Case Study | Discontinuing Long-Term Opioid Therapy for Chronic Pain Through a Biopsychosocial Lens Transcript

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Case Introduction and Referral

New-Onset Psychosis and Withdrawal History

a 61-year-old woman who was chronic pain a 61-year-old woman who was chronic pain psychiatry clinic psychiatry clinic in which individuals with chronic pain in which individuals with chronic pain but also mental health concerns be but also mental health concerns be evaluated for both coing or coexisting evaluated for both coing or coexisting problems is actually referred by her problems is actually referred by her primary care physician primary care physician and the reason or the chief complaint and the reason or the chief complaint Complaint was for psychosis Complaint was for psychosis Patient came with a past medical history Patient came with a past medical history of endometriosis, of endometriosis, mild degenerative joint disease, chronic mild degenerative joint disease, chronic pain syndrome in so many words. Uh that pain syndrome in so many words. Uh that included dismenorhea or irregular included dismenorhea or irregular menstrual cycles, migraines, sciatic menstrual cycles, migraines, sciatic pain that's nerve pain traveling down pain that's nerve pain traveling down the leg and muscularkeeletal pain.

the leg and muscularkeeletal pain. At this point, immediately might At this point, immediately might generate some questions. Good point to generate some questions. Good point to reflect what could be occurring right reflect what could be occurring right away based on the past medical history, away based on the past medical history, age, and other features that were age, and other features that were already shared.

already shared. It asks the question or begs the It asks the question or begs the question, what else do you want to know? question, what else do you want to know?

What else do you want to do in terms of What else do you want to do in terms of evaluations, tests, exams, evaluations, tests, exams, laboratory analysis, etc.

laboratory analysis, etc. And where is your mind going when it And where is your mind going when it comes to considering what could be comes to considering what could be causing this presentation, this set of causing this presentation, this set of symptoms, so-called differential symptoms, so-called differential diagnosis, as well as what are the diagnosis, as well as what are the therapeutics, treatments that you might therapeutics, treatments that you might be considering.

be considering. But we'll advance the story to see what But we'll advance the story to see what else unfolds. else unfolds. Turns out from the history of present Turns out from the history of present illness or HPI that for about four illness or HPI that for about four months, the patient has had a new onset months, the patient has had a new onset psychosis. So this is not something that psychosis.

Hallucinations, Delusions, and Distress

So this is not something that has been going on most of her life in has been going on most of her life in the context of recurrent opioid the context of recurrent opioid withdrawal meaning she's going through withdrawal meaning she's going through the after effects of stopping her opioid the after effects of stopping her opioid complicated by intermittent delirium.

complicated by intermittent delirium. Delirium is confusion or medical Delirium is confusion or medical confusion. So you have a lot to unpack confusion. So you have a lot to unpack there. You have a new there. You have a new or brand new set of symptoms in the or brand new set of symptoms in the context of some med changes important context of some med changes important ones. and and so you have a few hints ones. and and so you have a few hints there as to what could be going on.

there as to what could be going on. Turns out that uh you know psychosis is Turns out that uh you know psychosis is not typically something that presents at not typically something that presents at that age for the first time. Usually that age for the first time. Usually presents in younger age. Psychosis as in presents in younger age. Psychosis as in schizophrenia or schizopeeffective schizophrenia or schizopeeffective disorder or delusional disorders. Those disorder or delusional disorders. Those typically affect individuals starting in typically affect individuals starting in the ages of late teens or 20s. Turns out the ages of late teens or 20s. Turns out that the patient was running out of her that the patient was running out of her opioid early for about four months. So, opioid early for about four months. So, she was running out of the medication she was running out of the medication and was treating her withdrawal from and was treating her withdrawal from running out with over-the-counter running out with over-the-counter benadryil. And this was contributing to benadryil. And this was contributing to confusion and psychosis. We know that confusion and psychosis. We know that benadryil or dyenhydramine, which is an benadryil or dyenhydramine, which is an antihistamine, can cause confusion, antihistamine, can cause confusion, particularly when you're a bit older. So particularly when you're a bit older. So that plus running out of her opioid was that plus running out of her opioid was contributing to this confusion and contributing to this confusion and so-called psychosis.

so-called psychosis. She was never combative or agitated She was never combative or agitated throughout this. Never had safety throughout this. Never had safety concerns like suicidal ideation or concerns like suicidal ideation or homicidal ideiation thankfully.

homicidal ideiation thankfully. However, there were other psychiatric However, there were other psychiatric symptoms of note. So this psychosis symptoms of note. So this psychosis was characterized as having uh three was characterized as having uh three parts. Visual hallucinations, delusions parts. Visual hallucinations, delusions and auditory hallucinations. The visual and auditory hallucinations. The visual hallucinations for example included hallucinations for example included abnormal experiences of street lights.

abnormal experiences of street lights. These would resolve rapidly within days. These would resolve rapidly within days. And so this this was the least And so this this was the least distressing or problematic of the distressing or problematic of the symptoms. She did have delusions or symptoms. She did have delusions or fixed false beliefs about her neighbors fixed false beliefs about her neighbors conspiring against her. bugging her conspiring against her. bugging her place and broadcasting thoughts to her.

place and broadcasting thoughts to her. In other words, some paranoia. This did In other words, some paranoia. This did not resolve immediately and actually not resolve immediately and actually required some treatment. This persisted required some treatment. This persisted despite the visual hallucinations going despite the visual hallucinations going away quickly. Auditory hallucinations away quickly. Auditory hallucinations were characterized as negative were characterized as negative commentary or chatter from male and commentary or chatter from male and female voices. Maybe the neighbors, but female voices. Maybe the neighbors, but also some strangers. And there were some also some strangers. And there were some condemnatory religious themes meaning condemnatory religious themes meaning some u very harsh critical themes and some u very harsh critical themes and and religious sort of guilt themes. This and religious sort of guilt themes. This also did not resolve immediately and also did not resolve immediately and required treatment. You had some required treatment. You had some lingering effects lingering effects despite uh some of these symptoms despite uh some of these symptoms disappearing. All of these were each of disappearing. All of these were each of these were characterized as egoistonic.

these were characterized as egoistonic. That's fancy speak and psychiatry for That's fancy speak and psychiatry for symptoms that are really distressing and symptoms that are really distressing and bothersome. There are individuals who bothersome. There are individuals who have hallucinations and delusions and have hallucinations and delusions and that are not bothered by these or that that are not bothered by these or that do see them as consistent with reality.

do see them as consistent with reality. She understood that this was not her She understood that this was not her reality, her usual state of mind, and reality, her usual state of mind, and that something was wrong. She found it that something was wrong. She found it extremely distressing and uncomfortable extremely distressing and

uncomfortable and wanted it treated.

and wanted it treated.

Initial Workup and Medication Changes

So, with all the information that's been So, with all the information that's been shared, this is another good stopping shared, this is another good stopping point to reflect. What else do you want point to reflect. What else do you want to know at this point? What other to know at this point? What other information might be useful to information might be useful to disentangle what's been going on? What disentangle what's been going on? What else do you want to do in terms of else do you want to do in terms of tests, analyses, interviews, physical tests, analyses, interviews, physical exams, and again, where is your mind exams, and again, where is your mind taking you in terms of your differential taking you in terms of your differential diagnosis, your treatment diagnosis, your treatment considerations, and such.

considerations, and such. I'll advance further. The primary care I'll advance further. The primary care physician actually ordered a number of physician actually ordered a number of labs when she started to present with labs when she started to present with these symptoms. And the workup included these symptoms. And the workup included labs like complete blood cell count, labs like complete blood cell count, complete metabolic panel, thyroid complete metabolic panel, thyroid stimulating hormone, vitamin levels like stimulating hormone, vitamin levels like B12 and folic acid or folate and a CAT B12 and folic acid or folate and a CAT scan of the head. All of these were scan of the head. All of these were found to be within normal limits. So found to be within normal limits. So negative, they were normal. There were negative, they were normal. There were also no significant physical exam also no significant physical exam findings. She had no constitutional findings. She had no constitutional symptoms that she reported meaning like symptoms that she reported meaning like malaise fatigue. She had no weight loss.

malaise fatigue. She had no weight loss. So that was a negative exam as well. So that was a negative exam as well. Terms of treatment for about 2 months Terms of treatment for about 2 months the primary care doctor actually resumed the primary care doctor actually resumed Percoet which is an oxycodin acophen Percoet which is an oxycodin acophen opioid to prevent withdrawal. Tried to opioid to prevent withdrawal. Tried to resume opioids to offset that. also resume opioids to offset that. also started a medication known as cerakolar started a medication known as cerakolar quitipene 25 milligrams at bedtime and quitipene 25 milligrams at bedtime and increased it to 50 milligrams. This is increased it to 50 milligrams. This is an antiscychotic actually that can be an antiscychotic actually that can be helpful in states of confusion or in helpful in states of confusion or in psychosis.

psychosis. psychosis. Additionally started some zoloft or Additionally started some zoloft or certain ssrrii or conventional certain ssrrii or conventional anti-depressant 50 milligrams daily and anti-depressant 50 milligrams daily and increased that to 75 milligs. These were increased that to 75 milligs. These were the efforts by the primary care the efforts by the primary care physician to offset some of the symptoms physician to offset some of the symptoms that he was observing in his patient.

that he was observing in his patient. The effects included that the delusions The effects included that the delusions or the paranoia improved but had or the paranoia improved but had persistent auditory hallucinations persistent auditory hallucinations alongside the concern for over this alongside the concern for over this chronic opioid use. This all led to the chronic opioid use.

Psychiatric Exam and Symptom Summary

This all led to the referral to the chronic pain site referral to the chronic pain site clinic. So instead of referring to just clinic. So instead of referring to just conventional psychiatry conventional psychiatry or conventional pain management felt or conventional pain management felt that it was valuable to refer to a that it was valuable to refer to a clinic that can handle both issues given clinic that can handle both issues given that there were chronic opioids in the that there were chronic opioids in the mix as well as now psychiatric symptoms.

mix as well as now psychiatric symptoms. on exam by myself and psychiatry team on exam by myself and

psychiatry team found that the patient was u in terms of found that the patient was u in terms of appearance in uh no apparent distress so appearance in uh no apparent distress so was not overwhelmed or distressed was was not overwhelmed or distressed was age appearing matched her age well age appearing matched her age well nourished well-groomed so she was taking nourished well-groomed so she was taking care of herself eating well her behavior care of herself eating well her behavior was pleasant she was cooperative she was was pleasant she was cooperative she was a bit fidgety a bit fidgety and her mood was described by her as and her mood was described by her as depressed her affect meaning how she depressed her affect meaning how she looked physically in her face was full looked physically in her face was full range, meaning that she was range, meaning that she was appropriately changing how um her face appropriately changing how um her face would match her mood depending on what would match her mood depending on what she was talking about. In this case, it she was talking about. In this case, it was inongruent. It did not match what was inongruent. It did not match what she was stating as this persistent she was stating as this persistent sadness or depression. She would smile sadness or depression. She would smile at times and that didn't make entire at times and that didn't make entire sense, if you will. Her eye contact was sense, if you will. Her eye contact was within normal limits. Her speech was of within normal limits. Her speech was of normal rate and rhythm. Her thoughts normal rate and rhythm. Her thoughts were linear, meaning that they were were linear, meaning that they were normal, goal oriented, and organized.

normal, goal oriented, and organized. Her thought content lacked any suicidal Her thought content lacked any suicidal ideiation, homicidal ideiation. It also ideiation, homicidal ideiation. It also lacked illusions and paranoia. So lacked illusions and paranoia. So thankfully, that had gotten better. Her thankfully, that had gotten better. Her perception, meaning how she perceives perception, meaning how she perceives the world, did include those auditory the world, did include those auditory hallucinations I mentioned. In terms of hallucinations I mentioned. In terms of her sensorium or how aware or alert she her sensorium or how aware or alert she is, she was awake and alert as well as is, she was awake and alert as well as oriented times four meaning oriented to oriented times four meaning oriented to self, oriented to place, to time and to self, oriented to place, to time and to context. So she was quite intact in this context. So she was quite intact in this sense. Her insight and judgment were sense. Her insight and judgment were also very good. Insight is a measure of also very good. Insight is a measure of how aware you are of what's going on how aware you are of what's going on with you and judgment is also what kind with you and judgment is also what kind of behavioral choices you might be of behavioral choices you might be employing. they were both good and her employing. they were both good and her motor exam meaning how her body was sort motor exam meaning how her body was sort of moving um lacked any major findings.

of moving um lacked any major findings. It was within normal limits. It was within normal limits. So to summarize the presenting symptoms, So to summarize the presenting symptoms, she had the auditory hallucinations, she had the auditory hallucinations, depressed mood, insomnia both at the depressed mood, insomnia both at the beginning and during the night. So beginning and during the night. So that's onset and maintenance insomnia that's onset and maintenance insomnia respectively. She felt fatigued but had respectively. She felt fatigued but had reduced appetite, was also socially reduced appetite, was also socially withdrawing and also had some amount of withdrawing and also had some amount of guilt secondary to smoking um smoking guilt secondary to smoking um smoking cigarettes. She had some difficulty with cigarettes. She had some difficulty with concentration and focus as well as concentration and focus as well as anxiety over her auditory anxiety over her auditory hallucinations. They were egoistonic hallucinations. They were egoistonic again and distressing.

again and distressing. I've shared a lot of information thus I've shared a lot of information thus far. This is another good stopping point far.

Chronic Pain, Opioids, and Psychiatric Background

This is another good stopping point to reflect. to reflect. One might ask as a clinician, what else One might ask as a clinician, what else do you want to know at this point? What do you want to know at this point? What else do you want to elucidate? What else else do you want to elucidate? What else do you want to do in terms of again do you want to do in terms of again tests, analyses, interview questions, tests, analyses, interview questions, treatments, and where is your mind going treatments, and where is your mind going in terms of what's causing all of this?

in terms of what's causing all of this? It's important to stop, reflect, stop, It's important to stop, reflect, stop, reflect,

stop, reflect repeatedly so reflect, stop, reflect repeatedly so that we can really promote the best that we can really promote the best individualized care for the patient in individualized care for the patient in front of us. To advance the case a front of us. To advance the case a little bit more, little bit more, we learned that she had a chronic pain we learned that she had a chronic pain as well as psychiatric history. In terms as well as psychiatric history. In terms of chronic pain, her history included of chronic pain, her history included endometriosis, mild degenerative joint endometriosis, mild degenerative joint disease, chronic pain syndrome. I disease, chronic pain syndrome. I mentioned these earlier.

mentioned these earlier. She had chronic opioid history that She had chronic opioid history that actually amounted to 50 years. It's a actually amounted to 50 years. It's a very long time, five decades. Started at very long time, five decades. Started at age 12, so she was quite young for age 12, so she was quite young for dismenoria. So abnormal menstrual cycles dismenoria. So abnormal menstrual cycles um at the time of puberty. This is a um at the time of puberty. This is a very unusual trajectory, very young age.

very unusual trajectory, very young age. Um and yet she was placed on opioids Um and yet she was placed on opioids then and never quite discontinued off of then and never quite discontinued off of them. Her most recent dose from a them. Her most recent dose from a primary care physician included percoet primary care physician included percoet again oxycodone/ again oxycodone/ acceto medicine 5 to 10 milligrams every acceto medicine 5 to 10 milligrams every 4 to 6 hours as needed for any 4 to 6 hours as needed for any muscoskeleletal pain that she muscoskeleletal pain that she experienced. And remember she was on experienced. And remember she was on that but she was running out early for that but she was running out early for about 4 months. So she may have about 4 months. So she may have developed some kind of dependence and developed some kind of dependence and needed more of that of that agent. Also needed more of that of that agent. Also she was taking gabapentin 900 milligrams she was taking gabapentin 900 milligrams three times a day. That is an three times a day. That is an anti-epileptic that is used for anti-epileptic that is used for neuropathic pain. And rarely she would neuropathic pain. And rarely she would get some um articular injections meaning get some um articular injections meaning injections in the joints for her pain.

injections in the joints for her pain. In terms of past psychiatric history, In terms of past psychiatric history, she really had none none formally at she really had none none formally at least. She had no medication trials with least. She had no medication trials with anti-depressants and other meds. Uh she anti-depressants and other meds. Uh she had no inpatient or outpatient had no inpatient or outpatient psychiatric care and no suicide psychiatric care and no suicide attempts. Her attempts. Her family psychiatric history did include a family psychiatric history did include a history of a mother who had alcohol use history of a mother who had alcohol use Patient herself had a substance use Patient herself had a substance use history of remote alcohol use disorder history of remote alcohol use disorder that had been full and sustained that had been full and sustained remission. So at some point she also remission. So at some point she also struggled with controlling her alcohol struggled with controlling her alcohol intake. She also as mentioned earlier intake. She also as mentioned earlier smoked regularly. She smoked about a smoked regularly. She smoked about a She did share that she had a trauma She did share that she had a trauma history. She had childhood physical as history. She had childhood physical as well as emotional abuse. Physical trauma well as emotional abuse. Physical trauma did not result in any major injuries.

did not result in any major injuries. She just described her parents as quite She just described her parents as quite strict. She also had some emotional strict. She also had some emotional abuse in terms of that um strict abuse in terms of that um strict parenting but denied having to relive or parenting but denied having to relive or reexperience the symptoms and no reexperience the symptoms and no hypervigilance that she was aware of. So hypervigilance that she was aware of. So in other words, she was not revisiting in other words, she was not revisiting those moments in traumatic reminders those moments in traumatic reminders like flashbacks or nightmares. nor was like flashbacks or nightmares.

Treatment Plan and Medication Titration

nor was she on to her knowledge on pins and she on to her knowledge on pins and needles um scared of of anything that needles um scared of of anything that resembled her earlier trauma.

resembled her earlier trauma. Terms of her social history and Terms of her social history and developmental history, she completed developmental history, she completed high school and had numerous clerical high school and had numerous clerical jobs for decades, then went on jobs for decades, then went on disability for chronic pain at some disability for chronic pain at some point. She was married um and did point. She was married um and did describe her partner to be somewhat describe her partner to be somewhat doing meaning someone who would sort of doing meaning someone who would sort of take care of everything for her. um take care of everything for her. um arguably even enabling um but no arguably even enabling um but no children and they were financially children and they were financially stable. So they had no major stressors stable. So they had no major stressors when it came to money or the law or when it came to money or the law or anything of the sort.

anything of the sort. So at this point once again encouraging So at this point once again encouraging reflection and integration of all the reflection and integration of all the information you might ask what else do information you might ask what else do you want to know? What else do you want you want to know? What else do you want to do in terms of interview test, to do in terms of interview test, physical exam analyses and where is your physical exam analyses and where is your mind as a clinician going in thinking mind as a clinician going in thinking about the differential diagnosis or about the differential diagnosis or possible treatment directions?

possible treatment directions? I'll share that uh in terms of I'll share that uh in terms of psychopharmarmacologic treatment or psychopharmarmacologic treatment or medication treatment. We basically made medication treatment. We basically made the decision when we met her integrating the decision when we met her integrating all of this that we might want to rotate all of this that we might want to rotate her her antiscychotic medication. She her her antiscychotic medication. She was having persistent psychotic was having persistent psychotic symptoms. She was not delirious. She was symptoms. She was not delirious. She was not encphilopathic or confused. Um this not encphilopathic or confused. Um this no longer looked like it was just due to no longer looked like it was just due to withdrawal and benadryil. This was a withdrawal and benadryil. This was a lasting symptom that was not better lasting symptom that was not better explained by her benadryil use since she explained by her benadryil use since she had curbed that. So we decided to switch had curbed that. So we decided to switch over from quitipene or cerakquil over to over from quitipene or cerakquil over to zyprea also known as alanzipene and zyprea also known as alanzipene and started 2 and a half milligrams at night started 2 and a half milligrams at night uh excuse me twice a day and 15 uh excuse me twice a day and 15 milligrams at night. Now this was milligrams at night. Now this was gradually um increased um over time and gradually um increased um over time and this was titrated or increased every 2 this was titrated or increased every 2 to four weeks for up to 27.5 milligrams to four weeks for up to 27.5 milligrams total. And this finally did have a total. And this finally did have a significant reduction in her anxiety and significant reduction in her anxiety and auditory hallucinations.

auditory hallucinations. The the rationale for choosing this The the rationale for choosing this medication was based on a study that I medication was based on a study that I had performed a systematic review that had performed a systematic review that is shown in the box below where we had is shown in the box below where we had reviewed the role of atypical reviewed the role of atypical anticycchotics in chronic pain. In other anticycchotics in chronic pain. In other words, second generation anticycchotics.

words, second generation anticycchotics. Now there is no uh suggestion here that Now there is no uh suggestion here that these anticycotics are meant to treat these anticycotics are meant to treat pain but we wanted to choose the one pain but we wanted to choose the one that did have some possible role in that did have some possible role in muscularkeeletal pain, migraines, muscularkeeletal pain, migraines, fibromyalgia.

fibromyalgia. fibromyalgia. And for those who are interested in this And for those who are interested in this in this topic, they can you know visit in this topic, they can you know visit the systematic review and the and the the systematic review and the and the article that that dives into greater article that that dives into greater detail.

detail. detail. We also felt that it was important to We also felt that it was important to continue to increase the certuline or continue to increase the certuline or zoloft which was an SSRI and a zoloft which was an SSRI and a depressant. It is indicated for both depressant. It is indicated for both treatment of depression but also treatment of depression but also anxiety. And so we increased that to 100 anxiety. And so we increased that to 100 milligrams. We introduced a different milligrams. We introduced a different agent known as or hydroxazine which is a agent

known as or hydroxazine which is a cousin of benadryil. It is also an cousin of benadryil. It is also an antihistamine antihistamine antihistamine in order to help with anxiety.

in order to help with anxiety. And so she was instructed to use 25 And so she was instructed to use 25 milligrams three times a day or TID as milligrams three times a day or TID as needed and to avoid benadryil. This is a needed and to avoid benadryil. This is a less deliric or confuse confusionprone less deliric or confuse confusionprone We also went ahead and looked at how to We also went ahead and looked at how to manage the opioid in the midst of all of manage the opioid in the midst of all of this. Remember this is somebody who was this. Remember this is somebody who was for five decades on chronic opioids and for five decades on chronic opioids and as a result of of that uh was was as a result of of that uh was was starting to rely on it more frequently starting to rely on it more frequently was not doing well with it and uh needed was not doing well with it and uh needed to um you know was running out early and to um you know was running out early and and going into withdrawal. So we decided and going into withdrawal. So we decided actually to to change the short acting actually to to change the short acting opioid to a long acting opioid. The opioid to a long acting opioid. The short acting opioid was percoet every short acting opioid was percoet every six hours. We changed it to caden or mor six hours. We changed it to caden or mor mor morphine extended release 30 mor morphine extended release 30 milligrams daily. So, it's roughly uh milligrams daily. So, it's roughly uh you know a morphine equivalent to where you know a morphine equivalent to where we reduced it to about 30, but that's a we reduced it to about 30, but that's a 24-hour 24-hour 24-hour uh extended release version of morphine.

uh extended release version of morphine. And this led to a wean over time, a And this led to a wean over time, a reduction, a detox if you will, over reduction, a detox if you will, over time where we had Kadine 30 milligrams time where we had Kadine 30 milligrams per day for one week, then down to 20 per day for one week, then down to 20 millig per day for 3 weeks, then 10 millig per day for 3 weeks, then 10 millig per day for another 3 weeks, and millig per day for another 3 weeks, and then finally stopped. And of course we then finally stopped.

Outcome, Publication, and Clinical Lessons

And of course we followed her closely during this process followed her closely during this process so that we can assist with any uh so that we can assist with any uh symptoms, discomfort, etc. That's an symptoms, discomfort, etc. That's an image of what um the Cadian paperwork image of what um the Cadian paperwork looks like.

looks like. We also introduced a couple of other We also introduced a couple of other agents to help with pain and with mood. agents to help with pain and with mood.

Symbalta or deluxitine which is an SNRI Symbalta or deluxitine which is an SNRI and has some impact in muscoskeleletal and has some impact in muscoskeleletal pain and neuropathy was introduced and pain and neuropathy was introduced and it was increased to 60 milligrams a day it was increased to 60 milligrams a day and dicophenic an anti-inflammatory was and dicophenic an anti-inflammatory was introduced as well to assist with her introduced as well to assist with her arthritis and her muscularkeeletal pain.

arthritis and her muscularkeeletal pain. She was also She was also uh sent to physical therapy within our uh sent to physical therapy within our our division within our department and our division within our department and did physical therapy one to two times a did physical therapy one to two times a week for about 12 weeks to help week for about 12 weeks to help complement what we were doing with complement what we were doing with pharmarmacology.

pharmarmacology. pharmarmacology. In addition to that sort of as a perfect In addition to that sort of as a perfect you know biocschosocial you know biocschosocial model of care we included cognitive model of care we included cognitive behavioral therapy or CBT and with behavioral therapy or CBT and with cognitive be behavioral therapy. We were cognitive be behavioral therapy. We were trying to invite her to reflect more on trying to invite her to reflect more on some of the stressors that came about some of the stressors that came about with her chronic pain and also um social with her chronic pain and also um social stressors that she carried about from stressors that she carried about from her trauma. The focus was self-critical her trauma. The focus was self-critical cognitive distortions that we started to cognitive distortions that we started to identify early on. meaning that she had identify

early on. meaning that she had the propensity to have certain thoughts the propensity to have certain thoughts that were very negative about herself that were very negative about herself and we thought that they were not very and we thought that they were not very productive that they were distortions productive that they were distortions and they weren't helping really with and they weren't helping really with everything that she was experiencing.

everything that she was experiencing. She tended to have rejection She tended to have rejection sensitivities meaning that she was prone sensitivities meaning that she was prone to being very injured by others not to being very injured by others not accepting her. She had a lack of accepting her. She had a lack of assertiveness about her. Uh she would assertiveness about her. Uh she would not assert her needs. She had body image not assert her needs. She had body image issues as well and possibly uh some issues as well and possibly uh some alexathyia. It was very difficult for alexathyia. It was very difficult for her to name her emotions. Alexia is her to name her emotions. Alexia is Greek for lack for lack of words for Greek for lack for lack of words for mood. And so sometimes she just couldn't mood. And so sometimes she just couldn't access her feelings and describe them in access her feelings and describe them in appropriate ways. And CBT was meant to appropriate ways. And CBT was meant to assist her with this. This was done on a assist her with this. This was done on a weekly basis. We also included nicotine weekly basis. We also included nicotine replacement therapy. So that's where um replacement therapy. So that's where um she was able to reduce her nicotine down she was able to reduce her nicotine down from 15 cigarettes per day down to five from 15 cigarettes per day down to five cigarettes per day with the use of um cigarettes per day with the use of um nicoderm patches and and other coping nicoderm patches and and other coping strategies.

strategies. strategies. And while you know the CBT and the And while you know the CBT and the nicotine replacement therapy was started nicotine replacement therapy was started while on zipa 27.5 milligrams which is a while on zipa 27.5 milligrams which is a very high amount. We are aware of of how very high amount. We are aware of of how that can come with various side effects that can come with various side effects and and metabolic burdens. Um she did and and metabolic burdens. Um she did have actually some weight gain which have actually some weight gain which wasn't all bad. She came in actually wasn't all bad. She came in actually rather thin and underweight and um she rather thin and underweight and um she did have some CBT anxiety reduction. So did have some CBT anxiety reduction. So we were able to reduce her zip prea or we were able to reduce her zip prea or lanzipene from 27.5 all the way to 5 mg lanzipene from 27.5 all the way to 5 mg but her auditory hallucinations returned but her auditory hallucinations returned and we found the sweet spot finally at and we found the sweet spot finally at 7.5 milligrams a day. So we were able to 7.5 milligrams a day. So we were able to stabilize things. If you think about stabilize things. If you think about that dose, alanzipene 7.5 milligrams a that dose, alanzipene 7.5 milligrams a day, that really isn't a typical dose day, that really isn't a typical dose for conventional or typical psychiatric for conventional or typical psychiatric uh disorders with psychosis like uh disorders with psychosis like schizophrenia or schizophffective schizophrenia or schizophffective disorder. So this was an unusual case in disorder. So this was an unusual case in which 7.5 milligrams with some other which 7.5 milligrams with some other strategies of course took care of of the strategies of course took care of of the psychosis but um it's probably because psychosis but um it's probably because this we were dealing with a primary this we were dealing with a primary schizophrenia.

schizophrenia. schizophrenia. So what was the outcome? At 12 months, So what was the outcome? At 12 months, the patient was euthyic, meaning that the patient was euthyic, meaning that she had good normal mood without she had good normal mood without psychosis, psychosis, psychosis, was socially active and doing well. Her was socially active and doing well. Her pain was well controlled with no pain was well controlled with no resumption of opioids and she had no resumption of opioids and she had no cravings for them. So this was arguably cravings for them. So this was arguably a win and we were very pleased and so a win and we were very pleased and so was she with the outcome of this.

was she with the outcome of this. We actually published this case, we as We actually published this case, we as in myself and and a colleague um in the in myself and and a colleague um in the journal of psychiatric practice titled journal of psychiatric practice titled case report denovo and persistent case report denovo and persistent psychosis after withdrawal from chronic psychosis after withdrawal from chronic opioid therapy. So it's a very unusual opioid therapy. So it's a very unusual case. If somebody wants to read it in case. If somebody wants to read it in greater detail, they can of course read greater detail, they can of course read the article. Uh but it was uh a very the article.

Uh but it was uh a very important case to prevent to to present important case to prevent to to present excuse me to the literature because excuse me to the literature because number one it talked it was an unusual number one it talked it was an unusual case of somebody on opioids from a very case of somebody on opioids from a very early age. It was also an unusual case early age. It was also an unusual case of a mixed picture of delirium and of a mixed picture of delirium and psychosis in the context of stopping psychosis in the context of stopping those opioids. Additionally, it was very those opioids. Additionally, it was very interesting um case that sort of interesting um case that sort of illustrated how biocschosocial care can illustrated how biocschosocial care can be conducted with a mix of medication be conducted with a mix of medication adjustments, opioid we psychotherapy, adjustments, opioid we psychotherapy, physical therapy, and substance use care physical therapy, and substance use care in terms of nicotine replacement in terms of nicotine replacement therapy. All of these things working in therapy. All of these things working in concert to help an individual with a concert to help an individual with a complex presentation.

complex presentation. This is the timeline of the case that I This is the timeline of the case that I just presented. How it all sort of just presented. How it all sort of occurred. You see at the beginning 50 occurred. You see at the beginning 50 years of chronic opioids, a 4month years of chronic opioids, a 4month period of overuse/withdrawal period of overuse/withdrawal cycle mixed with not just opioids and cycle mixed with not just opioids and withdrawal but also dyenhydramine or withdrawal but also dyenhydramine or benadryil uh over the counter which was benadryil uh over the counter which was causing delirum and confusion. You had causing delirum and confusion. You had the psychosis onset. You had delusions.

the psychosis onset. You had delusions. this bar here that lasted up until a this bar here that lasted up until a certain point and visual hallucinations certain point and visual hallucinations which were very transient but the which were very transient but the auditory hallucinations were the longest auditory hallucinations were the longest of the psychotic symptoms that resumed of the psychotic symptoms that resumed or or that persisted excuse me. Here you or or that persisted excuse me. Here you have opioid resumption and have opioid resumption and psychopharmacologic titration that we psychopharmacologic titration that we just reviewed. We weaned off of the just reviewed. We weaned off of the opioid over time took about two months opioid over time took about two months and then we downtitrated or reduced and then we downtitrated or reduced alanzipene. So initially we really alanzipene. So initially we really relied heavily on alanzipene but then we relied heavily on alanzipene but then we decreased it and then achieved decreased it and then achieved maintenance cycle maintenance cycle um in terms of the final regimen and um in terms of the final regimen and again her symptoms disappeared again her symptoms disappeared eventually. So it took a while and the eventually. So it took a while and the other thing that's important from this other thing that's important from this image to to take home is that something image to to take home is that something that has been going on for 50 years or that has been going on for 50 years or or or longer is clearly not going to or or longer is clearly not going to take a week or two to address. um take a week or two to address. um something that has been uh treated with something that has been uh treated with you know highdosese opioids for a long you know highdosese opioids for a long time and then altered is not going to be time and then altered is not going to be fixed rather you know simplistically fixed rather you know simplistically with one or two interventions. It's with one or two interventions. It's going to take time. It's going to take going to take time. It's going to take individualized care. It's going to take individualized care. It's going to take biocschosocial interventions. So it's a biocschosocial interventions. So it's a good image to remind us that there are good image to remind us that there are Just as a reminder of the various things Just as a reminder of the various things that could have been at play in this that could have been at play in this case in terms of the differential case in terms of the differential diagnoses, the different uh conditions diagnoses, the different uh conditions to consider included a primary psychotic to consider included a primary psychotic process underneath these chronic process underneath these chronic opioids. What if for instance she had opioids. What if for instance she had all along a chronic primary all along a chronic primary schizophrenia, delusional disorder, schizophrenia, delusional disorder, something of that sort, but it was something of that sort, but it was masked or indirectly even treated by the masked or indirectly even treated by the opioids. If you think of opioids as uh opioids. If you think of opioids as uh CNS or central nervous system CNS or central nervous system suppressants, they can reduce anxiety.

suppressants, they can reduce anxiety. They can sometimes blunt some of those They can sometimes blunt some of those effects that are coming from the brain.

effects that are coming from the brain. So, who knows? She could have already So, who knows? She could have already had a chronic psychiatric disorder that had a chronic psychiatric disorder that was just masked, if you will, or covered was just masked, if you will, or covered up by the opioid. Um, maybe she had up by the opioid. Um, maybe she had obsessivempulsive disorder or OCD with obsessivempulsive disorder or OCD with some egoistonic or unpleasant features.

some egoistonic or unpleasant features. Maybe this could have been complex Maybe this could have been complex post-traumatic stress disorder with post-traumatic stress disorder with personality disorder and so-called personality disorder and so-called microcsychosis. These are these are microcsychosis. These are these are jargon terms from psychiatry where jargon terms from psychiatry where somebody with complex trauma might have somebody with complex trauma might have changes in their identity, personality changes in their identity, personality and then as a result of that also be and then as a result of that also be prone especially under stress to prone especially under stress to experience brief psychotic breaks from experience brief psychotic breaks from reality such as delusions, paranoia etc.

reality such as delusions, paranoia etc. Maybe she had major depressive disorder Maybe she had major depressive disorder or depression with psychotic features.

or depression with psychotic features. There are variants of major depressive There are variants of major depressive disorder that include psychotic disorder that include psychotic features.

features. features. It could have been an atypical delirium. It could have been an atypical delirium. So an atypical delirium would would be So an atypical delirium would would be again a medical confusion or again a medical confusion or encphylopathy secondary to medication encphylopathy secondary to medication effects, other medical matters. And of effects, other medical matters. And of course there could have been other course there could have been other considerations here. Um but it is a rich considerations here. Um but it is a rich case that illustrates that we must be case that illustrates that we must be thinking about all of these thinking about all of these possibilities and holding them possibilities and holding them simultaneously in our heads as simultaneously in our heads as clinicians.

clinicians. clinicians. terms of literature on this topic, terms of literature on this topic, there's actually very little out there. there's actually very little out there.

There's very few or sparse examples of There's very few or sparse examples of opioid withdrawal, quote unquote opioid withdrawal, quote unquote psychosis. In fact, what is described psychosis. In fact, what is described more often is a delirium, if you will, more often is a delirium, if you will, or encphylopathy. Um, where somebody or encphylopathy. Um, where somebody might have very transient, temporary, might have very transient, temporary, uh, reversible psychotic symptoms. Um, uh, reversible psychotic symptoms. Um, and it's really confounded or or or and it's really confounded or or or complicated by the possibility that this complicated by the possibility that this is actually more so confusion, temporary is actually more so confusion, temporary brain disruption from medication brain disruption from medication changes, not exactly the same as changes, not exactly the same as psychosis. Our case really stood out psychosis. Our case really stood out because after controlling for attention because after controlling for attention and orientation, we did feel strongly and orientation, we did feel strongly that this was no longer a delirium and that this was no longer a delirium and the person had for weeks, if not months, the person had for weeks, if not months, persistent psychotic symptoms. So this persistent psychotic symptoms. So this did stand out from what most of the did stand out from what most of the literature talks about when it comes to literature talks about when it comes to opioid withdrawal. And again, these are opioid withdrawal. And again, these are very rare reports.

very rare reports. This raises the question as to what was This raises the question as to what was going on here. What could be the going on here. What could be the mechanism of action of this? How does mechanism of action of this? How does this occur? One theory is that again this occur? One theory is that again maybe opioids as central nervous system maybe opioids as central nervous system suppressants meaning things that calm suppressants meaning things that calm the central nervous system or blunt it the central nervous system or blunt it basically simply reduce distress, basically simply reduce distress, anxiety and even psychosis. In other anxiety and

even psychosis. In other words, uh if you have strong opioids on words, uh if you have strong opioids on board, maybe you're just sort of board, maybe you're just sort of blunting again the brain so that one blunting again the brain so that one doesn't feel anxiety, distress, doesn't feel anxiety, distress, psychosis. I do see this clinically psychosis. I do see this clinically regularly where individuals uh tend to regularly where individuals uh tend to to feel like their psychiatric symptoms to feel like their psychiatric symptoms do improve as a result of opioids. Now do improve as a result of opioids. Now of course there are other side effects of course there are other side effects and other problems with that. So it's and other problems with that. So it's not meant to suggest that we should be not meant to suggest that we should be giving opioids for those conditions but giving opioids for those conditions but I have seen that before. Another theory I have seen that before. Another theory is that maybe the kappa opioid receptor is that maybe the kappa opioid receptor is being involved or implicated. So the is being involved or implicated. So the kappa opioid receptor is one that is is kappa opioid receptor is one that is is is is is rarely uh you know discussed in rarely uh you know discussed in medicine. So when we think of opioids medicine. So when we think of opioids and where they work in the brain, they and where they work in the brain, they work on mu receptors. Um these receptors work on mu receptors. Um these receptors are all named after Greek letters. And are all named after Greek letters. And so the mu receptor is really usually the so the mu receptor is really usually the one that that gets the most attention one that that gets the most attention because that's where opioids work and because that's where opioids work and activate and and they touch up on that activate and and they touch up on that little mu receptor and that causes little mu receptor and that causes analesia. In other words, reduction of analesia. In other words, reduction of pain. But opioids actually affect many pain. But opioids actually affect many different receptors as most of our meds different receptors as most of our meds do. And kappa receptors are a different do. And kappa receptors are a different uh opioid receptor that are important to uh opioid receptor that are important to consider. When you u involve the kappa consider. When you u involve the kappa receptor, it can be what's called receptor, it can be what's called psychotimedic. That's a long word for psychotimedic. That's a long word for saying it can induce psychosis. It can saying it can induce psychosis. It can induce psychotic symptoms. Uh which is induce psychotic symptoms. Uh which is very interesting. And so the chronic use very interesting. And so the chronic use of K receptor agonist meaning meds or of K receptor agonist meaning meds or opioids that activate the K receptor can opioids that activate the K receptor can lead to dopamine receptor up regulation lead to dopamine receptor up regulation in the misolyic and negro pathways.

in the misolyic and negro pathways. That's a long way of saying that if we That's a long way of saying that if we use opioids for a very long time and use opioids for a very long time and they activate the kappa receptor, you they activate the kappa receptor, you can get more dopamine in the brain can get more dopamine in the brain pathways that can themselves contribute pathways that can themselves contribute to psychosis. And so this is one to psychosis. And so this is one possible pathway or one mechanism that possible pathway or one mechanism that could be involved.

could be involved. The table that I'm showing here actually The table that I'm showing here actually shows um how through through certain you shows um how through through certain you know experiments we've shown that kappa know experiments we've shown that kappa opioid receptor agonism meaning again opioid receptor agonism meaning again activation of the kappa opioid receptor activation of the kappa opioid receptor can be blocked with opioid antagonist.

can be blocked with opioid antagonist. So in other words, we can prevent So in other words, we can prevent psychotic effects if we block that psychotic effects if we block that receptor. And and like that we learn receptor. And and like that we learn that these receptors, these kappa opioid that these receptors, these kappa opioid receptors really are involved in um in receptors really are involved in um in in kappa induced psychotic effects. And in kappa induced psychotic effects. And nlloxxone, which you hear a lot about, nlloxxone, which you hear a lot about, and now trexone as well are um blockers and now trexone as well are um blockers of these of these receptors. and um they of these of these receptors. and um they can prevent these kappa opioid receptor can prevent these kappa opioid receptor This image is also from the article that This image is also from the article that we published on this case that I just we published on this case that I just presented and it's basically presented and it's basically taking a stab at what the mechanism is taking a stab at what the mechanism is here. This is by no means um you know uh here. This is by no means um you know uh etched in sand. Uh this is or etched in etched in sand. Uh this is or etched in stone, excuse me. This is basically a a stone, excuse me. This is basically a a a potential mechanism as to why this a potential mechanism as to why this specific individual might have had uh

specific individual might have had uh you know psychotic effects or psychotic you know psychotic effects or psychotic symptoms way after uh many years of symptoms way after uh many years of taking chronic opioids. So obviously um taking chronic opioids. So obviously um there's the long-term opioid use in the there's the long-term opioid use in the middle here, but remember long-term middle here, but remember long-term opioid use mixed with certain risk opioid use mixed with certain risk factors is really what's most important.

factors is really what's most important. So somebody might have had psychiatric So somebody might have had psychiatric or psychosocial risk factors or genetic or psychosocial risk factors or genetic loading or diiathesis. Diiathesis is a loading or diiathesis. Diiathesis is a fancy word for risk. And so somebody fancy word for risk. And so somebody might have been loaded with certain risk might have been loaded with certain risk factors. Remember her her history factors. Remember her her history included trauma and included genetic included trauma and included genetic history of maternal alcohol use history of maternal alcohol use disorder. So, there may have been disorder. So, there may have been something already there that then with something already there that then with the mix of long-term opioid use might the mix of long-term opioid use might have led to psychotic disorder via these have led to psychotic disorder via these smaller arrows. Um, so you can see um smaller arrows. Um, so you can see um each one has smaller um header numbers.

each one has smaller um header numbers. These are all references in our article These are all references in our article that that are meant to um offer support that that are meant to um offer support for these theories. But one we talked for these theories. But one we talked about was chronic cappa opioid receptor about was chronic cappa opioid receptor activation. I just referred to that in activation. I just referred to that in the previous slide. This can lead to the previous slide. This can lead to misolyic or midbrain to limbic uh area misolyic or midbrain to limbic uh area dopamine release. DA being dopamine. Um dopamine release. DA being dopamine. Um you can also have some other changes you can also have some other changes over time in terms of neuron maturation.

over time in terms of neuron maturation. Oligodendrites are a type of neuron in Oligodendrites are a type of neuron in our brain. Um as well as abnormal our brain. Um as well as abnormal mileelination and and pruning. So these mileelination and and pruning. So these are these are complex processes that are are these are complex processes that are part of neurode development. how our part of neurode development. how our brains develop. And during adolescence, brains develop. And during adolescence, particularly when somebody so young as particularly when somebody so young as her, age 12, was exposed to highdosese her, age 12, was exposed to highdosese opioids, you might presume that that had opioids, you might presume that that had an impact actually on on brain pathways an impact actually on on brain pathways to the point of maybe impacting her risk to the point of maybe impacting her risk for psychotic disorder. Now, all of for psychotic disorder. Now, all of these things in concert, of course, and these things in concert, of course, and maybe even other factors contributed to maybe even other factors contributed to this picture.

this picture. [Music]