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MDD epidemiology

- Depression is the leading cause of disability worldwide.
- An estimated 350 million people of all ages suffer from depression.
- Unipolar depression ranks on top among contributors to the overall global burden of disease.
- MDD is the leading cause of reduced quality life- and years lived with disability (WHO).
• The WHO’s Mental Health Gap Action Programme (mhGAP) has called all countries for a public-health priority to reduce the ubiquitous burden caused by MDD.

• Joint Action on Mental Health and Wellbeing (EU, 2016) has provided guidelines.

• The need to understand the basal underpinnings that may prevent transition from predisposition in childhood- and adolescence to severe and consolidated MDD over the adult life span is urgent to improve the general public health.
Characteristics of MDD

Major Depressive Disorder

A1 Depressed Mood
A2 Diminished interest or pleasure

1) Weight loss- or gain
2) Insomnia or hypersomnia
3) Psychomotor agitation or retardation
4) Diminished ability to think or concentrate, or indecisiveness
5) Fatigue (loss of energy)
6) Feeling worthless or feeling guilt
7) Thought of death (suicidal ideation)

Present during the same 2-week period and represent a change from previous function.

Single episode or recurrent?
• Presence of two or more depressive episodes
Mechanism oriented research in MDD

• Braking down complex phenomena into key components that may enlighten mechanisms involved in the vulnerability, development, treatment and consolidation of symptoms in MDD.

• Supplements studies that aims to describe causes or demographical factors associated with MDD.
Choi & Kim (2010) PNAS

19/04/17
Mechanisms involved in MDD

Disner et al. (2011) *Nature Reviews, Neuroscience*
Mechanisms in Stress and depression

• A particular focus on cortisol and associated neuroendocrine processes has been motivated by the role of this steroid hormone in emotion processing through its interaction with serotonin metabolism, and neural –and brain structural plasticity,

• Particularly central in conventional depression treatment by the use of an antidepressants (SSRI/SNRI).
Stress activates
the hypothalamic-pituitary-adrenal (HPA) - axis

- Maladaptive: chronic stress.
Cortisol awakening response

Awakening +15min +30 +45 +60 +6Hrs +12hrs + 18hrs

Moderate depression

STRESS
Cortisol awakening response

Moderate depression

Severe depression

Awakening + 15min + 30 + 45 + 60 + 6Hrs + 12hrs + 18hrs
Consolidation of MDD via stress?

• Follow up studies have shown that depression in adolescent relapses within 5 years for 50-70% of the patients.
• An episode of depression during adolescence often heralds a chronic or relapsing disorder, and forecast a broad range of psychosocial difficulties and ill health.
• Moreover, early-onset depression might be a risk factor for late-life depression by contributing to brain abnormalities that predispose to depression.
• One such mechanism involves stress-related hormones leading to a reduction of neurotropic factor secretion, and ultimately a decrease in neurogenesis via serotonergic pathways.
Serotonergic signaling in the brain

Neurotransmitter affecting many processes

- Memory processing
- Neural plasticity
- HPA-axis activity

Serotonin transporter

- Popular target for antidepressant medication
- Genetic risk loci that influences synaptic serotonin levels
Neural plasticity

Generation of new neurons in adult individuals

- Neurogenesis
- Synaptogenesis
- Differentiation
- Axonal growth

Functional significance

- Learning and memory
- Spatial navigation
- Emotion processing
Neural plasticity and MDD recurrence

How does cortisol and serotonin influence neural plasticity?

Opposite effects

- Serotonin
- Cortisol

Short-term  Chronic
Caspi et al. (2003), Science
Mechanisms involved in MDD

Disner et al. (2011) *Nature Reviews, Neuroscience*
A Cognitive Vaccine against MDD?
The CNRG MDD database

• The CNRG database includes cortisol sampled longitudinally for more than 450 adults and extracted DNA for more than 1000 participants. Study specific questionnaires and extensive screening of demographics, function and symptoms.

• The database contains sMRI-, resting state MRI-, task fMRI- and DTI for 177 MDD patients and 75 HC from identical protocols in the same 3T MR scanner at IVS.

• Study specific questionnaires and extensive screening of demographics, function and symptoms.
Most urgent research topics!

• 1) How does conventional depression treatment lead up to better health by the moderation of depression courses in different age cohorts in different individuals?

• 2) How is function (social-, work-, school-) and subjective stress related and linked to MDD symptoms- and MDD consolidation over the life span?

• 3) Are neurocircuitry in emotion regulation relevant markers of individual MDD courses, recurrence, treatment individualisation and outcome over the life span?

• 4) What are the critical individual trajectories that prevent symptom consolidation after a single depressive episode?

• 5) Can mechanisms in MDD courses be modified directly to prevent MDD debut-, recurrence and consolidation?