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Introducing PEEP: The psychiatry early experience programme

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At Guy's King's and St Thomas' School of Medicine, a unique initiative is the Psychiatry Early Experience Programme (PEEP), which allows students to shadow psychiatry trainees at work several times a year. The students' attitudes towards psychiatry and the scheme are regularly assessed and initial results are already available.

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Epigenetic discoveries in psychiatric disorders

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Methylome modifications in monozygotic twins and in depression

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Epigenetics is the study of gene expression changes that are produced by heritable, though potentially reversible, modifications of chromatin structure or DNA methylation. DNA methylation is interesting in epidemiological studies, due to its accessibility and since previous evidence indicates that large inter-individual differences in methylation levels at some loci may correlate with phenotypic plasticity in changing environments.

Prior genome-wide methylomic research on depression has suggested that, together with differential DNA methylation changes, affected co-twins of monozygotic twin pairs have increased DNA methylation variability, probably in line with theories of epigenetic stochasticity. However, the putative biological roots of this variability remain largely unexplored.

This study evaluate whether DNA methylation differences within MZ twin pairs were related to differences in their depressive status. Genome-wide DNA methylation levels were measured in peripheral blood of 34 twins (17 MZ pairs) using Illumina Infinium Human Methylation450 Beadchip. Two analytical strategies were used

to identify differentially methylated probes (DMPs) and variably methylated probes (VMPs).

The majority of the DMPs were located in genes previously related to neuropsychiatric phenotypes, such as WDR26, a GWAS hit for MDD whose expression levels have been found altered in blood of depressed individuals.

VMPs were located in genes such as *CACNA1C*, *IGF2* and the p38 MAP kinase *MAPK11*, showing enrichment for biological processes such as glucocorticoid signaling.

The findings expand on previous research to indicate that both differential and variable methylation may play a role in the etiopathology of depression, and suggest specific genomic loci of potential interest in the epigenetics of depression.

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Longitudinal study of methylome profiles in subjects with psychosis and/or schizophrenia

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Background Schizophrenia is a complex disorder involving both genetic and environmental factors. Epigenetic is a growing theory to explain these interactions at a molecular level. It is well-known that schizophrenia begins with prodromal symptoms and patients undergoing subthreshold symptoms are named ultra-high risk (UHR) subjects. Therapeutic and prognostic attitude remain challenging for this population. According to the model of the gene-environment interactions, the psychotic transition in adolescence could be related to epigenetic changes during the psychotic transition.

Methods We designed and performed the first longitudinal study about whole-genome DNA methylation changes. Thirty-nine UHR patients were recruited in specialized center C'JAAD - Centre Hospitalier Ste Anne - Paris (France). During follow-up, 14 of them became psychotic (converters) according to the validated scale CAARMS. Initial and final methylation were investigated by Infinium Human Methylation450 BeadChip for 450,000 CpG after bisulfite conversion.

Results The psychotic transition was not associated with global methylation changes. Linear models failed to identify CpG and genes significantly associated with psychotic transition after Bonferroni correction. Analyses of the top results provided a cluster, which could classify perfectly converters and non-converters. These genes of interest are over-represented in biological pathways with relevance for psychotic physiopathology. Individual analyses highlighted the biological heterogeneity of the psychotic transition.

Conclusion Improving physiopathological understanding of psychotic transition is a current challenge to identify biomarkers and to develop targeted preventive interventions available in clinical practice for UHR subjects. The epigenetic processes and in particular DNA methylation could be interesting factors.

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Epigenetic modifications in anorexia nervosa patients and remitters compared to healthy control women

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Introduction Anorexia nervosa (AN) is the most severe in terms of morbidity psychiatric illness with the highest mortality rate increased by 23 fold. Treatments are limited effectiveness. AN has a strong genetic component with heritability at 70% but despite ~200 studies no major gene was identified. Epigenetics, such as DNA methylation, is another component of heritability that could explain the high heritability. Methylation is poorly studied in AN from small samples, and is focused on few candidate genes among publications. Under publication, a first genome-wide methylation study investigated 10 restrictive type AN patients, 19 bingeing/purging type of AN patients and 15 normal eaters using DNAs from whole blood (Booij, 2015). Of the 480K CpG sites that can be methylated of Infinium Human Methylation450 BeadChip Kit, authors focused on 24,000 sites located close to genes and they identified candidate genes with a different profile of methylation between AN and controls.

Objectives Our work is to replicate the results of Booji and also to investigate the AN remitters.

Aims Our goal is to identify epigenetic signatures of the AN disorder and the prognostic of remission.

Methods Twenty-four AN patients, 24 AN remitters will be compared to 48 healthy control women for methylation using the Infinium Human Methylation450.

Results As Booji et al., we will compare methylation for 24,000 sites located close to genes for 24 AN, 24 remitters and 48 controls.

Conclusions We expected to replicate the published results of Booji and to identify genes with a methylation signature specific of the AN remission.

Disclosure of interest The authors have not supplied their declaration of competing interest.

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Whole-genome epigenetic changes genome regarding childhood maltreatment in patients with borderline personality disorder or depression

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Early life adversity plays a critical role in the emergence of borderline personality disorder (BPD) and this could occur through epigenetic programming. In this perspective, we aimed to determine whether childhood maltreatment could durably modify epigenetic processes by the means of a whole-genome methylation scan of BPD subjects. Using the Illumina Infinium[®] Human Methylation450 BeadChip, global methylation status of DNA extracted from peripheral blood leucocytes was correlated to the severity of childhood maltreatment in 96 BPD subjects suffering from a high level of child adversity and 93 subjects suffering from major depressive

disorder (MDD) and reporting a low rate of child maltreatment. Several CpGs within or near the following genes (*IL17RA*, *miR124-3*, *KCNQ2*, *EFNB1*, *OCA2*, *MFAP2*, *RPH3AL*, *WDR60*, *CST9L*, *EP400*, *A2ML1*, *NT5DC2*, *FAM163A* and *SPSB2*) were found to be differently methylated, either in BPD compared with MDD or in relation to the severity of childhood maltreatment. A highly relevant biological result was observed for cg04927004 close to *miR124-3* that was significantly associated with BPD and severity of childhood maltreatment. *miR124-3* codes for a microRNA (miRNA) targeting several genes previously found to be associated with BPD such as *NR3C1*. Our results highlight the potentially important role played by miRNAs in the etiology of neuropsychiatric disorders such as BPD and the usefulness of using methylome-wide association studies to uncover such candidate genes. Moreover, they offer new understanding of the impact of maltreatments on biological processes leading to diseases and may ultimately result in the identification of relevant biomarkers.

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European alliances against depression: 4-level interventions targeting depression and suicidal behaviour

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Community-based 4-level approach: Background, implementation and evidence for efficacy

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The community-based 4-level-intervention concept developed within the “European Alliance against Depression” (<http://www.eaad.net/>) combines two important aims: to improve the care and treatment of patients with depression and to prevent suicidal behavior. It has been shown to be effective concerning the prevention of suicidal behavior [1–4] and is worldwide the most broadly implemented community-based intervention targeting depression and suicidal behavior. The 4-level intervention concept comprises training and support of primary care providers (level 1), a professional public relation campaign (level 2), training of community facilitators (teacher, priests, geriatric caregivers,