In this workshop I will present data from our research group and others pertaining to the biological mechanisms underlying accelerated cellular aging in PTSD. Most, but not all, studies have found that PTSD is associated with shorter mean leukocyte telomere length, an indicator of accelerated cellular aging. Mitochondrial dysfunction has been implicated in PTSD and our research group found evidence of a "u-shaped" relationship between PTSD symptom severity and mitochondrial DNA copy number. For what concerns immunity, we have recently found that PTSD subjects have increased blood levels of pro-inflammatory markers, a more senescent and dysfunctional profile of NK cells and impaired synthesis of nitric oxide. Finally, I will discuss the possibility of accelerated *epigenetic* aging in combat-exposed individuals with and without PTSD, using DNA methylation data.

Disclosure of interest   The author has not supplied his declaration of competing interest.

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Symposium: How to Integrate Stress - (Epi) Genetics and Imaging and What Does It Tell Us

S038

Stress Hormone System and Epigenetics in Depression

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Background   Exposure to early life adversity (ELA) has been identified as a major risk factor in the development of major depressive disorder (MDD). It is hypothesized that a mediating mechanism may be environmentally induced alterations in gene function. In our REDEEM (Research in depression: endocrinology, epigenetics and neuroimaging) project we are examining possible epigenetic difference in some previously investigated target genes relevant to depression. To this end, methylation of the following genes were measured: NR3C1 (HPA axis), SLC6A4 (serotonin neurotransmitter function), and CD3ε (T cell receptor gene). We also looked at possible trans-generational transmission of epigenetic markers in a mother-baby sample.

Methods   DNA was isolated from depressed patients and controls and babies and a portion of the above genes, encompassing our regions of interest, were amplified by PCR. Percentage methylation levels were measured by pyrosequencing. mRNA was also measured for some gene products to see if function was related to methylation. HPA axis function was measured with serial saliva samples throughout the day.

Results   to date: Methylation was increased in the CD3ε promoter in depressed subjects relative to controls. In the total group, those exposed to ELA had significantly increased methylation at this site. Levels of CD3ε mRNA levels were inversely related to methylation. There were some relationships between maternal ELA and baby methylation at the sites examined.

Conclusions   Consistent with an allostatic model of ELA damage, our findings suggest an alteration in epigenetic function in acquired

immunity and the HPA axis, mediated by ELA. Findings will be discussed.

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

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S039

Stress and the serotonergic system, observations from pet imaging

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Introduction   Stress response and the neuroendocrinologic factors through which it is mediated are disturbed in anxiety and in affective disorders. While acute stress is thought to result in hypothalamus-pituitary-adrenal- (HPA) axis hyperactivity (Varghese 2001), chronic stress may result in decreased HPA-response (Booji 2013). Antidepressant treatment, on the other hand, is thought to realign HPA–axis activity (Schüle 2007).

On the other hand, dysregulation within the serotonergic neurotransmitter system is understood as a central moderator in the pathophysiology of affective and anxiety disorders. Serotonergic transmission both regulates- and is regulated by- glucocorticoids. Cortisol results in an increase in serotonin synthesis and release while serotonergic transmission is thought to downregulate HPA-axis activity (Lanfumey, 2008). Positron emission tomography (PET) studies have demonstrated the link between the serotonergic system and the HPA-axis in humans in vivo. For example, a negative correlation between cortisol and $5HT_{1A}$ receptor levels in various brain regions has been shown (Lanzenberger, 2010). SERT expression, on the other hand, was shown using PET to be positively related to HPA-axis reactivity (Frokjaer 2013).

Methods   n.a.

Aims   Available literature on interactions between the HPA-axis and the serotonergic system will be discussed with a focus on data acquired via PET studies.

Results   n.a.

Conclusions   The interaction between the serotonergic system and the HPA-axis is likely bilateral and may be understood as a neurobiological link by which stress may foster the development of depression and anxiety.

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S040

Association of stress hormone system, epigenetics and imaging

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Introduction Major depressive disorder (MDD) is a common psychiatric condition, affecting up to 350 million people worldwide. Its pathogenesis seems to involve dysregulation of the hypothalamic-pituitary (HPA) axis and inflammation as key elements of the condition. Stressful life events and in particular early life adversity seem to play an important role as risk factors for MDD. Epigenetic, which has been found to impact in the transcription of genes, seem to be associated with brain structure and function. Aim of the research was to provide an overview about neuroimaging (epi)-genetics in MDD.

Methods Functional MRI, epigenetic and genetic information was obtained in a cohort of patients with MDD and healthy controls. Associations between, early life adversity, methylation of FKBP5 and SLC6A4, genetic variants and brain function and connectivity have been analysed.

Results Higher methylation of SLC6A4 gene was associated with higher BOLD response during emotion processing and lower BOLD response during higher order cognitive processes. Healthy participants with higher SLC6A4 methylation involved prefrontal cortical regions to a greater extent than the participants with lower SLC6A4 methylation, when trying to switch attention away from negative emotional stimuli (Frodl et al., 2015). Moreover, FKBP5 methylation was association with HPA axis functioning and amygdala brain function in patients with MDD. FKBP5 methylation also was related to grey matter volume.

Conclusions Our study provides further support to the hypothesis that DNA methylation plays a role. Particular peripheral DNA methylation states of MDD candidate genes are associated with brain function during emotion processing in patients with MDD.

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

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S041

Disadvantage of social sensitivity: interaction of oxytocin receptor genotype and child maltreatment on brain structure

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Background Oxytocin has received much attention as a pro-social and anxiolytic neuropeptide. In human studies, the G-allele of a common variant (rs53576) in the oxytocin receptor gene (*OXTR*) has been associated with protective properties such as reduced stress response and higher receptiveness for social support. In contrast, recent studies suggest a detrimental role of the rs53576 G-allele in the context of childhood maltreatment. To further elucidate the role of *OXTR*, gene by maltreatment (GxE) interactions on brain structure and function were investigated.

Methods $n = 309$ healthy participants genotyped for *OXTR* rs53576 underwent structural as well as functional MRI during a common emotional face-matching task. Childhood maltreatment was assessed with the Childhood Trauma Questionnaire (CTQ). Gray matter volumes were investigated by means of voxel-based morphometry (VBM) across the entire brain.

Results Structural MRI data revealed a strong interaction of rs53576 genotype and CTQ-scores, mapping specifically to the bilateral ventral striatum. GG homozygotes but not A-allele carriers showed strong gray matter reduction with increasing CTQ-scores. In turn, lower ventral striatum gray matter volumes were associated with lower reward dependence, a pro-social trait. Furthermore, the G-allele was associated with increased amygdala responsiveness to emotional facial expressions.

Conclusions The findings suggest that the G-allele constitutes a vulnerability factor for specific alterations of limbic brain structure in individuals with adverse childhood experiences, complemented by increased limbic responsiveness to emotional interpersonal

stimuli. While oxytocinergic signalling facilitates attachment and bonding in supportive social environments, this attunement for social cues may turn disadvantageous under early adverse conditions.

Disclosure of interest The author has not supplied his declaration of competing interest.

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Symposium: using technology to respond to the mental health needs of refugees in europe: mobile devices, telemedicine, and outcomes management

S042

The use of a telemedicine model and its logistics to reach as many european refugees as possible

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Current refugee crisis challenges mental health care systems all over the Europe. There is a number of research describing difficulties in dealing with cross-cultural patients. Access to relevant care as well as its availability are often limited due to: a) lack of respective qualified resources b) linguistically, cultural and even racial barriers in addressing of mental health care needs of cross-cultural patient population. By use of various e-Mental health applications, primarily videoconference, we may improve assessment and/or treatment of refugees and asylum seekers on distance e.g. Arabic speaking psychiatrist located in Sweden would be able to assess and/or treat refugees from Syria located in Germany). Specialized centers for treatment of refugees would also be able to get second-opinion service from remote experts and use it in order to confirm or re-consider diagnosis as well as the treatment options. Establishment of international network of cross-cultural experts enables to:

– Improve the mental health care across national boundaries by providing psychiatric consultations to other countries within EU

– Conduct International Treatment Team with Select Skills (e.g. Sign Language and Many Foreign Languages Staff)

– Provide Distance Supervision and Staff Consultation

– Provide Psycho Education of caregivers

– Improve Distance Learning via Case Conferencing and Best Practice Demonstration Across the National Boundaries

– Create Data Base over cross-cultural and other select skills professionals within EU

Disclosure of interest The author has not supplied his declaration of competing interest.

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S043

Preliminary results of USA-European field trial on the use of patient-reported measures in a mobile application and potential uses in refugee populations

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