

QUESTION

Should lifestyle changes (exercise, diet, social activities) vs. none or anti-anxiety treatment be used for anxiety patients with Friedreich ataxia?

POPULATION:	anxiety patients with Friedreich ataxia
INTERVENTION:	lifestyle changes (exercise, diet, social activities)
COMPARISON:	none or anti-anxiety treatment
MAIN OUTCOMES:	Less anxiety; Less anxiety; Better coping/outlook; Quality of life; Quality of life;

ASSESSMENT

Problem

Is the problem a priority?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> <input type="radio"/> No <input type="radio"/> Probably no <input checked="" type="radio"/> Probably yes <input type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 	<p>In cohort of 650 individuals with FA 20/560 (3.1%) reported anxiety. Within the subset of those in the typical age of onset group (n=540), 3.3% reported anxiety (Reetz et al, 2018). Notably, 60% of individuals with anxiety had co-morbidities related to visual disturbance.</p>	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of anxiety.</p> <p>4/6 indicated that the problem was serious, 2/6 indicated probably serious.</p> <p>4/6 indicated that the problem was urgent, 1/6 indicated probably urgent, 1/6 indicated probably not urgent.</p> <p>4/6 indicated that the problem was a priority, 2/6 indicated probably a priority. (Aug 2020)</p>

Desirable Effects

How substantial are the desirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS												
<ul style="list-style-type: none"> <input type="radio"/> Trivial <input checked="" type="radio"/> Small <input type="radio"/> Moderate <input type="radio"/> Large <input type="radio"/> Varies <input type="radio"/> Don't know 	<table border="1"> <thead> <tr> <th>Outcomes</th> <th>No of participants (studies) Follow up</th> <th>Certainty of the evidence (GRADE)</th> <th>Relative effect (95% CI)</th> <th colspan="2">Anticipated absolute effects* (95% CI)</th> </tr> </thead> <tbody> <tr> <td></td> <td></td> <td></td> <td></td> <th>Risk with none or anti-anxiety treatment</th> <th>Risk difference with lifestyle changes (exercise, diet, social activities)</th> </tr> </tbody> </table>	Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)						Risk with none or anti-anxiety treatment	Risk difference with lifestyle changes (exercise, diet, social activities)	<p>There is low-level evidence which suggest that exercise is associated with lower anxiety levels, particularly in those who are engaged in more vigorous sport activity. This may not be applicable to those with advanced FRDA.</p>
Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)										
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Less anxiety assessed with: State-Trait Anxiety Inventory	0 (1 observational study) ¹	_a,b,c,d,e,f	-	Participants with cerebral palsy (n=23), traumatic brain injury (n=6), multiple sclerosis (n=7) and Friedreich ataxia (n=7) were divided into 4 cohorts: 2 competitive Boccia (IC: independent competitive, and NIC: nonindependent competitive), recreational Boccia and control groups. The participants were followed for 4 months between pre and post tests and all underwent an individualised rehabilitation program. A one-way ANOVA and MANOVA were used to examine the effect of training on scores of psychosocial variables with one and multiple levels, respectively. There were no between-group differences in the STAI ($p \geq 0.05$).
Less anxiety assessed with: General Health Questionnaire-28	0 (1 observational study) ¹	_a,b,c,d,e,f	-	Participants with cerebral palsy (n=23), traumatic brain injury (n=6), multiple sclerosis (n=7) and Friedreich ataxia (n=7) were divided into 4 cohorts: 2 competitive Boccia (IC: independent competitive, and NIC: nonindependent competitive), recreational Boccia and control groups. The participants were followed for 4 months between pre and post tests and all underwent an individualised rehabilitation program. A one-way ANOVA and MANOVA were used to examine the effect of training on scores of psychosocial variables with one and multiple levels, respectively. There were no between-group differences in the GHQ-28.
Better coping/outlook assessed with: Rosenberg Self-Esteem Scale	0 (1 observational study) ¹	_a,b,c,d,e,f	-	Participants with cerebral palsy (n=23), traumatic brain injury (n=6), multiple sclerosis (n=7) and Friedreich ataxia (n=7) were divided into 4 cohorts: 2 competitive Boccia (IC: independent competitive, and NIC: nonindependent competitive), recreational Boccia and control groups. The participants were followed for 4 months between pre and post tests and all underwent an individualised rehabilitation program. A one-way ANOVA and MANOVA were used

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Quality of life assessed with: World Health Organization Quality of Life-BREF assessment	0 (1 observational study) ¹	_a,b,c,d,e,f	-	Participants with cerebral palsy (n=23), traumatic brain injury (n=6), multiple sclerosis (n=7) and Friedreich ataxia (n=7) were divided into 4 cohorts: 2 competitive Boccia (IC: independent competitive, and NIC: nonindependent competitive), recreational Boccia and control groups. The participants were followed for 4 months between pre and post tests and all underwent an individualised rehabilitation program. A one-way ANOVA and MANOVA were used to examine the effect of training on scores of psychosocial variables with one and multiple levels, respectively. Change in psychosocial parameters was not significantly influenced by the study group ($p \geq 0.05$). The four groups improved significantly from pre- to posttest in WHOQOL-BREF Physical: IC group (pretest mean 16.11, SD 5.25 to mean posttest 28.77 SD 3.15), NIC group (pretest mean 17.00, SD 6.65 to posttest mean 30.28, SD 12.60), recreational group (pretest mean 12.92, SD 5.45 to posttest mean 24.50, SD 6.69), control group (pretest mean 10.92, SD 4.57 to posttest mean 24.92, SD 5.34). In addition, the control group also showed improvements in WHOQOL-BREF Psychological (pretest mean 11.69, SD 5.60 to posttest mean 17.30, SD 7.36).
Quality of life assessed with: General Health	0 (1 observational study)	_a,b,c,d,e,f	-	Participants with cerebral palsy (n=23), traumatic brain injury (n=6), multiple sclerosis (n=7) and Friedreich ataxia (n=7) were divided into 4 cohorts: 2

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Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS														
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Certainty of evidence

What is the overall certainty of the evidence of effects?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ● Very low ○ Low ○ Moderate ○ High ○ No included studies 	<p>Very low certainty of effects as per the evidence profile table.</p>	

Values

Is there important uncertainty about or variability in how much people value the main outcomes?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Important uncertainty or variability ○ Possibly important uncertainty or variability ● Probably no important uncertainty or variability 		

o No important uncertainty or variability

Outcomes	Importance	Certainty of the evidence (GRADE)
Less anxiety assessed with: State-Trait Anxiety Inventory	CRITICAL ^a	_b,c,d,e,f,g
Less anxiety assessed with: General Health Questionnaire-28	CRITICAL ^a	_b,c,d,e,f,g
Better coping/outlook assessed with: Rosenberg Self-Esteem Scale	IMPORTANT ^h	_b,c,d,e,f,g
Quality of life assessed with: World Health Organization Quality of Life-BREF assessment	CRITICAL ⁱ	_b,c,d,e,f,g
Quality of life assessed with: General Health Questionnaire-28	CRITICAL ⁱ	_b,c,d,e,f,g

- a. Identified as important (3/6), critical (3/6) by people with FA and important by expert authors on this topic
- b. Participants with a diagnosis of FRDA n=7/43.
- c. Single study published.
- d. Confidence intervals not reported.
- e. Small sample size in each group (ranging from n=7 to n=14).
- f. Lack of allocation concealment and blinding.
- g. Recruitment bias (all from State Referral Centre)
- h. Identified as low importance (1/6), important (3/6), critical (2/6) by people with FA and important by expert authors on this topic
- i. Identified as important (3/6), critical (3/6) by people with FA and important by expert authors on this topic

Balance of effects

Does the balance between desirable and undesirable effects favor the intervention or the comparison?

JUDGEMENT

RESEARCH EVIDENCE

ADDITIONAL CONSIDERATIONS

<ul style="list-style-type: none"> ○ Favors the comparison ● Probably favors the comparison ○ Does not favor either the intervention or the comparison ○ Probably favors the intervention ○ Favors the intervention ○ Varies ○ Don't know 		
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Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no ● Probably yes ○ Yes ○ Varies ○ Don't know 	No published evidence.	<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if lifestyle changes for people with anxiety was acceptable (weighing up the balance between benefits, harms and costs).</p> <p>2/4 indicated the intervention was acceptable, 1/4 indicated probably acceptable, 1/4 indicated not acceptable. (Aug 2020).</p>

SUMMARY OF JUDGEMENTS

	JUDGEMENT						
PROBLEM	No	Probably no	Probably yes	Yes		Varies	Don't know
DESIRABLE EFFECTS	Trivial	Small	Moderate	Large		Varies	Don't know
UNDESIRABLE EFFECTS	Large	Moderate	Small	Trivial		Varies	Don't know
CERTAINTY OF EVIDENCE	Very low	Low	Moderate	High			No included studies
VALUES	Important uncertainty or variability	Possibly important uncertainty or variability	Probably no important uncertainty or variability	No important uncertainty or variability			
BALANCE OF EFFECTS	Favors the comparison	Probably favors the comparison	Does not favor either the intervention or the comparison	Probably favors the intervention	Favors the intervention	Varies	Don't know
ACCEPTABILITY	No	Probably no	Probably yes	Yes		Varies	Don't know

TYPE OF RECOMMENDATION

Strong recommendation against the intervention <input type="radio"/>	Conditional recommendation against the intervention <input checked="" type="radio"/>	Conditional recommendation for either the intervention or the comparison <input type="radio"/>	Conditional recommendation for the intervention <input type="radio"/>	Strong recommendation for the intervention <input type="radio"/>
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CONCLUSIONS

Recommendation

We conditionally recommend against 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 FRDA. Medication and/or counseling are likely to be more efficacious.

Subgroup considerations

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

Research priorities

Research on the effectiveness of lifestyle changes in treating anxiety in individuals with FRDA.

Reference

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).

