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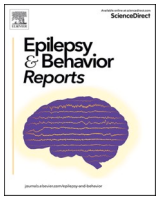

Using the hospital anxiety and depression scale in people with epilepsy: Is overlapping symptomatology a problem?

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ABSTRACT

The Hospital Anxiety and Depression Scale (HADS) is designed to screen for anxiety and depression in clinical settings. However, some items on the HADS may reflect symptoms associated with epilepsy and antiseizure medications rather than anxiety and depression. This study examined whether these items on the HADS contributed disproportionately to the reporting of anxiety and depression on the HADS in people with epilepsy (PWE). As part of a routine clinical assessment, 546 adults with epilepsy completed the HADS. In our sample, 56.2% reported elevated levels of anxiety, and 27.3% reported symptoms of depression with a score of 8 or more on the respective subscales. Scores on the anxiety and depression subscales were not associated with age, sex or epilepsy type. We did not find a relationship between endorsement of items related to panic, feelings of dread or butterflies in the stomach and a diagnosis of temporal lobe epilepsy. The most frequently endorsed item on the anxiety subscale of the HADS in the sample as a whole related to worrying thoughts, rather than the more somatic manifestations of anxiety. The item '*I feel as if I am slowed down*' was endorsed by the majority of people with epilepsy and may not reflect a symptom of depression in this group. Careful analyses of the pattern of endorsement of specific items on the HADS may improve the sensitivity of this screening measure to the presence of depression in people with epilepsy.

Introduction

Anxiety and depression are recognised as two of the most common psychiatric co-morbidities in epilepsy [1] with estimates of approximately one in four people suffering from anxiety and 15 % suffering from mood disorders [2]. Depression has a bidirectional relationship with epilepsy [3] and low mood precedes the diagnosis of epilepsy for many [4]. Whilst access to specialised neuropsychiatric treatment remains scarce even in high income countries [5], screening for mood disorders in epilepsy is increasingly recognised as a core component of care for this population [1]. Valid measurements of anxiety and depression in people with epilepsy are therefore required to identify and address the increased clinical needs in this group.

The Hospital Anxiety and Depression Scale (HADS) is a short 14 item, self-report scale designed to measure anxiety and depression in clinical settings [6]. It is widely used in epilepsy clinics and has been validated in people with epilepsy [7]. Wiglusz et al (2016) reported that the depression subscale had adequate sensitivity (90.5 %), acceptable specificity (70.7), and high negative predictive value (96.4 %) using a cut off of ≥ 7, in a sample of 118 adults with epilepsy whose psychiatric status was confirmed with a structured clinical interview with a trained psychiatrist. However, the positive predictive value was relatively low at 46.3 %. De Lemos et al also found a relatively low positive predictive value (55 %) of the HADS depression subscale in a sample of 103 people with temporal lobe epilepsy, using the higher cut off of ≥ 8. [8] Thus whilst the HADS depression subscale is effective at identifying those with depression, it may also identify a large number of people who would not fulfil the clinical criteria for the condition. Meanwhile, Gandy et al (2015) found that the anxiety subscale of the HADS had relatively poor sensitivity (61 %) in identifying those with anxiety with a high number of false negative cases identified on the subscale in their sample [9].

One of the reasons for the relatively low positive predictive value and reduced sensitivity of the HADS in people with epilepsy may be the overlap between seizure semiology and anti-epileptic medication side-effects, and some of the symptoms of anxiety and depression that the respondent is asked to rate on the questionnaire. It has long been recognised that focal seizures with retained awareness can produce feelings

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of anxiety and fear and autonomic features of heart rate and blood pressure changes which can be similar to anxiety attacks [10]. In 1887, Hughlings Jackson described a type of seizure as "There is the emotion of fear. I do not mean a fear of the fit, but fear which comes by itself." [11]. The items on the anxiety subscale of the HADS that could overlap with these ictal phenomena include '*I get a sort of frightened feeling as if something awful is going to happen*', '*I get sudden feelings of panic*' and '*I get a sort of frightened feeling like butterflies in the stomach*'. The 'butterflies' question may also be endorsed by those who experience a sensation of epigastric rising during focal seizures with retained awareness Furthermore, anti-epileptic medication can have adverse side-effects such as fatigue and slowed processing-speed [12]. The depression item on the HADS that could overlap with these side-effects is '*I feel as if I am slowed down*'. Misattribution of these epileptic/treatment phenomenon to anxiety and depression could lead to potential misdiagnosis of mood disorders in this population.

The aim of this study was to examine whether these specific items (three items on the anxiety subscale and one on the depression subscale) are disproportionately endorsed by people with epilepsy compared to other items on the respective subscales. Given the sensations of epigastric rising and emotional changes associated with temporal lobe semiology in focal seizures with retained awareness, we hypothesised that these symptoms would be more frequently endorsed by those with temporal lobe epilepsy compared to those with extra temporal foci or generalised epilepsy.

Material and methods

This study represents an analysis of the responses on the Hospital Anxiety and Depression Scale which were administered as part of a routine clinical assessment to 546 consecutive patients attending our department for a neuropsychological review between 2020 and 2021. (The National Hospital for Neurology & Neurosurgery, London and the UCLH Chalfont Centre for Epilepsy, UK). Participants were aged between 16 years to 81 years (Mean: 36.9 years, SD: 13.1); 307 were female, 239 were male. All patients had been referred to our department within the National Health Service by other professionals, primarily neurologists, neuropsychiatrists and general practitioners. Epilepsy diagnoses were made on a clinical basis, based on expert consideration of clinical history with seizure semiology, neuro-imaging findings and electroencephalography (EEG).

Two hundred and seventy-nine patients had temporal lobe epilepsy (n = 126 right; n = 132 left, n = 21 bilateral/unclear), the remaining 267 had extra temporal seizures (n = 91), generalised epilepsy (n = 36) or other/unclassified epilepsy (n = 140). See Table 1.

Measures

The HADS [6] is a 14-item scale yielding scores for anxiety (7 items) and depression (7 items). Each item is rated on a 4-point Likert scale resulting in a final score of anxiety ranging from 0 to 21 and a final score of depression ranging from 0 to 21. Higher scores represent higher levels of anxiety and depression. The cut-off points for the anxiety and depression subscales are as follows: 0–7 = normal; 8–10 = mild; 11–15 = moderate; 16–21 = severe.

Table 1
Clinical and demographic characteristics of the sample.

	Temporal Lobe Epilepsy (n = 279)	Other Epilepsy (n = 267)
AgeMean (s.d.)	38.8 (12.9)	35.0 (13.1)
Sex	149 Females 130 Males	158 Females 109 Males
Reading IQ	96.6 (10.3)	98.0 (10.7)
HADS Anxiety ScoreMean (s.d.)	8.4 (4.4)	8.6 (4.4)
HAD Depression ScoreMean (s.d.)	5.1 (3.8)	5.4 (4.1)

Ethical Approval

Permission to perform the audit of responses to the measures in this study was granted by the UCLH Quality and Safety Committee [Reference number 37–202122-SE]. All data was fully anonymised prior to analyses to ensure that the study conformed with local and national ethical guidelines for the study of routine data collected in clinical settings.

Statistical analyses

We used repeated measures MANOVA to see whether the target items in the anxiety subscale '*I get a sort of frightened feeling as if something awful is going to happen*', '*I get a sort of frightened feeling like butterflies in the stomach*', '*I get sudden feelings of panic*', were endorsed more strongly than other items in the subscale, as per our hypotheses. The seven items on the anxiety subscale were the within-subjects variables in the model. Epilepsy type (temporal vs other) was included in the model as a between-subjects factor to examine possible group differences in the level of endorsement. Total score on the HADS anxiety subscale was added as a covariate to control for overall level of anxiety reported across the subscale.

Following the MANOVA results indicating significant differences between strength of endorsement on the individual items, individual post-hoc pairwise analyses were conducted to see whether our target items were endorsed significantly more often than the other items on the subscale.

This MANOVA model was then repeated for the items in the depression subscale of the HADS to see whether the target item in the depression subscale '*I feel as if I am slowed down*' was endorsed significantly more strongly than other items in the subscale, as per our hypotheses, again epilepsy type as between-subjects factors and overall score on the depression subscale as the covariate. As with the analyses of the anxiety subscale, individual post-hoc pairwise analyses were conducted to see whether our target item was endorsed significantly more often than the other items on the subscale.

Results

Prevalence of anxiety and depression and clinical correlates

In the group as a whole, 56.2 % reported elevated levels of anxiety with a score of 8 or more on the HADS anxiety subscale whilst 27.3 % reported symptoms of depression with a score of 8 or more on the HADS

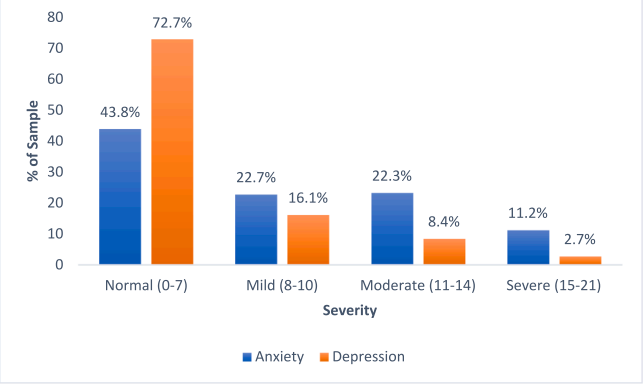

Fig. 1. Whole Sample: Severity of Anxiety and Depression Measured by the HADS.

depression subscale. See Fig. 1.

More than 75 % of people who obtained a score of 7 or less on the anxiety subscale endorsed the item '*I feel tense or wound up*'. See Fig. 2. Similarly, more than 75 % of people who obtained a score of 7 or less on the depression subscale endorsed the item '*I feel as if I am slowed down*' on the depression subscale. See Fig. 3.

Scores on depression and anxiety subtests were not related to age (Depression $r = 0.05$, $p > 0.05$; Anxiety $r = 0.02$, $p > 0.05$) or Reading IQ (Depression −0.13, $p > 0.05$; Anxiety −0.12, $p > 0.05$). There were no sex differences (males vs female) on the HADS anxiety subscale ($t = -1.3$, df 544, $p > 0.05$) or HADS depression subscale ($t = 0.15$, df 544, $p > 0.05$).

The 'temporal lobe' verses 'other epilepsy' groups did not differ in their overall scores on the anxiety and depression HADS subscales: Anxiety $t = 0.40$, df 544, $p > 0.05$, Depression $t = 0.71$, df 544, $p > 0.05$. The temporal lobe epilepsy group did not differ from those with other types of epilepsy in their average scores on any of the 14 individual items on the HADS.

Item analyses on the HADS anxiety subscale

Multivariate analysis of variance (MANOVA) with post hoc tests

Each question on the subscale was labelled with a single word for the analysis: Tense, Restless, Worrying, Relaxed, Awful, Butterflies, Panic (See Supplementary Table 1). The MANOVA revealed a significant effect for "Scale Item" ($f = 15.1$, df = 6, $p < 0.001$) indicating significant differences between the rates of endorsement across the 7 items that comprise the anxiety subscale of the HADS. There was no significant effect of epilepsy type (temporal vs other) on the level of endorsement of items across the subscale ($F = 1.6$, df = 6, $p > 0.05$).

Post hoc comparisons

Post hoc pairwise comparisons using Bonferroni corrections were conducted to investigate differences in endorsement levels between the individual subscale items '*I get a sort of frightened feeling as if something awful is about to happen*', '*I get a sort of frightened feeling like butterflies in the stomach*' and '*I get sudden feelings of panic*' and the other items on the anxiety subscale. See Supplementary Table 1 and Fig. 4.

I get a sort of frightened feeling as if something awful is about to happen: This item was endorsed significantly more strongly than '*I get sudden feelings of panic*', '*I can sit at ease and feel relaxed*' and '*I get a sort of frightened feeling like butterflies in the stomach*' (all $p < 0.01$). The item was endorsed significantly less often than '*Worrying thoughts go through my mind*' ($p < 0.001$) and '*I feel tense or wound up*' (both $p = 0.01$). There was no significant difference in the rates of endorsement of this item and '*I feel restless as I have to be on the move*' $p > 0.05$.

I get a sort of frightened feeling like butterflies in the stomach: This item was endorsed significantly less often than all of the other items in the anxiety subscale (all $p < 0.001$, except '*I can sit and feel relaxed*', $p = 0.02$).

I get sudden feelings of panic: This was endorsed significantly less often than '*Worrying thoughts go through my mind*', '*I feel tense or wound up*', '*I get a sort of frightened feeling as if something awful is about to happen*' (all $p < 0.001$). There was no significant difference in the rates of endorsement of this item and '*I can sit at ease and feel relaxed*' or '*I feel restless*' ($p > 0.05$).

In summary, we did not find a significant effect of epilepsy type on responses on the HADS. The items on the anxiety subscale were not uniformly endorsed across the subscale in our sample. The three items which may be associated with ictal phenomena ('*I get a sort of frightened feeling as if something awful is about to happen*', '*I get a sort of frightened feeling like butterflies in the stomach*' and '*I get sudden feelings of panic*') were not endorsed more often than other items including '*I feel tense and wound up*' and '*Worrying thoughts go through my mind*'.

Item analyses on the HADS depression subscale

Multivariate effects

Each question on the subscale was labelled with a single word for the analysis: Enjoy, Laugh, Cheerful, Slowed, Appearance, Book, Look Forward (See Supplementary Table 1).The MANOVA revealed a significant effect for "Scale Item" ($F = 25.9$, df 6, $p < 0.01$) indicating significant differences between the rates of endorsement across the 7 items that comprise the depression subscale of the HADS. There was no significant effect of epilepsy type (temporal vs other) on the level of endorsement of items across the subscale ($F = 0.73$, df = 6, $p > 0.05$) and no significant interactions between the subscale item and epilepsy type ($p > 0.05$).

Post hoc comparisons

Post hoc pairwise comparisons with Bonferonni corrections were conducted to investigate differences in endorsement levels between the item '*I feel as if I am slowed down*' and the other items on the subscale. See Supplementary Table 1 and Fig. 5.

This item was endorsed significantly more strongly than all of the other items on the subscale (all > 0.001) and was the most strongly endorsed item on the subscale.

In summary, as with the anxiety subscale, there was no significant effect of epilepsy type on responses on the depression subscale of HADS, but the items were not uniformly endorsed across the subscale. The feeling of being slowed down was endorsed significantly more than the other items on the subscale.

Discussion

In our large sample of consecutive patients referred for a neuropsychological assessment, over half of the sample (56.2 %) reported

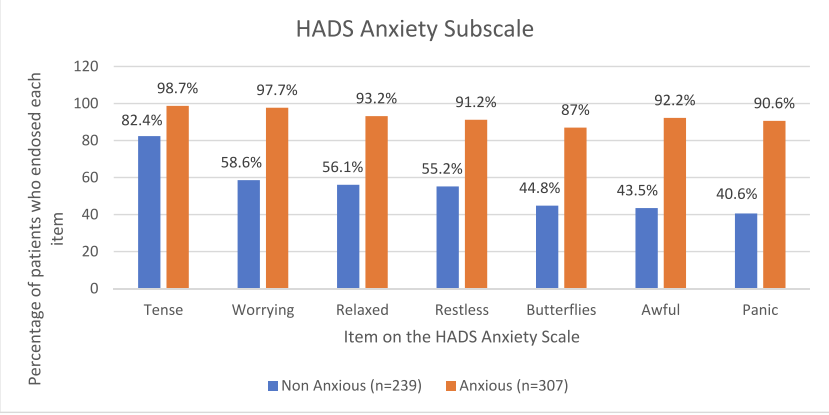

Fig. 2. Percentage of Patients in the Anxious/Non Anxious Group who Endorsed Each Item on the Anxiety Subscale (scoring 1 or more).

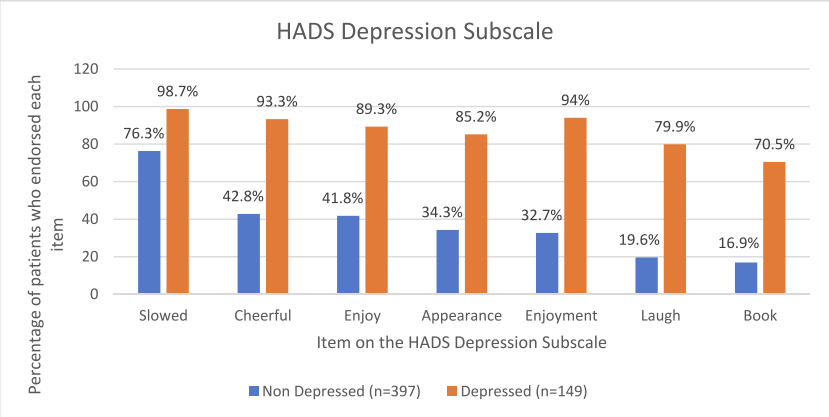

Fig. 3. Percentage of Patients in the Depressed/Non Depressed Group who Endorsed Each Item on the Depression Subscale (Scoring 1 or More).

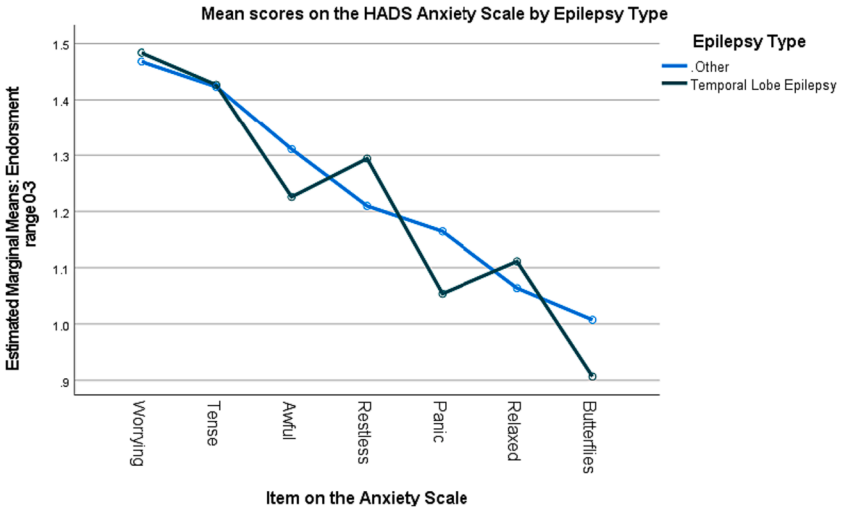

Fig. 4. Mean Scores on the HADS Anxiety Subscale by Epilepsy Type.

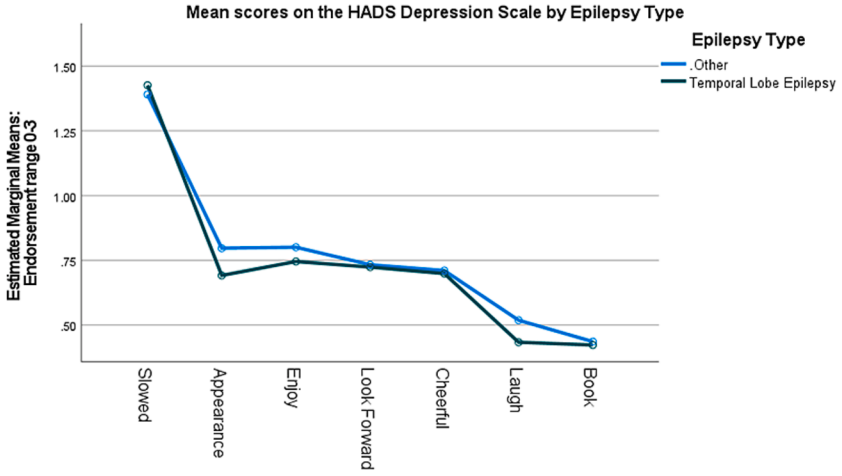

Fig. 5. Mean Scores on the HADS Depression Subscale by Epilepsy Type.

elevated levels of anxiety and more than one in four (27.3 %) reported symptoms of depression on the HADS. Scores on the anxiety and depression subscales were not related to age, sex or underlying epilepsy type. The results do not support our hypotheses that people with temporal lobe epilepsy would be more likely to endorse items associated with ictal symptomatology (including feelings of panic, dread and butterflies in the stomach) than those with other forms of epilepsy. We found no impact of epilepsy type on the level of endorsement on any of the items on the HADS.

Our results are reassuring with respect to the concerns discussed in

the introduction regarding the misattribution of possible ictal phenomena to anxiety. Anxiety is likely to be part of a complex presentation in people with epilepsy and the inclusion of symptoms that may overlap with ictal phenomena for some patients does not appear to have an undue influence on patient's responses on the subscale. This finding adds weight to previous studies that have found the HADS to be a valid screening tool for people with epilepsy [7,8] albeit with reduced sensitivity [8,9,13]. However, our findings do provide some insights into the factors that may reduce the specificity of the HADS in this population, particularly with respect to the ability of the depression scale to correctly identify those without the condition.

On the depression subscale, patients who reported elevated levels of depression and those who did not, endorsed the item '*I feel as if I am slowed down*' more strongly than the other items on the subscale. Our data indicates that feeling slowed down is very common in people with epilepsy with three quarters of the patients in our sample endorsing this symptom to some degree on the HADS. This symptom may not be a sensitive marker for underlying depression in people with epilepsy. From a practical, clinical perspective, our results suggest that the scores of people who score in the mild range for depression on the HADS should be examined for an anomalously elevated score on the '*I feel as if I am slowed down*' item to see if the classification indicates elevated symptomatology on a range of depressive symptoms, or just the feeling of being slowed down, in relative isolation from other features of depression. It is important to stress that the HADS, just like any other screening tool needs to be interpreted within the broader clinical context in which the patient presents, including individual seizure semiology, psychiatric history, and other medical concerns.

We did not have a non-epilepsy control group in this study and so we were not able to directly compare the pattern of endorsement across the items on the anxiety and depression subscales in people with epilepsy, with that seen in other patient groups. However, a number of studies have found similar discrepancies in the pattern of endorsement across the items on the HADS anxiety and depression subscales in other neurological groups. Interestingly '*I feel as if I am slowed down*' and '*I feel tense or wound up*' are also disproportionately endorsed in people with Parkinson's Disease [14,15]. Feeling slowed down can also be a feature of normal aging in non-neurological populations. Cameron et al [16] examined the impact of age, gender and educational background on the responses of 1,063 non neurological patients referred to primary care mental health services and found that older patients were more likely to report feeling slowed down than the younger patients in their study.

Limitations

We did not have access to formal psychiatric diagnoses for this sample and so it was not possible to formally examine the relationship between responses on the individual items on the HADS and clinically derived diagnoses of anxiety and depression. Whilst we had access to a relatively large sample of people with epilepsy, they had all been referred to our department for a neuropsychological assessment. Most people with epilepsy do not undergo a formal neuropsychological review and therefore the people in this sample may not be representative of the wider population of people with seizures. Given the well-established links between mood and cognitive complaints [17] it is likely that people referred for a neuropsychological assessment due to concerns about their cognitive function may well report elevated levels of low mood and experience more anxiety in general. This may be reflected by the very high level of endorsement of the 'worrying thoughts' item on the anxiety subscale. Again, this emphasises the importance of interpreting individual responses on the HADS in the broader clinical context. The majority of patients referred to our department are taking at least one anti-seizure medication with a sizable proportion on polytherapy. It is likely the pharmacological regime of each patient contributed to the feelings of being slowed down reported on the HADS and some medications are likely to have more effect than others. This should be considered in future studies.

Conclusions

We did not find a relationship between endorsement of items related to panic, feelings of dread or butterflies in the stomach and a diagnosis of temporal lobe epilepsy. The most frequently endorsed item on the anxiety subscale of the HADS in the sample as a whole related to worrying thoughts, rather than the more somatic manifestations of anxiety represented by feeling of dread, panic or butterflies. Feelings of being slowed down are very common in all forms of epilepsy and will be multifactorial in origin, reflecting features of the disease and its treatment. The item '*I feel as if I am slowed down*' is endorsed by the majority of people with epilepsy and may not reflect a symptom of depression. The responses of patients who score within the 'mild' range on the depression subscale of the HADS should be screened to ensure that this item is not exerting a disproportionate impact on the subscale.

Ethical approval

Permission to perform the audit of responses to the measures in this study was granted by the UCLH Quality and Safety Committee [Reference number 37-202122-SE]. All data was fully anonymised prior to analyses to ensure that the study conformed with local and national ethical guidelines for the study of routine data collected in clinical settings.

Declaration of Generative AI and AI-assisted technologies in the writing process

No AI tools were used in the production of this manuscript.

CRediT authorship contribution statement

Elisa Tye: Writing – review & editing, Writing – original draft, Project administration, Formal analysis, Data curation, Conceptualization. **Sallie Baxendale:** .

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ebr.2023.100641.

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