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## Suicide Risk Factors in Adult Bipolar Disorder

### AFFECTS OF CHILDHOOD ABUSE, UNEVENTUAL ADULT BIPOLAR DISORDER AND SELF-DESTRUCTIVE BEHAVIOR

It is reported that up to a-fifth of bipolar disorder patients will suicide. Yet, there are few studies looking at clinical risk factors in this population. What is the latest research? Welcome to the Clinician's Roundtable. I am Dr. Leslie Lundt, your host and with me today is Dr. Roger McIntyre. Dr. McIntyre is an associate professor of psychiatry and pharmacology at the University of Toronto and he heads the Mood Disorders Psychopharmacology Unit at the University Health Network in Toronto.

#### DR. LESLIE LUNDT:

Welcome to ReachMD, Roger.

**DR. ROGER MCINTYRE:**

Leslie, thanks for having me.

**DR. LESLIE LUNDT:**

Roger, what don't we know about risk factors for completed suicide in bipolar patients?

**DR. ROGER MCINTYRE:**

There has been a large body of evidence that has documented many social demographic clinical and treatment factors that affects suicidality and bipolar disorder. What emerges from that literature, in fact what surrounded entirely are couple of key messages and that is that suicidality and bipolar disorder is often presaged by depressive symptoms and usually depressive symptoms that have been mixed with agitation and anxiety. The second message that I think is important to highlight is that we are learning that medical comorbidity, obesity, overweight, diabetes also increases the risk for suicidality in individuals with bipolar and that is a relatively new finding. The third of 3 comments in response, Leslie is that we often think about suicide as a behavior, obviously a very destructive behavior in response to proximal stressors, the loss of a job, the loss of a relationship in, you know, the last month or two and indeed that is inexorably true. We are also learning that distal stressors, in other words, childhood adversity, trauma, abuse and so on may set a very unfortunate groundwork that leads to maladaptive behavior, i.e. suicidality as an adult and that was really the focus of our work.

**DR. LESLIE LUNDT:**

Now, you have been interested in the effects of stress inflicted in childhood, tell us about that.

**DR. ROGER MCINTYRE:**

I would particularly start over the years with meeting individuals, who have bipolar disorder, major depressive disorder and how often they report history of maltreatment. It has been a compelling unequivocal body of evidence that links these types of unfortunate experiences to suicide, not just ideation, not just attempt, but completion as an adult. I think what is particularly interesting from the research perspective is trying to pursue what is the link. I think we can certainly begin the high positive signs around the areas of psychological risks that are inherent, what been exposed to abuse, I think there has been a body of literature that has really grown remarkably only while in 5 to 7 years that document interesting neurobiological changes that occurs in individuals, who have been exposed to trauma, Sjogren or during critical periods of development. For example, we now know that during critical periods of development, when, you know, all of us are developing our ability to really respond to stress in appropriate and adaptive fashion, which really in biological terms meaning issues around cortisol, issues around immune activation or inflammatory activation and the autonomic response in individuals, who are developing if you are exposed to a so-called environmental pathogenic experience that may disrupt permanently some of those response pattern and a lot of these types of biological processes and sub-processes remain largely, if you say, this way in quiet, the silent, and they are only activated down stringing at 20, 25, 30 years old when a person is exposed to a traumatic experience, it really awakens this maladaptive pattern and often overwhelms the person's homeostatic abilities leading to these types of chaotic behaviors.

**DR. LESLIE LUNDT:**

Tell us about the papers you published on this.

**DR. ROGER MCINTYRE:**

One of the papers we published on this was some work from our clinic, where and what we did was, we looked at the first 1000 patients, who came to our clinic and these were individuals, who are consecutive referrals to a tertiary university based mood disorders program. Half the referrals are from primary care providers and half are from specialty providers in the community. It is total about 50-50 split and what we found was is and this correlates with other investigators is that the rate of trauma as

a child, these were adult patients over the age of 18 up into the age of 65 and as children, they historically would often report during an amnestic inquiry a high rate of childhood maltreatment. In fact, we had rates between 20 and 40%, depending on what type of abuse we are talking about, physical, sexual, emotional and also neglect is a very, very common phenomenon and I think what we have learnt from the abuse literature if I can call that in the last decade is that not all abuse is created equal, and I think that there has been a thought that, for example emotional abuse is not as toxic as other forms of views, we are believing that probably it is not the case that there are indeed high level of toxicity associated with emotional abuse. So, we found very high rate. Again, that is in addition to what we have already known. What we then did is we looked at current and more recent and past histories of self-harm behaviors and usually we will define it with unequivocal description of what a self-harm is, as you know in psychiatry, there is a thin line between what is truly suicide and what some use to refer to as suicide or behaviors that are not intended to destroy the life, but are intended to either alleviate distress or to seek out help or a whole long list of other rationales and reasons behind the behavior. So, we are talking serious suicide attempts and what we found was is that adults yet have very high rates of suicidality as the term, but specifically high rates of self-harm in terms of shooting themselves, hanging themselves, and surviving remarkably. This is a larger concern on trial and we have a subway system, people jump in front of subways and survive, I mean these are unequivocal self-harm attempts and we found that individuals, who have bipolar disorder and depressive disorder, particularly pronouncing bipolar disorder who in fact reported such unfortunate events also with the individuals who all reported childhood adversity and we found the relationship work both ways. Now, when you are looking at these types of relationships, there are many types of variables I could possibly confound this association. Economics, there is a host of issues around course of illness, people for example, who attempt suicide tend to have much more severe course and that may be actually more of the explanatory variable rather than the distal stressor of abuse and we did as best as we could to control for some of these more obvious confounding factors and remarkably is that there has been relatively diffuse studies that have looked at relationship between suicide and bipolar disorder as a function of childhood adversity and we hope to, if you will, sort of issue or query on call the clinicians that they close retention to that in evaluating risky patients.

### **DR. LESLIE LUNDT:**

If you are new to our channel, you are listening to the Clinician's Roundtable on ReachMD, the Channel for Medical Professionals. I am Dr. Leslie Lundt, your host and with me today is Dr. Roger

McIntyre. We are discussing the affects of childhood abuse, uneventual adult bipolar disorder and self-destructive behavior.

Roger, did you see a gender difference in your study?

**DR. ROGER MCINTYRE:**

There was a suggestion in our study that men, who are exposed to childhood adversity may be at a higher risk when compared to the female counterparts, if they were exposed to childhood trauma and I don't want to overstate that, that finding was a suggestion, but when we carried a host of multiple analyses to strike that association has diminished considerably. So, I think that there has been a lot of literature that has documented women are more likely to attempt suicide, men are more likely to complete suicide and most of these folks have bipolar or major depression. We have done relatively few studies looking at this gender or I guess, more specifically sex relationship, male/female with this. So, our look was very preliminary and there was a suggestion that men were more at risk, but I think it still remains an open question.

**DR. LESLIE LUNDT:**

How about the type of abuse, whether it is physical or sexual or emotional? Did that make a difference?

**DR. ROGER MCINTYRE:**

It seems though with our analysis that individuals, who have been exposed to sexual trauma, particularly sexual trauma that had been perpetuated by a first degree family member, a father, a brother, a mother, things like that, they were particularly disadvantaged and those individuals are particularly at risk and so, as I said earlier that there has been, you know, not all abuse is created equal in terms of the toxic effect on the individual and there are several lines of evidence that do suggest that sexual abuse may be particularly toxic, particularly when perpetuated by what should be our safety

object that is our first-degree relatives in our lives, I think it has a particularly detrimental effect, not only the psychological aspects, but there is a whole host of family dysfunctional aspects that are implicated by that type of behavior as well.

**DR. LESLIE LUNDT:**

And what your best <\_\_\_\_\_> to counsel pathway here?

**DR. ROGER MCINTYRE:**

Well, my <\_\_\_\_\_> is that beyond I think well established association between trauma and negative is the cognitive, you know, outcomes in terms of negative ischemia cognitively, you know, literature is very compelling. I have put forth an additional, these are not rival, but additional hypothesis that individuals with bipolar disorder in addition to having this in propensity to disturbances and affect of processing and affect of perception, this environmental pathogenic exposure then I think further disrupts the neural systems that underlie or sub-serve stress, management, coping with stress, and general affect as cognitive processing abilities and perceptual abilities and so in short, we are organizing this neurobiology in a very detrimental way for the individuals so that downstream left so terribly disadvantaged and so when faced with terrible trauma, they react in the most maladaptive ways.

**DR. LESLIE LUNDT:**

Are there treatment implications here that we can learn?

**DR. ROGER MCINTYRE:**

I think that the sort of direct instruction to me as a clinician from this work that we did was when I in fact

assessed the patient with bipolar disorder and my practice is in the adult population, you know, we haven't typically thought about childhood adversity linking at the suicidality for the risk inherent now and although we do take a history of childhood trauma in all of our patients, we haven't typically drawn that line as close to adult suicidality as we now do at this type of work and similar research has been published by other colleagues at NIH, for example, there has been similar work that has similar findings. So, when assessing my patient, who has bipolar disorder, key issues are around depression, around depressive symptoms mixed with agitation, and we make a strong point of trying to sort out some of the factors around these abuse experiences and trying to say what they mean for patients. I think what are the criticisms that I have of some of the literature in suicidality, we have many, many, many factors that are associated with suicide, but what is the predictive value, what is the net predictive value and I think that really is the query on call to us in research to further characterize how predictive is this. It's 1 thing to be associated, but really in sort of mathematical terms, how much weight does it actually have and I think that is what we are going to try and look at with some other data basis that we are currently analyzing.

**DR. LESLIE LUNDT:**

If we think about the neurobiology, if there are any hints to what or not, a medication might do for these folks?

**DR. ROGER MCINTYRE:**

Interesting question, you know, there has been a body of evidence down to fix it for a number of years that of the various agents that we employ in the management of bipolar disorder treating bipolar disorder, lithium has surfaced as 1 agent that appears to lower not only overall suicide completion rates, but what interesting is it also seems to reduce the lethality of the message chosen by the individual and there has been some contradictory data on recent, but there has been a number of papers that I think give us some competence, saying that this may be a real effect. Beyond lithium, we don't really know if any other sort of "bipolar medications" or actually anti-suicidal and there is of course as you know clozapine was looked at in primarily psychotic patients with a beneficial effect on suicidality, but I think that is the key issue and that is can we determine an anti-suicide effect with some

of these agents. As you know, clinical trials will never allow us to enroll these types of, patients at least in terms of pivotal trials, but we hope epidemiological as they may shed some more lives.

**DR. LESLIE LUNDT:**

Well, thank you so much for enlightening us on this today, Roger.

**DR. ROGER MCINTYRE:**

Thanks Leslie for having me here, I really appreciate it.

**DR. LESLIE LUNDT:**

We have been speaking with psychiatrist, Dr. Roger McIntyre about the relationship between childhood abuse and suicidality in adult bipolar patients. I am Dr. Leslie Lundt. You have been listening to ReachMD XM157, the Channel for Medical Professionals. For complete program guide and download of podcast, visit our website at [www.reachmd.com](http://www.reachmd.com). Thank you for listening.

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