Tomas J Ekström[4], Jesper Tegnér[2,‡], and Carl Johan Sundberg[1,‡]



Karolinska Institute:
23 men and women to bicycle using only one leg for 45 minutes, four times a week over three months.

Muscle biopsies before and after the experiment

new methylation-gene expression patterns on genes associated with insulin response, inflammation and energy metabolism

EWAS and RNA-seq

Pidsley *et al. Genome Biology*
http://genomebiology.com/20

RESEARCH

Methylomi
supports a
schizophre

Ruth Pidsley[1,2], Joana Vi
Gustavo Turecki[4], Leona

logy

Access

r[4],

DOI 10.1186/s13059-016-1041-x

Genome Biology

RESEARCH Open Access

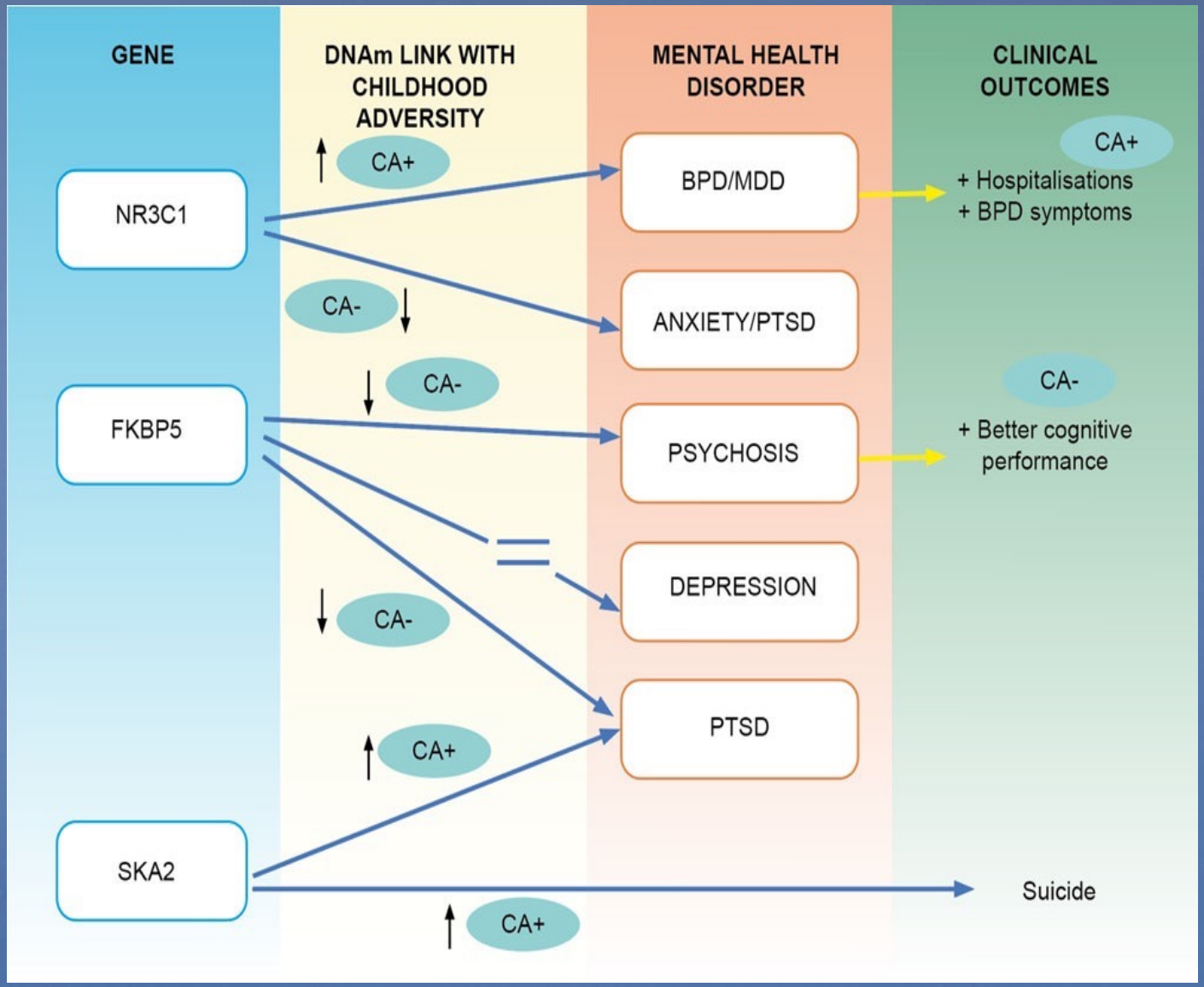
CrossMark

An integrated genetic-epigenetic analysis of schizophrenia: evidence for co-localization of genetic associations and differential DNA methylation

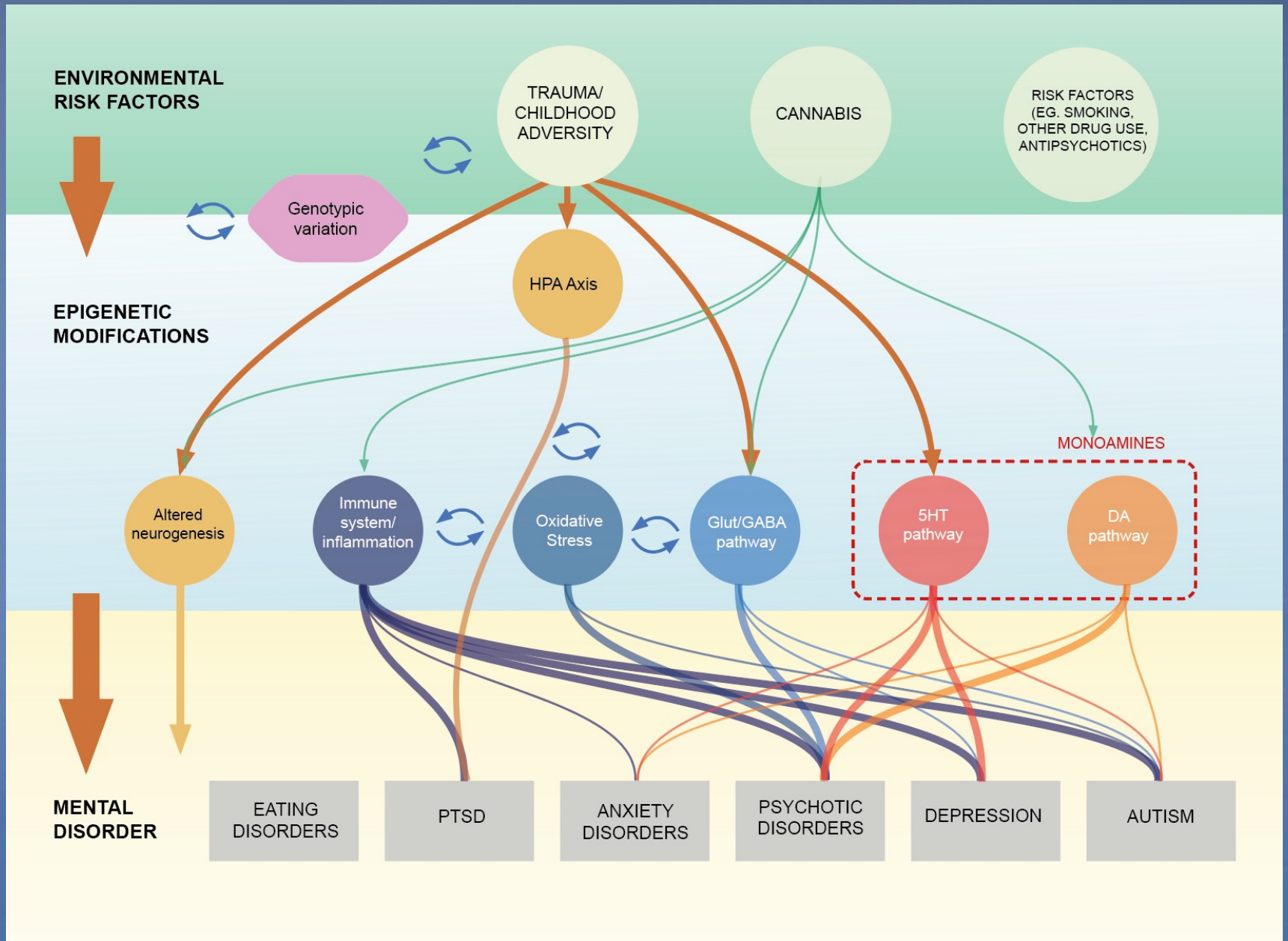
Eilis Hannon[1], Emma Dempster[1], Joana Viana[1], Joe Burrage[1], Adam R. Smith[1], Ruby Macdonald[1], David St Clair[2], Colette Mustard[3], Gerome Breen[4], Sebastian Therman[5], Jaakko Kaprio[5,6,7], Timothea Toulopoulou[8], Hilleke E. Hulshoff [illegible][9], Marc M. Bohlken[9], Rene S. Kahn[9], Igor Nenadic[10], Christina M. Hultman[11], Robin M. Murray[4], David A. Collier[4,12], Nick Bass[13], Hugh Gurling[13], Andrew McQuillin[13], Leonard Schalkwyk[4,14] and Jonathan Mill[1,4,15*]

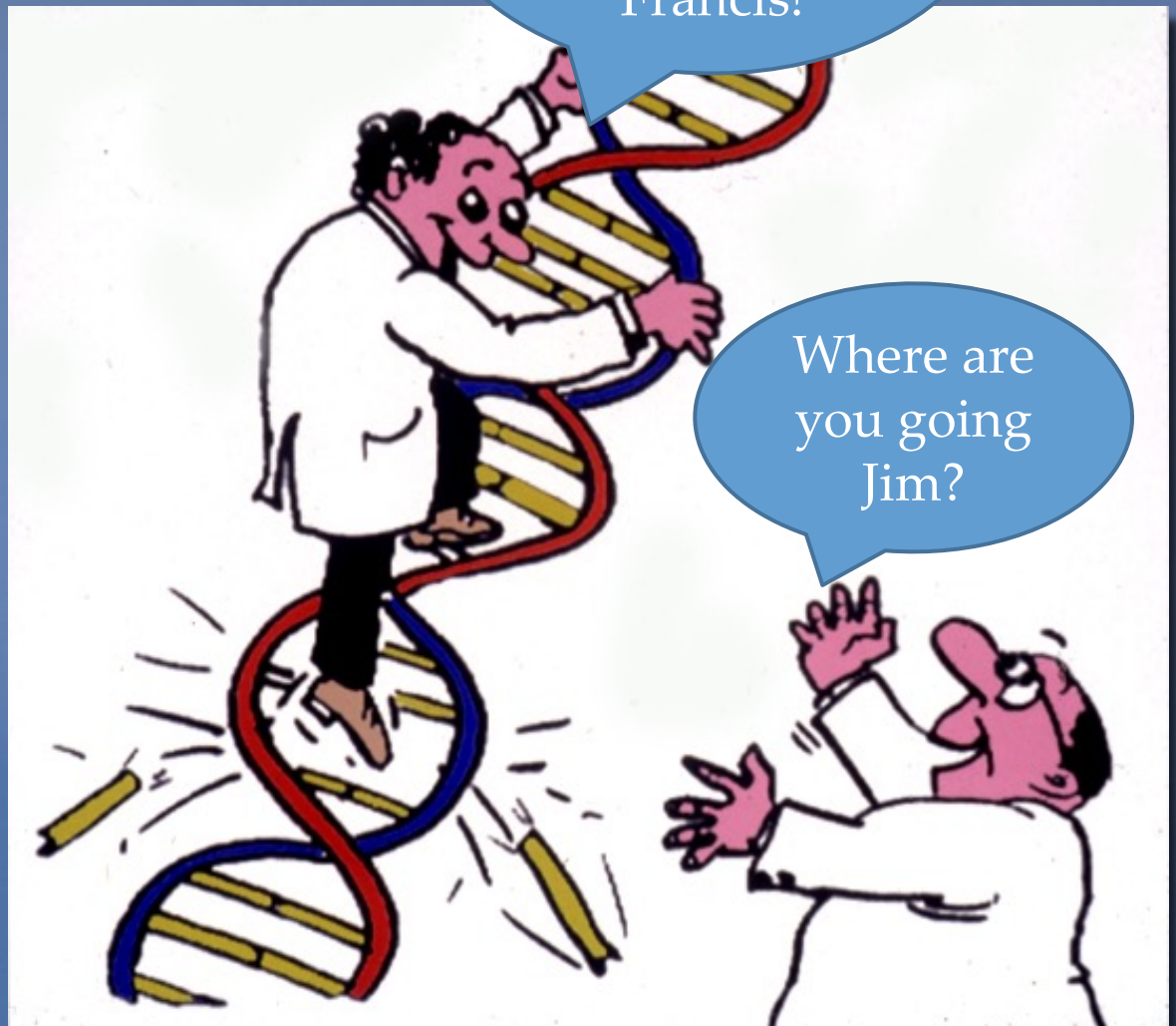
"We have identified multiple differentially methylated positions and regions consistently associated with schizophrenia across the three cohorts; these effects are independent of important confounders such as smoking. We also show that epigenetic variation at multiple loci across the genome contributes to the polygenic nature of schizophrenia"

Can epigenetics shine a light on the biological pathways underlying major mental disorders? Alameda L, **Trotta G**, Quigley H, Rodriguez V, Gadelrab R, Dwir D, Dempster E, Wong CCY, Forti MD. Psychol Med. 2022



And more broadly




I am following the trails left by the environment, Francis!
Where are you going Jim?

THANK YOU!