

QUESTION

Should sensory specific training vs. no training be used for all individuals with Friedreich ataxia?	
POPULATION:	all individuals with Friedreich ataxia
INTERVENTION:	sensory specific training
COMPARISON:	no training
MAIN OUTCOMES:	Sensation; Neurological Function; Neurological function; Neurological function; Independence in daily activities;
SETTING:	
PERSPECTIVE:	
BACKGROUND:	
CONFLICT OF INTERESTS:	

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 type="radio"/> Probably yes <input checked="" type="radio"/> Yes <input type="radio"/> Varies <input type="radio"/> Don't know 		<p>The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were interviewed on the consequences, urgency and priority of the topic.</p> <p>8/8 indicated upper limb dysfunction was serious.</p> <p>1/7 indicated upper limb dysfunction was not urgent; 1/7 indicated probably not urgent; 1/7 indicated probably urgent; 4/7 indicated urgent.</p> <p>1/7 indicated upper limb dysfunction was probably not a priority, 3/7 indicated probably a priority, 3/7 indicated 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 		

- Moderate
- Large
- Varies
- Don't know

Outcomes	No of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
				Risk with no training	Risk difference with sensory specific training
Sensation - not measured	-	-	-	-	-
Neurological Function assessed with: SARA follow up: mean 6 weeks	9 (1 observational study) ¹	⊕○○○ VERY LOW ^{a,b,c,d,e}	-	11 people with autosomal dominant spinocerebellar ataxia (n=6) or Friedriech ataxia (n=5) wore a wearable proprioceptive stabilizer for 5 days/week, 180 min/day for 3 weeks. The Friedman analysis of variance by ranks was used to identify treatment effects across timepoints and the Wilcoxon-signed rank test was used to identify post hoc comparisons in the case of statistically significance. Statistically significant improvement in the SARA between baseline (mean 10.7, SD 3.1) and 3 weeks of device use (mean 9.55, SD 3.06, $p=0.027$) was identified.	
Neurological function assessed with: 9HPT follow up: mean 6 weeks	9 (2 observational studies) ^{1,2}	⊕○○○ VERY LOW ^{a,b,c,d,e}	-	11 people with autosomal dominant spinocerebellar ataxia (n=6) or Friedriech ataxia (n=5) wore a wearable proprioceptive stabilizer for 5 days/week, 180 min/day for 3 weeks. The Friedman analysis of variance by ranks was used to identify treatment effects across timepoints and the Wilcoxon-signed rank test was used to identify post hoc comparisons in the case of statistically significance. Statistically significant improvement in the 9HPT (dominant hand) between baseline (mean 35.6 seconds, SD 9.1) and 3 weeks of device use (mean 31.2 seconds, SD 4.99, $p=0.008$) was identified. (Leonardi et al 2016)	
				25 people with multiple sclerosis	

				underwent an 8-week controlled whole-body vibration training (CWBV), 3x/week. Paired t-tests were used to analyse 9HPT scores pre and post training. There were no statistically significant changes between either dominant ($p=0.053$) or non-dominant 9HPT ($p=0.059$). (Yang et al 2016).
Neurological function assessed with: Grooved Pegboard test	0 (1 observational study) ³	⊕○○○ VERY LOW ^{e,f}	-	13 people with multiple sclerosis and 12 age and sex matched controls underwent sensory nerve stimulation (aTENS) in two sessions with current applied only during the second visit. A within-group comparison of mean values identified significant improvements in the time taken to complete the groove pegboard (mean 110 seconds, SD 43 to mean 99 seconds, SD 37, $p=0.004$).
Independence in daily activities - not measured	-	-	-	-

1. Leonardi L, Aceto MG, Marcotulli C et al.. A wearable proprioceptive stabilizer for rehabilitation of limb and gait ataxia in hereditary cerebellar ataxias: a pilot open labeled study. *Neurol Sci*; 2017.
 2. Yang F., Estrada E.F., Sanchez M.C.. Vibration training improves disability status in multiple sclerosis: A pretest-posttest pilot study. . *J. Neurol. Sci.*; 2016.
 3. Almuklass A.M., Capobianco R.A., Feeney D.F., Alvarez E., Enoka R.M.. Sensory nerve stimulation causes an immediate improvement in motor function of persons with multiple sclerosis: A pilot study. . *Mult. Scler. Relat. Disord.* ; 2020.
- a. Five people with FRDA (n=5) within a sample of 11 people (n=11).
 - b. One study published only.
 - c. N=2 withdrawals from the study.
 - d. Small sample size.
 - e. Confidence intervals not provided. (Non-parametric data.)
 - f. No participants with an FRDA diagnosis.

Undesirable Effects

How substantial are the undesirable anticipated effects?

JUDGEMENT	RESEARCH EVIDENCE					ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ Large ○ Moderate ○ Small ○ Trivial ○ Varies ● Don't know 	Outcomes	№ of participants (studies) Follow up	Certainty of the evidence (GRADE)	Relative effect (95% CI)	Anticipated absolute effects* (95% CI)	
					Risk with no training	Risk difference with sensory specific training
	Sensation - not measured	-	-	-	-	-
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				<p>baseline (mean 35.6 seconds, SD 9.1) and 3 weeks of device use (mean 31.2 seconds, SD 4.99, $p=0.008$) was identified. (Leonardi et al 2016)</p> <p>25 people with multiple sclerosis underwent an 8-week controlled whole-body vibration training (CWBV), 3x/week. Paired t-tests were used to analyse 9HPT scores pre and post training. There were no statistically significant changes between either dominant ($p=0.053$) or non-dominant 9HPT ($p=0.059$). (Yang et al 2016).</p>
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	f. No participants with an FRDA diagnosis.	
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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 	Very low certainty of evidence as per the evidence profile table.	

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 ● No important uncertainty or variability 	<table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="width: 40%;">Outcomes</th> <th style="width: 20%;">Importance</th> <th style="width: 40%;">Certainty of the evidence (GRADE)</th> </tr> </thead> <tbody> <tr> <td>Sensation - not measured</td> <td>IMPORTANT^a</td> <td style="text-align: center;">-</td> </tr> <tr> <td>Neurological Function assessed with: SARA follow up: mean 6 weeks</td> <td>IMPORTANT^b</td> <td style="text-align: center;">⊕○○○ VERY LOW^{c,d,e,f,g}</td> </tr> <tr> <td>Neurological function assessed with: 9HPT</td> <td>IMPORTANT^b</td> <td style="text-align: center;">⊕○○○</td> </tr> </tbody> </table>	Outcomes	Importance	Certainty of the evidence (GRADE)	Sensation - not measured	IMPORTANT ^a	-	Neurological Function assessed with: SARA follow up: mean 6 weeks	IMPORTANT ^b	⊕○○○ VERY LOW ^{c,d,e,f,g}	Neurological function assessed with: 9HPT	IMPORTANT ^b	⊕○○○	
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Independence in daily activities - not measured	IMPORTANT ⁱ	-									
	<p>a. Identified as important (6/6) by people with FA and important by expert authors on this topic.</p> <p>b. Outcome listed as important by people with FA (3/3) and expert authors for this topic.</p> <p>c. Five people with FRDA (n=5) within a sample of 11 people (n=11).</p> <p>d. One study published only.</p> <p>e. N=2 withdrawals from the study.</p> <p>f. Small sample size.</p> <p>g. Confidence intervals not provided. (Non-parametric data.)</p> <p>h. No participants with an FRDA diagnosis.</p> <p>i. Identified as critical (3/6) and important (3/6) by people with FA and important by expert authors on this topic.</p>										

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 		

Acceptability

Is the intervention acceptable to key stakeholders?

JUDGEMENT	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
<ul style="list-style-type: none"> ○ No ○ Probably no 	No published research.	The Friedreich's ataxia Clinical Management Guideline Patient and Parent Advisory Panel were asked if the intervention was

<ul style="list-style-type: none"> ● Probably yes ○ Yes ○ Varies ○ Don't know 		<p>acceptable (weighing up the balance between benefits, harms and costs). 2/4 indicated that sensory specific training of the arm and hand for all people with FA was reasonable, 1/4 indicated that training varies or was sometimes reasonable, 1/4 indicated that they didn't know if training was reasonable. (Aug 2020).</p>
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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 type="radio"/>	Conditional recommendation for either the intervention or the comparison <input checked="" 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 cannot recommend either the use or non-use of sensory specific training of the upper limbs for individuals with Friedreich ataxia in a clinical setting.

Justification

We acknowledge the role of sensory input, particularly proprioception, on upper limb functional task performance and that sensory specific training attempts to mitigate the loss of sensation. However, the pathology of sensory impairment in FRDA is different to like populations and therefore we are unable to say that sensory impairment secondary to FRDA is amenable to intervention.

Subgroup considerations

None.

Research priorities

Further research is needed to assess the effects of sensory interventions for individuals with FRDA in relation to neurological upper limb function, quality of life and activities of daily living.