Clinical Management Guidelines for Friedreich Ataxia

Chapter 14. Mental health issues in Friedreich ataxia

Contents
14.1 Literature review of prevalence of mental health issues in Friedreich ataxia3
14.2 Management of depression in Friedreich ataxia5
Best practice statements6
Recommendations6
Lay summary8
14.3 Management of anxiety in Friedreich ataxia9
Recommendations9
Lay summary10
14.4 Management of psychosis in Friedreich ataxia11
Recommendations
Lay summary12
Author details
References

This chapter of the Clinical Management Guidelines for Friedreich Ataxia and the recommendations and best practice statements contained herein were endorsed by the authors and the Friedreich Ataxia Guidelines Panel in 2022.

Disclaimer

The Clinical Management Guidelines for Friedreich ataxia ('Guidelines') are protected by copyright owned by the authors who contributed to their development or said authors' assignees.

These Guidelines are systematically developed evidence statements incorporating data from a comprehensive literature review of the most recent studies available (up to the Guidelines submission date) and reviewed according to the Grading of Recommendations, Assessment Development and Evaluations (GRADE) framework © The Grade Working Group.

Guidelines users must seek out the most recent information that might supersede the diagnostic and treatment recommendations contained within these Guidelines and consider local variations in clinical settings, funding and resources that may impact on the implementation of the recommendations set out in these Guidelines.

The authors of these Guidelines disclaim all liability for the accuracy or completeness of the Guidelines, and disclaim all warranties, express or implied to their incorrect use.

Intended Use

These Guidelines are made available as general information only and <u>do not constitute medical advice</u>. These Guidelines are intended to assist qualified healthcare professionals make informed treatment decisions about the care of individuals with Friedreich ataxia. They are not intended as a sole source of guidance in managing issues related to Friedreich ataxia. Rather, they are designed to assist clinicians by providing an evidence-based framework for decision-making.

These Guidelines are not intended to replace clinical judgment and other approaches to diagnosing and managing problems associated with Friedreich ataxia which may be appropriate in specific circumstances. Ultimately, healthcare professionals must make their own treatment decisions on a case-by-case basis, after consultation with their patients, using their clinical judgment, knowledge and expertise.

Guidelines users must not edit or modify the Guidelines in any way – including removing any branding, acknowledgement, authorship or copyright notice.

Funding

The authors of this document gratefully acknowledge the support of the Friedreich Ataxia Research Alliance (FARA). The views and opinions expressed in the Guidelines are solely those of the authors and do not necessarily reflect the official policy or position of FARA.

14. Mental health issues in Friedreich ataxia

Caroline Spencer, Alexandra Durr, George Wilmot, Susan Perlman and Louise Corben

This chapter describes important mental health issues for individuals with Friedreich ataxia, including depression, anxiety and psychosis, and strategies for investigation and management. In making recommendations for management of these mental health conditions, the authors were tasked with answering the following questions:

For individuals with Friedreich ataxia, what is the best management for depression? (see 14.2) For individuals with Friedreich ataxia, what is the best management for anxiety? (see 14.3) For individuals with Friedreich ataxia, what is the best management for psychosis? (see 14.4)

14.1 Literature review of prevalence of mental health issues in Friedreich ataxia

Jennifer Farmer is acknowledged for much of the content of the literature review and overview of depression, taken from the previous version of the guidelines (2014).

While psychiatric symptoms are not part of the presenting or diagnostic clinical features of Friedreich ataxia (FRDA), published literature and clinical experience indicate that many individuals with FRDA experience depression, anxiety and associated mental health issues. Literature from the early 1900s suggests the presence of dementia and psychosis in individuals with FRDA. However, these reports were prior to clear diagnostic criteria and, in later publications thought to be complicated by misdiagnosis and selection bias (individuals reported were institutionalized and not a representative sample of individuals with the disease) (1, 2).

In a later study, Flood and colleagues (1) reported their clinical experience and a retrospective medical record review of 38 individuals who met the clinical diagnostic criteria for FRDA and attended the Ataxia Clinic at University of California Los Angeles. They found that whilst dementia and severe cognitive disturbances were rare, most (92%) individuals with FRDA had mood disturbances, ranging from a mild, grief-related, reactive depression to severe depression. They concluded that the depression was a consequence of living with a chronic, progressively disabling, neurological disease rather than being intrinsic to FRDA. This report elegantly reminds the clinician of the likely psychological impact of living with a disease that causes continual loss of abilities, loss of livelihood and loss of future. The authors further suggest that what are initially normal responses of grief and depression can become prolonged and clinicians need to consider that individuals with FRDA may be at an increased risk for major depression and suicide (1). Giordani and colleagues (2) also examined the psychological status of individuals with FRDA and reported significantly higher levels of anxiety, depression and social isolation than in controls. Both studies identified that FRDA not only affects the individual diagnosed with FRDA, but has a far-reaching effect on the entire family, particularly the burden and loss that they face over the prolonged course of the disease.

Others have also reported the frequency of affective disorders in small cohorts of individuals with FRDA (3-5). White and colleagues (4) reported neuropsychological and neuropsychiatric characteristics of 15 adults with FRDA (mean age 36.1 years). While finding some differences in performance on cognitive tests, there was no difference in mood disorders when screened with the Symptom Checklist-90 (SCL-90) and Hamilton depression scale compared to age-matched controls. A few of the subjects with FRDA did have a history of adjustment disorder with depressed mood. The authors specifically mentioned that one third of the individuals with FRDA demonstrated inappropriate jocularity during testing (4). Ciancarelli and colleagues (5) found that 29% of

individuals with FRDA (24 adults) had mood disorders, mostly depression, when assessed for cognitive disorders with a neuropsychiatric battery.

Mantovan and colleagues (3) administered the Minnesota Multiphasic Personality Inventory (MMPI) to eight adults with FRDA and half of the individuals showed a profile outside the normal range. None of the control participants demonstrated similar profiles. The personality pattern of the individuals with FRDA was characterized by increased irritability, poor impulse control, or blunting of affect. In addition, those with FRDA had low scores on the MMPI K scale and negative dissimulation index suggesting reduced defensiveness and a poor self-presentation. The authors point out that the significant physical disability associated with FRDA and having an onset in childhood and adolescence may play a significant role in the development of personality or lead to maladaptive behavior observed in this profile (3). Despite being a small cohort, the results of this investigation provide a fascinating insight into the little investigated area of personality characteristics related to FRDA. Findings from a more recent study support the existence of specific personality characteristics in FRDA (6). The authors hypothesize that diagnosis of FRDA during the crucial period of adolescence could partly explain this specific personality development (6).

Studies examining cognitive function in FRDA screened participants with and without FRDA for depression using the Beck Depression Inventory (BDI). The first two studies (7, 8) demonstrated significantly greater scores on the BDI in 15 and 13 individuals with FRDA, respectively, compared to a similar number of individuals without FRDA. Two later studies (9, 10) did not show a significant difference in BDI scores between participants with FRDA and those without FRDA (n = 13 and n = 10, respectively).

An exploratory study of transitional life events in individuals with FRDA highlighted that the usual transitional events in a person's life are exacerbated by the presence of FRDA. Moreover, such transitional events are accompanied by significant grief and loss associated with challenges to identify and self-esteem (11). As such it is not unusual to find a greater incidence of reactive depression in a cohort of individuals with FRDA compared to a control group. Indeed, one study has examined depression in individuals with FRDA in the context of neuroimaging (12). Twenty-two individuals with FRDA were screened for depression using the BDI followed by cerebral 3T MRI scans to examine volumetric differences between individuals with depression and those without. A little more than a third (36.3%) of individuals with FRDA fulfilled the DSM-IV criteria for major depression. Whilst this is higher than in the general population, it is similar to reports in other neurodegenerative diseases (12). There was no correlation between age, disease severity or disease duration and the BDI score. The MRI studies showed grey matter atrophy in the frontal lobe of depressed individuals with FRDA. In addition, the severity of depression correlated with atrophy in the right superior frontal gyrus. As discussed by the authors, whether the observed atrophy is due to long-term major depression or the neurodegenerative process of the disease cannot be ascertained (12).

Nieto and colleagues (13) surveyed 57 individuals with FRDA with the BDI and revealed significantly more depressive symptoms, as compared to a normative sample. Within the FRDA group, over half (59%) scored in the "minimal" range, while 19%, 18% and 4% scored in the "mild", "moderate", and "severe" ranges, respectively. Recently Perez-Flores and colleagues (14) surveyed 62 individuals with FRDA on health-related quality of life using the SF-36 Health Survey. Participants with FRDA scored significantly lower than the general population used for comparison on all domains of quality of life. The largest group differences were observed in the physical health and general health domains, with individuals with FRDA reporting significantly lower scores than the comparison group. Social and emotional dimensions were also significantly lower in individuals with FRDA, although differences

from the comparison group were smaller. These findings remained significant even when taking age and gender into account, leading the authors to conclude that FRDA is associated with significant negative effects on quality of life, including physical, social, and emotional impacts.

14.2 Management of depression in Friedreich ataxia

Clinicians should be highly attuned to the possibility of depression and associated mental health issues in individuals with FRDA and ensure these issues are proactively and effectively managed. In a large cohort of individuals with FRDA (n=650), 14.2% reported depression (15). Grief and sadness are common among individuals with FRDA, particularly as they deal with significant transitional times such as ceasing to walk, and dealing with adolescence and early adulthood (11). Transitional times often highlight the sense of loss and present significant challenges to an individual's sense of identity (11). Many of these individuals also present with irritability due to frustration of trying to perform activities of daily living. As one person with FRDA stated "Every small detail of their lives consumes more and more of the time they used to devote to work, play and other independent activity" (1).

If depression or other mental health issues are suspected in individuals with FRDA, proactive management should include referral to appropriate clinicians, instigation of pharmacological therapy if indicated and referral for counseling. In particular, given the prevalence of depression in individuals with FRDA and the impact on quality of life, clinicians should be vigilant to the possibility of depression and provide timely intervention. The clinical experience of the authors indicates there is no difference in response to antidepressant medication in individuals with FRDA compared to those without FRDA. For this reason, it is important to make sure individuals with FRDA are screened for depression, particularly as the consequences of depression are major (suicidal thoughts, hospitalization, lack of engagement in social activities and/or physical therapy programs) and clinical experience suggests that individuals with FRDA may not recognize depressive symptoms. Clinicians also need to consider both the degree of depression and the possibility of masking of symptoms by associated FRDA-related symptoms such as fatigue. As such, careful assessment of the severity of depression is warranted. Given individuals with FRDA may be reluctant to recognize symptoms of depression, the first line of clinical management may be counseling. However, it is important to explore what will work best for individual with FRDA, particularly in the context of the other aspects of their lives, such as accessibility requirements of face-to face counseling and time constraints for work/study/family. The clinician may consider treating depressive symptoms with both counseling and medication. Preventive measures such as counseling at major life stages such as going to college, or leaving home may be very helpful. Counseling may also be appropriate for parents/carers of individuals with FRDA.

Lifestyle changes (such as exercise, diet, social activities) may have a positive impact on depression. Conversely, depression may impact on the motivation to engage with lifestyle changes. This could be helped by the use of antidepressants. As such, lifestyle changes may be used in in conjunction with other treatments, particularly medication. There may, however, be significant barriers to participation related to FRDA that would need to be addressed to enable lifestyle changes and these FRDA—related factors may also exacerbate underlying depression. A multidisciplinary approach to facilitating engagement in lifestyle changes may assist. Suicidal or more severely depressed individuals with FRDA are likely to need more targeted therapy.

While it is apparent that depression and associated mental health issues may be a greater risk for individuals with FRDA, it is still not clear if the greater prevalence is due to the pathology associated with FRDA, the environmental/lifestyle changes imposed by the presence of the condition, or a combination of the two. Further research is required to understand the mechanism associated with

mental health issues in individuals with FRDA. Further research is also required to identify significant periods during the disease process when an individual may be at greater risk and therefore requiring prophylactic intervention including, but not confined to, intense and targeted counseling.

Best practice statements

Individuals with Friedreich ataxia require regular evaluation in terms of risks for developing depression and/or other mental health issues.

Individuals with Friedreich ataxia may benefit from regular counseling to assist in adjusting to transitional events and possibly prevent the emergence of related depression.

Individuals with Friedreich ataxia identified with depression should be treated with established interventions including counseling +/- pharmacological agents.

The risk of suicide in individuals with Friedreich ataxia should be considered and managed proactively.

Recommendations

Grading for strength of recommendation and level of evidence

For the rating of the **strength** of the recommendation, in addition to evidence from studies in FRDA, evidence from like conditions, clinical experience and expert consensus are taken into account when published evidence is not available.

The **level of evidence** is based on published evidence from studies in FRDA. If there is no published evidence in FRDA, evidence from other like conditions or clinical expertise may have been used to make the recommendation – this is graded as 'very low' or in some cases 'low' level evidence. See the table below for an explanation of the symbols used to grade recommendations.

Strength of recommendation	Symbol	Level of evidence	Symbol
Strong for intervention	$\uparrow \uparrow$	High	$\oplus \oplus \oplus \oplus$
Conditional for intervention	↑	Moderate	$\oplus \oplus \oplus \bigcirc$
Neither intervention nor comparison		Low	$\oplus \oplus \bigcirc\bigcirc$
Conditional against intervention	→	Very low	\oplus
Strong against intervention	$\downarrow \downarrow$		

Antidepressant medication

Should antidepressant medication versus none be used for depressed individuals with Friedreich ataxia?	Strength	Level of evidence
We conditionally recommend the use of antidepressant medication in individuals with Friedreich ataxia who present with symptoms of depression.	↑	⊕○○○

Justification: Cohort studies indicate that the presence of depressive symptoms may be greater in individuals with Friedreich ataxia than those without Friedreich ataxia. Whilst there is no published evidence in Friedreich ataxia, if treatment is efficacious then the desirable effect on

individuals who are depressed would be large. Clinical experience of the authors indicates there is no difference in response rate in individuals with Friedreich ataxia compared to those without Friedreich ataxia, when they accept use of medication. Individuals with Friedreich ataxia are less likely to accept a diagnosis of depression; however, there is no reason why they would not respond to treatment after accepting that treatment may be of benefit. For this reason, it is important to make sure individuals with Friedreich ataxia are screened and clinicians are alert to the possibility of depression.

Note, the consequences of depression are major (suicidal, hospitalization) and the experience of the expert authors indicate individuals with Friedreich ataxia may not recognize depressive symptoms. Clinicians need to be very careful in considering both the degree of depression and the possibility of masking of symptoms. As such, careful assessment of severity of depression is warranted.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and depression and should be implemented according to an assessment of the severity of depression. Balance of side effects versus efficacy needs to be taken into account when considering treatment options.

Counseling for depression

Should counseling or therapy versus none or antidepressant prescription be used for depressed individuals with Friedreich ataxia?	Strength	Level of evidence
We recommend counseling or therapy over no counseling in individuals with Friedreich ataxia who present with symptoms of depression.	个个	⊕○○○

Justification: Cohort studies indicate that the presence of depressive symptoms may be greater in individuals with Friedreich ataxia than those without Friedreich ataxia. Whilst there is no published evidence in Friedreich ataxia, if counseling is efficacious then the desirable effect on individuals who are depressed would be large. Given individuals with Friedreich ataxia may be reluctant to recognize symptoms of depression, the first line of clinical management may be counseling. It is important that clinicians explore what will work best for individuals with Friedreich ataxia, particularly in the context of the other aspects of their lives (accessibility requirements of face to face counseling, time constraints for work/study/family, etc.). The clinician may need to consider treating depressive symptoms with both counseling and medication. In addition, it is important for the clinician to be aware of the role of fatigue in depression (and perhaps presenting as depression).

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and depression. It may be difficult for a person with severe dysarthria to engage in counseling. Counseling may be very helpful at major life stages such as going to college, leaving home etc. Counseling may also be appropriate for parents/carers of individuals with Friedreich ataxia.

Lifestyle changes for depression

Should lifestyle changes (exercise, diet, social activities) versus none or antidepressant treatment be used for depressed individuals with Friedreich ataxia?	Strength	Level of evidence
We recommend lifestyle changes (exercise, diet, social activities) either prior to or in conjunction with other interventions, including antidepressants, for individuals with Friedreich ataxia who have symptoms of depression.	↑ ↑	⊕○○○

Justification: Lifestyle changes may have a positive impact on depression. However, the use of antidepressants may assist in facilitating participation if depression is associated with lack of motivation. Therefore, lifestyle changes may be used in in conjunction with other treatments, particularly medication. There may be significant barriers to participation related to Friedreich ataxia that would need to be addressed to enable lifestyle changes.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and depression. Consideration should be given to the stage of Friedreich ataxia, the age of the person, and the level of depression (mild vs severe). Suicidal or more severely depressed individuals with Friedreich ataxia may need more targeted therapy.

Lay summary

Lay summary of clinical recommendations for depression in Friedreich ataxia

Individuals with Friedreich ataxia often report mental health concerns. These issues can vary in nature throughout the person's life, and often include depression. Mental health concerns can affect physical, emotional, and social wellbeing.

Why these recommendations?

There are various strategies that may help a person with Friedreich ataxia experiencing depression.

Medication

Due to a lack of studies, there is no direct evidence showing the benefits of medication for treating depression in individuals with Friedreich ataxia. However, if medication is effective for treating depression, the benefit to the individual would be large, so it may be worth trying. Ways to limit undesirable side effects (such as dizziness or worsening balance), which would likely have a greater impact on individuals with Friedreich ataxia than other people, should be considered.

Counselling

While there is no direct evidence for the benefits of counselling in individuals with Friedreich ataxia who have depression, we recommend counselling to treat depression. If counselling is effective, the benefit would be large and there are unlikely to be any undesirable effects.

Lifestyle changes

We recommend lifestyle changes (e.g., exercise, healthy diet, greater social activities) before, or at the same time as other treatments for depression in Friedreich ataxia. Although there is little research evidence that lifestyle changes will improve depression symptoms, the clinical experience of the authors supports the benefits of lifestyle changes.

What does this mean for you as a person living with Friedreich ataxia or caring for someone living with Friedreich ataxia?

Research shows that individuals with Friedreich ataxia experience depression more frequently than others in the general population. It is important to talk to your doctor or other healthcare professional if you feel this may be an issue for you or someone you care for. A health professional will assess whether the use of behavioural management, counselling, medication, alternative therapies and/or a specific diet may be appropriate for you.

Who are these recommendations specifically for?

These recommendations are relevant to all individuals with Friedreich ataxia who have symptoms of depression. Consideration should be given to treatments that are best suited to the age of the individual, the specific diagnosis and the severity of symptoms.

14.3 Management of anxiety in Friedreich ataxia

Whilst anxiety has not often been explicitly studied in individuals with FRDA, it appears to not be as common as depression. In a large cohort (n=650) of individuals with FRDA, 20 (3.1%) reported experiencing anxiety (15). Importantly, 18 of those 20 were in the typical onset group, which had a prevalence of 3.3% (15). The clinical experience of the authors indicates there is no difference in response to anti-anxiety medication in individuals with FRDA, compared to those without FRDA. There have not been any studies in FRDA, but if anti-anxiety medication is efficacious as in the general population, then the desirable effect on individuals who are anxious would be large.

It is important to make sure individuals with FRDA are screened and clinicians are alert to the possibility of anxiety. In addition, clinicians should explore what will work best for an individual with FRDA, particularly in the context of other aspects of their lives, such as accessibility requirements of face-to-face counseling and time constraints for work/study/family. The clinician may need to consider treating symptoms of anxiety with both counseling and medication.

Recommendations

Anti-anxiety medication

Should anti-anxiety medication versus none be used for anxiety in individuals with Friedreich ataxia?	Strength	Level of evidence
We conditionally recommend the use of anti-anxiety medication in individuals with Friedreich ataxia who present with symptoms of anxiety.	↑	⊕○○○

Justification: Cohort studies indicate the presence of anxiety symptoms in individuals with Friedreich ataxia. Whilst there is no published evidence in Friedreich ataxia, if treatment is efficacious then the desirable effect on individuals who are anxious would be large. Clinical experience of the authors indicates there is no difference in response to medication in individuals with Friedreich ataxia, when they accept the use of medication, compared to those without Friedreich ataxia. It is important to make sure individuals with Friedreich ataxia are screened and clinicians are alert to the possibility of anxiety.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and symptoms of anxiety and should be implemented according to an assessment of the severity of anxiety. Balance of side-effects versus efficacy needs to be taken into account when considering treatment options.

Counseling for anxiety

Should counseling or therapy versus none or anti-anxiety prescription be used for anxiety in individuals with Friedreich ataxia?	Strength	Level of evidence
We recommend counseling or therapy over no counseling for individuals with Friedreich ataxia who present with symptoms of anxiety.	个个	⊕○○○

Justification: While there is no published evidence in Friedreich ataxia, if counseling is efficacious then the desirable effect on individuals who are anxious would be large. It is important clinicians explore what will work best for an individual with Friedreich ataxia, particularly in the context of other aspects of their lives (accessibility requirements of face-to-face counseling, time constraints for work/study/family, etc.). The clinician may need to consider treating symptoms of anxiety with both counseling and medication.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and symptoms of anxiety. It may be difficult for a person with severe dysarthria to engage in counseling. Consideration should be given to a possible link between visual disturbance and the emergence of anxiety.

Lifestyle changes for anxiety

Should lifestyle changes (exercise, diet, social activities) versus none or anti-anxiety treatment be used for anxiety patients with Friedreich ataxia?	Strength	Level of evidence
We conditionally recommend <i>against</i> lifestyle changes as a primary intervention to treat anxiety in individuals with Friedreich ataxia, favoring anti-anxiety medication or counseling prior to or in conjunction with any lifestyle changes.	\	⊕○○○

Justification: There is a lack of research on the effectiveness of lifestyle changes in treating anxiety in individuals with Friedreich ataxia. Medication and/or counseling are likely to be more efficacious.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and symptoms of anxiety.

Lay summary

Lay summary of clinical recommendations for anxiety in Friedreich ataxia

Individuals with Friedreich ataxia often report mental health concerns. These issues can vary in nature throughout the person's life, and often include anxiety. Mental health concerns can affect physical, emotional, and social wellbeing.

Why these recommendations?

There are various strategies that may help a person with Friedreich ataxia experiencing anxiety.

Medication

Due to a lack of studies, there is no direct evidence showing the benefits of anti-anxiety medication for treating anxiety in individuals with Friedreich ataxia. However, if medication is effective for treating anxiety symptoms, the benefit to the individual would be large. Ways to limit undesirable side effects (such as dizziness or worsening balance), which would likely have a greater impact on individuals with Friedreich ataxia than other people, should be considered.

Counselling

While there is no direct evidence for the benefits of counselling in individuals with Friedreich ataxia who have anxiety, we recommend counselling to treat these conditions. If counselling is effective, the benefit would be large and there are unlikely to be any undesirable effects.

Lifestyle changes

There is little research or clinical experience indicating that lifestyle changes will improve anxiety. Thus, we recommend other interventions, such as medication or counselling, over lifestyle changes for individuals experiencing anxiety.

What does this mean for you as a person living with Friedreich ataxia or caring for someone living with Friedreich ataxia?

It is important to talk to your doctor or other healthcare professional if you feel anxiety may be an issue for you or someone you care for. A health professional will assess whether the use of behavioural management, counselling or medication may be appropriate for you.

Who are these recommendations specifically for?

These recommendations are relevant to all individuals with Friedreich ataxia who have symptoms of anxiety. Consideration should be given to treatments that are best suited to the age of the individual, the specific diagnosis and the severity of symptoms.

14.4 Management of psychosis in Friedreich ataxia

The clinical experience of the expert authors and case reports (16-19) supports the existence of psychosis in individuals with FRDA, albeit rare, particularly in end-stage disease. Medications such as quetiapine (19), aripiprazole (16) and risperidone (18) are all reported as effective in treating psychosis in FRDA. It should be noted, however, that as psychosis is more likely to be in end-stage rather than earlier stage FRDA, it may be hard to judge the efficacy of medication, particularly if severe dysarthria is present. Therefore, involving family and carers in treatment monitoring is important.

For those individuals in the earlier stage of FRDA who experience an onset of psychosis it is important to exclude other sources of psychosis such as use of recreational or prescription drugs, hypoxia due to sleep disordered breathing or an onset of schizophrenia. Ganos and colleagues (17) reported a case of a 29-year-old male with FRDA who developed irrationality, paranoid delusions, auditory hallucinations and somatic sensations four days after receiving intravenous amiodarone to manage an episode of paroxysmal tachyarrhythmia. It is imperative that primary health care providers are alert to and consider psychosis in individuals, particularly in those with advanced FRDA, but also those earlier in the disease trajectory. In addition, interdisciplinary management, including treating neurologists, psychiatrists, and tertiary health care givers, will ensure best possible treatment for these individuals (17).

Recommendations

Anti-psychotic medication

Should antipsychotic medication versus none be used for psychosis in individuals with Friedreich ataxia?	Strength	Level of evidence
We conditionally recommend the use of antipsychotic medication in individuals with Friedreich ataxia with confirmed episodes of psychosis.	↑	⊕○○○

Justification: Antipsychotics should work as well in individuals with Friedreich ataxia as in those without Friedreich ataxia. It is important for the primary healthcare provider to be alert to and consider psychosis in individuals with advanced Friedreich ataxia.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and a confirmed diagnosis of psychosis. Individuals who have severe dysarthria require careful screening to ensure accurate diagnosis.

Counseling for psychosis

Should counseling or therapy versus none or antipsychotic prescription be used for psychosis in individuals with Friedreich ataxia?	Strength	Level of evidence
We conditionally recommend <i>against</i> the use of counseling or therapy over antipsychotic medication in cases of acute psychosis in Friedreich ataxia.	\	⊕○○○

Justification: The expert authors consider counseling in cases of acute psychosis to be not as efficacious as antipsychotic medication. Counseling for the family may be useful and counseling post-psychotic episode may be of benefit.

Subgroup considerations: This recommendation is for individuals with Friedreich ataxia and a confirmed diagnosis of psychosis. Individuals who have severe dysarthria require careful screening to ensure an accurate diagnosis of psychosis.

Lay summary

Lay summary of clinical recommendations for psychosis in Friedreich ataxia

Individuals with Friedreich ataxia often report mental health concerns. These issues can vary in nature throughout the person's life and can affect physical, emotional, and social wellbeing. Although rare, some individuals of advanced age and severity of Friedreich ataxia can experience symptoms of psychosis including sensory hallucinations and paranoia.

Why these recommendations?

Medication

For individuals with Friedreich ataxia who experience episodes of psychosis, we recommend the use of antipsychotic medication, according to the specific diagnosis. Management of psychosis with antipsychotic medication should be no different for people with Friedreich ataxia than for other people.

Counselling

Although counselling can be beneficial for some mental health issues, in the case of psychosis, we recommend using medication rather than counselling because medication is likely to be more effective.

What does this mean for you as a person living with Friedreich ataxia or caring for someone living with Friedreich ataxia?

An individual experiencing an episode of psychosis will need to be assessed by a doctor or psychiatrist. Once a diagnosis of psychosis is made, the doctor will assess which medication may be appropriate to treat your particular symptoms.

Who are these recommendations specifically for?

These recommendations are relevant to all individuals with Friedreich ataxia experiencing an episode of psychosis. Consideration should be given to treatments that are best suited to the age of the individual and the severity of symptoms.

Author details

Louise Corben, PhD

Principal Research Fellow, Murdoch Children's Research Institute, Melbourne, Victoria, Australia Email: louise.corben@mcri.edu.au

Alexandra Durr, MD, PhD

Professor of Neurogenetics, Sorbonne Université, Paris, France

Email: alexandra.durr@icm-institute.org

Susan Perlman, MD

Clinical Professor of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California, USA

Email: sperlman@ucla.edu

Caroline Spencer, PhD

Postdoctoral Fellow, Boston University, Boston, Massachusetts, USA

Email: cspencer@bu.edu

George Wilmot, MD, PhD

Associate Professor, Department of Neurology, Emory University, Atlanta, Georgia, USA

Email: gwilmot@emory.edu

References

- 1. Flood MK, Perlman SL. The mental status of patients with Friedreich's ataxia. J Neurosci Nurs. 1987;19(5):251-5.
- 2. Giordani B, Boivan M, Berent S, Gilman S, Junck L, Lehtinen S, et al. Cognitive and emotional function in Friedreich's ataxia (Abstract). J Clin Exp Neuropsychol. 1989;11(1):53-4.
- 3. Mantovan MC, Martinuzzi A, Squarzanti F, Bolla A, Silvestri I, Liessi G, et al. Exploring mental status in Friedreich's ataxia: a combined neuropsychological, behavioural and neuroimaging study. Eur J Neurol. 2006;13:827-35.
- 4. White M, Lalonde R, Botez-Marquard T. Neuropsychologic and neuropsychiatric characteristics of patients with Friedreich's ataxia. Acta Neurol Scand. 2000;102(4):222-6.
- 5. Ciancarelli I, Cofini V, Carolei A. Evaluation of neuropsychological functions in patients with Friedreich ataxia before and after cognitive therapy. Funct Neurol. 2010;25(2):81-5.
- 6. Sayah S, Rotge JY, Francisque H, Gargiulo M, Czernecki V, Justo D, et al. Personality and neuropsychological profiles in Friedreich ataxia. Cerebellum. 2018;17(2):204-12.
- 7. Corben LA, Delatycki MB, Bradshaw JL, Horne MK, Fahey MC, Churchyard AC, et al. Impairment in motor reprogramming in Friedreich ataxia reflecting possible cerebellar dysfunction. J Neurol. 2010;257(5):782-91.
- 8. Corben LA, Delatycki MB, Bradshaw JL, Churchyard AJ, Georgiou-Karistianis N. Utilisation of advance motor information is impaired in Friedreich ataxia. Cerebellum. 2011;10(4):793-803.
- 9. Corben LA, Akhlaghi H, Georgiou-Karistianis N, Bradshaw JL, Egan GF, Storey E, et al. Impaired inhibition of prepotent motor tendencies in Friedreich ataxia demonstrated by the Simon interference task. Brain Cogn. 2011;76(1):140-5.
- 10. Corben LA, Georgiou-Karistianis N, Bradshaw JL, Hocking DR, Churchyard AJ, Delatycki MB. The Fitts task reveals impairments in planning and online control of movement in Friedreich ataxia: reduced cerebellar-cortico connectivity? Neuroscience 2011;192(382-390).
- 11. White BV, Leib JR, Farmer JM, Biesecker BB. Exploration of transitional life events in individuals with Friedreich ataxia: implications for genetic counseling. Behav Brain Funct. 2010;6(65).

- 12. da Silva CB, Yasuda CL, D'Abreu A, Cendes F, Lopes-Cendes I, Franca MC, Jr. Neuroanatomical correlates of depression in Friedreich's ataxia: a voxel-based morphometry study. Cerebellum. 2013;12(3):429-36.
- 13. Nieto A, Hernandez-Torres A, Perez-Flores J, Monton F. Depressive symptoms in Friedreich ataxia. Int J Clin Health Psychol. 2018;18(1):18-26.
- 14. Perez-Flores J, Hernandez-Torres A, Monton F, Nieto A. Health-related quality of life and depressive symptoms in Friedreich ataxia. Qual Life Res. 2020;29(2):413-20.
- 15. Reetz K, Dogan I, Hohenfeld C, Didszun C, Giunti P, Mariotti C, et al. Nonataxia symptoms in Friedreich Ataxia: Report from the Registry of the European Friedreich's Ataxia Consortium for Translational Studies (EFACTS). Neurology. 2018;91(10):e917-e30.
- 16. Chan YC. Aripiprazole treatment for psychosis associated with Friedreich's ataxia. Gen Hosp Psychiatry. 2005;27(5):372.
- 17. Ganos C, Schottle D, Zuhlke C, Munchau A. Psychosis complicating Friedreich ataxia. Mov Disord Clin Pract. 2015;2(1):84-5.
- 18. Salbenblatt MJ, Buzan RD, Dubovsky SL. Risperidone treatment for psychosis in end-stage Friedreich's ataxia. Am J Psychiatry. 2000;157(2):303.
- 19. Oruç S, Gulseren G, Kusbeci OY, Yaman M, Geçici O. Quetiapine treatment for psychosis in Friedreich's ataxia. Klinik Psikofarmakoloji Bulteni Bulletin of Clinical Psychopharmacology. 2012;22:357-8.