BIOPSYCHOSOCIAL ROUNDS PRESENTATION FORMAT & EXAMPLES

Rev. 9-4-13

1. Identifying Data and Present Illness:

Demographics (e.g., 56 year old divorced Caucasian male, living with a girlfriend), chief complaint (e.g., "I am depressed"), present illness (this is a history of present episode if the patient has a long history of psychiatric illness, e.g., The patient has a chart diagnosis of bipolar disorder, with a history of multiple psychiatric hospitalizations at this medical center. The present episode was ushered in about a month ago when the patient noticed that his mood was becoming progressively depressed...He presented himself to the evaluation unit, accompanied by his girlfriend, who was concerned that he had expressed suicidal thoughts... etc.)

2. Life Chart

Life chart is a chronological map of the patient as a person, beginning from birth leading up to the present. First used by Adolph Meyer at John Hopkins University, this is a good way of integrating the patient's history with his/her adaptation and maladaptation to stress that may result in pathology.

Life chart should consist of three columns, the left one being milestones and events, the middle column being actual year and chronological age of the patient, and the right column being any pathology, contact with health care system, and medications. The students will be given some example life charts.

3. Mental Status Examination/Pertinent Medical Findings/Lab Results

The life chart should be followed by a presentation of the patient's admission mental status (or the first mental status the student was able to perform on the patient), and presentation of any pertinent physical findings and lab results.

4. Summary of Salient History and Abnormalities

On the basis of the present illness, the life chart, and mental status examination, the salient features and abnormalities should be summarized to prepare the way for a differential diagnosis.

5. Differential Diagnosis

The presenter will do a differential diagnosis using DSM-5 format. First, present all possibilities, and then discuss how certain diagnoses may be ruled out, ruled in, and

certain factors may contribute to the possible diagnoses, and how to evaluate the patient further.

6. Working Diagnoses

These are the diagnoses on the basis of which you will begin to treat/manage the patient acutely.

7. Formulation

Formulation is the way you understand how the person who is the patient got to be the way you have presented him/her. Ordinarily, the formulation should integrate the biological and psychosocial factors in the course of development, i.e., present the biologic/genetic predisposition/vulnerabilities on the basis of family history or other findings, and an understanding of the psychologic/personality development of the patient in interaction with the environment. While there is no right or wrong formulation, the formulation is of critical importance in our ability to understand and empathize with the patient, and develop a comprehensive management plan that is appropriate for the individual patient. In formulation, you may speculate using various theories or approaches. It is highly recommended that you use several *different theoretical frameworks* to explain or understand the patient.

8. Management Plan

On the basis of your formulation, and the diagnosis, propose a comprehensive, multidimensional management plan.

9. Bibliography

List the articles/book chapters that you read concerning this patient/syndrome/treatment. Did you encounter something that is particularly interesting, timely, or new, present a summary of the paper. A scholarly discussion of the literature in the context of formulation or as a separate presentation is highly recommended and will be a consideration for Honors.

Examples 1-3

Example 1.

Identifying Data and Present Illness

MT is a 28 year-old male with a history of excessive alcohol use who presented to the ED with a fractured pelvis, fractured vertebrae, and lacerations sustained after he dove into his family's empty swimming pool. His family reported that he had a history of delusions, hallucinations, and increasingly erratic behavior, especially in the last few months. MT reported that "God" told him to dive into the pool.

MT was apparently was able to pull himself out of the pool and onto the patio where he was found. He sustained a laceration of left forehead, bilateral superior pubic rami fractures, and an avulsion fracture of his right talo-fibular ligament.

MT stated that "God" gives him commands continuously. He also stated that he always feels compelled to obey the commands that he receives. He stated that has killed people who were attempting to hurt or persecute him, although he then clarified that what he meant is that God eliminates his enemies by sending them to Hell. In addition, the patient stated that he is an alien, and that he is all-powerful, capable of healing himself using his mind. He stated that he forgot to conceal or repair his injuries before he arrived in the hospital. He further explained that he can "manifest" objects or phenomena with his mind. He provided a demonstration by explaining that he was conjuring fire in his hand and asking expectantly whether I could see it. He insisted that the objects and phenomena that he "manifests" are invisible to him but visible to others. He stated that he can read minds and see when people around him are trying to hurt him. He called me "Ryan Brown", the name of his deceased best friend.

During the interview, MT became increasingly agitated and insisted that God commanded him to get up from bed. He attempted to get out of the bed and partially succeeded, although he appeared to be in great pain. Later in the morning, when we returned with the whole team, he insisted variously that there was a bomb under the bed, or that he was commanded by God to get out of the bed lest he be sent to hell. He appeared floridly psychotic, agitated, and terrified of remaining in bed. Nursing staff attempted to convince him to remain in bed so as to avoid the risk of fall and to prevent aggravation of his injuries. MT insisted on standing up, despite the fact that he was clearly in great pain. He was able to stand but found that walking was too painful. We held him and helped him to remain balanced until security arrived. Meanwhile, nursing began administration of IV haloperidol and lorazepam. He was cooperative with hospital security. He was placed in 4-point restraints and on a PRN pharmacologic restraint cocktail, after which he slept.

Life Chart

Personal History	Year (age)	Psych/medical history
Born in Fresno, CA to a family of Hispanic heritage. Middle of 5 children. Two older sisters, a younger sister, a youngest brother, Isaac. Grew up in Fresno. His father is an ordained minister. His mother is a hair stylist. The family attends the Four Square church. The household was devoutly religious. MT says "They forced their Christian beliefs on me, and I'm more spiritual than all of them, and they hate me for it."	1985 (0)	Describes suffering head injuries as a child but is unable to provide details ("I got hit by a bat"). Mother recalls no perinatal health issues. MT's birth was quick and painless.
Attends kindergarten and meets his future best friend, Ryan Brown	1989 (4)	
Home-schooled by his mother (continues through high school). Mother reports that the family did not have trust in local schools but gave children the option of attending public school.	1990- (5)	
The family belongs to a home- schooling cooperative, so the children met other children despite being home-schooled.		
Abusing Robitussin cough syrup (codeine, guaifenesin, pseudoephedrine)	1998 (13)	
Smoking cigarettes. MT later becomes attached to marijuana, cigarettes and alcohol.	1998 (13)	
Smoking marijuana.	1998 (13)	
Smoking cigarettes routinely	2003 (18)	
Smoking marijuana routinely	2003 (18)	
Drinking alcohol routinely	2003 (18)	
Says that he saved the life of a friend, Philip, who was contemplating suicide by introducing that friend to	~2003 (~18)	

marijuana.		
Best friend, Ryan, died suddenly,	2005 (20)	
possibly of a medication or drug		
overdose.		
overdose.		
MT claims that his family did not		
tell him about the death and that		
he only found out a couple		
weeks later from his pastor.		
Der his mether he did not se te		
Per his mother, he did not go to the funeral because his family		
-		
was out of town.	2005 (20)	
Stops going to church regularly.	2005 (20)	
MT works at various jobs,	Mid-2000s (Early-mid 20s)	
including carpet cleaning,		
landscaping, and as a cook in a		
nursing home.		
Started using methamphetamine	Mid-2000s (Early-mid 20s)	
heavily		
Meets his first serious girlfriend,	2009 (24)	
Helen. Helen becomes pregnant.		
Helen goes back to Coffeyville,	2009 (25)	
Kansas, where she is from, to be		
near her family.		
MT has frequent and easy access		
to meth. Helen's brother, Scott,		
makes meth in the family's		
house.		
MT's daughter, Kali, is born in	2009 (25)	
Kansas.		
MT and Helen plan to get		
married and come back to		
Fresno. MT's parents say of		
Helen that "she was very		
immature" and that "MT had to		
take care of the baby. MT's		
mother says that MT would		
frequently say to her, "If I leave,		
the baby will die; Helen does not		
know how to take care of the		
baby."		
MT returns to Fresno briefly.	Winter 2009 (25)	
interestion of the structure of the stru		

Kali has recently had pneumonia		
but was better.		
MT gets a call from Helen saying that Kali is not breathing. MT tries to walk her through CPR over the phone, but Kali passes away. MT gets drunk that evening. MT's mother says that he does not express grief and does not attend the funeral. He says "she's dead, and there's nothing I can do."	Winter 2009 (25)	
Per MT's mother, Helen's family ignores requests from MT's family to establish cause of death.		
MT says to his mother: "I don't believe that Kali is dead".	2009-2010 (25)	
It unclear exactly when MT begins to hear the voice of God issuing commands to him. When asked, he repeatedly says that he has always been able to hear God.	~2009-2013	
MT is unable to hold a regular job. Living at his parents' house and working odd jobs	2013 (28)	
MT spends many of his days at Fresno and Shaw, behind the Burger King. "I'm friends with the homeless people."	2013 (28)	
MT calls his father to say that there is an intruder in the house. MT's younger brother, Isaac, comes by the house and reports that there is no intruder.	2/2013 (28)	
Presents to ED after being found down at the side of the road, intoxicated.	5/13/2013 (28)	Per chart, MT states that he smoked marijuana and drank excessively. Per chart, he states that he thinks he was hit by a car as it turned the corner. (MT later says that this episode
		represented a suicide attempt,

		and that he threw himself into traffic.) MT is uncooperative, refuses imaging and wound care. He self clears his c-spine. He is able to ambulate, and he is discharged home when his mother comes to the ED to pick him up. ED differential was "alcohol intoxication, illicit drug intoxication, ICH less likely, dehydration, hyperthermia." No psychiatry consult.
MT's mother hears him banging on the walls of the home. She walks into his room and finds that he has set the mattress on fire.	6/29/2013 (28)	
MT hears God telling him to dive into his parents' swimming pool. The pool is empty. He starts filling it with water but dives in before it is close to full.	7/1/2013 (28)	MT suffers multiple pelvic and vertebral fractures. He is agitated and floridly psychotic. Psychiatry is consulted. MT describes years of heavy cannabis and alcohol use. "I drink so much I should be dead". MT also describes years of methamphetamine use, although he says, "I don't use meth anymore". He describes a past episode, not recent, where "a friend injected me with meth, and I was up for two weeks." MT says, "I used meth to unlock my powers." MT associates meth with increased auditory acuity. "I can hear cockroaches and rats."
MT remains floridly psychotic on risperidone, despite modestly increased doses. Appears to be very frightened in the hospital. He states that he will be studied	7/1/13-7/10/13 (28)	

and dissected. He is transferred to CBHC on 7/10, where he has been hospitalized since.		
MT's degree of psychosis and delusion is unchanged. He is able, briefly, to talk about Kali and becomes very tearful.	7/30/13 (28)	
Treating team at CBHC decides to start MT on clozaril with his consent.	8/2/13 (28)	

Mental Status Exam and Pertinent Medical Findings

<u>General</u>: a tall man with a large build, in distress, complaining of pain and hunger. Unkempt, with a large periorbital laceration. Appears stated age.

Psychomotor: agitated.

Eye Contact: poor.

<u>Mood:</u> labile. Often veering between anger and panic. Angry that he is unable to eat and unable to leave his bed. Panicked that he will die if he does not leave the hospital.

Affect: variable

<u>Speech:</u> normal volume, rate slightly fast.

Thought Process: tangential with loose association.

Thought Content: paranoid and delusional with persecutory and grandiose elements.

Perception: command auditory hallucinations.

Attention: alert and attentive

<u>Orientation</u>: unable to assess due to tangential speech.

Insight: no insight into his illness.

Judgment: no capacity to assess extent of his injuries or to recognize behavioral norms in the hospital.

Lab Test	Result
INR	1.2
Protime	14.8
TSH	0.652
Free T4	1.30
UTox	Positive only for opiates, which MT received in the ED
HIV	NR

Alcohol	None detected
AST	22
ALT	20
ALKPHOS	49
TBILI	0.8

EKG: normal sinus rhythm with normal axis, regular rate, and regular intervals. Tall T waves in V2-V5 have rounded tops, broad bases, and asymmetric ascent, all suggestive of normal repolarization variant. Qtc 437 ms.

Summary of Salient History and Abnormalities

MT is a 28 year-old male with a history of excessive alcohol use who presents with multiple traumatic injuries after he obeyed a command auditory hallucination ordering him to dive into his family's empty swimming pool. Although this is MT's first presentation to our service, and, according to his parents, his first encounter with psychiatric care, there appears to be a pattern of psychologic decompensation over the past several months, with worsening delusions and increasingly troubling behavior. MT has a history of excessive substance use involving marijuana, alcohol, and methamphetamine, and he himself associates methamphetamine use with the onset of changes in his personality. According to his parents, MT was high-functioning about 3-4 years ago, living in Coffeyville, Kansas at that time and engaged to be married to a woman named Helen. Helen, like MT, was from a deeply religious family. With her he had an infant child, Kali Joy Grace. MT had difficulty finding work in Kansas, and he returned for a period of time to Fresno. While back in Fresno, he received a call from Helen stating that Kali was unresponsive. MT attempted to walk Helen through CPR over the phone, but Kali did not survive. MT's father feels that MT never recovered from the loss of his child, that he did not grieve properly and instead began drinking more heavily. The engagement was dissolved thereafter. MT subsequently increased his alcohol intake, lost interest in school, and was able to work only at odd jobs. He was recently laid off. In February, the family observed for the first time that MT was perhaps hallucinating, when the father received a call from MT stating that there was an intruder in the house (there apparently was not). In May, MT presented to the ED after he was found down, intoxicated. He claimed that he had been struck by a car rounding the corner, but he explained during his July hospitalization that he had sought to end his life in May by walking into traffic. The day before the current hospital admission (6/30), the patient's mother found him beating and kicking down a wall in the house and then noticed that a mattress had been set on fire. The patient ran out of the house and was not seen until the next day, the day on which he dove into the empty pool. On presentation, MT was floridly psychotic, with grandiose and persecutory delusions, and showed no insight into his illness.

Differential Diagnosis

<u>Medical Issues</u>: lumbar transverse process fractures, laceration of face (left forehead), bilateral superior pubic rami fractures, avulsion fracture of the right talo-fibular ligament, alcohol withdrawal.

Psychiatric differential:

• Schizophrenia spectrum disorders (schizophrenia, schizoaffective, schizophreniform)

- Bipolar mania with psychosis
- Alcohol withdrawal
- Major depressive disorder with psychotic features
- Substance-induced psychotic disorder (e.g. methamphetamine, PCP)
- Post-traumatic stress disorder
- Delirium
- Psychosis secondary to a medical condition (i.e. other metabolic, toxic, infectious, or autoimmune encephalopathy with psychosis)

MT's CT Head was negative for any focal finding. Alcohol withdrawal was likely a contributing factor in his presentation. He did not endorse depressed mood. Neither the limited history that he could provide nor the more extensive history provided by his family was suggestive of mood cycling or of any cyclic quality to his illness. Above all, his history, especially the history provided by his parents, indicated a process of gradual but relentless psychologic decompensation over months and possibly years, suggestive of a neurodegenerative disease and pointing toward schizophrenia. We felt that a schizophrenia spectrum disorder was likely but could only be diagnosed after extended observation.

Working Diagnosis

Schizophrenia spectrum disorder

Formulation

<u>Biological:</u> schizophrenia is a highly heritable neurodegenerative disease with an erratic course. It classically presents in adolescence or early adulthood. Although erratic, with some patients recovering to very near their prior baseline function after initial psychotic episodes, its natural history is usually one of decline. GWAS have uncovered a large number of genes associated with schizophrenia, but none is very strongly linked, leading to the conclusion that a complex interaction between genetic susceptibility and environment is required to induce disease. Recently, there has been interest in retrospective studies of perinatal and childhood illnesses and their linkage to schizophrenia, under the assumption that a pathogenic interaction between genes and environment leads to initiation of low-level disease very early life followed by acute exacerbation due to further stresses in the classic onset period. Perinatal and early childhood risk factors that may be linked to schizophrenia include infections, nutritional deficiencies, and obstetric complications. It is difficult to elucidate the role of these possible risk factors with only retrospective epidemiological analysis, but they appear to be linked even after conducting studies by chart review instead of interview (to control for recall bias). It is unclear whether MT suffered injuries in early childhood that increased his risk of developing schizophrenia.

Of possibly greater significance to the development of schizophrenia in MT is his heavy use of cannabis and methamphetamine. These drugs have been linked not only to acute psychosis but to the onset of schizophrenia.

Although MT's parents report no known family history of schizophrenia, many of MT's aunts and uncles are not in touch with his family. MT's parents report that multiple family members suffer from

substance abuse. Susceptibility to substance abuse is heritable, involving physiologic properties of the brain's reward system and physiologic predisposition to compulsivity.

<u>Psychological:</u> the pathways by which psychologic stress lead to acute mental illness require further elucidation, but it has long been evident that psychologic stress leads to physiologic changes, including increased glucocorticoid release, with myriad downstream effects on gene transcription. Glucocorticoids are known to be neurotoxic in excess, with toxic effects particularly evident in hippocampal tissue. The event that stands out in the life of MT as a particularly acute stressor is the death of his daughter, and the psychologic suffering induced by this event was compounded by his inability to grieve in a mature and healthy way. His stress also caused him to increase his use of drugs that in turn predispose to psychosis.

<u>Social:</u> social factors linked to schizophrenia include urbanicity, minority/migrant status, and childhood developmental trauma, such as bullying, family conflict, or abuse. MT comes from an ethnic minority family. It appears that his childhood was free of abuse, but his social environment provided him with ubiquitous access to drugs, including methamphetamine and marijuana.

Biologic Management Plan

MT was considered likely to be withdrawing from alcohol in addition to suffering from a primary psychosis, so he was initially treated with thiamine and folate. Chronic alcoholism is common, and the rate of thiamine deficiency in chronic alcoholism approaches 80% (*Markowitz, 2000*). In addition, the rate of anaphylaxis in thiamine supplementation is a handful out of a million, and the consequences of a prolonged thiamine deficient state are grave and irreversible. Thus thiamine supplementation is routinely indicated for any person presenting to the ED with altered mental status.

Soon after his hospitalization, MT became sufficiently agitated that restraints were necessary. We assessed him as unsafe and likely to injure himself by getting out of bed. He was therefore placed in restraints emergently. As soon as possible, we replaced his physical restraints with pharmacologic restraints (haloperidol 2 mg/lorazepam 1 mg/benadryl 25-50 mg q8 hrs PRN). Concomitant with emergent administration of haloperidol, an EKG was obtained to confirm that his QTc was in the safe range (< 470 ms and < 60 ms above baseline).

MT was continued on CIWA protocol for alcohol withdrawal over several days while we observed him. We obtained urine toxicology, blood alcohol, liver function, thyroid function, and HIV tests to rule out substance-induced psychotic disorder, hepatic encephalopathy, thyrotoxicosis or hypothyroidism, and HIV dementia. All of these tests were negative/normal.

MT was initially treated with a low dose of risperidone, 1 mg PO BID, and the progression of his psychosis was observed over time. His psychosis did not respond to increasing doses of risperidone. It has also not responded to olanzapine. He is now being started on clozapine.

Choice of Initial Medication

A rule of thumb is that one attempts to treat the patient's psychosis with at least two anti-psychotics before a clozaril trial, due to the risk of agranulocytosis with clozaril. Clozaril is the most effective anti-psychotic, but it also, along with olanzapine, causes the most weight gain and metabolic derangements. The side effect profile should be taken into account to determine which medication is best for a particular patient. A further disadvantage of clozaril is that it is not available as a depot medication.

Risperidone has advantages as a starting medication. It is not among the anti-psychotics with the greatest effect on the QTc interval. In addition, as a second-generation anti-psychotic, it has fewer EPS effects than first-generation anti-psychotics. Finally, of the second-generation drugs, the metabolic effects of risperidone are the least.

An EKG should be obtained first if prescribing one of the anti-psychotics that prolongs the QT interval: clozapine, thioridazine, iloperidone, ziprasidone. The QTc should be < 460-470. (*Leucht, 2011*)

Sedation Strategies

Combinations of haloperidol and an antihistamine, or haloperidol and lorazepam, have been found to be more effective than haloperidol alone. Diphenhydramine is preferred among the antihistamines because it a well-established drug with anticholinergic properties that help prevent EPS.

On a medical ward IV access is available, it is straightforward to opt for parenteral administration. In settings where one does not have IV access, enteral administration or intramuscular injection are reasonable options. There are rapidly-dissolving tablets and liquid formulations of some anti-psychotics. *(Leucht, 2011)*

Assessment of Negative Symptoms of Schizophrenia

EPS may be incorrectly interpreted as negative symptoms. Rule out EPS by doing a trial of an anti-Parkinsonian med, or by changing the AP to one with few EPS symptoms. (*Leucht, 2011*)

Assessing Non-Response to Anti-Psychotic Medication

Delusions may remain even after the hyperdopaminergic mesolimbic state has been partially corrected. The goals of anti-psychotic therapy are therefore modest: coping with delusions and avoiding hallucinations – especially command hallucinations – so that the patient is as safe as possible. If the patient is not yet safe, consider increasing the dose of the anti-psychotic that the patient is on. A rule of thumb is to wait two weeks to assess response. It is also important to reassess the diagnosis, since the patient could be bipolar.

CYP or other metabolic interactions that decrease drug availability should be taken into account.

Medication adherence should be taken into account. Measuring serum levels can be useful in some of these situations. Depot formulations (long-acting injectables) are available, although not for clozapine, given its risks of agranulocytosis.

To change therapy, cross-titrate. It is important to plan for cholinergic rebound with some drugs, so titrating down instead of stopping is essential. Withdrawal-emergent movement disorders also reported with clozapine. (*Leucht, 2011*)

Adjunctive therapy

There is no convincing evidence thus far for adding other drug classes (mood stabilizers, sedativehypnotics, AEDs, beta blockers) in a patient with a diagnosis of schizophrenia. (*Leucht, 2011*)

Psychologic Management Plan

Cognitive behavioral therapy is indicated for patients with persistent delusions or hallucinations. In CBT, a supportive environment is combined with emphasis on building cognitive skills to permit patients to distinguish reality from psychosis and to ignore unwanted intrusive thoughts.

To emphasize reality, the CBT therapist will directly challenge delusions and help the patient develop alternative explanation involving recognition of the fact that he or she is mentally ill. Since CBT involves challenging the patient's deeply-held psychotic beliefs, it is inappropriate at the initial presentation, when gaining rapport is the first priority. *(Kingdon, 2002.)*

Meta-analyses have demonstrated that CBT is effective as compared to placebo, and is stronger in managing delusions as opposed to hallucinations. (Wykes, 2008)

Social Management Plan

The effect of the patient's home emotional environment and family dynamic on schizophrenia relapse has been studied using the construct of Expressed Emotion. Using a standardized interviewing tool (the Camberwell Family Interview), relatives who live with the patient are interviewed, and the number of critical or hostile comments they make are scored. Higher critical expressed emotion is associated with higher rates of relapse.

This finding has been replicated and established with a very thorough meta-analysis, and it has also been extended to other mood disorders. The share of relapse causality due to expressed emotion appears to be about 1/3rd. The expressed emotion score is a stronger predictor of relapse in more longstanding illness. (*Butzlaff, 1998*)

Goals of family psychoeducation include the following:

- Emphasize to the family that schizophrenia has genetic, perinatal, and environmental risk factors.
- Educate families on the stress-diathesis model: set family expectations so that family members do not place undue stress on the patient (e.g. avoid "you are doing better, so why not get a job").
- Understand that asociality and avolition are elements of the disease process, not laziness.
- Promote medication adherence.
- Prevent the onset of therapeutic nihilism.
- Educate regarding the importance of avoiding substance abuse. (Schooler, 1997))

Literature Review

Schizophrenia is a syndrome that may in fact represent multiple diseases. It is marked by three coinciding symptom clusters. The so-called "positive" symptoms include hallucinations, delusions (often of a persecutory or paranoid nature), and disorganization of speech (tangential or circumstantial speech, derailed speech, neologisms, or word salad). The so-called "negative" symptoms include decreased affect and an avolitional state. Schizophrenia patients also exhibit global cognitive and social impairment. In addition, there are "soft signs" for schizophrenia that tend not to be used for diagnosis but point toward the fact that the disease is not limited cognitive and limbic deficits, but also involves sensory and motor functions, albeit subtle: agraphesthesia (inability to identify letters traced on skin) and astereognosia (inability to identify object by touch) are often present. Right/left confusion may also be apparent.

Early in the development of modern psychiatry, Kraeplin recognized that schizophrenia is distinguished from mood disorders with psychotic symptoms by its declining course. The initial presentation is often marked by florid psychosis and productive symptoms, followed by progressive cognitive impairment, predominance of negative symptoms, and eventually advanced dementia. Although some patients diagnosed with schizophrenia appear to recover much of their prior function and are spared this natural history of decline, today we perceive schizophrenia as a neurodegenerative disease. Even those patients who seem to recover, as judged by dissipation of positive or negative symptoms, often remain cognitively impaired on neuropsychological testing (*Heaton, 2001*). On MRI, the brains of schizophrenic patients tend to show marked atrophy in the specific areas of the frontal and prefrontal cortex, parietal lobe, and temporal lobe (*Bonilha, 2008*). Areas of atrophy are correlated with different symptom clusters: reduced volume in frontal parietal and temporal regions is linked to delusion, whereas reduced volume of the prefrontal cortex is linked to negative symptoms. (*Bonilha, 2008*)

Schizophrenia is unusual among the neurodegenerative diseases in that it is devastatingly common and strikes in early adulthood, instead of old age. Although many neurodegenerative diseases are poorly understood, schizophrenia is even less well-characterized than most others. There is no definitive histopathologic property of the brain with schizophrenia. The cellular pathways involved in its pathogenesis remain almost entirely obscure.

The so-called dopamine hypothesis – that the symptoms of schizophrenia arise from excess dopamine in the mesolimbic tract – arose straightforwardly from the observation that early anti-psychotic drugs were potent D2 receptor antagonists. However, potency of D2 receptor antagonism does not correlate perfectly with anti-psychotic drug efficacy. More importantly, an imbalance of neurotransmitters is an incomplete explanation for a disease with a degenerative course.

In the past few decades, a renewed focus on the neurodegenerative aspects of schizophrenia has led to the idea of schizophrenia as a disease of inadequate neurotrophic support. Considering the erratic course of the schizophrenia, as well as the fact that its typical onset in adolescence or early adulthood coincides with a time of cortical remodeling, investigators have speculated that schizophrenia is marked by an exacerbated imbalance between normal processes of neuronal disconnection and degeneration on the one hand, and neuronal growth and plasticity on the other. Seen this way, schizophrenia is a

disease of unbalanced neurotrophic support in certain areas of the brain. The neurotransmitter imbalances observed in schizophrenia may simply be the downstream consequences of imbalances in neural connections. While neuroleptic drug development has traditionally focused on blockage or promotion of specific neurotransmitter activity, this focus may be misplaced. The degree to which a drug can slow or retard the course of neurodegeneration, or modulate neurotrophic activity, may be the more fundamental concern.

Neurotrophins determine the global balance of neurotransmitters by altering the architecture and pattern of neural differentiation. Recently there has been significant interest in the role of brain-derived neurotrophic factor (BDNF) in the pathogenesis of mood and psychotic symptoms across multiple mental illnesses. BDNF is a mediator of neuronal survival and plasticity for dopaminergic, cholinergic, and serotonergic neurons in the CNS. The critical role of BDNF as a survival-promoting neurotrophin has been established for hippocampal ad cortical neurons, cholinergic neurons, nigral dopaminergic, and 5-HT neurons using mouse knockout models to show the effects of deficiency and then exogenous supplementation. One hypothesis is that BDNF deficiency leads to a fragile neurocytoarchitecture and reduced capacity for plasticity in adults in specific regions of the brain. Antidepressants and antipsychotics restore normal plasticity, growth capability, and survival signaling by normalizing levels of BDNF. BDNF is a secreted protein with autocrine and paracrine functions. It has recently emerged, however, that BDNF may undergo anterograde and retrograde transport, and so may act at the synapse, possibly in a signal-graded fashion. (*Angelucci, 2005*)

Substance use – and particularly methamphetamine and cannabis – is linked to the development of schizophrenia. Cannabis is associated with the development of schizophrenia in patients with a single amino acid substitution polymorphism of the COMT allele. (*Avshalom, 2006*) Amphetamine increases striatal DA transmission in schizophrenia, triggering psychotic symptoms as compared to controls. It is evident, therefore, how amphetamine makes disease more florid acutely through dopaminergic effects. A mechanism by which repeated exposure to methamphetamine leads to chronic disease remains to be elucidated.

Like most diseases, schizophrenia is characterized by missing heritability, indicating that environment plays a crucial role in activating the cellular program leading to pathology. Retrospective studies have established a long list of environmental phenomena that may contribute to the risk of developing schizophrenia. Many of these environmental influences have not yet been studied prospectively, or cannot be easily analogized to animal models in the way that neurotrophic and neurotransmitter hypothesis can. Factors implicated in schizophrenia include childhood and perinatal infections, nutritional deficiencies, and obstetric complications, such as hypoxic brain damage. Social factors linked to schizophrenia include living in an urban environment, minority/migrant status, and childhood developmental trauma.

As the field moves closer toward reconceptualizing schizophrenia as a neurodegenerative disorders, it is important to remember that psychosocial factors directly influence the physiology of the brain and may contribute to neurologic fragility. Some of the social factors thought to be linked to schizophrenia – including urbanicity, minority/migrant status, and childhood developmental trauma – are thought to act

by causing stress through the mechanism of "social defeat", wherein a person eventually comes to understand himself or herself as alienated and as a social outsider. Acute emotional stress, as well as chronic social and psychologic factors, probably influence pathogenesis by activating the body's physiologic stress response. (Schooler, 1997)

The schizophrenia phenotype may in fact be several different but related phenotypes with different underlying etiologies. Investigators are now working not with cohorts of schizophrenic patients but instead with cohorts that are strictly defined around a specific "endophenotype", i.e. a particular mental phenomenon among the many that characterize schizophrenia. For example, the sensory and motor deficits found in many schizophrenic patients could be a considered an endophenotype; paranoid psychosis could be considered an endophenotype. As more research is done, the hope is that endophenotypes will turn out to be more tightly correlated than a schizophrenia diagnosis with some of the biopsychosocial risk factors already identified. If so, these correlations will enhance our understanding of the disease, possibly leading to a new, more pathophysiologically-guided delineation of the schizophreniform disorders in the next DSM.

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Example 2.

HPI

C.O. is a 34 year-old homeless Caucasian male admitted for traumatic injuries sustained in a bicycle vs. motor vehicle accident. His injuries included R basilar skull fracture, L occipital fracture, bilateral frontal subarachnoid hemorrhage (R>L) and a small tentorial subarachnoid hematoma. In addition, he had a lacerated spleen, pneumothorax, upper and lower proximal extremity fractures and presented with altered mental status. At admission, he screened positive for EtOH, methamphetamines, benzodiazepines and marijuana.

Psychiatry was consulted 4 weeks into his hospital course to evaluate the patient's agitation, impulsivity and refusal to cooperate with staff. The patient demonstrated aggression, impulsivity, hyperorality, and perseveration on food, his restraints, and voiding. The primary team had initiated Ativan PRN and Seroquel 100 mg BD prior to consulting us. We added Depakote starting at 250 mg BID and recommended a Neurology consult to evaluate the patient's neurocognitive function. Neurology found impairments on tests of frontal cortex function.

The patient's agitation continued, accompanied by numerous complaints from the staff. We titrated up Depakote (to 750 mg BID) and Seroquel (to 150 mg BID) with the aim of reducing PRN Ativan use, which we were worried might be exacerbating his agitation. However, at 6 weeks into the patient's hospital stay, the primary team initiated scheduled Ativan and Haldol with the goal of discontinuing physical restraints to facilitate placement of the patient at a skilled nursing facility. Restraints were removed but the patient continued to have frequent falls and injuries and, at week 7, began to refuse medications. In anticipation of placement in a SNF with rehab, we recommended replacing the frequent Ativan with scheduled Klonapin (2mg Q8hrs) and discontinuing scheduled Haldol. The patient agreed with the plan and was transferred to CSTCC.

Life Chart

Milestones/Events	Year/Age	Pathology/Contact with Healthcare System/Medications
Patient born in Mariposa and raised by mother – biological father unknown/uninvolved	1979 birth	Possible perinatal exposure to cocaine and other substances
Half-sister born	1982 3 yo	

Patient lives with mother, stepfather and half-sister in Mariposa. Patient's mother is a "crack-addict". Describes this time as "freedom" since his mother never paid attention to what he was doing. Sometimes he "despised her" because she would use their rent money to buy drugs and the "showers were always cold".	1981-1993 2-14 yo	
Patient beat up by a "street gang". Refers to this as a	1990	Identification with the aggressor

formative experience in which he learned "strength is in numbers".	11 yo	
Patient leaves to live with Grandmother in "the	1993 14 yo	
mountains" because stepfather favored his half-sister		
over him: "She got the world and I got nothing".		
Living with his grandmother: "too much rope and I hung	1993-1995	Conduct disorder?
myself with it". He and his friends would break into empty	14-16 yo	First reported alcohol use
vacation homes to spend the night and drink their liquor. He states that his friends would steal from the houses		
but that he "was just there to party".		
Caught breaking in to a house and spent 40 days in a	1995 16 yo	
juvenile detention facility with 4 other boys	1995 16 yu	
Formed the MK3 (Mariposa Klu Klux Klan) with other	1995-1997	Conduct disorder?
boys from his high school. They talked about how much	16-18 yo	Antisocial personality disorder?
they hated "niggers" but never attacked anyone outside	10 10 yo	
the group. Instead, they "made zip guns and beat the		
crap out of each other".		
Finish high school and became involved with the mother	1997 18 yo	Escalating alcohol use along with first
of his two children. She "was a drinker" and that they	,	reported drug use
would drink heavily together with occasional drug use.		
Episode of methamphetamine-induced psychosis. Believed that every car was after him and assigned significance to the color of each car.	1998 19 yo	Treated at Fresno Rehabilitation Center (now Quest House). Treated with Depakote and Elavil. Reports that they also tried Haldol but "it made him all crazy". States "they believed I was bipolar" because of his family history and because of reports from his probation officer. His theory is that the probation officer thought he was bipolar because he was constantly coming on and off drugs and his moods would vary accordingly.
On a visit home, sister told him that his best friend had		Impairment of inhibition. Antisocial
been stealing from them. He "just got really angry and		personality disorder? Intermittent
lost control", severely beating his friend. Convicted of		explosive disorder?
assault and spent 2 years in prison. It was a "new		
situation" so he "kept his head down and made his way		
through". (His son was 5 months old at the time)		

After being released, he returned to Mariposa and to be near his ex and their children. Her boyfriend reportedly became jealous and told the patient to stay away from the children. Once again, the patient became violently angry and attacked the boyfriend, resulting in a second 3-year incarceration for assault. This time, it was "a different yard". The inmate situation was chaotic and he was invited by the "big boys" to join them in creating a new hierarchy. He says that he "held the keys" and would target sexual predators and inmates who had committed crimes against children for beatings by "his crew" but states that he never participated in the beatings himself.	2006-2009 27-30 yo	Impairment of inhibition. Antisocial personality disorder? Intermittent explosive disorder?
Began parole in Madera. Stayed at the Mission for a while but "left because of the bedbugs" and lived in a tent by the river where he "had a girl".	2009 30 уо	
Transfer to Fresno for his final year of parole. Started taking accounting classes at Fresno Community College along with his aunt Susan.	2011 32 уо	
Alternated between living with his grandmother (now in	2011-2013	Escalating substance use

F		
Fresno but remarried and her new husband didn't like having the patient around), homelessness and short stays with friends. Reports heavy drinking (~1 pint liquor / day + beer) and escalating drug use during this time.	32-34 уо	
Period of several weeks where he "felt exuberant, above normal" and describes heavy alcohol/drug use and numerous sexual encounters with his girlfriend in public places, including at school. Continued to perform well in classes, receiving "straight A's".	2011 32 уо	Hypomanic / Manic episode?
Rehab (required/suggested by parole officer?)		28-day program at Quest House. "There were more drugs here than on the street".
Second episode lasting several weeks during which he "felt like a king" and "had a whole harem" of sexual partners, both male and female. Continued to perform well academically.	2013 34 уо	Hypomanic / Manic episode?
Visit to psychiatrist to obtain benzodiazepines.	2013 34 уо	Diagnosed with an anxiety disorder and prescribed benzodiazepines. However, the patient states that he tailored his answers to convince the doctor that he needed benzos because he thought they would help him stop drinking.
Bicycle vs. MV	2013 34 yo	Admitted to CRMC. Seen by us. Transferred to CSTCC.

Mental Status and Neurocognitive testing/Pertinent Medical Findings

Mental Status Exam at 1st encounter Appearance/Behavior: Lying in bed in hospital clothing and 4

point restraints. Normal body build. Appears stated age. Alert and attentive but frequently distracted by perseveration on needs. Oriented to name, place, situation and date. Psychomotor: Agitated, pulling at restraints and repeatedly requesting their removal. Repeatedly kicks sheet aside and then urgently requests to be covered. Intermittent eye contact. Intermittently cooperative but repeatedly requested food and then refused to continue with interview until food was provided. Mood/Affect: Anxious with appropriate affect. Speech: Loud whisper, normal rate with frequently interrupted rhythm Thought Process: Coherent with normal association but frequent interruption to ask about food and removal of restraints. Thought Content: No delusional content expressed. Marked perseveration on hunger, food and restraints Perception: denies auditory or visual hallucinations. Memory impairment: recall of 2/3 objects at 5 minutes Social judgment: intact. Insight: cannot remember accident, does not understand why he is currently in restraints but has some awareness of prior mental illness.

<u>Imaging</u> Neurology's read of the initial head CT 6/7/2013 showed bilateral frontal subarachnoid hemorrhage R>L and subarachnoid hemorrhage at the tentorial margins (interpreted by radiology as a possible subdural hematoma).

Subsequent imaging showed underlying hemorrhagic traumatic injury in the right frontal lobe.

Neurology's read of the most recent CT (6/13/2013) showed a large hypoattenuating defect in the R frontal lobe with midline shift and possibly some areas of injury in the R temporal lobe. Sulci in the L frontal cortex are possibly more prominent than would be expected for the patient's age.

Assessment of Frontal Executive Function

C.O. was able to copy alternating figures with no difficulty. He completed the MOCA trails test with two mistakes, which he self identified and returned to correct. He was able to perform the alternating hand movement tasks but, when asked to tap hand only when hearing the letter A in a string of letters, he was unable to suppress tapping with his fist for other letters. He did however differentiate between a fist tap for other letters and an open palm tap for the letter A with only 3 mistakes. On the Stroop test, he had marked difficulty on the second phase but then insisted on naming the colors in Spanish and was able to progress through quickly.

<u>Mental Status Exam on day of discharge</u> Appearance/Behavior: Standing beside bed in hospital clothing, leaning on walker for support. Clean shaven. Oriented to name, place, situation and date.

Attention: Able to spell Fresno backwards, digit recall intact to 8 but grouped digits (ex - 5 7 9 2 3 became fifty-seven ninety-two three) Memory: 3/3 objects recalled at 5 min. Psychomotor: Calm but with frequent shifts in position to relieve back pain. Good eye contact. Cooperative but mildly antagonistic ("I hate being asked questions early in the morning. They wake me up to poke at me every hour. It's asinine. Asin*seven*, asin*eight*, asi*nine*.") Mood/Affect: Annoyed with appropriate affect. Speech: Normal volume, normal rate, normal rhythm Thought Process: Coherent with normal association Thought Content: No delusional content expressed. Perception: Denies auditory or visual hallucinations. Social judgment: intact. Insight: Understands the impact that substance use has had on his life and plans to remain sober after discharge. However, believes that he has already achieved this goal and is "looking forward to finding other people who haven't figured it out yet at this place I am going to and forcing them to see how it's done." He dismisses the possible contribution of mental illness to his life prior to the accident and does not incorporate his new attentional deficits into his immediate plans for the future (he is planning to sign up for a full course load this fall).

Summary of Salient History and Abnormalities

C.O. is a 34 year-old homeless Caucasian male admitted for traumatic injuries sustained in a bicycle vs. motor vehicle accident. He has a family history of substance use and bipolar disorder. Beginning in adolescence, he describes heavy drinking with occasional marijuana and methamphetamine use. He reports numerous incidents of violence perpetuated both against and by him throughout adolescence and into adulthood. He describes two episodes of elevated mood accompanied by high-risk behaviors but states that he continued to perform well academically during these times.

Escalating substance use culminated in the accident in which he sustained a R basilar skull fracture, L occipital fracture, bilateral frontal subarachnoid hemorrhage (R>L) and a small tentorial subarachnoid hematoma. CT and MRI showed large regions of pathology in the R frontal lobe and smaller regions of injury in the L frontal lobe. During his recovery, he began to exhibit dangerous impulsivity, perseveration and poor planning skills. Neurocognitive testing showed corresponding deficits in frontal executive functioning. However, he was able to quickly identify strategies that allowed him to partially compensate for these deficits. C.O.'s attention and organizational skills improved dramatically over the course of his hospitalization, but were still significantly impaired at the time of discharge. He had good insight into his condition at times but often forgot his psychiatric

and neurocognitive impairments in his excitement about the future.

Differential Diagnoses

(organized chronologically by first reported incidence)

Substance Use Disorder

Rule in

A maladaptive pattern of substance use leading to clinically significant impairment or distress, as

manifested by one (or more) of the

following, occurring within a 12-month period:

- 1. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home
- 2. Recurrent substance use in situations in which it is physically hazardous
- 3. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance Tolerance: A need for markedly increased amounts of the substance to achieve intoxication or desired effect Withdrawal: The substance is often taken in larger amounts or over a longer period than was intended, There is a persistent desire or unsuccessful efforts to cut down or control substance use, A great deal of time is spent in activities necessary to obtain the substance, use the substance, or recover from its effects

Rule out: None

Conduct Disorder

A prolonged pattern of antisocial behavior such as serious violation of laws and social norms and rules.

Rule Out: Many teens with substance use disorder display traits of conduct disorder that resolve when the substance use disorder is treated.¹

Characterization: Adolescent vs. Childhood onset. Adolescent onset is associated with better outcomes and less lifetime impairment.² From the obtained history, C.O.'s conduct problems

began at age 14 but it would be helpful to have a more detailed early school history in order to be able to rule out childhood onset.

Antisocial Personality Disorder

Rule in:

There is a pervasive pattern of disregard for and violation of the rights of others occurring since age

15 years, as indicated by the following:

- 1. failure to conform to social norms with respect to lawful behaviors as indicated by repeatedly performing acts that are grounds for arrest;
- 2. impulsivity or failure to plan ahead;
- 3. irritability and aggressiveness, as indicated by repeated physical fights or assaults;
- 4. reckless disregard for safety of self or others;
- 5. consistent irresponsibility, as indicated by repeated failure to sustain consistent work behavior or honor financial obligations;
- 6. *lack of remorse, as indicated by being indifferent to or rationalizing having hurt, mistreated, or stolen from another.* (When asked whether he was sorry about the 2 assaults that resulted in imprisonment, he said "Not really, it was meant to be. But actually, yes, because now I am at risk for a 3rd strike." When further questioned, he said he was "a little sorry for beating up the first guy because he was smaller than me but not for beating up the second because he was bigger.")

The individual is at least age 18 years. There is evidence of conduct disorder with onset before age 15 years.

Rule out: The occurrence of antisocial behavior is not exclusively during the course of

schizophrenia or a manic episode. The patient's history is supportive of episodes of hypomania.

Without further history, it is impossible to rule out the possibility of true manic episodes that may

have been coincident with greatest disinhibition.

Intermittent Explosive Disorder Rule in:

1. several episodes of impulsive behavior that result in serious damage to either persons or property

2. the degree of the aggressiveness is grossly disproportionate to the circumstances or

provocation Rule out:

3. *the episodic violence cannot be better accounted for by another mental or physical medical condition.* Other mental disorders that may cause violent outbursts (ex -antisocial personality disorder) must first be ruled out.

Bipolar Disorder

Rule in:

- Euphoria and/or an irritable mood with the following symptoms: Grandiosity Racing thoughts Overactivity, especially in goal-directed areas Excessive participation in risky behaviors, such as hypersexuality
- Rule out: No clear reported evidence of depression. (The patient avoided answering questions about possible depressive episodes but his grandmother reports that she observed periods of what she thought was depression.) If patient's and family's reports of high function during episodes of euphoria are untrue or exaggerated, these may represent episodes of true mania.

Frontal Disinhibition Secondary to Traumatic Brain Injury

- Rule in: Behavioral perseverations despite self-harm, impulsivity, poor-planning and hyperorality Evidence of bilateral frontal lobe injury on CT and MRI Poor performance on tests of frontal executive function
- Rule out: Patient demonstrated marked impulsivity and poor decision making prior to injury. Without baseline testing of frontal functioning, it is impossible to determine the relative contributions of chronic vs. acute frontal dysfunction on neurocognitive testing.

Other Diagnoses to consider: Intrauterine Substance Exposure

- Early Head Trauma Rule in: multiple beatings sustained as a child and adolescent Rule out: no report of hospitalizations or persistent deficits following beatings, no clear evidence of prior injury on CT (MRI would be more sensitive than CT for this purpose but was not obtained)
- Oppositional Defiance Disorder Rule out: obtained history shows aggression directed towards peers rather than towards authority figures, supporting Conduct Disorder over ODD. Bipolar I Disorder Rule in: if patient's and family's reports of high function during episodes of euphoria are untrue or exaggerated, these may represent episodes of true mania. Rule out: obtained history supports episodes of hypomania over mania.

Anxiety Disorder Rule in: prior diagnosis Rule out: patient reports manipulating encounter to obtain benzodiazepines

Post-Traumatic Stress Disorder Rule in: The patient describes several beatings and his descriptions of his time in prison includes significant amounts of violence. His grandmother believes that he suffers from PTSD related to his prison experiences. Rule out: He denies nightmares/flashbacks/avoidance and describes the above incidents as positive experiences.

Working Diagnosis

Adolescent conduct disorder with resultant

Antisocial personality disorder and

Bipolar II disorder complicated by overlying

Substance use and

Acute frontal cortex dysfunction secondary to traumatic brain injury

Pervasive substance use makes it difficult to definitively establish a diagnosis but the history is strongly suggestive of both conduct disorder and subsequent antisocial personality disorder.

Based upon the obtained history, the patient has experienced at least two periods of hypomania. If, however, the reports of good academic performance during these episodes are exaggerated, it is possible that these were instead episodes of true mania, pointing towards a Bipolar I diagnosis instead.

Formulation

Biological

Based upon his family history, C.O. has a biological predisposition to both bipolar disorder and substance dependence. Interestingly, while bipolar disorder and schizophrenia share several susceptibility alleles, genomic structural variation is thought to play a smaller role in the predisposition to bipolar disorder.³

Given his mother's substance use history, it is likely that C.O. was exposed to crack cocaine and other drugs both pre- and postnatally. While several recent studies looking intrauterine cocaine exposure in various developmental outcomes have found minimal effect once socioeconomic status has been controlled for, a recent systematic review showed an increase in behavioral problems and adolescent illicit substance use, albeit with small effect sizes.^{4,5}

In addition to perinatal exposures, C.O.'s own long-term substance use is likely to have altered the gene expression profile and chemistry of his brain, resulting in altered behavioral patterns. For example, chronic methamphetamine use is associated with disinhibition and executive dysfunction, independent of mood disorders and other substance use.⁶

Psychological

C.O.'s history is notable for recurrent abandonment. His mother chose drug use over her family and subsequently died while he was in prision. His step-father overtly favored his sister over him. His ex left the area and took their children with her. His grandmother, who took him in as a teenager, is now unable to have him live with her because her new husband is not willing to tolerate C.O.'s aggressive behaviors. His aunt is financially unable to have him come live with her after discharge. C.O. was often tearful and would shut down when discussing these experiences.

A second theme, viewed as a positive one by C.O., is his search for the power he perceived in groups. He cites the beating he received as an 11 year-old as a formative experience in which he learned "strength is in numbers". This *identification with the aggressor* drove him to seek out violent groups that he could assume leadership of, including his "gang" in high school and his prison "crews".

C.O.'s pre-existing constellation of conduct disorder, antisocial personality disorder, hypomanic episodes and pervasive substance use was characterized by impulsivity and poor insight.⁷⁹With his bilateral frontal lobe injuries, he acquired further disinhibition, impaired

attention, and an impaired ability to plan.¹⁰⁻¹⁴

<u>Social</u>

As discussed above, C.O. sought out groups of his peers throughout his life "I have no enemies, only friends", possibly trying to re-assemble the family he lost. Despite his maladaptive behaviors, he continues to maintain relationships with his grandmother and aunt, both of whom visited him in the hospital and asked to be involved in discharge planning. His children spend summers with his grandmother in Fresno and he regained contact with them during this hospitalization. They came to visit him the week he was discharged and he spent the days before anxiously asking the nursing staff to assist him with showering, shaving and ambulating so that he could sit with them in the visitors' lounge.

Management Plan

Summary of discharge recommendations:

. Though much improved, patient continues to demonstrate poor planning and impulsivity with impaired attention and requires intensive PT/OT in a supervised environment.

Continue Depakote 750 mg BID, Seroquel 150 mg BID and Klonapin 2mg Q8hrs

. Facilitate a long-term psychotherapy relationship for medication management and to provide CBT addressing frontal lobe dysfunction secondary to TBI in addition to pre-existing psychiatric disinhibition

. Facilitate the patient's interest in drug/alcohol acute rehab Facilitate patient's interest in finding an AA/NA program to participate in long-term Facilitate patient's interest in finding housing and employment resources <u>Biological</u>

Treatment Plan

We can't change C.O.'s genetic predispositions or perinatal exposures, but we can help him to halt the damage caused by his escalating substance use. He has repeatedly expressed a desire to stop drinking, which he believes is the gateway to his other substance use. We recommended a short inpatient rehab program followed by connection of the patient to long-term support groups such as Alcoholics Anonymous and Narcotics Anonymous.

Psychological Treatment Plan

A study looking at the incidence of impulsivity in the general population found that, even after controlling for comorbid psychiatric disorders, impulsivity was associated with a 2-3 fold increased risk of difficulty controlling anger, problems with gambling and excessive spending,

trouble paying attention to details, lack of planning, starting fights, shoplifting, and suicide attempts.¹⁵We recommended long-term treatment of his impulsivity with mood stabilizers. He tolerated moderate dosages of Seroquel and Depakote well while in the hospital and stated that he was willing to take them after discharge. Given that he sought out benzodiazepines prior to his accident, they may not be the best choice for long-term pharmacotherapy but, in the short-term, we recommended continuing scheduled Klonapin as an adjunct therapy to help control his agitation to a level where he is capable of participating in his own physical rehabilitation at CSTCC.

Another shared characteristic of his pre and post-injury presentations is a marked lack of insight. TBI Patients with low self-awareness are more likely to exhibit disinhibition, interpersonal problems, and more difficulties in total competency.¹⁶ C.O. demonstrated understanding of his deficits at each in-depth discussion but was unable to hold on to these ideas from one day to the next. We recommended establishment of a long-term therapeutic relationship to guide his recovery after discharge.

On neurocognitive testing, C.O. had already begun to demonstrate conscious compensatory strategies to address his acquired attentional deficits. At a structural level, studies show that there is a global compensatory recruitment of an adaptive fronto-parietal network after localized frontal lobe damage.¹⁷ We suggested cognitive behavioral therapy to address the wide array of maladaptive behaviors exhibited by C.O., with a particular focus on frontal cortex dysfunction.

Social Treatment Plan

C.O.'s desire to be a positive force in his children's lives can be a strong motivating factor for self-driven recovery. He hopes to find a stable housing situation, complete a community-college certificate in Accounting, and find a job. In addition, given his drive to be part of a group and to assume a leadership role within it, organizations such as NA/AA may be the ideal environment to facilitate his long-term recovery and sobriety.

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Example 3.

Example 3.

Identifying Data and Present Illness

63 year old male with a past medical history of COPD, hypertension, type 2 diabetes mellitus, and a reported schizophrenia diagnosis was BIBA when he was found unresponsive. The patient was found unresponsive at his home by his adult foster daughter at around 11 am. EMS found patient with GCS 8 and by the time he arrived at the hospital he had a GCS 7. He did not respond to naloxone and was intubated with an initial GCS 3T. His medication list included Valium, Vicodin, Risperidone, and Zolpidem. His utox revealed benzodiazepines and opiates. Flumazenil was not given due to unknown benzodiazepines dosing history. Patient was transferred to the ICU where he eventually woke up with a GCS 10T. Upon waking, he was able to follow commands and he was subsequently extubated.

Life Chart

Personal History	Year (age)	Psych/Medical History
CHILDHOOD		
Born in Riverside, California.	March 12, 1950 (0)	
Patient describes good parents and one sister.		
In elementary school he said he liked school but that he "wasn't as quick as others," and that he "did the best he could." He had a hard time reading and understanding what he read. He was never held back. He got along well with his friends.		Reading comprehension difficulty.
In high school, he described "off and on" relationships with girls but nothing serious.		

DROPPED OUT OF HIGH SCHOOL		
He "couldn't wait to get out," of high school so		
he dropped out in the 11 th grade.		
FIRST WIFE/BIRTH OF DAUGHTER	1966-1967 (16-17)	
Began working for a fencing company and	1900-1907 (10-17)	
married first wife, M. Around this time he also		
worked for a moving van company, doing factory work with forklifts and boxcars. His		
goal was "to better myself." He also worked at		
Beverly Manor, a nursing home, as an orderly	1966-1967 (16-17)	
where he cleaned and waxed floors but he "couldn't handle watching people die" so he	1900 1907 (10 17)	
quit after six months. The patient and his first		
wife, M, had a daughter C. He describes the		
relationship with M as "not too good." They rented a small house that was next to his		
parents' home. He reported that M would		
leave C with his parents and "go out flirting."		
This made the patient very upset to the point that his parents' were "afraid of what [he'd]		
do." He said that all he wanted was answers		
and that he never had a chance to fight with		
because she left too quickly. Patient would "wonder about [his] daughter," and wondering		
why things had happened the way they did.		
After his first wife left, he coped with the loss		
by working. He got a job at Amox Aluminum.		
Later, he was an overhead crane operator at a		
steel mill in Fontana, CA. He gradually "worked [his] way up in the company." He left the steel		
mills to work in a food distribution warehouse		
for Stator Brothers.		
SECOND WIFE		

He married his second wife T who was ready		
to have kids but the patient "wasn't ready." This lead to their divorce.		
This lead to their divorce.		
THIRD WIFE		
His third wife was J. He describes this		
relationship as "temporary." He met her in a		
bar and she and her kids moved in with him.		
He reports that the just "showed up." He		
wasn't ready for kids and this relationship ended when J took his bank account and left.		
ended when I took his bank account and left.		
FOURTH WIFE		
B is the patient's current wife. He describes		
her as a "good, Christian woman," who has		
"issues of her own." B had five sons from a		
previous relationship. At that time he felt		
ready to have children in his life. He describes his relationship with B as "OK."		
ACCIDENT		
While working at the food distribution		
warehouse, the patient was walking	Late 1960's to early	
backwards pulling a load with a pallet mover when he slipped in a puddle of water. He hurt	1970's (late teen to	
his knee when he fell. The patient was	early 20's)	
distraught at the thought of not being able to		
work. He said at that point, "[his] mind started		
going," and he wondered, "what am I going to		
do?" The injured knee was repaired with arthroscopic surgery after which he was	Early 1970's (early 20's)	
unable to go back to work. While in the	20 31	
hospital the patient reports that his knee		
doesn't bother him.		

1983 (33)	
1984 (34)	

DRUG CESSATION/FRESNO		
DRUG CESSATION/FRESING		
Patient reports getting "burnt out on [speed]" and that it wasn't worth it. Both he and his wife were able to quit. He said he was able to quit because he, "just made up [his] mind." Reports being clean for 7 years since quitting. Around this time, patient moved with wife to Fresno to be closer to her sons from another relationship.	1984 (34)	
WIFE'S LUMBAR FRACTURE		
Wife has osteoporosis and has been bedridden		
since fracturing lumbar vertebrae.	1984 (34)	
		PSYCHIATRIC
GOLDEN LIVING		DIAGNOSIS
		Diagnosed with
Patient had pneumonia and stayed at Golden		schizophrenia. Per B,
Living for a few days. He was not pleased with		the patient often
his care there and a class action law suit was filed.		believes that people
med.		are out to get him or
		following him. He has
SETTLEMENT		had illusions where he
		has seen telephone
Patient reported getting a settlement from the		poles as shadows at the end of a street
class action lawsuit filed against Golden Living.		which he interpreted
The settlement is for a reported \$153,000. It		as "people plotting
appears that the patient attempted to conceal the settlement from his wife. Upon learning of		against him."
the settlement, his wife stated that she		
wanted her half so that she could buy a new		
electric wheelchair, a walk-in bathtub, and a		
new house. Wife reports that patient may be		
concerned that the settlement will "tip off the		
police" to the patient's "four to five warrants		
in Riverside for misdemeanors." The patient is afraid that the police will find out and he will		

"lose everything."	1984 (34)	
	2006 (56)	
ARGUMENT WITH WIFE Patient reports arguing with wife just prior to OD. He was unsure what he should do about the settlement so he reportedly gave it to Catholic Charities. (This portion of the history is unclear as patient has told different versions of the story which have conflicted with the wife's understanding of what happened.)		
	February 2013 (62)	

2013 (63)	
May 2013 (63)	DEPPRESSIVE SYMPTOMS Patient stated he is depressed with worsening anxiety, loss of pleasure, insomnia, and weight loss of 40 pounds.
T 1010Y 2013 (03)	FIRST SUICIDE ATTEMPT Patient took ~10 Vicodin in a suicide attempt before bed.

	He awoke then next
	day.
August 22, 2012 (C2)	SECOND SUICIDE
August 22, 2013 (63)	ATTEMPT
	Patient left a note for
	his wife stating that he
	was "sorry for
	, everything," and that
	he "really did love"
	her, and that he
	would" hopefully see
	[her] soon." He then
	took 10-12 Valium, 20
	Vicodin, and a full
	bottle of ibuprofen.
August 23, 2013 (63)	
0 / (/	INPATIENT
	PSYCHIATRIC
	HOSPITAL
	Patient transferred to
	CBHC. Per note,
	"patient stated he is
	depressed [with]
	worsening anxiety,
	loss of pleasure,
	insomnia, weight loss
	of 40 pounds since
	May, 2013. Feels hopeless, helpless,
	and worthless. Patient
	lacks energy is tired
	and not sleeping at
	night.

August 29, 2013 (63)	

* Medications were not listed above because patient had difficulty recalling all medications and timeline. Medications include: Vicodin, Valium, risperidone, ibuprofen, lisinopril, albuterol, metoprolol, zolpidem, saxagliptin, and diphenhydramine.

Mental Status Examination/Pertinent Medical Findings/Lab Results

On Arrival, 8/23 (day 1): GCS E1, V1, M1, Total: 3T.

Lab Results:

Basename	Value 8/23 (day 1)	Value 8/25 (day 3)	Value 8/26 (day 4)
HGB	13.5*	14.0	14.5
НСТ	37.1*	40.0	41.4
WBC	5.3	8.2	6.3
PLT	153	164	182
MCV	85		
INR	1.1		
PROTIME	13.7		
Na+	136	138	141
К+	3.9	4.1	4.8

CI-	109	108	112*
CO ₂	22	25	25
BUN	14	25*	15
CREATININE	0.8	1.6*	0.7
Glucose	146*	90	90
AST	18		
ALT	11		
ALKPHOS	51		
BILIT	0.2*		
Protein	6.4		
LABALBU	3.8		
Troponin	<0.006		
TSH	0.596		
HgA1c	5.0		

MSE on 8/26 (day 4 in the hospital):

Appearance/Behavior: Patient appears disheveled, worried, and distressed. Wearing hospital attire and sitting on the edge of the bed eating breakfast. Normal body build. Appears older than stated age.

Psychomotor: Appearing uncomfortable, constantly shifting in bed

Eye contact: Good eye contact.

Mood/Affect: Sad, anxious mood with congruent affect. He was tearful intermittently throughout the encounter.

Speech: Normal volume, rate, and rhythm

Thought Content: Appropriate content and topicality of thought. No delusional content expressed.

Perception: Denies hallucinations.

Attention: Alert but unable to spell WORLD backwards

Orientation: x4

Memory impairment: Recall of 1 object at 5 minutes and another 1 object with a hint.

Abstraction: Intact

Insight: intact. He understands that his actions could have lead to his death.

Social Judgment: Intact.

MSE on 8/27 (day 5 in the hospital)

Appearance/Behavior: NAD. Normal body build. Appears older than stated age.

Psychomotor: Appearing uncomfortable, constantly shifting in bed

Eye contact: Good eye contact.

Mood/Affect: Euthymic to sad. He was tearful intermittently throughout the encounter but occasionally smiled.

Speech: Normal volume, rate, and rhythm

Thought Content: Appropriate content and topicality of thought. No delusional content expressed.

Perception: Denies hallucinations.

Attention: Alert and attentive

Orientation: x4

Memory impairment: Recall of 2/3 objects at 5 minutes.

Abstraction: Intact

Insight: intact. He understands that his actions could have lead to his death.

Social Judgment: Intact.

Summary of Salient History and Abnormalities

RD was born and raised in Riverside, California. He grew up with both of his parents and a sister. He described a normal childhood except for academic challenges that began in elementary school. Reading was difficult for RD as he found it difficult to process what he was reading which required him to read over the material more than once. His difficulties in school continued and contributed to his desire to get out of school.

During his junior year of high school he dropped out when he became a father. He had a series of jobs to support his newborn daughter and new wife. RD's first marriage was short lived after his parents informed him that his wife had been cheating on him. After the divorce, he became estranged from his first wife and his daughter. This took a significant toll on him and made future relationships more challenging.

The patient was married two more times during the late 1960's and 1970's. The patient's second marriage ended quickly when he realized that his second wife was ready for kids but he was not. He married his third wife whom he met in a bar. The marriage ended when she moved her kids in with her and the patient again felt like he wasn't ready for children. The third wife drained his bank account and left the patient. RD married his current wife in 1983. This wife had five sons from a previous marriage but by this time the patient felt that he was ready to have children in his life again.

While working at a food distribution warehouse, the patient sustained an accident that left him unable to work. He has been on SSI since which is his only source of income.

Per the current wife, the patient has schizophrenia. It is unclear if a psychiatric diagnosis was made by a physician. The wife explained that the patient often believes that people are out to get him or following him. He has had illusions where he has seen telephone poles as shadows at the end of a street which he interpreted as "people plotting against him."

Around the time of his injury the patient and his wife started using methamphetamine. They used drugs until seven years ago when the patient reports getting "burnt out on [speed]" and that it wasn't worth it. Both he and his wife were able to quit cold turkey and they have been clean for seven years.

The patient has HTN, hyperlipidemia, and COPD. His wife suffers from osteoporosis and has been wheelchair bound since sustaining lumbar fractures. The patient helps care for his wife with the help of their adult foster daughter. The patient was hospitalized in February 2013 for pneumonia. He was discharged from the hospital to Golden Living. He was not pleased with his care and filed a class action law suit which he expects to yield him a \$153,000 settlement. The patient did not fully disclose this with his wife. The wife reports that patient may be concerned that the settlement will "tip off the police" to the patient's "four to five warrants in Riverside for misdemeanors." The couple argued about finances and the wife stated that she wanted her half to buy a new electric wheelchair and a new house. He was unsure what he should do about the settlement so he reportedly gave it to Catholic Charities. (This portion of the history is unclear as patient has told different versions of the story which have conflicted with the wife's understanding of what happened.) The conflict proceeded to the patient's first suicide attempt where he took ~10 Vicodin but he awoke then next day. Before his second suicide attempt, the patient left a note for his wife stating that he was "sorry for everything," and that he "really did love" her, and that he would" hopefully see [her] soon." He then took 10-12 Valium, 20 Vicodin, and a full bottle of ibuprofen. The patient was found unresponsive at his home by his adult foster daughter at around 11 am. EMS found patient with GCS 8 and by the time he arrived at the hospital he had a GCS 7. He did not respond to naloxone and was intubated with an initial GCS 3T. His utox revealed benzodiazepines and opiates. Flumazenil was not given due to unknown benzodiazepines dosing history. Patient was transferred to the ICU where he eventually woke up with a GCS 10T. Upon waking, he was able to follow commands and he was subsequently extubated.

Psychiatric consult revealed that the patient had taken the pills with the intention of ending his life. He was sad, anxious, and tearful during interviews. Patient stated that his desire to hurt himself came upon him suddenly. He denied current suicidal ideation but remains at a high risk for another suicide attempt.

RD was transferred to CBHC. Per note, "patient stated he is depressed [with] worsening anxiety, loss of pleasure, insomnia, and weight loss of 40 pounds since May, 2013. He feels hopeless, helpless, and worthless. Patient lacks energy is tired and not sleeping at night.

Differential Diagnosisⁱ

Major Depressive Disorder

- Rule in: depressed mood most of the day, loss of pleasure, significant weight loss, insomnia, loss of energy, feelings of worthlessness and guilt, decreased concentration, and suicide attempt
- Rule out:
- Further evaluation: determine objective agitation or retardation, time course of symptoms

Dysthymic Disorder

- Rule in: insomnia, low energy, poor concentration, feelings of hopelessness, low self-esteem
- Rule out: unclear if feelings existed before May 2013
- Further evaluation: determine if nearly lifelong depression has been present

Dysthymia with Superimposed Major Depressive Disorder (Double Depression)

- Rule in: depressed mood most of the day, loss of pleasure, significant weight loss, insomnia, loss of energy, feelings of worthlessness and guilt, decreased concentration, and suicide attempt
- Rule out: unclear if feelings existed before May 2013

• Further evaluation: determine if nearly lifelong depression has been present

Generalized Anxiety Disorder

- Rule in: patient very concerned about settlement, appeared anxious at each encounter
- Rule out: unclear timeline of anxiety
- Further evaluation: verify with patient timeline and effect on marriages

Methamphetamine Induced Mood Disorder

- Rule in: history of dependence, history of hallucination, depressed mood
- Rule out: patient denies, not apparent on utox
- Further evaluation: verify with patient

PTSD

- Rule in: sleep disturbance, difficulty concentrating,
- Rule out: no evidence of traumatic event or intense fear, no nightmares or flashbacks
- Further evaluation: further evaluate possible sources of trauma

Schizoaffective Disorder

- Rule in: symptoms of major depressive disorder
- Rule out: hallucinations not reported during time of depressive episode
- Further evaluation: evaluate precise timing of all episodes of hallucinations, evaluate for substance use during around hallucinations

Schizophrenia

- Rule in: history of hallucinations, patient given respiridone by foster daughter and claims that it "cleared his mind", possible tardive dyskinetic movements (patient attributes these to back pain)
- Rule out: patient denies current hallucinations
- Further evaluation: evaluate for most recent hallucinations, determine if hallucinations occurred while the patient was on methamphetamine

Avoidant Personality Disorder

- Rule in: feeling of inadequacy
- Rule out: was able to move up in occupational hierarchy to an extent
- Further evaluation: assess for social inhibition and hypersensitivity to negative evaluation

Medical Diagnoses

Recovering from Valium, Vicodin, and ibuprofen overdose. History of HTN, hyperlipidemia, and COPD. Arthroscopic knee surgery to repair damage sustained from a work related injury.

Stressors: reading, marital conflict, SSI, recent settlement

Assets: recent settlement

GAF 10 due to serious suicidal act with clear expectation of death.

Working Diagnosis

Major Depressive Disorder but cannot rule out schizoaffective disorder or substance abuse.

Formulation

RD has multiple risk factors that contributed to the development of the patient's mood disorder and subsequent suicide attempt. The patient's current state is a result of the accumulation of biological, psychological, and social factors which influence and contribute to one another.

BIOLOGICAL

While the patient denies knowledge of any psychiatric diagnoses in his family, he has evidence of early biological factors contributing to his current state. The most prominent biological factors contributing to the patient's condition are learning impairment, substance abuse, and comorbid medical conditions. The patient endorsed difficulty in school due to a reading problem. According to the patient, he was able to read but had difficulty processing the information requiring him to read the material again to understand. This is a problem that has followed him into adulthood that may be indicative of an underlying cognitive impairment. He stated that he "couldn't wait to get out" of high school. It is unclear if he would have graduated if he had not become a father when he was seventeen. An underlying cognitive impairment could help explain his reduced resilience to stress and his multiple marriages which ended in divorce.

After the patient was injured at work and became dependent on Social Security Insurance (SSI), the patient and his wife began using methamphetamine which may have been a coping mechanism for the patient. The patient reported using methamphetamine for roughly 23 years. Substance use disorders are one of the most common comorbid conditional associated with depression, and it is a possible organic cause of depression^{ii,iii}. A variation for the GRIN1 gene, which codes the NMDA receptor subunit NR1, has been shown to be a risk factor for methamphetamine dependence and methamphetamine induced psychosis^{iv}. While the patient has not been tested for such, it is possible that he has the gene and is more susceptible to methamphetamine dependence and would provide an explanation of his past psychotic symptoms^v. Methamphetamine also increases ACTH and thyroxine while decreasing cotrisol, triiodothyroxine, and TSH. It has also been noted that subjects who use methamphetamine score higher on the Beck Depression Inventory (BDI-13) than those who are not using methamphetamine^{vi}. The patient has not used methamphetamines for the past seven years but is currently taking barbiturates and opiates which can contribute to depression³. Abstinence from methamphetamine has been shown to be protective and there is a gradual time dependent improvement in decision making capacity^{vii}. Methamphetamine use increases dopamine in the brain eventually leading to damage to dopaminergic neural networks. When used chronically, methamphetamine is capable of damaging memory and executive function and increases the risk for developing anxiety, depression and psychosis^{viii}.

As the patient has aged he has also begun to struggle with comorbid medical conditions including hypertension, hyperlipidemia, type II diabetes mellitus, and back pain. It is unlikely that a single biological factor is responsible for RD's depression and ultimate suicide attempt². The end result is due to contributions from an early reading impairment, substance abuse, and comorbid medical conditions.

PSYCHOLOGICAL

Several psychological factors have contributed the state that resulted in the patient's suicide attempt. He had problems associated with early fatherhood, disturbed family atmosphere^{ix}, disability, substance abuse⁹, and caring for his disabled wife⁹. The patient described a happy childhood with both of his parents and his sister. He grew up in Riverside, California and spent most of his life in that area. He described difficultly reading and understanding in school that continues to the present⁹. When he was seventeen years old he became a father and married his first wife. The patient's first marriage was short lived when he became aware that she was leaving their daughter with his parents and going out to flirt with other men. His first marriage ended and made it difficult for the patient to have healthy relationships in his successive marriages. The second and third marriages ended because the patient didn't feel ready for children again so soon after losing his daughter⁹. The repeated interpersonal

problems took their toll on the patient⁹. By the time he married his forth and current wife, he was able to be around children again. Shortly after his last marriage the patient sustained a work related injury and has been on SSI ever since. During the first two decades with his current wife, the couple began using methamphetamine. They did not quit until seven years ago around the time that they moved to Fresno. Currently the patient is serving as a caregiver for his wife who is bedridden⁹ and is only mobile with the help of an electric wheelchair which has broken recently. The patient is also in the process of receiving a settlement from Golden Living where he feels he was not treated adequately. The patient didn't initially disclose the \$153,000 settlement with his wife which caused an argument immediately before the suicide attempt. Angry that the patient was trying to conceal the money, the wife demanded her half.

SOCIAL

Social factors influencing the patient's situation include poverty, disability, and possible outstanding warrants. While there are several social factors contributing to the patient's depression, the most influential factor at this time appears to be finances. Since 1983 the patient has been on SSI after sustaining a work related injury. The patient's wife is also on disability and they lived on a fixed income. Their combined income is roughly \$18,000 annually. Prior to the suicide attempt the patient was informed that he was going to receive a \$153,000 settlement from Golden Living which he did not disclose to his wife. He was concerned that by receiving the settlement, he would forfeit his SSI benefits. The wife became inflamed when she found out about the settlement resulting in an argument. During a phone interview with the wife, she mentioned that the patient was afraid that the settlement would tip off the police because of his outstanding warrants and that he would loose everything.

Management Plan

BIOLOGICAL

The patient overdosed on Valium, Vicodin, and ibuprofen resulting in his altered mental status (AMS) and Acute Kidney Injury (AKI). Diazepam overdose results in AMS which gradually improves within 48 hours. The AMS improves before diazepam is fully cleared from the body. After a large overdose, diazepam can be detectable for one to two weeks^x. Opiates also induce AMS and can lead to respiratory depression. Upon arrival the patient was intubated and mechanically ventilated in response to his respiratory depression. NSAID overdoses are common in the United States but death rarely occurs following overdose. Ibuprofen overdose rarely results in symptoms. Due to renal clearance of ibuprofen, kidney damage is the most common concern and is avoided by urine alkalinization and diuresis. Hemodialysis does not aid in clearing ibuprofen but may become necessary if kidney damage is severe

enough^{xi}. The patient would also benefit from neuropsychiatric testing to determine deficits and if they are due to dementia or some other cause.

The patient should also receive treatment for his chronic conditions and be in contact with a PCP for primary care.

- COPD: continue albuterol prn
- Back Pain: Percocet 5-325 mg q6 prn
- Monitor cholesterol
- Monitor BP: continue lisinopril 5 mg PO daily
- Monitor DM: Periodic HgA1c
- Health Maintenance (vaccinations, cancer screenings, etc.)

PSYCHOLOGICAL

- 5 mg Valium PO BID
- Inpatient psychiatric facility for stabilization at CBHC.
- Outpatient psychiatry for long term management due to his high risk state (male, age > 60, previous suicide attempt, depression, lack of support, and comorbid medical illnesses^{xii}).
 Goals of treatment are to alleviate the depressive symptoms and prevent future suicide

attempts. This has traditionally been monitored by monitoring symptoms through interviewing the patient or through standardized questionnaires. Neurotrophins are brain regulators that are involved in neuronal plasticity, specifically brain derived neurotrophic factor (BDNF). BDNF interacts with its receptor TrkB to reorganizes the brain and optimize the neural networks in response to environmental stimuli. A polymorphism of the BDNF gene has been linked to mood disorders. The link between BDNF and depression has also been shown by measuring serum levels in depressed patients and comparing postmortem BDNF levels in the brains of people with known depression to those who without depression^{xiii}. BDNF levels can be improved with both medication and psychotherapy. It is important to address stressors in the patient's life that cannot be alleviated with medication such as improving community integration and quality of life^{xiv}. There are many approaches to non medicine based psychotherapy.

Due to the patients financial constraints it may be wise to consider Brief Psychotherapy taking into account the narrow window of time that the patient will have to take advantage of therapy at the inpatient psychiatric facility. This therapy will help the patient to cope with stress using healthy ways that he has in the past with a finite number of sessions. Cognitive Therapy would also be beneficial by recognizing and combating negative thoughts and giving the patient a more realistic view of his situation^{xv}.

SOCIAL

It would help alleviate stressors on the patient to involve a social worker to help the patient establish long term outpatient psychiatric care. It would also help the patient to have his home set up to more easily take care of his wife. This could include a more accessible bathroom and a replacement electric wheelchair for his wife.

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