Symposium: The role of the telomere-telomerase system in psychiatric disorders and treatments: Underlying mechanisms linking mental illness with cellular aging

S034

Telomere length and depressive and anxiety disorders: Longitudinal associations and underlying mechanisms

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Many psychiatric disorders have been associated with increased risk of mortality and various aging-related somatic diseases. In addition to unhealthy lifestyles, also various stress-related physiological processes likely play a role in explaining these detrimental health consequences of psychiatric disorders. The impact could be visible at the cellular level, with psychiatric patients presenting more signals of physiological aging for instance as determined by measuring telomere length. In this talk we will first highlight the current state-of-the art evidence that various psychiatric conditions, including e.g. depression, anxiety and PTSD, are associated with shorter telomere length. Second, we will provide results from the Netherlands Study of depression and anxiety ($n = 2981$) that tested longitudinal associations using 6 year data on psychiatric status and telomere length. These results indicate that the association between depressive and anxiety disorders with telomere length is stable over time, and doesn't show many dynamic associations. Finally, in the same study we have also tested to what extent lifestyle and dysregulations of physiological stress systems such as the immune, HPA-axis and autonomic nervous systems are partly responsible for the observed shorter telomere length in depressed or anxious patients. Results indicate that especially smoking behavior and systemic inflammation partly contribute to the shorter telomere length, but can't completely explain found associations.
In sum, this talk will highlight the current state-of-evidence for an association between various psychiatric conditions with shorter telomere length, and will provide insights into its dynamics and its contributing mechanisms.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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S035

The role of telomeres and telomerase in the clinical effect and mechanism of action of psychopharmacological interventions

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Originally studied in relation to aging and cancer research, telomeres and telomerase are now also investigated in relation to psychiatric disorders and treatments. Based on findings emerging from clinical and preclinical data, we hypothesize that the telomere–telomerase system represents a novel element mediating the mechanism of action of certain psychopharmacological interventions.
In this symposium I'll present the preliminary evidence on the complex translational relationships between specific psychiatric medications (i.e. antidepressants, lithium and antipsychotics), the telomere–telomerase system and clinical outcomes. The modulation of intracellular Wnt/b-catenin or PI3 K/Akt signaling pathways, the interaction with BDNF and 5-HT, and the antioxidant properties could represent possible mechanisms by which the different types of psychiatric medications could modulate telomere length and telomerase activity. The potential of the telomere–telomerase system in promoting cellular survival and/or function in the brain and in the periphery could, in turn, represent a neurobiological substrate through which these molecules can mediate the therapeutic effect of such interventions.
Further, in the present symposium I'll show data from our research team on telomere length and telomerase activity in leukocytes predicting clinical response to serotonin–specific reuptake inhibitors (SSRIs) in subjects with major depressive disorder.
Disclosure of interest The author has not supplied his declaration of competing interest.

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S036

Can reducing psychological distress slow down the rate of telomere attrition?

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Specific types of cognitions and mental processes may lead to greater stress arousal and may subsequently impact cell longevity. The study of telomeres and telomere-related molecular systems may provide a pathway for exploring the link between psychological domains and cell physiology. Based on findings emerging from clinical and preclinical data, we hypothesize that the telomere-telomerase system contributes to explain certain biological underpinnings of psychological interventions.
In this symposium we'll present the preliminary evidence on the complex translational relationships between specific psychological domains (i.e. childhood adversities, stressful life events, mindfulness-based interventions and perceived distress), the telomere-telomerase system and clinical outcomes. Further, we'll discuss preliminary data on the effect of mindfulness- and meditation-based interventions on cellular ageing and disease-associated molecular phenotypes.
Disclosure of interest The authors have not supplied their declaration of competing interest.

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S037

Evidence of accelerated biological ageing in post-traumatic stress disorder

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Post-traumatic stress disorder (PTSD) is a common and debilitating condition, affecting between 10–20% of soldiers returning from combat zones, and with even higher prevalence rates in Veterans Affairs healthcare settings. PTSD is associated with an increased risk for various medical illnesses, many of which are commonly seen with older age. This raises the possibility that PTSD is associated with accelerated biological aging at the cellular level. Accelerated biological aging occurs when biological age outpaces chronological age, and this process is driven by a number of biological mechanisms including immune activation, oxidative stress, and mitochondrial dysfunction.

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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.

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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- glucocortocoids. 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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