Northamptonshire Healthcare NHS
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Alpha Stim for anxiety in Primary Care – Final report

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Background

Alpha-Stim AID is a cranial electrotherapy stimulation (CES) device with evidence of effectiveness in treating symptoms of anxiety; it is a self-administered treatment. Prior to recommending for adoption, the United Kingdom's (UK's) National Institute for Health and Care (NICE) stated the need for collection of real-world data to better understand issues around people's treatment preferences, uptake of the device, response rates, and treatment completion rates (NICE, 2021). In this project, Alpha-Stim AID was offered through a United Kingdom (UK) primary care social prescribing service to patients who reported symptoms of anxiety.

Alpha-Stim AID intervention

Once the participants provided informed consent to try the Alpha-Stim AID (Conformite Europeenne [CE] marked as a class IIa medical device) they were sent it or given it by their SPLW with instructions for how to use it. They were advised to use this once a day for an hour for six weeks, and to use the device at level 1 (2 bars on screen) (0.5 Hz, 100 - 500 µA, 50% duty cycle, biphasic asymmetrical rectangular waves). Alpha-Stim AID is a mobile phone sized device worn via a neck lanyard delivering small electric currents via soft pad conducting metal clips to the earlobes. SPLWs could be contacted to ask any questions about the device, side effects and its use. Patients remained on any physical or medical health medication they were taking and continued any other medical or psychological interventions. Following 6 week's use they were required to return the Alpha-Stim AID.

Results

Demographics

Average age was 42 years

65% females, 35% males

Uptake

84 patients signs of anxiety were approached by social prescription liaison workers (SPLWs) and offered Alpha-Stim, 77 consented, a 91.6% uptake rate.

Statistical analysis

33 (43%) of participants fully completed baseline and follow-up measures, and so were included in analysis.

GAD-7 (anxiety)

Reliable improvement and remission rates at the end of the study were 53.39% and 33.3% for the GAD-7, respectively. Remission rates exceeded expected outcome (20%).

The reduction in GAD-7 scores were statistically significant, $F(2, 64) = 24.60$, $p < 0.001$, a large effect size was observed partial $\mu 2 = 0.435$. Thus, 44% of the improvement in GAD score was attributed to the intervention. Post hoc analysis with a Bonferroni adjustment revealed that there was a decrease in GAD-7 score from baseline ($M = 15.52$, $SD = 3.84$) to week 3 ($M = 10.73$, $SD = 5.72$), a statistically significant mean decrease of 4.79, 95% CI [2.75, 6.83], $p < 0.001$; and from baseline to week 6 ($M = 10.15$, $SD = 5.05$).

PHQ-9 (depression)

Reliable improvement and remission rates at the end of the study were 46.7% and 29.5% for the PHQ-9, respectively. Remission rates exceeded expected outcome (20%).

The reduction in PHQ-9 scores were statistically significant at all time points during the intervention, $F(2, 64) = 23.49$, $p < 0.001$, a large effect size was observed partial $\mu 2 = 0.423$. The large effect size confers 42% of the improvement in PHQ-9 was accounted for by the intervention. Post hoc analysis with Bonferroni adjustment revealed that there was a decrease in PHQ-9 score from baseline ($M = 16.85$, $SD = 4.66$) to week three ($M = 11.67$, $SD = 6.37$), a statistically significant mean decrease of 5.18, 95% CI [3.05, 7.32], $p < 0.001$; Similarly, a decrease in PHQ-9 score is observed between

baseline and week 6 (M = 11.00, SD = 5.97), a statistically significant decrease of 5.85, 95% CI [3.25, 8.45], p < 0.001.

EQ=5D-5L (quality of life) scores

Perceived quality of life significantly increased by 0.17 on the health index score (meeting the expected outcome), this intervention adds 1.68 Quality Adjusted Life Years (QALYs).

Table 3 illustrates the descriptive data for each of the five dimensions as well as the mean health index and VAS at baseline, week 3 and week 6. From baseline to week 6, quality of life increases with an improvement of 0.17 reported. Measured across ten years, this intervention adds 1.68 QALYs.

Table 1. Means and standard deviations within each dimensions across time with corresponding mean variation, significance and effect size.

EQ-5D Dimension	Baseline	Week 3	Week 6	*F*	*p*	*μ2*
	M (SD)	*M (SD)*	*M (SD)*			
Mobility	1.81 (1.06)	1.63 (1.04)	1.66 (.90)	1.00	.374	
Self-care	1.94 (1.22)	1.88 (1.07)	1.56 (.80)	2.179	.132	
Usual activity	2.88 (1.45)	2.34 (1.36)	2.19 (1.03)	4.223	.019*	.120
Pain/discomfort	2.44 (1.29)	2.53 (1.34)	2.16 (1.08)	2.45	.110	
Anxiety/depression	3.25 (1.11)	2.53 (1.16)	2.69 (.93)	8.99	< 0.001*	.225
Health index score	.46 (.36)	.55 (.37)	.63 (.26)	6.150	< 0.001*	.166
EQ-VAS score	51.69 (22.19)	58.78 (20.77)	62.56 (20.60)	3.956	.024*	.113

*Significant at p < 0.05 level

Furthermore, data screening permitted the use of a one-way repeated measure ANOVA to determine whether there was a statistically significant difference in participants' EQ dimensions, as well as their health index score and VAS over the course of the 6-week alpha stim intervention. The improvement was statistically significant for two ED dimensions (usual activity and depression/anxiety), for the health index score and the VAS score, ranging from medium to large effect sizes. As anticipated, post hoc analysis with a Bonferroni adjustment revealed there was an improvement from baseline to weeks 3 and/or 6 but not between weeks 3 and 6.

Treatment completion rates

Out of 57 who completed baseline assessments, 35 completed treatment and follow-up assessments (61.4%).

Patient usage questionnaire

Fourteen patients completed a usage questionnaire. The majority were mostly compliant with usage instructions (6 every day and 5 virtually every day [79%]).

Table 2. Usage questionnaire

ID	Frequency of use	Routinely use device at set time	Reason for use	Was anxiety reduced	Was AS useful	Why/impact	Use it again?	If stopped using it why?
01	Virtually every day	Yes	Anxiety	Yes	Yes	• Helps me get through the day • Helped in morning – feeling calmer and more relaxed	Yes	
03	Every day for the period	Yes	Anxiety	No	No	• Stopped using it, as didn't like way felt using it	No	Stopped participating and using device as made feel dizzy
05	Every day for the period	Yes	Anxiety	Yes	Yes	• Noticed a significant reduction in anxiety, is more relaxed • Feels more confident	Yes	
08	A couple of times	No	Anxiety	No	No	• No differences noticed in anxiety	Yes	Kept forgetting to use it, very busy personal and work life
12	Every day for the period	Yes	Severe anxiety	Yes	Yes	• Significantly improved sleep • Feeling much less anxious • Improved quality of life	Yes	
42	Virtually every day	Yes	Severe anxiety	Yes	Yes	• Feeling of lightness in mood • Could concentrate more • Reduced anxiety	Not given	

ID	Frequency of use	Routinely use device at set time	Reason for use	Was anxiety reduced	Was AS useful	Why/impact	Use it again?	If stopped using it why?
44	Most days	Yes	Anxiety / Sleep	Not given	Don't know.	• Major things happening in life going well, so unsure if placebo effect	Not given	
45	Virtually every day	Yes	Anxiety / Pain/ Sleep	Don't know	Yes	• Motivation and purpose • Feels had positive affect • Gave a routine	Not given	
46	Virtually every day	Yes	Anxiety / Depression/ grief	Not given	Yes	• Feels different and positive • Dealing better with my grief	Not given	
47	Every day for the period	Yes	Severe anxiety / grief	Not given	Yes	• Felt relaxed and calm • Helped with sleep	Not given	
48	Virtually every day	Yes	Anxiety / Depression	Yes	Yes	• More relaxed	Yes	
50	Every day for the period	Yes	Anxiety / Depression	Yes	Yes	• Able to do things without feeling pain • Helped controlling emotions (crying)	Yes	
52	Every day for the period	Yes	Anxiety/ Pain/ Sleep	Yes	Don't know	• Struggling overall with general health	Yes	
58	Half of the days	Yes	Depression/ Natural therapy	Yes	No	• Ex-partner stopped her using it, causing anger and stress	Yes	When circumstances at home were difficult

Table 3. Analysis of usage questionnaire

Usage	***n* (%)**
Frequency of use:	
Every day	6(43)
Virtually every day	5(36)
Most days	1(7)
Half the time	1(7)
A couple of times	1(7)
Routinely used at set time	
Yes	12(86)
No	2(14)
Anxiety reduced	
Yes	8(57)
No	2(14)
Don't know	1(7)
No answer	3(21)
Was it useful	
Yes	9(64)
No	3(21)
Don't know	2(14)
Use it again	
Yes	8(57)
No	1(7)
No answer	5(35)

Patient Feedback

Fifteen participants consented to be interviewed. The age range of the participants was 26 – 65 years (M = 46.6); 10 (67%) female and 5 (33%) male. In-depth interviews on the experience and feedback of individuals with symptoms of anxiety who have used the Alpha-Stim AID provided support for the acceptability, useability, and positive outcomes. Virtually all (14 out of 15, [93%]) were mostly compliant with usage instructions, see table 4.

There were fewer prior feelings of uneasiness about receiving Alpha-Stim AID treatment and less discomfort reported that has been reported for using tDCS (Gordon et al., 2021; Grycuk et al., 2021). Participants found engagement with the Alpha-Stim AID was enabled through the useability of the device, in that it was accessible, easy to use, reliable, could be embedded into their daily routine, and did not have any adverse side effects preventing use; these factors promoted treatment compliance. The findings add to and aligns with evidence of useability, feasibility, ease of use, and lack of side effects found in other studies (Barclay & Barclay, 2014; Griffiths et al. 2021; Morriss et al. 2019; Royal et al. 2022; Shekelle et al. 2018). Medication side-effects can cause treatment failure (Sundbom & Bingefors, 2013); and the lack of Alpha-Stim AID side effects, meant that some participants perceived the Alpha-Stim AID as a preferred alternative to medication.

Positive impact was experienced majority of the participants; participants associated positive benefits with using the Alpha-Stim AID. The participants described reductions in their anxiety and panic attacks, and increases in feeling of calmness and relaxation. This is supported by prior quantitative research, which found Alpha-Stim AID significantly reduces anxiety symptoms (Barclay & Barclay, 2014; Griffiths et al 2021; Morriss et al. 2019; Royal et al. 2022; Shekelle et al. 2018). Participants reported improvements in sleep quality and duration. This finding is aligned to studies that have quantitatively measured CES and its impact on sleep (Kirsch & Gilula, 2007; Kirsch et al. 2019; Wagenseil et al., 2018). The positive experience described by the participants were interlinked, giving insight into factors related to experiencing wellbeing and good quality of life. The Alpha-Stim AID was associated with breaking negative cycles of mental illness and promoting positive cycles of mental health, well-being and recovery.

Participants described changes in their thoughts and thought processes, or a mindset shift. Some reported a reduction in harmful and unhelpful thoughts (which are known to be associated with distress), and an increase in their ability to make connections with others and be able to actively participant in activities. Some participants reported cognitive reframing which enabled them to shift their mind-set to look at situations and experiences from a constructive perspective and finding alternative ways of perceiving ideas, events or situations (Robson & Troutman-Jordan, 2014). This seemed to be a key recovery element and linked to self-reflection and greater resilience.

Some participants experienced no effect following the use of the Alpha-Stim AID, and it is not effective for all people (Barclay & Barclay, 2014; Griffiths et al. 2021; Morriss et al. 2019; Royal et al. 2022; Shekelle et al. 2018). Those who did not experience a positive impact, experienced psychological distress due to failure of hopes that it would work. Practitioners need to be aware of this and prepare patients for this potential outcome and ensure that patients receive ongoing support, and to suggest other solutions for their anxiety. Patients need to be informed of possible treatment not working and trajectories before the initiation so they know that they may need to try a number of options until an effective treatment is found (Toledo-Chávarri et al. 2020).

Table 4: Interviewed participants' use of Alpha-Stim AID

Participant	Reason for use	How often used AS	When used it	Level used at
P1	Anxiety and panic attacks	Every day	Different times of day, predominantly mornings	Level 1 only
P2	Anxiety	Every day initially, reduced to once every 2 days, then once every 3 days	Before bedtime	Level 1 only
P3	Anxiety and depression	Every day	Before bedtime	Twice increased – didn't like feeling, returned to level 1
P4	Anxiety	Every day initially, then sporadically	Around mid-day	Level 1 only
P5	Anxiety and depression	Initially every day, then 3-4 times a week dependent on mood	No set time, when feels low mood	Level 1 only

Participant	Reason for use	How often used AS	When used it	Level used at
P6	Anxiety, stress and panic attacks	Every other day initially, then every day	In the morning	Tried higher level, felt dizzy, returned to level 1
P7	Anxiety and panic attacks	Used when felt overwhelmed	Before bedtime	Tried higher level, experienced headache returned to level 1
P8	Anxiety and panic attacks (has PTSD)	Every day	In the evening	Level 1 only
P9	Anxiety and depression	Every day	In the morning	Tired it at top level (5), no effect at any level
P10	Anxiety (has OCD)	Every day (2 times a day)	Early afternoon, and before bedtime	Level 1 only
P11	Anxiety (has PTSD)	Sporadically initially, then every day	Before bedtime	Level 1 only
P12	Anxiety	Every day	In the evening after work	Level 1 only
P13	Anxiety	Every day	Before bedtime	Level 1 only
P14	Anxiety (has PTSD)	Every day (2 times per day)	In the morning (20 mins after awake) 1 hour before bedtime	Tried higher level, experienced memory loss, returned to level 1
P15	Anxiety and depression	Every day	In the evening	Level 1 only

Record of devices returned

Out of 29 devices 26 have been returned, three were recorded as lost (10%). Less than 20% expected non-returns.

30 are in the process of being retrieved/returned

Record of devices returned damaged beyond use

Around 10% were returned damaged beyond use

Feedback from staff

Overall, feedback was positive

Operationalization issues identified:

1. Potential additional Alpha-Stim AID treatment course repeat requirements for patients (i.e. worked first time but now anxiety symptoms have returned), costs and process required for this
2. Some patients do not start using or delay starting to use the Alpha-Stim once given it
3. Can be difficult, costly and time-consuming to get the device back
4. None return of devices means devices cannot be sent out to newly identified patients
5. Quite a high level of device loss due to damage, too dirty or non-return
6. Requires considerable time and effort to clean and test and get device ready for next patient
7. Outcome measure completion rates can be low
8. A cultural shift and investment is needed to implement Alpha-Stim, the process of prescribing anxiety medication and referring people to counsellors and IAPT is backed by decades of experience, solid infrastructures, and millions of pounds of investment. There is not this funding and process for offering devices such as the Alpha-Stim.

Increased patient and clinician choice of treatment:

- There is a demand from patients for the Alpha-Stim
- There is a demand from SPLWs to offer the Alpha-Stim to patients
- Patients like having alternative to taking anti-anxiety medication

SPLWs are very well suited to deploying Alpha-Stim AID, as they gain an in-depth understanding of the patient, their needs and circumstances; and see a patient over a course of time.

<u>Assessment of staff time and other costs</u>

Estimated costs of £62 per patient

Results related prior assumptions

People will choose Alpha-Stim as a form of treatment

Alpha-Stim significantly reduces anxiety, enabling reliable improvement and remission rates of 53.39% and 33.3% respectively

Majority of people will use the device as per instructions

A primary care provider can set up and deliver the Alpha-Stim treatment and collect data, but completed data collection rates allowing analysis of change were less than expected at 43%.

Patient and Public Involvement and Engagement

NHFTs lived experience advisors were involved in reviewing and contributing to the project's Proof of Value Assessment Form (PVAF), advising on what is important to patients; advising on patient facing materials; input into analysis and interpretation of interview results. Lived experience advisors contributed to the development of a bid for research funding to the NIHR in relation to social prescribing which could consider the role of Alpha-Stim.

Outputs

A proposed route for patient and NHS staff access

Proposed referral routes:

1. GP other members of GP team, community and district nursing teams or hospital discharge teams refers a patient to a SPLW who offers Alpha-Stim
2. Person is sent a link to Spring Northamptonshire and directly refers themselves or someone they care for to SP service https://www.springnorthamptonshire.org/
3. NHS staff can access by above routes
4. NHS staff could potentially access via their employers wellbeing or counselling services
5. Possible funding routes include: 'personal budgets'

Patient flow diagram

See document entitled: 'Alpha-Stim Social Prescribing Service Pathway'

A protocol for implementation

See document entitled: 'Staff instructions V1'

Scientific paper

A paper is planned to be written and submitted

Dissemination and stakeholder engagement

September 2022 online meeting entitled 'Alpha-Stim in primary care meeting'

Aims - discuss:

1. Progress to usual model of care that includes Alpha-Stim in primary care and how this could be presented to commissioners
2. Discuss development of a "toolkit" to support progress and overcome barriers towards enabling a primary care pathway as "usual practice"

Presentations delivered on:

1. Alpha-GP project background, design, delivery, and preliminary results
2. Alpha-Stim training programme
3. Nottingham based nurse-led Alpha-Stim cranial electrostimulation to treat anxiety and depression in university students project

Roll-out

GPA has agreed in principal funding from GPA board to roll-out Alpha-Stim in GPA.

Additional work

Bid for further funding

Submitted a bid for research funding to the NIHR RfPB in October 2022 in relation to social prescribing which could consider the role of Alpha-Stim if this is part of social prescribing service delivery.