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Alpha-Stim AID Cranial Electrotherapy Stimulation (CES) Anxiety and Depression Treatment for Adults in a Social Prescribing Service: Anxiety and Depression Outcomes

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Abstract

Background: Generalised anxiety disorder (GAD) is common and can negatively impact people's wellbeing and functioning. GAD treatment includes psychotherapy and/or anti-anxiety medication, which are not acceptable to or effective for many people experiencing GAD. Alpha-Stim AID cranial electrotherapy stimulation (CES) has evidence of effectiveness in the treatment of anxiety and depression. Purpose: Evaluation of Alpha-Stim AID on anxiety and depression for adults with GAD symptoms using a social prescribing service. Methods: An open-label patient cohort design with no control group. Twenty-six adult patients, 22 females and 4 males, with an age range of 24 to 68 years and an average age of 49 years, completed 6 weeks of Alpha-Stim AID use. Pre- and post-intervention assessments were undertaken using participant self-report measures: Generalised Anxiety Disorder (GAD-7) and Patient Health Questionnaire (PHQ-9). Results: Reliable improvement and remission rates were 42% and 19% for GAD-7; 38% and 27% for PHQ-9. GAD-7 and PHQ-9 significantly improved with large effect sizes. Conclusions: A social prescribing service can offer, and patients will choose to use Alpha-Stim AID, which may be useful in the treatment of anxiety and depression. This study addresses the need for real-world data on Alpha-Stim AID in relation to response rates. It contributes to how Alpha-Stim Aid can be used in social prescribing services, including through a group-based pathway.

Keywords

Alpha-Stim, Non-Invasive Brain Stimulation, Social Prescribing, Cranial

Electrotherapy Stimulation, Anxiety, Depression

1. Introduction

Anxiety disorders (generalised anxiety disorder (GAD), phobias, panic disorders) are the most prevalent mental illness (up to 33.7% lifetime prevalence) (data mostly from Western countries) (Bandelow & Michaelis, 2015; Michael et al., 2007). The most common anxiety disorder is GAD, defined as excessive and difficult-to-control anxiety or worry about issues, activities, and/or events (APA, 2013). The effects of GAD can negatively impact functioning, wellbeing, and quality-of-life (Locke et al., 2015; Kessler et al., 2012; Wittchen et al., 2011). Epidemiology data shows that 59% of people with GAD are comorbid with major depressive disorder (MDD) (Carter et al. 2001).

GAD pharmacotherapy includes serotonin norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), benzodiazepines, and buspirone (Bespalov et al., 2010; Muntingh et al., 2016). SSRIs and SNRIs are first-line treatments and can be effective in treating anxiety disorders (small to moderate effect sizes) (Jakubovski et al., 2019). Adverse side effects, including dizziness, nausea, fatigue, insomnia, weight gain, involuntary physical movement, gastrointestinal problems, and sexual dysfunction can result in poor compliance or stopping use (Bandelow et al., 2017; Jiménez-Jiménez & Molina, 2000); and there can be an increased suicide risk (Amendola et al., 2024; Strawn et al., 2018). Between 18% to 30% of people stop using their medication before the end of course of treatment (Mochcovitch et al., 2017), there is a high risk of relapse (Culpepper, 2009) and withdrawal effects can be long-lasting and severe for some people (Davies & Read, 2019). There can be stigma related to antidepressant use (Castaldelli-Maia et al. 2011). Adverse side effects can result in additional costs, for example, additional GP visits for medication change or treating side effects (Mark et al., 2011). Benzodiazepines are recommended only for severe anxiety symptoms and under four weeks of use, due to dependence risk and withdrawal issues (NICE, 2019a).

Psychotherapy is recommended for treating anxiety disorders and is effective for some people; however, multiple appointments over multiple weeks or months mean it is costly and lengthy, and non-response rates are 60% - 66% (Gyani et al., 2013; Griffiths & Griffiths, 2014; NICE, 2019b). Psychotherapy is not acceptable for some people due to cultural or religious beliefs, physical mobility issues, travel costs, or/and work or family caring responsibilities (Bandelow et al., 2017). Patients should have a range of choices of treatment options for anxiety symptoms that best suit their needs, lives, and concerns.

Cranial electrotherapy stimulation (CES) is a non-invasive brain stimulation (NIBS) via a pulsed low-intensity electrical current that causes an effect in the brain (Nardone et al., 2014). CES has very few side effects and was first used to

induce sleep and relaxation (Guleyupoglu et al., 2013), and subsequently for treating depression, anxiety, insomnia, pain, and post-traumatic stress disorder (PTSD) (Kirsch et al., 2019). CES treatment can be used alongside pharmacological and psychotherapy treatment or as a standalone alternative treatment (Kirsch et al., 2019). A meta-analysis and systematic review of the efficacy of CES for anxiety symptoms found CES to be well tolerated and significantly reduced anxiety symptoms (moderate effect sizes) (Ching et al., 2022); however, there is a lack of evidence from appropriately powered and designed GAD primary outcome RCTs for CES's beneficial effects (Brunyé et al., 2021).

The mechanisms of action effects when using CES may be related to modulation of the central and peripheral nervous system, altering resting state and limbic system activation, then increasing cortical alpha-based activity and the release of hormones and neurotransmitters (Brunyé et al., 2021; Ching et al., 2022). Electroencephalography (EEG) data shows changes from delta (0.1 - 3.5 Hz) and beta (12.5 - 30 Hz) frequencies to more alpha frequencies (8 - 12 Hz) and increased left frontal region theta activity, which is associated with relaxation (Kennerly, 2004; Kim et al., 2021).

The Alpha-Stim AID (Anxiety, Insomnia, and Depression) CES device delivers very low voltage current to cause changes to electrical activity of the brain, from beta and delta frequencies (associated with stress) to alpha frequencies (associated with relaxation) (Kennerly, 2004), and potentially similar effects to practicing meditation/mindfulness (Morriss et al., 2019). The Alpha-Stim AID is mobile phone-sized and connected via mental clips to both earlobes for up to an hour a day by users "at home"; it is easy to use and is European Economic Area (EEA) Conformité Européene (CE) marked for intended purpose (Griffiths et al., 2021). A reduction in anxiety by 32% has been found (Barclay & Barclay, 2014); a systematic review of evidence concluded that Alpha-Stim AID may reduce symptoms of anxiety and depression and is safe without serious side effects (Shekelle et al., 2018). Anxiety and depression can be linked, and an RCT in people seeking help for primary major depression who scored moderate generalised anxiety disorder (GAD) whose depression symptoms were not responsive to antidepressant treatment found clinically important change on depression and anxiety, but no additional benefit compared with sham (Morriss et al., 2023), placebo responsiveness is a real effect for the patient (Burke, 2023).

Non-randomised open-label no control group studies of Alpha-Stim AID in a social prescribing service, nurse-led university student services, and psychotherapy services, reported significant improvements in quality of life, anxiety and depression for people experiencing anxiety symptoms (Griffiths et al., 2021; Griffiths et al., 2023; Morriss et al., 2019; Royal et al., 2022). Alpha-Stim AID has few and minor physical sensations and side effects (some users report mild tingling sensations at skin contact points and slight dizziness but generally this does not prevent use); Alpha-Stim is safe, well-tolerated and acceptable, and can be used with anxiety medication, and people will mostly follow the required treatment protocol

(Griffiths et al., 2021; Griffiths et al., 2023; Morriss et al., 2019; Royal et al., 2022).

Social prescribing in the United Kingdom (UK), part of the NHS long-term plan (NHS, 2019), is an approach used to identify needs and provide access to resources to address needs, and connect patients to health services, community-based activities and social care in their local area (Drinkwater et al., 2019). Social prescribing services support social capital development and engagement with community-based groups and provide peer support. There are increasing overlaps between mental health services and social prescribing services to address the increased incidence of anxiety disorders; social prescribing services can help improve outcomes for people with anxiety and depression, including people with health inequalities.

This study addresses the need to collect real-world data to report Alpha-Stim AID's response rates (NICE, 2021). In this study, Alpha-Stim AID was offered through a United Kingdom (UK) social prescribing service to patients reporting symptoms of anxiety and the study assessed anxiety and depression outcomes.

2. Methods

2.1. Design

An open-label patient, non-randomised, with no control group design and no predetermined sample size. Pre- and post-outcome assessment using self-report measures.

2.2. Approval

Ethical approval was granted by a reviewing panel of the NHS healthcare provider (Reference: Alpha-SPRING1). Participants provided informed written consent and the study was delivered in accordance with the World Medical Association (WMA) Declaration of Helsinki. The study was undertaken from October 2023 to November 2024 as part of routine social prescribing services.

2.3. Medical Records

Following participants' informed consent, demographic information (sex, date of birth, ethnicity) was extracted from digital clinical records of routinely collected data.

2.4. Setting

Participants were recruited through a social prescribing service in one county in the United Kingdom (UK). An NHS patient is referred to a community-based social prescribing link worker (SPLW), who assesses their needs and goals (what matters to them) and provides health, practical and emotional support. SPLWs make appropriate links and referrals to healthcare and community-based resources and services to facilitate the adoption of healthier lifestyles (NHS England, 2021).

2.5. Alpha-Stim AID Intervention

Alpha-Stim AID, Conformité Européenne (CE) is marked as a class IIa medical device and delivers small electric currents via soft pad-covered metal clips soaked with electrical conducting fluid conducting electricity to the earlobes. Treatment protocol was once a day for an hour over six weeks at level 1 (2 bars on screen) (0.5 Hz, 100 - 500 μA, 50% duty cycle, biphasic asymmetrical rectangular waves).

The SPLW demonstrated how to use the Alpha-Stim AID CES device and described the support available while using it. SPLWs could be contacted to ask questions during the intervention period (6 weeks). Patients were not required to change prescribed medication. Following six weeks' use, participants returned the Alpha-Stim AID.

2.6. Inclusion/Exclusion

Informed consent and agreement to return Alpha-Stim AID at the end of the study were required. The inclusion criterion: patient reporting anxiety symptoms, aged 18 or over and having capacity to consent. The exclusion criteria: implantation with a pacemaker, an implantable cardioverter device (ICD) and pregnancy.

2.7. Procedure

Patients were referred to a SPLW by their GP or other NHS professional, and the SPLW then identified if a patient had anxiety symptoms and met inclusion/exclusion criteria. Patients were given information about Alpha-Stim AID and study evaluation. Informed consent was required, and patients could withdraw consent or stop at any point without the need to provide a reason. Outcome measures were completed at baseline prior to Alpha-Stim AID use and at six weeks post Alpha-Stim AID use.

Following previous patient feedback requesting peer support, and the continued need to improve cost effectiveness of social prescribing service, a group-based approach was employed. Potential participants were given a date and time to meet at a community centre. Two SPLWs ran a clinic for around eight patients at a time and comprised a demonstration of how to use the device, time for questions and answers, and completing consent and baseline questionnaires. Once the forms were completed, the participants would be given a device along with written instructions and FAQs to take home. They would also be given a return clinic date in six weeks' time, after which they would come back to the same venue to give the devices back and complete follow-up measures. All participants who attended the groups were allocated an SPLW who they could ask any questions during the 6 weeks regarding the devices and the process or raise any concerns.

2.8. Measures

The Generalised Anxiety Disorder-7 (GAD-7) seven-item self-report measure of GAD (Spitzer et al., 2006). A score of 0 - 4: no or minimal anxiety, 5 - 9: mild anxiety, 10 - 14: moderate anxiety, and 15 - 21: severe anxiety. Remission is 7 or

less, and reliable improvement is a reduction of 5 points (Kroenke et al., 2007; Spitzer et al., 2006). The GAD-7 has good sensitivity and specificity and has good internal consistency, as shown by Cronbach's Alpha value of α = 0.92 (Kroenke et al., 2007).

The Patient Health Questionnaire-9 (PHQ-9) self-report measure of depression has good sensitivity and specificity for major depression and good internal consistency (Kroenke et al., 2001). Scores for depression severity are 0 - 4: none, 5 - 9: mild, 10 - 14: moderate, 15 - 19: moderately severe, and 20 - 27: severe (Kroenke et al., 2007). Remission is a 9 or less, and reliable improvement is a reduction of 6 points (Richards & Borglin, 2011).

2.9. Statistical Analysis

Data were analysed using the statistics software package SPSS® Statistics v28. Data screening confirmed the dataset met requirements of the general linear model. One-way repeated measures ANOVAs were conducted to determine statistically significant change.

3. Results

3.1. Participant Characteristics

Twenty-six participants completed six weeks of treatment, baseline, and six-week follow-up assessments. The sample comprised twenty-two (84.62%) females and four (15.38%) males, with an age range of 24 to 68 years with an average age of 49 years. Ethnicity characteristics were: "White British" (English, Welsh, Scottish, Northern Ireland) = 21 (80.77%), "White Irish" = 1 (3.85%), White (Any other) = 1 (3.85%), "Asian or Asian British" = 1 (3.85%), "Mixed white and black Afro-Caribbean" = 1 (3.85%), and "Other" = 1 (3.85%).

Participants were asked if they were undertaking psychotherapy; eighteen (69.23%) stated no, four (15.38%) stated cognitive behavioural therapy (CBT), two (7.69%) stated applied relaxation therapy (7.69%), and one stated (3.85%) psychodynamic psychotherapy. Participants were asked if they were taking medication for anxiety or depression; nine (34.62%) stated no, five (19.23%) stated (SSRIs), one (3.85%) stated Pregabalin, nine (34.62%) stated other anxiety/depression medication, and one (3.85%) "unsure".

As illustrated by **Table 1**, participant mean baseline scores were in the "moderate" range for anxiety and depression (Spitzer et al., 2006; Kroenke et al., 2001).

Table 1. Baseline characteristics (n = 26).

Variable	Mean ± SD
GAD-7	13.7 ± 4.49
PHQ-9	14.5 ± 5.33

3.2. GAD-7 and PHQ-9

GAD-7 results: Mean scores showed a significant improvement in GAD-7 from

13.73 (*SD* = 4.49) at baseline to 8.96 (*SD* = 4.20) at follow-up, with large (Cohen's *d* = 0.907) effect size. At follow-up, five participants (19.23%) experienced remission (a GAD-7 score of 4 or less at post-intervention follow-up) and eleven participants (42.31%) reliable improvement (a reduction of 5 or more points on the GAD-7 from baseline). Table 2 shows baseline and follow-up GAD-7 scores and levels.

Table 2. Baseline and follow-up GAD-7 scores and levels.

GAD-7		
Score	Number of participants at Baseline	Number of participants at Follow-up
0 - 4 (No or minimal anxiety)	1 (3.85%)	5 (19.23%)
5 - 9 (Mild anxiety)	3 (11.54%)	10 (38.46%)
10 - 14 (Moderate anxiety)	10 (38.46%)	8 (30.77%)
15 - 21 (Severe anxiety)	12 (46.15%)	3 (11.54%)

PHQ-9 results: Mean scores showed a significant improvement in PHQ-9 from 14.54 (*SD* = 5.33) at baseline to 9.85 (*SD* = 4.88) at follow-up, with a large (Cohen's *d* = 0.831) effect size. At follow-up, seven participants (26.92%) experienced remission (a PHQ-9 score of 5 or less at post-intervention follow-up), and ten participants (38.46%) showed reliable improvement (a reduction of 6 points on the PHQ-9 from baseline). Table 3 shows baseline and follow-up PHQ-9 scores and levels.

Table 3. Baseline and follow-up PHQ-9 scores and levels.

PHQ-9		
Score	Number of participants at Baseline	Number of participants at Follow-up
0 - 4 (No depression)	2 (7.69%)	4 (15.38%)
5 - 9 (Mild depression)	2 (7.69%)	9 (34.62%)
10 - 14 (Moderate depression)	9 (34.62%)	8 (30.77%)
15 - 19 (Moderately severe depression)	8 (30.77%)	5 (19.23%)
20 - 27 (Severe depression)	5 (19.23%)	0 (0%)

A participant usage survey indicated that the majority of participants (n = 18, 69%), would use Alpha-Stim again to address their anxiety symptoms.

4. Discussion

This study showed that using Alpha-Stim AID whilst receiving social prescription services can reduce anxiety and depression symptoms in patients with symptoms of anxiety, supporting findings of published research and health service based

studies (Barclay and Barclay, 2014; Shekelle et al., 2018; Morriss et al., 2019; Griffiths et al., 2021; 2023; Royal et al., 2022). The depression and anxiety remission and reliable improvement rates results from the current study add to evidence from three other NHS service based Alpha-Stim AID studies that community based patients' depression and anxiety symptoms can be reduced with the Alpha-Stim AID (Griffiths et al., 2021; Griffiths et al., 2023; Morriss et al., 2019; Morriss et al., 2023; Royal et al., 2022).

This study showed that a social prescribing service can offer the Alpha-Stim AID treatment. The service developed a group-based process of recruitment, training, support, distribution, and collection. Social prescribing services are potentially a good route to deliver this treatment as they are available across the UK and seek to address patients' holistic needs, issues, and goals (NHS England, 2021). Addressing anxiety and depression symptoms through social prescribing services may reduce demand for primary care, secondary care, and psychotherapy services; therefore, reducing healthcare demands and costs. Social prescribing prescription of Al-ha-Stim can be less stigmatising than using antidepressants or face-to-face psychotherapy provided by mental health services. Using a group approach opens up the possibility of the use of Alpha-Stim AID within group consultations and long term condition management groups; peer support can benefit anxiety management. Alpha-Stim AID may offer an alternative treatment for those experiencing anxiety symptoms who have failed to respond to medication or psychotherapy or for who medication side effects or factors related to psychotherapy are unacceptable.

Future studies could include further data collection points, e.g. 12 and 24-week follow-up, to assess whether the effectiveness on decreasing depression and anxiety symptoms is long-lasting, relapse rates, and whether the Alpha-Stim AID needs to be used periodically in order to maintain its effects. An appropriately designed and powered RCT on effectiveness and cost-effectiveness for GAD is required: comparing Alpha-Stim AID with individual cognitive behavioural therapy (CBT), anti-anxiety medication or combination of both (NICE, 2021). A double-blinded, sham controlled trial can eliminate the potentially large placebo effects of CES (Brunyé et al., 2021; Morriss et al., 2023).

5. Limitations

There was an open-label, no control group or non-randomisation design. Participants continue using existing medication, therapy, and social prescribing services. Alpha-Stim AID treatment was adjunct to existing anxiety or other treatments or therapies, which were not recorded. Additional disease diagnosis was not recorded or reported. The sample was over-represented by females (85.6%), and so the results are less generalisable to males. This study only collected 6-week follow-up data. Relapse data was not collected.

6. Conclusion

The social prescribing service developed an effective Alpha-Stim AID pathway

and delivery processes for patients with anxiety. This study's findings provide evidence that patients with anxiety symptoms will choose to use the Alpha-Stim AID and that, along with social prescribing service support, Alpha-Stim may reduce anxiety and depression symptoms.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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