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A postmortem study

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CHAPTER 1

GENERAL INTRODUCTION AND SCOPE OF THE PRESENT THESIS

GENERAL INTRODUCTION

Suicide is a worldwide health problem that terminates approximately 700,000 reported human lives every year, which may even be an underestimation and according to the WHO, many more people likely commit suicide (WHO, 2021). It is one of the leading causes of death during the period of late adolescence (WHO, 2021). Suicide rates in European countries have been gradually rising and, in the Netherlands, the number of suicides is increasing 3–6% annually. The effect of preventive interventions is hard to establish and almost half of the suicides in Netherlands are committed by individuals who are receiving psychiatric therapies.

Suicide and comorbid psychiatric illnesses

Among the various risk factors for suicide, the occurrence of pre-existing psychiatric disorders increase the chance to attempt suicide (CDC, 2021). Suicide risks are generally associated with the presence of mental disorders, in particular when multiple ones are involved. Individuals with a tendency for suicide e.g. have a 6 times higher chance to combine multiple psychiatric illnesses when compared to control subjects (Préville et al., 2005). The type of co-existing psychiatric disorders varies substantially, however, (Qin et al., 2014; Tidemalm et al., 2008) with in particular (combinations of) major depressive disorder (MDD), bipolar disorder (BD) and schizophrenia (SCZ) having a stronger relationship than other disorders (de Medeiros Alves et al., 2015; San Too et al., 2019).

Epidemiological studies have shown that adult patients with psychiatric illnesses have robust tendencies for suicide, relative to those without mental diagnoses (Choi et al., 2020; Sorenson and Golding, 1988). However, two topics in this respect deserve our attention. First, geographical variations due to culture specificities and lack of medical care reduce the proportion of reported mental disorders among suicide cases. East Asian countries such as China and India, that are generally short of psychiatric interventions, report a lower prevalence of mental disorders in individuals with suicide compared to North America and Europe (Cho et al., 2016; Milner et al., 2013). Adolescent and young adult suicide attempters without a diagnosable psychiatric disorder are generally linked to substance misuse that impacts their mental states adversely (Cao et al., 2015; Marttunen et al., 1998). In addition, subclinical psychiatric symptoms that did not meet the full diagnostic criteria of a mental disorder also appeared to be present in a great majority of individuals who died by suicide (Joiner Jr et al., 2017). These unnoticed and ‘subthreshold’ forms of psychiatric disorders that coexist in approximately half of the suicide attempters should be taken into account when considering prevalence and the relation between psychiatric health and suicide risk (Balázs et al., 2000).

In addition, among individuals with mental comorbidity, death by suicide is not only considered the final outcome of the mental illness, but is also underpinned by independent genetic features (Zhao et al., 2019). Clinical studies have shown that individuals with a first-

degree relative who had mental disorders and died by suicide, are more likely to commit suicide (Qin et al., 2002). This effect can be even stronger in the case of a parental history of suicide, regardless of the presence or absence of a psychiatric disorder (Ballard et al., 2019; Sørensen et al., 2009). Genetic studies further support the idea that the etiology of suicidal behavior cannot be solely explained by psychiatric background (Erlangsen et al., 2018; Zhang et al., 2020a, b; Zhao et al., 2015; Zhao et al., 2018). We hypothesize that pre-existing mental disorders may contribute to genetic vulnerability of suicide, instead of being a deterministic factor in suicide pathophysiology.

Age-associated suicide portraits

Throughout the whole lifespan, personal, familial and/or societal events may have varying effects on people in terms of mental factors related to suicide. For instance early life circumstances and related adversities, including a higher birth order, childhood exposure to psychological trauma (violence, sexual abuse or neglect), difficulties at school, a younger maternal age and adult internalizing disorders, are early signs for later mental disorders, which will eventually enhance the risk of suicide in adulthood (Geoffroy et al., 2018; Ligier et al., 2020; Park et al., 2015; Rossi et al., 2020). In addition, it is suggested that these early life stressful events, particularly in patients with MDD, BD or SCZ, can predict the aggregation of a mental condition, including mental extremes such as suicide attempts (Adigüzel et al., 2019; Alli et al., 2019; Tanti et al., 2017; Tasmim et al., 2020). Mental disorders that represent the largest risk for suicide in teenagers and young adults typically include posttraumatic stress disorder, dysthymia, MDD and borderline personality disorder (Lesage et al., 1994; Miché et al., 2018). For individuals who do not have specific mental diagnoses, comorbidities involving substance abuse (alcohol, nicotine or drug dependency) can also contribute to psychiatric illnesses and are frequently associated with suicide attempts (Cao et al., 2015; Lesage et al., 1994; Miché et al., 2018; Shafii et al., 1988). The processes that lead to suicide completion from the moment of ideation onset, appear to be relatively short, which obviously limits opportunities for therapeutic interventions (Marttunen et al., 1998).

Compared to the young population, diagnosable mental disorders are more often seen in elderly individuals who commit suicide (de Raykeer Pascal et al., 2018; Henriksson et al., 1995). Age appears less important in assessing suicide risks when compared to personal or socioeconomic factors, like personality traits, physical illness, domestic violence, poverty, recent bereavement and public disgrace (Harwood et al., 2001, 2006; Maselko and Patel, 2008; Pridmore, 2015).

Gender differences in suicidal behaviors

Suicidal behavior show a prominent gender difference, that starts from adolescence and persists throughout the lifespan. Worldwide suicide rates in males are 2-3 times higher than in females,

and a long-term risk of suicide in the context of mental illness shows a similar sex difference, particularly in subjects above thirty (Babanejad et al., 2014; Gunnell et al., 2002; Organization, 2014). The most prevalent mental disorder and risk factor in males is substance abuse, while MDD and anxiety disorder are the most common ones in females (Liu et al., 2018; Taylor et al., 2004). In addition, suicide attempts were independently associated with sexual orientation minority status. Homosexual and bisexual populations have much higher lifetime prevalence of suicide attempts than heterosexual populations (Bolton and Sareen, 2011). Interestingly, in older adults, the presence of mental disorders that are related to an elevated risk of suicide was more common in women (Vasiliadis et al., 2017), which seems to imply that the impact of mental health on suicide tendency is stronger in this group.

Of concern, however, in aged males, either before or after suicide attempts, fewer psychiatric disorders are detected, most likely due to a more limited mental health follow-up than for females of the same age (Niederkrötenhaler et al., 2019; Schmutte and Wilkinson, 2020). The sex-biased variables mentioned above that take effect from childhood to adolescence have been linked to higher suicide tendencies throughout the age range, but their influence appears to be reduced in males of advanced age.

Suicide prevention

Efforts to prevent suicide have consistently shown a poor response, even when compared to the pharmaceutical treatment of mental disorders. According to a complete follow-up of the patient records, more than 5% of the patients with MDD, BD or SCZ continue to be at the risk for suicide even when they are receiving active mental health service (Nordentoft et al., 2011). Death by suicide occurs most frequently within the first three months after the initial psychiatric diagnosis and during the first year after hospital discharge (Orme et al., 2020; Randall et al., 2014), indicating that switching therapeutic approaches may possibly trigger psychobiological alterations that could perhaps contribute to suicide behaviors ('treatment-emergent suicidality') (Jick et al., 2004).

Apart from their improvement of psychotic symptoms, most antipsychotics are similar in their effect and not different from placebo treatment when it comes to suicide prevention (Garlow et al., 2013; Khan et al., 2001; Tauscher-Wisniewski et al., 2007). Among the selective serotonin reuptake inhibitors, fluoxetine, when considered in relation to suicide prevention, is more effective in females (Beasley et al., 1991; Milane et al., 2006), but paroxetine treatment resulted in an increased intensity of attempted suicides (Aursnes et al., 2005). As to serotonin-norepinephrine reuptake inhibitors, milnacipran appears to induce a rapid improvement from suicidality (Kirino and Gitoh, 2011). In contrast, a higher risk of suicide has been consistently linked to the prescription of venlafaxine, regardless of whether the patient suffered from severe mental illnesses (Mines et al., 2005; Rubino et al., 2007). It is thus important to be aware of the

differences and possible links between the prescription of specific antidepressants and the risk of suicidality.

Tricyclic antidepressants and benzodiazepines have proved to alleviate suicidal thoughts in adults with anxiety disorders, posttraumatic stress disorder, and in adolescents under chronic stress, on the condition that it is prescribed alone (Boggs et al., 2020; Soreni et al., 1999). Clozapine and olanzapine have demonstrated improvements in preventing suicide risk among patients with schizophrenia and schizoaffective disorder, especially when this coincided with other public health and psychosocial interventions (Bastiampillai et al., 2017; Meltzer et al., 2003; Ringbäck Weitoft et al., 2014). However, a possible link between benzodiazepines over-prescription and increased potential for suicide attempts in males and adolescents is also worth discussing (Neutel and Patten, 1997; Niederkrotenthaler et al., 2019). A concurrent use with antidepressants like zolpidem may have increased the suicide risk compared to the use of zolpidem solo (Sung et al., 2019). Of note, there are cases that document a relationship between abrupt clozapine discontinuation and the subsequent rise in suicide events (Patchan et al., 2015).

Lithium has been broadly prescribed in patients with mental health diagnoses (MDD and BD in particular) and a history of suicide ideation and attempts (Roberts et al., 2017; Smith and Cipriani, 2017; Terao et al., 2018). Its discontinuation within six months has been linked to increased suicide death rates (Oquendo et al., 2011; Smith et al., 2014). Since the majority of antipsychotics do not reverse suicidal ideations or behaviors, and can even trigger suicide tendencies in some circumstances, it is concluded that novel anti-suicide treatments should focus on understanding of the molecular mechanisms specific for suicide, rather than for the pre-existing mental disorders per se.

LEGALIZED EUTHANASIA AND PHYSICIAN-ASSISTED SUICIDE

Euthanasia and physician-assisted suicide (PAS) are legally practiced in the Netherlands but concern a relatively small number of people and is performed only under very strict regulations. Euthanasia is defined as the administration by a physician of a medication, such as a sedative and neuromuscular relaxant, to intentionally end a patient's life upon the explicit and repeated request of the mentally competent patient (Emanuel et al., 2016). For the practice of euthanasia, the euthanatic agents are administered intravenously. First, a coma is introduced by thiopental (2000 mg) or propofol (1000 mg). Subsequently, when the patient is determined to be in a medically induced coma, a neuromuscular blocker, such as rocuronium (150 mg), atracurium (100 mg) or cisatracurium (30 mg) is administered. This paralyzes all striated muscles, with the exception of the heart and cause the patient to die (KNMG/KNMP, 2012).

PAS is defined when the physician provides medication to a patient at his or her explicit request with the understanding that the patients intends to use the medications to end his or

her life (Emanuel et al., 2016). With PAS, the patient takes the euthanistic agents him/herself. A sufficiently high dose of an orally administered barbiturate (pentobarbital or secobarbital) results in depression of the respiratory system, causing respiratory acidosis. This coupled with vascular and/or cardiogenic shock results in death (KNMG/KNMP, 2012).

Studies based on human brain tissue have so far never investigated subjects who died by legal euthanasia and PAS. In our following studies, individuals who died of legal euthanasia will be subdivided into patients with mood disorders (MD) (to compare the differences between suicidal behaviors and suicidal ideations) and controls without a neuropsychiatric disorder (to correct for the effect of drug overdose and death ideation, that occurred in patients with MD who died of legal euthanasia and controls who died of incurable physical diseases such as cancer).

BRAIN REGIONS IMPLICATED IN SUICIDE

Prefrontal cortex

The prefrontal cortex (PFC) has been implicated as the executive center, in processes like planning, decision making, short-term memory, personality expression, and the moderation of social behavior and control of speech and language (Siddiqui et al., 2008). Both structural and functional abnormalities of the PFC have been linked to suicide and mental disorders. In patients with MDD, suicide attempters have shown alterations in functional connectivity and cortical protein markers in the dorsolateral prefrontal cortex (DLPFC), as compared to non-suicide attempters (Dean et al., 2019; Wang et al., 2019). Suicide attempters with MDD or BD also share specific structural alterations, suggesting there could be common neural pathways for suicide in mood disorders (Wei et al., 2020; Zhao et al., 2018).

Apart from suicide, neuroimaging alterations in the PFC are often related to psychosis. Information processing in the DLPFC, which has been related to the etiology of psychotic features (McIntosh et al., 2008), was preferentially reduced in psychotic BD patients. This suggests that psychosis might be accompanied by a disruption of the prefrontal control network which could possibly result in a relative stronger activation of the default network (Baker et al., 2014). In addition, abnormal brain activation in the ACC, as measured by functional magnetic resonance imaging (fMRI), has been related to impairments in emotional processing, attention and neurotransmitter levels in pediatric and euthymic individuals with BD (Lee et al., 2018; Li et al., 2018; Soeiro-de-Souza et al., 2018).

Consistent with this, patients in their first manic episode with psychosis also had a significant volume reduction of the entire ACC (Keramatian et al., 2016), whereas the right dorsal ACC volume was found to be increased in recent-onset psychosis (de Azevedo-Marques Perico et al., 2011). Similarly, in SCZ, a frontal cortex-targeted MRI study showed that an ACC-

based disturbance in cognitive control was related to long-term suicidal ideations and behaviors, whereas no such relation was present in the DLPFC (Minzenberg et al., 2014). In addition, transcranial magnetic stimulation that targeted the PFC can improve clinical symptoms and have anti-suicidal effects in patients with SCZ (George et al., 2014; Linsambarth et al., 2019; Mehta et al., 2019). The abovementioned observations indicate that the PFC is associated with the pathogenesis of suicidal behavior in conditions of mental illness. This implies that therapies targeting the PFC may be potentially effective for suicide prevention.

Hypothalamus

The hypothalamus is part of the limbic system and links the nervous system to the endocrine system. One of its major functions is its involvement in the stress response. This thesis will focus on the paraventricular nucleus (PVN) and supraoptic nucleus (SON), which are two primary drivers of the hypothalamo-pituitary-adrenocortical axis, and the infundibular nucleus (INF), a nucleus exposed outside the blood-brain barrier, that regulates hormone release and provide inputs to the other hypothalamic nuclei. So far, only a few studies that focused on the human hypothalamus have addressed the neurobiological alterations in relation to suicide (Merali et al., 2006). However, the functions dominated by the hypothalamus strongly indicate that this structure may play a critical role in the pathophysiology of suicide.

Hippocampus

The human hippocampus contains a high density of of glucocorticoid receptors, which make it more vulnerable to long-term stress than other brain areas (Wang et al., 2013). Many structural and functional imaging studies have shown that the hippocampus is dynamically and volumetrically altered in patients with mental disorders who have suicidal ideations or attempts (Zhang et al., 2022). Of note, MDD, as a major comorbidity of suicide, is associated with structural changes to the hippocampus. Previous meta-analyses have shown a reduction in the volume of the hippocampus in subjects with MDD, which was absent in bipolar disorder (BD) (Campbell et al., 2004). Depressed patients with suicidal ideation did not show volumetric alterations, but did display decreased functional dynamics (determined by the amplitude of low-frequency fluctuations) in the hippocampus (Jiao et al., 2019; Lan et al., 2019). Different from suicide ideators, suicide attempters, independent of their prior psychiatric disorder, exhibited a reduced regional homogeneity in their left hippocampus, indicating hippocampal dysfunction in the predisposition to suicidal behaviors (Cao et al., 2015). For example, suicide attempters in MDD displayed a higher hippocampal functional connectivity (Wagner et al., 2021; Weng et al., 2019). MDD patients with repeated or acute suicide attempts showed much smaller hippocampal volumes than patients with a first suicide attempt, non-suicidal patients or healthy controls (Colle et al., 2015; Kang et al., 2020; Sarkinaite et al., 2021). In addition, suicidal attempters with BD had significantly reduced gray matter volume in the hippocampus (Johnston et al.,

2017; Niu et al., 2019). However, this suicide attempt-related cortical atrophy did not appear in schizophrenia (Spoletini et al., 2011), suggesting that reduced hippocampal volume promises to be a possible neuroimaging marker to predict suicidality in MDD.

Furthermore, as whole-brain functional neuroimaging studies have shown that the connectivity of the hippocampus with the hypothalamus and PFC specifically predicts the subjective sensation of stress in humans (Goldfarb et al., 2020), we decided to include these three brain regions in our research.

SCOPE OF THE PRESENT THESIS

Previously, our group has studied changes in glutamate- and GABA-related gene expression in the PFC in relation to stress, specific neurotransmitters, suicide and MDD (Zhao et al., 2015; Zhao et al., 2018; Zhao et al., 2016). However, very few studies have examined glial genes in patients with mental disorders and controls, accounting for confounding factors like suicide, gender and psychosis. Therefore, in **Chapter 2**, we studied whether suicide and psychotic features, either as parts of the symptoms of MDD, or as separate entities, are characterized by differences in glial gene expression in the human PFC. In **Chapter 3**, we focus on the question whether suicide and psychotic features are characterized by glia alterations in the human PFC in BD, and whether glia genes are differently expressed between genders in relation to suicide and psychotic features. As an extension of Chapter 3, we review in **Chapter 4** the evidence on sex differences of BD in terms of epidemiology, cognition, clinical manifestation, neuroimaging, neurobiological mechanisms, and highlight the role of the DLPFC as a key brain region in providing molecular landscape. In **Chapter 5**, we study whether suicide, either as part of the symptoms of schizophrenia, or as a specific entity, is characterized by differences in glia expression in the human PFC.

Chapter 6 focuses on the hypothalamus in relation to a possible hormonal risk factor for suicide. In this chapter, we hypothesize, on the basis of epidemiological data, that progesterone in the hypothalamus may play a role in suicide behaviors. In order to validate our hypothesis, two experiments were performed. Firstly, we investigated the distribution of the progesterone receptor (PR) in the human hypothalamus and determined whether some common parameters (age and gender) affect its expression in specific hypothalamic nuclei. This first human hypothalamic map of PR distribution allows to localize the most probable site for progesterone action at the central level. Secondly, we studied alterations in PR/proopiomelanocortin (POMC)- and PR/neuro-peptide Y (NPY)-co-expressing neuronal densities, and their ratios in the INF and compared MD, suicide and control subjects. Two groups of individuals with euthanasia, i.e., MDs with euthanasia and controls (i.e., donors without psychiatric disorders) who also died by legal euthanasia, were included in order to distinguish the changes going together with the possible differences between a completed suicide and suicide ideation, and the pharmacological

and possible other effects of the euthanasia. Subsequently, corticotropin-releasing hormone (CRH) and thyrotropin-releasing hormone (TRH) positive neurons were quantified, in order to explore differential projections of the POMC and NPY innervation of the PVN in brains of suicide and MD cases. A better understanding of the molecular mechanisms underlying the involvement of progesterone in suicide pathophysiology may have future consequences for the prescription of oral anticonception types.

Brain imaging and postmortem studies in suicide have demonstrated a reduction in the volume of the hippocampus as well as alterations in its cytobiology. Studies in the human hippocampus of suicide victims have shown alterations in neuronal-glial morphology and composition. A better understanding of the cellular and molecular mechanisms that underlie suicidal behavior and pharmacological responses may lead to the identification of novel targets that might make diagnoses and therapies more personalized. **Chapter 7** therefore contains a review that discusses several leading theories of the neurobiological factors in the hippocampus that may contribute to suicide, including the serotonin system, Wnt signaling pathway, brain-derived neurotrophic factor/tropomyosin receptor kinase B (BDNF/TrkB) signaling and the androgen receptors. We review in detail evidence for the role of these factors in suicide and in treatment response. In addition, cognitive dysfunction is discussed as a risk factor for suicide since novel evidence hints at a role for cognitive therapies in decreasing suicidal ideations, in addition to antidepressant therapy.

Chapter 8 is based on the finding that medications that regulate purine metabolism have antidepressant and anti-suicidal effects, indicating a pathophysiological involvement of purinergic disturbance in depression and suicide. Since the different psycho-pharmacological effects involve separate pathways, differences in purinergic receptor expression or activation may relate to suicide and MD, respectively. In addition, a hypothalamic involvement in suicide, MD and legal euthanasia has not been reported before, even though this subcortical region is driving key roles in emotion and stress regulation. Thus, in this chapter, we investigate in detail the expressions of stress-associated purinergic receptors in key stress regions of the human brain: the hippocampus, hypothalamus and PFC.

On the basis of our research findings shown in the above chapters, we discuss in **Chapter 9**, the feasibility and significance of using bio-samples from donors who died by legal euthanasia as potent novel research materials in suicide research. We also propose detailed strategies in both antemortem and postmortem studies in relation to this research cohort.

In **Chapter 10** and **11**, we provide an overview of the main findings, and hypothesize how the different brain areas and systems studied here and, in the literature, may lead to a better understanding of the mechanisms underlying depression and different aspects of suicidality. In all, our research aims to unravel the novel pharmacological targets that are widely applicable to suicidal populations, independent of their psychiatric diagnoses, which sheds light on the direct control of global suicides.

REFERENCES

- Adigüzel, V., Özdemir, N., Şahin, Ş.K., 2019. Childhood traumas in euthymic bipolar disorder patients in Eastern Turkey and its relations with suicide risk and aggression. *Nordic journal of psychiatry* 73, 490-496.
- Alli, S., Tasmim, S., Adanty, C., Graff, A., Strauss, J., Zai, C., Geretsten, P., Borlido, C., De Luca, V., 2019. Childhood trauma predicts multiple, high lethality suicide attempts in patients with schizophrenia. *Psychiatry research* 281, 112567.
- Aursnes, I., Tvette, I.F., Gaasemyr, J., Natvig, B., 2005. Suicide attempts in clinical trials with paroxetine randomised against placebo. *BMC medicine* 3, 14.
- Babanejad, M., Delpisheh, A., Asadollahi, K., Khorshidi, A., Sayehmiri, K., 2014. Attribution of mental disorders in suicide occurrence. *OMEGA-Journal of Death and Dying* 69, 311-321.
- Baker, J.T., Holmes, A.J., Masters, G.A., Yeo, B.T., Krienen, F., Buckner, R.L., Ongur, D., 2014. Disruption of cortical association networks in schizophrenia and psychotic bipolar disorder. *JAMA Psychiatry* 71, 109-118.
- Balázs, J., Bitter, I., Lecrubier, Y., Csiszér, N., Ostorharics, G., 2000. Prevalence of subthreshold forms of psychiatric disorders in persons making suicide attempts in Hungary. *European psychiatry* 15, 354-361.
- Ballard, E.D., Cui, L., Vandeleur, C., Castela, E., Zarate, C.A., Preisig, M., Merikangas, K.R., 2019. Familial Aggregation and Coaggregation of Suicide Attempts and Comorbid Mental Disorders in Adults. *JAMA psychiatry* 76, 826-833.
- Bastiampillai, T., Sharfstein, S.S., Allison, S., 2017. Increasing the use of lithium and clozapine in US suicide prevention. *JAMA psychiatry* 74, 423-423.
- Beasley, C.M., Dornseif, B.E., Bosomworth, J.C., Saylor, M.E., Rampey, A.H., Heiligenstein, J.H., Thompson, V.L., Murphy, D.J., Masica, D.N., 1991. Fluoxetine and suicide: a meta-analysis of controlled trials of treatment for depression. *BMJ (Clinical research ed.)* 303, 685-692.
- Boggs, J.M., Lindrooth, R.C., Battaglia, C., Beck, A., Ritzwoller, D.P., Ahmedani, B.K., Rossom, R.C., Lynch, F.L., Lu, C.Y., Waitzfelder, B.E., 2020. Association between suicide death and concordance with benzodiazepine treatment guidelines for anxiety and sleep disorders. *General hospital psychiatry* 62, 21-27.
- Bolton, S.-L., Sareen, J., 2011. Sexual orientation and its relation to mental disorders and suicide attempts: Findings from a nationally representative sample. *The Canadian Journal of Psychiatry* 56, 35-43.
- Campbell, S., Marriott, M., Nahmias, C., MacQueen, G.M., 2004. Lower hippocampal volume in patients suffering from depression: a meta-analysis. *American Journal of Psychiatry* 161, 598-607.
- Cao, J., Chen, J.-m., Kuang, L., Ai, M., Fang, W.-d., Gan, Y., Wang, W., Chen, X.-r., Xu, X.-m., Wang, H.-g., 2015. Abnormal regional homogeneity in young adult suicide attempters with no diagnosable psychiatric disorder: a resting state functional magnetic imaging study. *Psychiatry Research: Neuroimaging* 231, 95-102.
- CDC, 2021. Suicide Prevention.

- Cho, S.-E., Na, K.-S., Cho, S.-J., Im, J.-S., Kang, S.-G., 2016. Geographical and temporal variations in the prevalence of mental disorders in suicide: Systematic review and meta-analysis. *Journal of Affective Disorders* 190, 704-713.
- Choi, J.W., Lee, K.S., Han, E., 2020. Psychiatric disorders and suicide risk among adults with disabilities: A nationwide retrospective cohort study. *Journal of affective disorders* 263, 9-14.
- Colle, R., Chupin, M., Cury, C., Vandendrie, C., Gressier, F., Hardy, P., Falissard, B., Colliot, O., Ducreux, D., Corruble, E., 2015. Depressed suicide attempters have smaller hippocampus than depressed patients without suicide attempts. *Journal of psychiatric research* 61, 13-18.
- de Azevedo-Marques Perico, C., Duran, F.L., Zanetti, M.V., Santos, L.C., Murray, R.M., Scazufca, M., Menezes, P.R., Busatto, G.F., Schaufelberger, M.S., 2011. A population-based morphometric MRI study in patients with first-episode psychotic bipolar disorder: comparison with geographically matched healthy controls and major depressive disorder subjects. *Bipolar Disord* 13, 28-40.
- de Medeiros Alves, V., Goncalves Bezerra, D., Gomes de Andrade, T., Leao de Melo Neto, V., E Nardi, A., 2015. Genetic polymorphisms might predict suicide attempts in mental disorder patients: a systematic review and meta-analysis. *CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders)* 14, 820-827.
- de Raykeer Pascal, R., Hoertel, N., Blanco, C., Olfson, M., Wall, M., Seigneurie, A.-S., Schuster, J.-P., Lemogne, C., Limosin, F., 2018. Effects of psychiatric disorders on suicide attempt: similarities and differences between older and younger adults in a national cohort study. *The Journal of clinical psychiatry* 79.
- Dean, B., Tsatsanis, A., Lam, L.Q., Scarr, E., Duce, J.A., 2019. Changes in cortical protein markers of iron transport with gender, major depressive disorder and suicide. *The World Journal of Biological Psychiatry*, 1-8.
- Emanuel, E.J., Onwuteaka-Philipsen, B.D., Urwin, J.W., Cohen, J., 2016. Attitudes and practices of euthanasia and physician-assisted suicide in the United States, Canada, and Europe. *Jama* 316, 79-90.
- Erlangsen, A., Appadurai, V., Wang, Y., Turecki, G., Mors, O., Werge, T., Mortensen, P.B., Starnawska, A., Børglum, A.D., Schork, A., 2018. Genetics of suicide attempts in individuals with and without mental disorders: a population-based genome-wide association study. *Molecular psychiatry*, 1.
- Garlow, S.J., Kinkead, B., Thase, M.E., Judd, L.L., Rush, A.J., Yonkers, K.A., Kupfer, D.J., Frank, E., Schettler, P.J., Rapaport, M.H., 2013. Fluoxetine increases suicide ideation less than placebo during treatment of adults with minor depressive disorder. *Journal of psychiatric research* 47, 1199-1203.
- Geoffroy, M.C., Gunnell, D., Clark, C., Power, C., 2018. Are early-life antecedents of suicide mortality associated with psychiatric disorders and suicidal ideation in midlife? *Acta psychiatrica Scandinavica* 137, 116-124.
- George, M.S., Raman, R., Benedek, D.M., Pelic, C.G., Grammer, G.G., Stokes, K.T., Schmidt, M., Spiegel, C., Dealmeida, N., Beaver, K.L., Borckardt, J.J., Sun, X., Jain, S., Stein, M.B., 2014. A two-site pilot randomized 3 day trial of high dose left prefrontal repetitive transcranial magnetic stimulation (rTMS) for suicidal inpatients. *Brain Stimul* 7, 421-431.
- Goldfarb, E.V., Rosenberg, M.D., Seo, D., Constable, R.T., Sinha, R., 2020. Hippocampal seed connectome-based modeling predicts the feeling of stress. *Nat Commun* 11, 1-10.

- Gunnell, D., Rasul, F., Stansfeld, S., Hart, C.L., Smith, G.D., 2002. Gender differences in self-reported minor mental disorder and its association with suicide. *Social psychiatry and psychiatric epidemiology* 37, 457-459.
- Harwood, D., Hawton, K., Hope, T., Jacoby, R., 2001. Psychiatric disorder and personality factors associated with suicide in older people: a descriptive and case-control study. *International journal of geriatric psychiatry* 16, 155-165.
- Harwood, D., Hawton, K., Hope, T., Jacoby, R., 2006. Suicide in older people without psychiatric disorder. *International journal of geriatric psychiatry* 21, 363-367.
- Henriksson, M.M., Marttunen, M.J., Isometsä, E.T., Heikkinen, M.E., Aro, H.M., Kuoppasalmi, K.I., Lönnqvist, J.K., 1995. Mental disorders in elderly suicide. *International Psychogeriatrics* 7, 275-286.
- Jiao, L., Duan, X., Cui, Q., Chen, H., Liao, W., 2019. More than just statics: temporal dynamics of intrinsic brain activity predicts the suicidal ideation in depressed patients. *Psychological medicine* 49, 852-860.
- Jick, H., Kaye, J.A., Jick, S.S., 2004. Antidepressants and the risk of suicidal behaviors. *Jama* 292, 338-343.
- Johnston, J.A., Wang, F., Liu, J., Blond, B.N., Wallace, A., Liu, J., Spencer, L., Lippard, E.T.C., Purves, K.L., Landeros-Weisenberger, A., 2017. Multimodal neuroimaging of frontolimbic structure and function associated with suicide attempts in adolescents and young adults with bipolar disorder. *American journal of psychiatry*.
- Joiner Jr, T.E., Buchman-Schmitt, J.M., Chu, C., 2017. Do undiagnosed suicide decedents have symptoms of a mental disorder? *Journal of clinical psychology* 73, 1744-1752.
- Kang, W., Shin, J.H., Han, K.M., Kim, A., Kang, Y., Kang, J., Tae, W.S., Paik, J.W., Lee, H.W., Seong, J.K., 2020. Local shape volume alterations in subcortical structures of suicide attempters with major depressive disorder. *Human brain mapping* 41, 4925-4934.
- Keramatian, K., Dhanoa, T., McGirr, A., Lang, D.J., Honer, W.G., Lam, R.W., Yatham, L.N., 2016. Structural brain changes in first episode mania with and without psychosis: Data from the Systematic Treatment Optimization Program for Early Mania (STOP-EM). *The world journal of biological psychiatry : the official journal of the World Federation of Societies of Biological Psychiatry*, 1-11.
- Khan, A., Khan, S.R., Leventhal, R.M., Brown, W.A., 2001. Symptom reduction and suicide risk among patients treated with placebo in antipsychotic clinical trials: an analysis of the Food and Drug Administration database. *American Journal of Psychiatry* 158, 1449-1454.
- Kirino, E., Gitoh, M., 2011. Rapid improvement of depressive symptoms in suicide attempters following treatment with milnacipran and tricyclic antidepressants—a case series. *Neuropsychiatric disease and treatment* 7, 723.
- KNMG/KNMP, 2012. Guidelines for the practice of euthanasia and physician-assisted suicide.
- Lan, M.J., Rizk, M.M., Pantazatos, S.P., Rubin-Falcone, H., Miller, J.M., Sublette, M.E., Oquendo, M.A., Keilp, J.G., Mann, J.J., 2019. Resting-state amplitude of low-frequency fluctuation is associated with suicidal ideation. *Depression and anxiety* 36, 433-441.
- Lee, M.S., Anumagalla, P., Talluri, P., Pavuluri, M.N., 2018. Attentional engagement increases inferior frontal gyrus activity and mutes limbic activity in pediatric bipolar disorder: Meta-analyses of fMRI studies. *Progress in neuro-psychopharmacology & biological psychiatry*.

- Lesage, A.D., Boyer, R., Grunberg, F., Vanier, C., Morissette, R., Ménard-Buteau, C., Loyer, M., 1994. Suicide and mental disorders: a case-control study of young men. *The American journal of psychiatry*.
- Li, L., Ji, E., Tang, F., Qiu, Y., Han, X., Zhang, S., Zhang, Z., Yang, H., 2018. Abnormal brain activation during emotion processing of euthymic bipolar patients taking different mood stabilizers. *Brain imaging and behavior*.
- Ligier, F., Giguère, C.-E., Notredame, C.-E., Lesage, A., Renaud, J., Séguin, M., 2020. Are school difficulties an early sign for mental disorder diagnosis and suicide prevention? A comparative study of individuals who died by suicide and control group. *Child and Adolescent Psychiatry and Mental Health* 14, 1-9.
- Linsam Barth, S., Jeria, A., Avirame, K., Todder, D., Riquelme, R., Stehberg, J., 2019. Deep Transcranial Magnetic Stimulation for the Treatment of Negative Symptoms in Schizophrenia: Beyond an Antidepressant Effect. *J ECT*.
- Liu, B.-P., Qin, P., Liu, Y.-Y., Yuan, L., Gu, L.-X., Jia, C.-X., 2018. Mental disorders and suicide attempt in rural China. *Psychiatry research* 261, 190-196.
- Marttunen, M.J., Henriksson, M.M., Isometsa, E.T., Heikkinen, M.E., 1998. Completed suicide among adolescents with no diagnosable psychiatric disorder. *Adolescence* 33, 669.
- Maselko, J., Patel, V., 2008. Why women attempt suicide: the role of mental illness and social disadvantage in a community cohort study in India. *Journal of Epidemiology & Community Health* 62, 817-822.
- McIntosh, A.M., Whalley, H.C., McKirdy, J., Hall, J., Sussmann, J.E., Shankar, P., Johnstone, E.C., Lawrie, S.M., 2008. Prefrontal function and activation in bipolar disorder and schizophrenia. *Am. J. Psychiatry* 165, 378-384.
- Mehta, U.M., Naik, S.S., Thanki, M.V., Thirthalli, J., 2019. Investigational and Therapeutic Applications of Transcranial Magnetic Stimulation in Schizophrenia. *Curr Psychiatry Rep* 21, 89.
- Meltzer, H.Y., Alphas, L., Green, A.I., Altamura, A.C., Anand, R., Bertoldi, A., Bourgeois, M., Chouinard, G., Islam, M.Z., Kane, J., 2003. Clozapine treatment for suicidality in schizophrenia: international suicide prevention trial (InterSePT). *Archives of general psychiatry* 60, 82-91.
- Merali, Z., Kent, P., Du, L., Hrdina, P., Palkovits, M., Faludi, G., Poulter, M.O., Bédard, T., Anisman, H., 2006. Corticotropin-releasing hormone, arginine vasopressin, gastrin-releasing peptide, and neuromedin B alterations in stress-relevant brain regions of suicides and control subjects. *Biological psychiatry* 59, 594-602.
- Miché, M., Hofer, P.D., Voss, C., Meyer, A.H., Gloster, A.T., Beesdo-Baum, K., Lieb, R., 2018. Mental disorders and the risk for the subsequent first suicide attempt: results of a community study on adolescents and young adults. *European child & adolescent psychiatry* 27, 839-848.
- Milane, M.S., Suchard, M.A., Wong, M.-L., Licinio, J., 2006. Modeling of the temporal patterns of fluoxetine prescriptions and suicide rates in the United States. *PLoS medicine* 3.
- Milner, A., Svetcic, J., De Leo, D., 2013. Suicide in the absence of mental disorder? A review of psychological autopsy studies across countries. *International journal of social psychiatry* 59, 545-554.
- Mines, D., Hill, D., Yu, H., Novelli, L., 2005. Prevalence of risk factors for suicide in patients prescribed venlafaxine, fluoxetine, and citalopram. *Pharmacoepidemiology and drug safety* 14, 367-372.
- Minzenberg, M.J., Lesh, T.A., Niendam, T.A., Yoon, J.H., Rhoades, R.N., Carter, C.S., 2014. Frontal cortex control dysfunction related to long-term suicide risk in recent-onset schizophrenia. *Schizophrenia research* 157, 19-25.

- Neutel, C.I., Patten, S.B., 1997. Risk of suicide attempts after benzodiazepine and/or antidepressant use. *Annals of epidemiology* 7, 568-574.
- Niederkrötenhaler, T., Mittendorfer-Rutz, E., Thurner, S., Endel, G., Klimek, P., 2019. Healthcare utilization, psychiatric medication and risk of rehospitalization in suicide-attempting patients with common mental disorders. *Australian & New Zealand Journal of Psychiatry*, 0004867419895112.
- Niu, J., Tsai, H.-H., Hoi, K.K., Huang, N., Yu, G., Kim, K., Baranzini, S.E., Xiao, L., Chan, J.R., Fancy, S.P., 2019. Aberrant oligodendroglial–vascular interactions disrupt the blood–brain barrier, triggering CNS inflammation. *Nature neuroscience* 22, 709-718.
- Nordentoft, M., Mortensen, P.B., Pedersen, C.B., 2011. Absolute risk of suicide after first hospital contact in mental disorder. *Archives of general psychiatry* 68, 1058-1064.
- Oquendo, M.A., Galfalvy, H.C., Currier, D., Grunebaum, M.F., Sher, L., Sullivan, G.M., Burke, A.K., Harkavy-Friedman, J., Sublette, M.E., Parsey, R.V., 2011. Treatment of suicide attempters with bipolar disorder: a randomized clinical trial comparing lithium and valproate in the prevention of suicidal behavior. *American journal of psychiatry* 168, 1050-1056.
- Organization, W.H., 2014. Preventing suicide: A global imperative. World Health Organization.
- Orme, W.H., Szczepanek, A.E., Allen, J.G., Oldham, J.M., Madan, A., Frueh, B.C., Fowler, J.C., 2020. Lifetime and prospective associations among personality trait domains and suicide-related behaviors in patients with severe mental illness. *Journal of affective disorders* 266, 492-497.
- Park, S., Hong, J.P., Jeon, H.J., Seong, S., Cho, M.J., 2015. Childhood exposure to psychological trauma and the risk of suicide attempts: the modulating effect of psychiatric disorders. *Psychiatry investigation* 12, 171.
- Patchan, K.M., Richardson, C., Vyas, G., Kelly, D.L., 2015. The risk of suicide after clozapine discontinuation: Cause for concern. *Annals of clinical psychiatry: official journal of the American Academy of Clinical Psychiatrists* 27, 253.
- Préville, M., Hebert, R., Boyer, R., Bravo, G., Seguin, M., 2005. Physical health and mental disorder in elderly suicide: a case-control study. *Aging & Mental Health* 9, 576-584.
- Pridmore, S., 2015. Mental disorder and suicide: A faulty connection. *Australian & New Zealand Journal of Psychiatry* 49, 18-20.
- Qin, P., Agerbo, E., Mortensen, P.B., 2002. Suicide risk in relation to family history of completed suicide and psychiatric disorders: a nested case-control study based on longitudinal registers. *The Lancet* 360, 1126-1130.
- Qin, P., Hawton, K., Mortensen, P.B., Webb, R., 2014. Combined effects of physical illness and comorbid psychiatric disorder on risk of suicide in a national population study. *The British Journal of Psychiatry* 204, 430-435.
- Randall, J.R., Walld, R., Finlayson, G., Sareen, J., Martens, P.J., Bolton, J.M., 2014. Acute risk of suicide and suicide attempts associated with recent diagnosis of mental disorders: a population-based, propensity score—matched analysis. *The Canadian journal of psychiatry* 59, 531-538.
- Ringbäck Weitoft, G., Berglund, M., Lindström, E.A., Nilsson, M., Salmi, P., Rosén, M., 2014. Mortality, attempted suicide, re-hospitalisation and prescription refill for clozapine and other antipsychotics in Sweden – a register-based study. *Pharmacoepidemiology and drug safety* 23, 290-298.

- Roberts, E., Cipriani, A., Geddes, J.R., Nierenberg, A.A., Young, A.H., 2017. The evidence for lithium in suicide prevention. *The British Journal of Psychiatry* 211, 396-396.
- Rossi, R., Talevi, D., Gregori, E., Quarta, E., Lucaselli, A., Pacitti, F., 2020. Early interpersonal violence mediates the effect of family history of mental disorder on suicide attempts in a non-clinical sample. *Rivista di psichiatria* 55, 37-40.
- Rubino, A., Roskell, N., Tennis, P., Mines, D., Weich, S., Andrews, E., 2007. Risk of suicide during treatment with venlafaxine, citalopram, fluoxetine, and dothiepin: retrospective cohort study. *BMJ (Clinical research ed.)* 334, 242.
- San Too, L., Spittal, M.J., Bugeja, L., Reifels, L., Butterworth, P., Pirkis, J., 2019. The association between mental disorders and suicide: A systematic review and meta-analysis of record linkage studies. *Journal of affective disorders*.
- Sarkinaite, M., Gleizniene, R., Adomaitiene, V., Dambrauskiene, K., Raskauskiene, N., Steibliene, V., 2021. Volumetric MRI analysis of brain structures in patients with history of first and repeated suicide attempts: a cross sectional study. *Diagnostics* 11, 488.
- Schmutte, T.J., Wilkinson, S.T., 2020. Suicide in Older Adults With and Without Known Mental Illness: Results From the National Violent Death Reporting System, 2003–2016. *American journal of preventive medicine*.
- Shafii, M., Steltz-Lenarsky, J., Derrick, A.M., Beckner, C., Whittinghill, J.R., 1988. Comorbidity of mental disorders in the post-mortem diagnosis of completed suicide in children and adolescents. *Journal of affective disorders* 15, 227-233.
- Siddiqui, S.V., Chatterjee, U., Kumar, D., Siddiqui, A., Goyal, N., 2008. Neuropsychology of prefrontal cortex. *Indian J. Psychiatry* 50, 202.
- Smith, E.G., Austin, K.L., Kim, H.M., Miller, D.R., Eisen, S.V., Christiansen, C.L., Kilbourne, A.M., Sauer, B.C., McCarthy, J.F., Valenstein, M., 2014. Suicide risk in Veterans Health Administration patients with mental health diagnoses initiating lithium or valproate: a historical prospective cohort study. *BMC psychiatry* 14, 357.
- Smith, K.A., Cipriani, A., 2017. Lithium and suicide in mood disorders: updated meta-review of the scientific literature. *Bipolar disorders* 19, 575-586.
- Soeiro-de-Souza, M.G., Otaduy, M.C.G., Machado-Vieira, R., Moreno, R.A., Nery, F.G., Leite, C., Lafer, B., 2018. Anterior Cingulate Cortex Glutamatergic Metabolites and Mood Stabilizers in Euthymic Bipolar I Disorder Patients: A Proton Magnetic Resonance Spectroscopy Study. *Biological psychiatry. Cognitive neuroscience and neuroimaging*.
- Soreni, N., Apter, A., Weizman, A., Don-Tufeled, O., Leschiner, S., Karp, L., Gavish, M., 1999. Decreased platelet peripheral-type benzodiazepine receptors in adolescent inpatients with repeated suicide attempts. *Biological psychiatry* 46, 484-488.
- Sørensen, H.J., Mortensen, E.L., Wang, A.G., Juel, K., Silvertov, L., Mednick, S.A., 2009. Suicide and mental illness in parents and risk of suicide in offspring. *Social psychiatry and psychiatric epidemiology* 44, 748-751.
- Sorenson, S.B., Golding, J.M., 1988. Suicide ideation and attempts in Hispanics and non-Hispanic whites: demographic and psychiatric disorder issues. *Suicide and Life-Threatening Behavior* 18, 205-218.

- Spoletini, I., Piras, F., Fagioli, S., Rubino, I.A., Martinotti, G., Siracusano, A., Caltagirone, C., Spalletta, G., 2011. Suicidal attempts and increased right amygdala volume in schizophrenia. *Schizophrenia research* 125, 30-40.
- Sung, H.G., Li, J., Nam, J.H., Won, D.Y., Choi, B., Shin, J.-Y., 2019. Concurrent use of benzodiazepines, antidepressants, and opioid analgesics with zolpidem and risk for suicide: a case-control and case-crossover study. *Social psychiatry and psychiatric epidemiology* 54, 1535-1544.
- Tanti, A., Kim, J., Wakid, M., Davoli, M., Turecki, G., Mechawar, N., 2017. Child abuse associates with an imbalance of oligodendrocyte-lineage cells in ventromedial prefrontal white matter. *Molecular psychiatry*.
- Tasmim, S., Dada, O., Wang, K.Z., Bani-Fatemi, A., Strauss, J., Adanty, C., Graff, A., Gerretsen, P., Zai, C., Borlido, C., 2020. Early-life stressful events and suicide attempt in schizophrenia: machine learning models. *Schizophrenia Research*.
- Tauscher-Wisniewski, S., Disch, D., Plewes, J., Ball, S., Beasley, C.M., 2007. Evaluating suicide-related adverse events in clinical trials of fluoxetine treatment in adults for indications other than major depressive disorder. *Psychological medicine* 37, 1585-1593.
- Taylor, R., Page, A., Morrell, S., Carter, G., Harrison, J., 2004. Socio-economic differentials in mental disorders and suicide attempts in Australia. *The British Journal of Psychiatry* 185, 486-493.
- Terao, T., Kanehisa, M., Shiotsuki, I., Ishii, N., 2018. Mixed features in bipolar I disorder and the effect of lithium on suicide. *American Journal of Psychiatry* 175, 80-80.
- Tidemalm, D., Långström, N., Lichtenstein, P., Runeson, B., 2008. Risk of suicide after suicide attempt according to coexisting psychiatric disorder: Swedish cohort study with long term follow-up. *BMJ (Clinical research ed.)* 337, a2205.
- Vasiliadis, H.-M., Lamoureux-Lamarche, C., Guerra, S.G., 2017. Gender and age group differences in suicide risk associated with co-morbid physical and psychiatric disorders in older adults. *International psychogeriatrics* 29, 249-257.
- Wagner, G., Li, M., Sacchet, M.D., Richard-Devantoy, S., Turecki, G., Bär, K.-J., Gotlib, I.H., Walter, M., Jollant, F., 2021. Functional network alterations differently associated with suicidal ideas and acts in depressed patients: an indirect support to the transition model. *Translational psychiatry* 11, 1-11.
- Wang, L., Zhao, Y., Edmiston, E.K., Womer, F.Y., Zhang, R., Zhao, P., Jiang, X., Wu, F., Kong, L., Zhou, Y., Tang, Y., Wei, S., 2019. Structural and functional abnormalities of amygdala and prefrontal cortex in major depressive disorder with suicide attempts. *Frontiers in psychiatry* 10, 923.
- Wang, Q., Van Heerikhuizen, J., Aronica, E., Kawata, M., Seress, L., Joels, M., Swaab, D.F., Lucassen, P.J., 2013. Glucocorticoid receptor protein expression in human hippocampus; stability with age. *Neurobiology of aging* 34, 1662-1673.
- Wei, S., Womer, F.Y., Edmiston, E.K., Zhang, R., Jiang, X., Wu, F., Kong, L., Zhou, Y., Tang, Y., Wang, F., 2020. Structural alterations associated with suicide attempts in major depressive disorder and bipolar disorder: A diffusion tensor imaging study. *Progress in neuro-psychopharmacology & biological psychiatry* 98, 109827.
- Weng, J.-C., Chou, Y.-S., Tsai, Y.-H., Lee, C.-T., Hsieh, M.-H., Chen, V.C.-H., 2019. Connectome analysis of brain functional network alterations in depressive patients with suicidal attempt. *Journal of clinical medicine* 8, 1966.

WHO, 2021. Suicide.

Zhang, L., Lucassen, P.J., Salta, E., Verhaert, P.D., Swaab, D., 2022. Hippocampal neuropathology in suicide: Gaps in our knowledge and opportunities for a breakthrough. *Neurosci. Biobehav. Rev.* 132, 542-552.

Zhang, L., Verwer, R.W., Lucassen, P.J., Huitinga, I., Swaab, D.F., 2020a. Prefrontal cortex alterations in glia gene expression in schizophrenia with and without suicide. *J. Psychiatr. Res.* 121, 31-38.

Zhang, L., Verwer, R.W., Lucassen, P.J., Huitinga, I., Swaab, D.F., 2020b. Sex difference in glia gene expression in the dorsolateral prefrontal cortex in bipolar disorder: Relation to psychotic features. *J. Psychiatr. Res.* 125, 66-74.

Zhao, J., Lucassen, P.J., Swaab, D.F., 2019. Suicide is a confounder in postmortem studies on depression. *Biol. Psychiatry* 86, e37-e40.

Zhao, J., Qi, X.-R., Gao, S.-F., Lu, J., van Wamelen, D., Kamphuis, W., Bao, A.-M., Swaab, D., 2015. Different stress-related gene expression in depression and suicide. *Journal of psychiatric research* 68, 176-185.

Zhao, J., Verwer, R., Gao, S.-F., Qi, X.-R., Lucassen, P., Kessels, H., Swaab, D., 2018. Prefrontal alterations in GABAergic and glutamatergic gene expression in relation to depression and suicide. *J. Psychiatr. Res.* 102, 261-274.

Zhao, J., Verwer, R., Van Wamelen, D., Qi, X.-R., Gao, S.-F., Lucassen, P., Swaab, D., 2016. Prefrontal changes in the glutamate-glutamine cycle and neuronal/glial glutamate transporters in depression with and without suicide. *Journal of psychiatric research* 82, 8-15.