

Abstract 21-2-01

**Abstract Title:** Two Hits, but the First Matters Most: Childhood Trauma Predisposes to Adult PTSD and Influences Adult Interpersonal Dynamics

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Introduction/Background: Despite traumatic events being as old as human life itself, our understanding of post-traumatic stress disorder (PTSD) is recent, formally dating to 1980 in the DSM (Scott, 2014). New, phenotypically distinct entities have been recognized as different from the post-traumatic disorders described by survivors of 20th century warzones, such as complex post-traumatic stress disorder (CPTSD), now recognized in the International Classification of Diseases, version 11 (ICD-11). Whereas classic PTSD was understood solely through the lens of reexperiencing, avoidance, and hyperarousal, entrained by a well-defined traumatic event such as combat or motor vehicle collision, ICD-11 CPTSD includes these same criteria and further adds affect dysregulation, alterations of consciousness, disturbed self-perception, disturbed perceptions of offender(s), relational dysfunction, and an altered values system developing progressively in the context of chronic, developmentally adverse interpersonal trauma (Maercker, 2021). There is a possible link between developmentally entrained CPTSD and adult PTSD, with the former having a permissive effect for the development of the latter. In a Dutch study of 85 veterans examined pre- and post-deployment to Afghanistan during Operation Enduring Freedom, methylation of SKA-2, a biomarker correlate of suicidality and cortisol dysregulation (often seen in PTSD), was predictive of PTSD symptoms; strikingly, while greater combat related trauma exposure predicted increasing methylation and cortisol blunting, this appeared to be a pro-compensatory response. Severity of PTSD symptoms was predicted by a longitudinal decrease in SKA-2 methylation, and pre-deployment SKA-2 levels together with childhood trauma exposure significantly predicted PTSD symptoms independently of wartime trauma exposure (Boks et al., 2016). While it is not clear if childhood trauma directly mediates these epigenetic changes, its interaction with biomarkers raises its likelihood of being part of a causal mechanism. While recent studies have shown that gene methylation is associated with severity of Adverse Childhood Experiences (ACEs), no distinct pattern of methylation was discovered in PTSD cohorts, despite such associations being seen with military and combat trauma inventories (Hossack et al., 2020). This may be because of a heterogeneity of epigenetic phenotypes in those with ACEs or because the remoteness of the temporal association results in an indistinct epigenetic phenotype.

**Description:** Patient is a 44 year old female who was hospitalized for treatment of lacerations and orthopedic injuries sustained during an accident while riding an all-terrain vehicle with her child. Her history was significant for motor vehicle collision (MVC) approximately ten years ago in which her other child had also been in the vehicle with her. Subsequent to the most recent accident, she reported reexperiencing of the prior MVC, with her first thought subsequent to impact being who would take care of her child if she did not survive. Current symptoms includes muscle tension, greatly increased frequency of nightmares (increasing from approximately three yearly to multiple nightly), flashbacks about first MVC and intrusive thoughts about it. She reports having avoided "crazy drivers" subsequent to the first MVC, but feels able to drive because she remains in control of her own vehicle. Her social history was significant for childhood parental physical abuse and subsequent abandonment, death of

friends and family members during adolescence and early adulthood, and a prolonged abusive relationship with a substance abusing partner who physically and sexually abused her during adolescence. Patient reports recent oral-maxillofacial surgery performed for cosmetic reasons (related to perceived need to improve attractiveness) and recently terminated a relationship with a different partner who was also substance abusing. Patient is involved in caregiving for others and has adopted parentless children, despite multiparity. She has mainly self-managed PTSD hyperarousal by developing calming breathing practices and nightmares through imaginative exercises to plan non-distressing dreams before falling asleep.

**Discussion and Conclusion:** This patient's presentation is interesting because it demonstrates both classic PTSD (symptoms within the reexperiencing, avoidance, and hyperarousal clusters) and CPTSD (disturbed self-perception resulting in surgery, disturbed perception of abusers leading to renewed harmful relationships, and relational dysfunction in which patient is a caregiver to many people despite personal history of abandonment). Her PTSD development and exacerbation subsequent to both accidents were expressed through concerns regarding interpersonal attachments (her concern for injury or death was mainly for caregiving for children), further connecting PTSD symptoms to a background of interpersonal abandonment and trauma. Though she demonstrates adaptive responses to trauma, such as self-calming techniques and altruism, this second MVC demonstrates that she is at risk of PTSD relapse, with childhood traumatic exposures being a significant risk factor. This case report should encourage clinicians to always screen patients with classic PTSD symptom clusters for childhood adverse experiences and history of physical, sexual, emotional, or other abuse in childhood, because a growing body of evidence indicates the existence of multiple traumatic phenotypes and potential mechanistic effects of early life trauma on post-traumatic pathogenesis.

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Abstract 21-2-02

Abstract Title: Psychosis in Paraneoplastic Syndrome and its Complications

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**Introduction/Background:** The International Classification of Diseases, tenth revision (ICD-10) defines "psychosis" as the "presence of hallucinations, delusions, or a limited number of abnormalities of behavior, such as gross excitement or overactivity, marked psychomotor retardation and catatonic behavior"; the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) similarly defines "psychotic features" to be delusions, hallucinations, or formal though disorder [1]. Psychosis is commonly seen in various psychiatric, neurodevelopmental, neurologic, and medical conditions and can occur due to a primary or secondary cause [2]. Primary psychosis is due to a psychiatric disorder while a secondary cause of psychosis is due to a medical or neurologic disorder [1].

Psychiatric manifestations like psychosis, as well as other symptoms like seizures, movement disorders, personality change, autonomic dysfunction, and even death can be seen in paraneoplastic syndromes [3, 4]. These syndromes occur due to malignancies secreting peptides, hormones, and cytokines or when there is a cross-reaction between the malignant tissue and non-malignant tissue [5]. There are two subtypes of antibodies seen in paraneoplastic syndromes: ones that target neural intracellular antigens and ones that target cell-surface antigens [3]. Antibodies that target neural intracellular antigens have a high association with cancer whereas the association is weaker with the other subtype [3]. Antibodies in both subtypes can be seen in the cerebrospinal fluid and patients can also present with abnormal neuroimaging and electroencephalography (EEG) [3, 6]. Studies have shown that early intervention leads to positive outcomes, and oftentimes, allow patients to almost completely return to baseline [7].

Description: Patient is a 50-year-old white male with a history of multiple myeloma who presented with altered mental status and acute psychosis. The patient was unable to give a clear history of the events preceding the hospitalization due to his clinical condition. Patient displayed disorganized thought process, flight of ideas, and aggressive behavior. A few days after admission, the patient started experiencing visual and auditory hallucinations. The acute onset of the patient's psychosis raised concern for an organic cause. A lumbar puncture (LP) was recommended at this time to assess for paraneoplastic syndrome. Neuroimaging was obtained and MRI showed T2/flair hyperintensities in a distribution that was slightly atypical of chronic microvascular change but without associated enhancement or restricted diffusion. Radiology recommended that correlation with a LP may be helpful. However, neurology believed that there was a low likelihood that the underlying cause is a paraneoplastic syndrome, and that they did not believe a LP was necessary at this time. Despite medication modifications and various tests, the patient's psychosis did not improve over a lengthy hospitalization nor was an underlying cause of the psychosis able to be determined. Due to the lack of answers and the patient's symptoms resembling delirium rather than a primary psychiatric disorder, a LP became more important and was performed. One week following the LP (with autoantibody assessments still in progress at the Mayo clinic), the patient was found to have rhythmic shaking of his

left arm and was unresponsive. Following the episode, he had a post-ictal confusion and brief lack of movement on the right side. EEG is also now in progress.

**Discussion and Conclusion:** Although the results for the LP are still pending, the focus of this case report is not the results, but rather the importance of a thorough evaluation of all organic causes of psychosis, as it can commonly occur due to secondary causes [1]. Even if CSF analysis comes back unrevealing, a LP is a procedure that should have been done earlier in the hospital stay that could have very well determined the underlying cause of the psychosis or just as importantly, ruled out potential underlying causes. Depending on what the underlying cause of the psychosis is, treatment can vastly vary, thus emphasizing again the importance of a thorough work-up and specifically in this case, the LP, regardless of the results. Detection of the secondary cause and then appropriately treating it can effectively eliminate the psychosis.

The importance in treating psychosis lies in the complications that occur. Psychosis presents as a roadblock for not only the deliverance of effective healthcare but also participation from the patient in their own healthcare [2]. Patients who are experiencing psychosis may not have the proper insight to effectively weigh treatments presented to them. Outside of the medical setting, patients with psychosis can face challenges in everyday life. Depending on the severity of the psychosis, patients may not be able to take care of themselves or function appropriately outside or inside the home. This leads to further complications like being unable to hold a job, being unable to take care of other health concerns, or even perform activities of daily living.

Due to the domino effect that psychosis can have on all aspects of a patient's life, a thorough and prompt work-up of all organic causes is crucial in patients who are experiencing acute psychosis. The longer treatment for psychosis is delayed, the consequences can become more and more severe.

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Abstract 21-2-03

Abstract Title: Suicidality in Huntington's Disease

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**Introduction/Background:** Chronic non-communicable diseases have been strongly associated with depression (5). In Huntington's disease, up to 98% of patients develop a psychiatric disorder or experience psychiatric symptoms at some point during their disease, with the most frequent being depression (1). The prevalence of depression in Huntington's disease has been estimated between 9 and 63% with suicidal ideation occurring in 20-30% of patients and suicide attempts in approximately 7% of patients (1,6). This association between Huntington's disease, depression, and suicidality is inadequately characterized but is thought to go beyond the life disruption and psychological toll of motor symptoms, being at least in part organic (2,3).

**Description:** The patient is a 38-year-old male with a past medical history significant for Huntington's disease diagnosed in 2017 who presented after leaping from a 3-story building in an apparent suicide attempt, sustaining multiple traumatic fractures of the lower extremities and spine. The patient reported increasing depression leading up to the suicide attempt focused on the progression of his disease. The patient's mother died from complications of Huntington's disease at age 36, and his worry has increased as he is now past this age. He also lost two other relatives in his mother's family to Huntington's disease. In addition, he reported a continuous feeling of stress that he attributed to being homeless. He denies any previous suicide attempts and reports feeling glad his attempt failed. The patient was initially resistant to contacting family, stating that he did not want to further burden his sister, stating that she had done enough already.

Upon obtaining collateral from sister, conflicting information was obtained. The patient has been living in an apartment supplied by his sister. The sister manages the patients' finances, provides him with groceries, and delivers his medications. His sister has been supporting the patient in this manner for the last three years. The patient's sister reported that just prior to this event, the patient abruptly left home without any notice, and the sister was about to file a missing person's report. She was glad to hear that he was in the safe care of the local hospital.

**Discussion and Conclusion:** This patient's presentation is significant for its ability to bring both awareness to the burden and severity of depression in patients with Huntington's Disease and the unique social stressors that these patients face. With the alarming rate of depression and suicidality in patients with Huntington's disease, it is crucial that suicidal thoughts and behaviors are closely followed in this patient population (5). There is some debate on how rates of suicidality differ with the stages of Huntington's disease. One prominent school of thought is that rates of suicidality peak bimodally, first with symptom onset and second with a patient's loss of independence. This is followed by a subsequent decrease in suicidality as disease progression impacts cognition and personality with apathy and affect blunting becoming increasingly prevalent (1,4). This patient presents well past symptom onset with several years of diminished independence and a first-time suicide attempt. This was contrary to the suggested bimodal distribution of suicidality and seemed to be driven by two specific factors. First, his

anticipation of death, having watched his mother succumb to the same disease earlier in life, and second, his guilt for having to rely on his sister for such extensive care. Upon further interactions with the patient, however, it became apparent that his guilt for burdening his sister was the overwhelming driver of his suicidality. Social workers who were actively engaged with the patient at the Huntington's Clinic were unaware of the patient's distress. Our case underscores the need to understand a patient's perspective on his condition and social setting, factors that could easily be overlooked if a patient's perspective is not clearly investigated. In this case, the basic needs of the patient such as food, clothing, and shelter were provided, but his feelings about it were not addressed. This highlights the importance of engaging the feelings and perceptions of all patients who might have concerns about the terminal nature and dependency caused by their illness.

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Abstract 21-2-04

Abstract Title: A Case Report of Menstrual Psychosis: Could this be a new sub-type of PMDD?

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**Introduction/Background:** Menstrual psychosis is a rare occurrence that has only been described in case reports thus far in the literature. This phenomenon is characterized by a cyclical onset of psychosis that coincides with menstruation, usually starting around the onset of the menstrual cycle with resolution of psychotic symptoms when menstruation ends.<sup>1</sup> This subtype of psychosis is particularly important to recognize as the approach to medication management is influenced by fluctuations in hormones, which is the target of treatment.<sup>1</sup>

**Description:** Here we present a case of a 36-year-old Caucasian female with PPH of moderate-to-severe intellectual disability who was brought to the ED for overdose on her home Risperidone and admitted for observation. She was reportedly on Risperidone for many years due to behavioral disturbances related to her intellectual disability. The patient was in a state of extreme agitation when she took an overdose of Risperidone, which was only a total of 3 0.5mg tablets. The patient's mother described these periods of agitation as occurring in congruence with the patient's menstrual cycles, starting about 5 days prior to the onset of menstruation and subsiding at the end of the cycle. The patient's mother also described psychotic symptoms during this time, including laughing/talking to herself, making gestures, and scratching/hitting herself. The patient's psychotic symptoms subside towards the end of her menstrual cycle, and she has a return to her baseline. Her baseline is described as doing most of her ADLs with minor assistance, ability to have simple conversations with family, and the absence of psychotic symptoms. This repeated behavioral change with psychosis associated with the perimenstrual period started about 10-15 years ago. The mother reports that the patient has previously been on Depo-Provera birth control for 2 years in which psychotic symptoms had completely resolved. However, the patient had gained a significant amount of weight so Depo was discontinued. This apparent menstrual psychosis then returned after Depo was discontinued and patient's symptoms worsened further over the last year after the death of her father. The patient was prescribed an OCP during this hospitalization to take daily to achieve amenorrhea, and Risperidone was increased. On initial presentation, patient appeared to be responding to internal stimuli, seen laughing and talking to herself and making gestures. After an increase in Risperidone and a short period of observation, it was reported by the mother that the patient had returned to her baseline. She was discharged with plan to follow up outpatient with a psychiatrist and an OB/GYN.

**Discussion and Conclusion:** Menstrual psychosis has been described as having several distinct characteristics, including acute onset, brief duration with full return to patient's baseline, and the presence of psychotic symptoms exclusively associated with the timing of the menstrual cycle.<sup>1</sup> There have been many case reports that have been presented in the literature and it could be argued that it should have its place in the DSM-5, potentially as a subtype of Premenstrual dysphoric disorder. It is particularly important to highlight this interesting phenomenon because the management is unique to other primary psychotic disorders, as the target of treatment is managing the fluctuations of hormones,

particularly estrogen.<sup>1</sup> Similarly to our patient we are presenting, there have been other cases that have shown resolution of psychotic symptoms with contraceptive medication alone, which ultimately reduces fluctuations of sex steroid hormones.<sup>2</sup> It has been hypothesized that estrogen is protective against psychosis and that marked reductions in estrogen as seen at the start of the menstrual cycle is what precipitates the emergence of psychotic symptoms seen in menstrual psychosis.<sup>3</sup> This hypothesis of the protective effect of estrogen could also be part of the explanation for later onset of psychotic disorders seen in women as opposed to earlier onset in men.<sup>3</sup> This hypothesis has been further illustrated in life cycle studies that have shown that women are more vulnerable to either first episode psychosis or relapse of an existing psychotic disorder during periods of acute decreases in estrogen and psychotic symptoms highlights the complexity and influence of hormones on the body. Furthermore, this case presentation along with other case reports of menstrual psychosis facilitates the need for further diagnostic recognition to ensure that medication management is appropriately targeted towards abating fluctuations of sex hormones.

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Abstract 21-2-05

Abstract Title: A unique presentation of Misidentification Syndrome, a syndrome of subjective doubles

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Additional Authors/Affiliations: Alexandru Ghilezan, DO; Candace Lynn Perry, MD: AltaPointe

**Introduction/Background:** The syndrome of subjective doubles is a rare form of delusional misidentification syndrome. It describes a person who believes they have a clone, double, or doppelgänger. The syndrome belongs to a group of disorders including: Capgras' syndrome, Frégoli syndrome, and intermetamorphosis syndrome; all psychopathologic phenomena that occur primarily in the setting of psychosis in Schizophrenia. In Capgras Syndrome, the patient expresses the belief that familiar persons have been replaced by clones. These conditions form a syndrome due to their tendency to co-occur and interchange, and their basic theme is the concept of the double. It has been determined that these syndromes arise from a change in the way the brain processes visual signals, specifically the ability to recognize familiar faces. These delusions have been shown to exist upon face-to-face interaction and subsequently resolve during telephone communications.

**Description:** Here we present the case of a 26-year-old male who presented after an acute decompensation and worsening of psychotic features for an involuntary evaluation. The patient reported visualizing several identical replicas of himself. Despite seeing these replicas numerous times, the patient did not express fear of harm by these doubles and noted they often did not speak to him. For example, the patient reported that the 2 officers who detained him prior to hospital admission both appeared and sounded identical to himself. The patient also expressed the delusion that his mother had been replaced. He believed his mother was cloned and reported a great number of different identical clones. These delusions appeared to be fixed and persisted at the end of inpatient evaluation.

**Discussion and Conclusion:** This case highlights a combination of the syndrome of subjective doubles and Capgras syndrome where the patient has delusions regarding self and others. It is particularly interesting as it illustrates the tendency of these delusions to occur simultaneously. It is atypical that this patient had the impression that he was being pursued by his doubles, as patients with this syndrome historically believe their "doppelgänger" leads an entirely separate life. This showcases the presentations that medical students and clinicians should recognize to identify and manage patients with this rare symptom of psychosis.

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Abstract 21-2-06

Abstract Title: Evaluation of Psychotic Symptoms in Patient with Underlying Partial Seizures

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**Introduction/Background:** Psychosis is categorized by a group of symptoms that may include hallucinations, delusions, or disorganized thinking, speech and behavior. Primary psychosis is thought to be caused by a psychiatric disorder, whereas secondary psychosis is caused by a specific medical condition (4). Psychosis of epilepsy is a potential secondary cause in which underlying mechanisms are correlated with an existing seizure disorder (2). Epileptic psychoses are defined as either peri-ictal or interictal, depending on their timing compared to the occurrence of seizures. Peri-ictal psychosis may present before (preictal), during (ictal) or after seizures (postictal). These episodes have well-defined initial and final phases. Symptom duration is short and completely resolves, but peri-ictal psychosis can be a recurring condition (3). Peri-ictal psychosis can also be the result of an iatrogenic process to pharmacologic and/or surgical interventions (2).

**Description:** A 33-year-old male with no past psychiatric hospitalizations who is on disability due to partial seizures secondary to a traumatic brain injury at age 18 presents with worsening episodes of agitation and psychosis. Evaluation by the psychiatric team concluded the psychotic episodes were in the context of seizures and diagnosed him with psychotic disorder due to another medical condition. The seizures were well controlled with the addition of Lamictal by a neurologist before the patient was transferred to a psychiatric facility. The patient ceased having any psychotic or mood symptoms or behavioral issues since admission to the psychiatric hospital. They determined the patient had adequate insight into his condition and recommended outpatient follow up. However, an independent psychiatric evaluation suggested the diagnosis of bipolar disorder, manic with psychotic features, which led to the patient continuing in-patient hospitalization.

**Discussion and Conclusion:** This case highlights the complications involved in diagnosing psychiatric conditions in the context of underlying medical conditions. When psychotic symptoms are described as only occurring in the context of having a seizure, it is reasonable to conclude the events are correlated. However, according to the independent evaluation, focusing primarily on the seizure symptoms and timing could possibly result in oversights in the psychiatric evaluation.

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Abstract 21-2-07

Abstract Title: Case of Oxcarbazepine Induced Hyponatremia

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**Description:** A 66-year-old Caucasian male with a history of bipolar II disorder, post-traumatic stress disorder, generalized anxiety disorder and insomnia has been treated with 600 mg of oxcarbazepine for over 20 years. He was experiencing 3-4 episodes of diarrhea day as well as 3-4 episodes of nocturia per night. On investigation by his primary care provider, his basic metabolic panel was remarkable for hyponatremia, which was asymptomatic. Patient remained hyponatremic consistently for a year even after diet change and sodium supplementation. His lowest plasma sodium concentration was 126 mEq/L. Upon evaluation by urologist, urinalysis showed high concentration of sodium. Oxcarbazepine dose was decreased to 300 mg and plasma sodium concentration increased to 135 mEq/L.

**Discussion and Conclusion:** Studies show there is an increased risk of hyponatremia with oxcarbazepine therapy with approximately fifty nine percent of patients experiencing symptomatic hyponatremia within two years of initial therapy.1 Many risk factors increase the chances of developing hyponatremia, but diuretic use and advanced age were of particular importance.1 Patients are also at risk during events that may require an increase in fluid intake such as post-op or during hot weather.2 Patients taking oxcarbazepine should be regularly monitored for hyponatremia and educated about signs and symptoms of severe hyponatremia. Patients with previously well controlled seizures who become refractory to treatment, have altered mental status or other abnormal behaviors should be evaluated for possible hyponatremia. Patients should be instructed about the concomitant use of common other drug therapies such as non-steroidal anti-inflammatory drugs, diuretics, calcium channel blockers, tricyclic antidepressants.1 They should also be educated on symptoms of hyponatremia, such as dizziness, somnolence, headache, abnormal vision, insomnia, or ataxia. Routine monitoring of anti-diuretic hormone levels is not indicated as investigations indicate that levels remain within normal range during therapy.2

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Abstract 21-2-08

Abstract Title: Chronic Tic Disorder and Comorbidities

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**Introduction/Background:** Chronic Tic Disorders (CTD) are long-lasting neuropsychiatric disorders of childhood that present with a waxing and waning pattern in severity and frequency. CTD have an estimated prevalence of 0.5% to 3% and male predominance with a gender ratio of approximately 2:1. Patients with CTD may present with vocal and/or motor tics that are preceded by premonitory urges. Pathophysiology is not entirely understood, but evidence suggests improper modulation of motor programs at cortical and subcortical areas in the brain. CTD is associated with many neuropsychiatric conditions including OCD, ADHD and ASD.

**Description:** A 14-year-old female presented with a 7-year history of progressively worsening motor tics, reaching peak severity in Summer 2020. Tics were exacerbated by stress and ameliorated by relaxing or focusing activities. At the initial appointment, tics consisted of clapping her hands together, followed by her hitting herself in the forehead with the palm of her hand or fist. She also reported occasionally unintentionally punching friends. She endorsed slow auditory processing, dislike of loud noises and bright lights, and sensitivity to being touched by people or things such as tight clothing. She reported intrusive thoughts such as repeatedly checking the mailbox to ensure properly closure and applying lotion immediately after washing her hands. She also complained of insomnia, spending an average of 1.5 hours to fall asleep. Apart from tics, her mental status exam was normal. She was started on Clonidine 0.1mg at night to lessen tic severity and assist with sleep. At follow-up, patient stated decreased premonitory urges with a significant reduction in severity and frequency in her tics. She is no longer hitting herself in the head and noted the ability to proactively prevent tics by applying deep pressure on her body. At both visits, she insisted on treatments that lessened the severity and frequency of her tics rather than effectively stopping tics altogether as she feels her tics are part of her identity.

**Discussion and Conclusion:** Many patients with chronic tic disorders present with comorbid conditions such as ADHD and OCD/OCB. Studies have shown that these conditions are associated with abnormalities in the cortico-basal ganglia pathway, suggesting how tics can be actively suppressed by the frontal cortex. Hence tics can be exacerbated by stress and ameliorated by concentration and relaxation. In addition, tics must be discerned from stereotypies, especially when suspecting ASD. Stereotypy can also occur in tic disorders; however, stereotypy is not preceded by premonitory urges and symptoms do not wax and wane in severity and frequency. Differentiating between compulsions and tics may prove difficult. Tics may be misinterpreted as a feeling of relief rather than a means to alleviate distress from a compulsion. In addition, sensory sensitivities have been observed in patients with tic disorders due to interceptive awareness, which is associated with enhanced activity of the insula, motor, and cingulate cortices. In all, this case demonstrates the necessity to discern comorbid conditions when suspecting Chronic Tic Disorders.

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Abstract 21-2-09

Abstract Title: MicroRNA Correlates of Childhood Maltreatment and Suicidality

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**Introduction/Background:** Early life trauma, especially physical, sexual, or emotional abuse, are strong risk factors for both depression and suicide. However, the precise mechanisms that link abuse with depression and suicide risk are not well understood. One hypothesis is that these environmental events induce chemical modifications of DNA, and that these changes link early life abuse with later development of depression and suicide attempts. However, this has received very little systematic study. Our preliminary data indicate that chemical modification of the DNA sequences for micro RNAs (miRNAs) link early trauma with depression and suicide. Micro RNAs are short regulatory RNAs that are an important mechanism for environmental regulation of RNA and protein expression. These are significantly altered in people with early life trauma, and specific miRNA changes are associated with depression and suicide risk. The overarching hypothesis of this study is that childhood maltreatment can induce long-term chemical modifications of DNA for micro RNAs. The net effect of these changes may lead to long-term cellular (mal)adaptations which may lead to depression and suicide vulnerability in people with a history of childhood maltreatment.

**Methods:** Our research group has developed a novel method of extracting miRNAs that are specific to neurons, which are contained in small vesicles called exosomes in peripheral blood samples. We have shown that the patterns of miRNA expression are very similar in neuron-specific exosomes and human post-mortem brain samples. This study will recruit participants in three groups – depression with recent serious suicidal ideation or attempt, depressed without recent ideation or attempt, and normal volunteer controls.

Only depressed and suicidal participants will be recruited at Huntsville Hospital. Non-suicidal depressed patients and controls will be recruited at the UAB HRMC. Hospitalized patients will be approached by their respective attending physicians who will serve as co-investigators on the project about participating. People who assent to participation will be contacted by a research staff person. Written informed consent will be obtained prior to any research procedure. A screening interview will be conducted by the research staff person to ensure that inclusion and exclusion criteria are met. However, the remainder of the procedures will be conducted at the UAB HRMC after discharge.

We will also conduct a widely used experimental stressor called the Trier Social Stress Test (TSST). Both depression and suicidality are increased by stressful life events. The TSST is a standardized mildly stressful experience that reliably induces an increase in blood cortisol. We have also shown that the TSST induces changes in miRNA expression that are different in people with a history of childhood maltreatment who are depressed and suicidal. The TSST consists of people presenting a 5-minute speech on any topic of their choosing and then doing some mental arithmetic in front of a panel of two or more observers. Ten ml. blood samples will be obtained at baseline and immediately post-TSST and

15, 30, 60, and 90 minutes after the test. The blood samples will be immediately processed and stored at -80°C. Exosomes will be extracted from the blood plasma samples and miRNA analyzed using an RNA sequencing method. We have conducted hundreds of TSSTs with blood sampling without incidents in a wide range of psychiatric patients and normal volunteer controls.

All data collected in this study will be kept in a HIPAA-compliant REDCAP database for subsequent analysis. The data reported from the study will be done in aggregate and no personally identifiable information will be released.

**Results:** This is an ongoing study.

**Discussion and Conclusion:** If successful, this study may lead to reliable, blood-based biomarkers for depression and suicide risk.

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