S37

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

S38

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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S39

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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S40

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

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