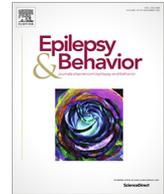




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Anhedonia in epilepsy

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ABSTRACT

Background: Anhedonia, the impaired ability to experience pleasure, is a core feature of major depressive disorder, one of the most common comorbidities in epilepsy. It is also reported as a clinical feature independent of depression in a number of other neurological conditions. This study aimed to establish the prevalence of anhedonia in a sample of people with epilepsy, with and without a diagnosis of depression, and to examine the clinical and demographic characteristics of those who present with this symptom.

Methods: A consecutive sample of 211 people (118 female, 93 male, mean age 38.09 years) completed the Snaith-Hamilton Pleasure Scale (SHAPS) to determine the presence of anhedonia and the Hospital Anxiety and Depression Scale to determine levels of anxiety and depression. The majority of patients had focal epilepsy ($n = 165$), and the remaining patients had generalized epilepsy ($n = 22$), or unclassified epilepsy ($n = 24$). Sixteen percent of the sample had a clinical diagnosis of depression at the time of the study.

Results: Over one in three of the sample (35%) reported significant anhedonia on the SHAPS. While these patients were more likely to have a diagnosis of depression ($p < 0.01$), 30% of people without a diagnosis of depression also reported significant anhedonia. Difficulties gaining pleasure on 12 of the 14 items on the SHAPS were associated with cognitive difficulties, with those reporting an inability to feel pleasure on the item scoring significantly lower on tests of cognitive function than those who were able to gain pleasure. Of the three cognitive domains examined (overall intellectual ability, verbal memory, and processing speed), a poor memory had the strongest relationship; with lower memory function associated with an impaired ability to experience pleasure on 9 of the 14 items.

Conclusion: While anhedonia is well recognized as a feature of depression, our data suggests that it can be present in up to a third of people with epilepsy who do not have a diagnosis of depression. Cognitive difficulties, particularly impaired memory function may mediate some features of anhedonia. The implications of these findings for the clinical management of anhedonia in people with epilepsy are discussed.

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1. Introduction

Mood and anxiety disorders are one of the most frequent comorbidities of people with epilepsy [1,2]. Depressive disorders are estimated to have a lifetime prevalence rate of 30–35% in people with epilepsy [3,4]. In a recent review, the overall pooled estimate for the incidence rate of active depression in people with epilepsy was 23.1% [5]. However, symptoms of depression may be even more widespread than these studies suggest, since depression in epilepsy can be missed when symptoms are masked or mimicked by the side effects of medication or seizures [6–9]. The presence of anhedonia may be a more clinically sensitive sign of

developing future depression in people with epilepsy than traditional markers [10,11].

Anhedonia, the reduced ability to feel pleasure, is a core feature of major depressive disorder [12]. Increased anhedonia is prevalent across several neurological conditions including Parkinson's disease [13,14] and traumatic brain injury [15,16], significantly reducing the quality of life [13]. Research into the prevalence and presentation of anhedonia in epilepsy populations is scarce.

Clinically abnormal rates of anhedonia have been reported in 12% of children with epilepsy, with significantly higher levels of anhedonia compared to healthy age, sex, and reading ability-matched peers [17–19] reported that children with frontal lobe epilepsy had significantly higher anhedonia severity scores than children with temporal lobe epilepsy. A recent study reported that 15/51 (29.4%) of adults with mesial temporal lobe epilepsy reported elevated levels of anhedonia on the Snaith-Hamilton

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Pleasure Scale after social restrictions associated with COVID-19 were lifted, compared to 19.6% prior to the pandemic [20]. Levels of anhedonia significantly correlated with levels of stress, depression, and anxiety ($p < 0.001$) confirming the strong link between anhedonia and depressive and anxiety symptoms in this population.

Rayner et al. [11] proposed 2 symptom-based phenotypes of depression in focal epilepsy: a cognitive phenotype and a somatic phenotype. The somatic phenotype of depression includes anhedonia as a core feature alongside high levels of anxiety. In their sample of ninety-one patients with focal epilepsy, 7% were classified as having symptoms of somatic depression, characterized by vegetative depressive symptoms and anhedonia. As with the later Sammarra et al. study [20], these symptoms were associated with greater levels of anxiety. The cognitive phenotype was more common, present in 17% of the sample, and was characterized by self-critical cognitions and pervasive memory deficits.

The current study aimed to establish the prevalence of anhedonia in a clinical population of people with epilepsy, with and without a diagnosis of depression, and to characterize the clinical and demographic factors associated with this presentation in this population.

2. Methods

2.1. Design and clinical setting

This study represents an analysis of the responses on the SHAPS [21] and the Hospital Anxiety and Depression Scale [22] which were administered as part of a routine clinical assessment of 211 consecutive patients with epilepsy who attended our department for a neuropsychological review between August 2021 and May 2022 at the National Hospital for Neurology & Neurosurgery, London and the UCLH Chalfont Centre for Epilepsy, UK. 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). Depression had been diagnosed by a general practitioner or psychiatrist and the presence of the diagnosis was identified via clinical review and examination of the medical records at the time of the neuropsychological assessment.

2.2. Measures

Participants completed the SHAPS [21], a 14-item scale measuring anhedonia. Participants respond to each item along a 4-point Likert scale, covering the ability to experience pleasure in domains of social interaction, food, sensory experience, and interests. Responses of strongly disagree or disagree are given one point, and responses of strongly agree or agree are scored zero points. Each participant's final score ranges from zero to 14, with higher scores indicating higher levels of present-state anhedonia. Final scores from the SHAPS were used to determine the presence of clinical anhedonia with a score of 3 or above indicating the presence of clinically abnormal anhedonia and scores of 2 or below reflecting normal levels of hedonic response. This cut-off was based on the original SHAPS study which confirmed that a cut-off score of 2 provided the best discrimination between 'normal' and 'abnormal' levels of hedonic tone [21]. The SHAPS is recognized as a user-friendly tool in clinical populations with high levels of reliability, and convergent and discriminant validity [23–25].

Participants also completed the Hospital Anxiety & Depression Scale [22]. The HADS is a 14-item scale yielding scores for anxiety

and depression. Each item is rated on a 4-point scale. Cut-offs for the total scores are used to categorize anxiety and depression; 0–7 (Normal) 8–10 (Mild) 11–15 (Moderate) 16–21 (Severe). This scale has been shown to have satisfactory construct validity and acceptable internal consistency in populations with epilepsy [26].

The neuropsychological measures used in the analyses were the National Adult Reading Test (NART), a reading test that gives an estimate of optimal intellectual reserve (IQ), the coding subtest from the Wechsler Adult Intelligence Scales – 4th edition (a measure of processing speed) and the learning score from the list learning test of the BIRT Memory and Information Processing Battery (a measure of verbal learning/memory).

2.3. Participants

Patients who were unable to read or whose intellectual disabilities prevented them from completing the questionnaire were excluded from the sample. The demographic and clinical characteristics of the patient series are presented in Table 1.

2.4. Ethical approval

We obtained prior permission to perform the audit of responses to the measures in this study from the UCLH Quality and Safety Committee [Reference number 37-202122-SE]. All data was fully anonymized 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.

2.5. Statistical analyses

Pearson Chi-square analyses were used to examine the associations between the presence/absence of anhedonia identified on the SHAPS and epilepsy type. The relationship between the overall SHAPS score and measures from the HADS was examined using Pearson Chi-square and Pearson r correlations.

The relationship between the endorsement of difficulty deriving pleasure on each item on the scale and cognitive function was examined using independent t -tests. A binary logistic regression model was used to identify significant demographic and clinical predictors of the presence of anhedonia. All analyses were conducted using SPSS v27 for windows.

Table 1
Demographic and clinical characteristics of the sample.

Age	Mean age 38.09 (sd 13.7) range 17–72
Sex	118 female, 93 male
Epilepsy Type	Focal $n = 165$ Generalised $n = 22$ Unclassified $n = 24$
History of depression	$N = 56$ (26%)
Current clinical diagnosis/treatment for depression	$N = 34$ (16%)
Reading IQ (National Adult Reading Test)	Mean 102.3 (standard deviation 11.0)
HADS Anxiety Score	Normal 40.3% Mild 19.4% Moderate 22.3% Severe 18%
HADS Depression Score	Normal 68% Mild 16% Moderate 12.1% Severe 3.9%

3. Results

3.1. Prevalence of anhedonia, depression and anxiety

Responses to the individual items on the SHAPS are represented graphically in Fig. 1. Seventy-four people (35%) of the group as a whole reported significant levels of anhedonia on the SHAPS (a score of 3 or more). The prevalence of anhedonia ranged from 22.7% in those with generalized epilepsy, 35% in those with focal to 45.8% in those with unclassified epilepsy (Pearson Chi-square = 2.96, $df = 2$, $p = 0.26$).

The distributions of mild, moderate, and severe levels of anxiety and depression in the epilepsy groups, as measured by the HADS are presented in Fig. 2. There was no significant effect of epilepsy type on the distribution of patients in each of the categories for anxiety (Pearson Chi-Square = 4.1, $df = 6$, $p = 0.65$) or depression (Pearson Chi-Square = 3.9, $df = 6$, $p = 0.68$).

3.2. Clinical associations with the presence of anhedonia

In the group as a whole, the total score on the SHAPS was highly correlated with the depression scale on the HADS (Pearson $r = 0.42$, $p < 0.001$). Anhedonia was also significantly associated with the endorsement of anxiety symptoms on the HADS (Pearson $r = 0.31$, $p < 0.001$).

As expected, the presence of anhedonia was significantly associated with a current clinical diagnosis of depression (Pearson Chi-Square = 10.0, $df = 1$, $p = 0.002$). However, 30% of the sample without a clinical diagnosis of depression also reported significant anhedonia ($n = 54$).

In the group reporting anhedonia ($n = 74$), those with a diagnosis of depression tended to be younger than those without a current diagnosis of depression; No diagnosis of depression and anhedonia; mean age 39.3 years (standard deviation 12.1); diagnosis of depression and anhedonia; mean age 33.3 years (standard deviation 10.6); $t = 1.9$, $df = 72$, $p = 0.02$). Sex was evenly distributed in the patients with anhedonia with and without a current

diagnosis of depression (Pearson Chi-Square = 0.08, $df = 1$, $p = 0.77$).

Patients with anhedonia who had a concurrent diagnosis of depression reported significantly greater levels of anxiety on the HADS than those reporting anhedonia without a diagnosis of depression ($t = -2.2$, $df = 69$, $p = 0.01$). In those who reported anhedonia, there were no significant differences between the groups with and without a diagnosis of depression on the depression scale of the HADS ($t = -1.4$, $df = 69$, $p = 0.08$).

3.3. Regression analyses

Binary logistic regression was used to examine the demographic and clinical predictors of anhedonia in the sample. Age (years), sex (categorical/F), type of epilepsy (categorical: Generalized, Focal, Unclassified), verbal memory (list learning score), and processing speed (coding score) was used as the predictor variables of significant anhedonia reported on the SHAPS (a score of 3 or greater).

Multicollinearity between independent variables was examined via correlations and the variance inflation factor (VIF). Whilst age and processing speed and memory are significantly correlated, they are not highly correlated (Pearson correlation < 0.40). See Supplementary Table 1. The VIF and tolerance collinearity statistics for each variable are presented in Supplementary Table 1. The VIF scores are below 10 [27] and none of the tolerance statistics are below 0.2 [28]. The assumptions for including these variables in the binary logistic model were met.

The logistic regression model is presented in Table 2. Anhedonia was significantly associated with poor verbal memory and the presence of generalized epilepsy in the model.

3.4. Cognitive correlates

There were no significant differences between the patients who reported significant anhedonia on the SHAPS and those who did not on our measure of overall cognitive reserve (NART IQ;

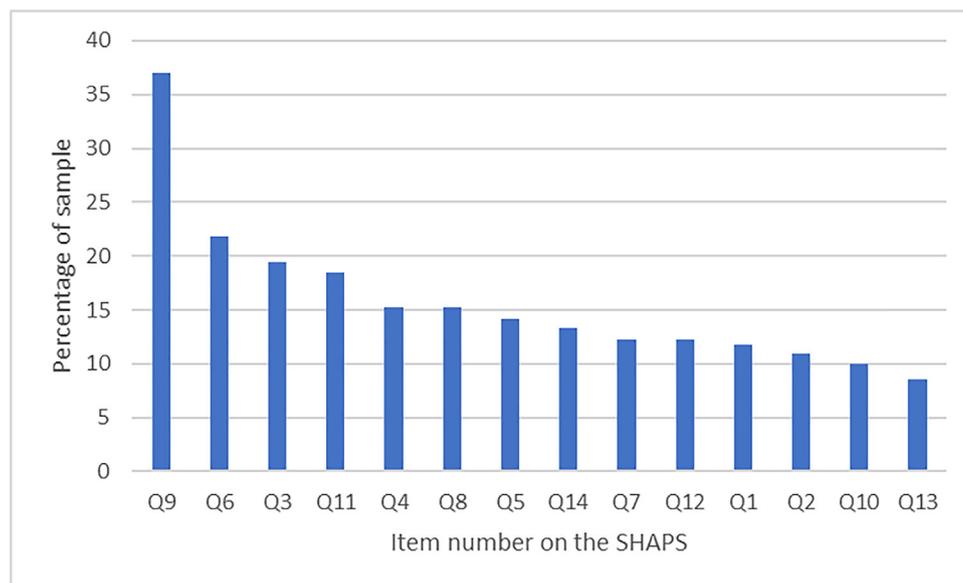


Fig. 1. Percentage of sample who reported difficulties experiencing pleasure on each item of the SHAPS. Key: 1. I would enjoy my favourite television or radio programme. 2. I would enjoy being with my family or close friends. 3. I would find pleasure in my hobbies and pastimes. 4. I would be able to enjoy my favourite meal. 5. I would enjoy a warm bath or refreshing shower. 6. I would find pleasure in the scent of flowers or the smell of a fresh sea breeze or freshly baked bread. 7. I would enjoy seeing other people's smiling faces. 8. I would enjoy looking smart when I have made an effort with my appearance. 9. I would enjoy reading a book, magazine or newspaper. 10. I would enjoy a cup of tea or coffee or my favourite drink. 11. I would find pleasure in small things, e.g. bright sunny day, a telephone call from a friend. 12. I would be able to enjoy a beautiful landscape or view. 13. I would get pleasure from helping others. 14. I would feel pleasure when I receive praise from other people.

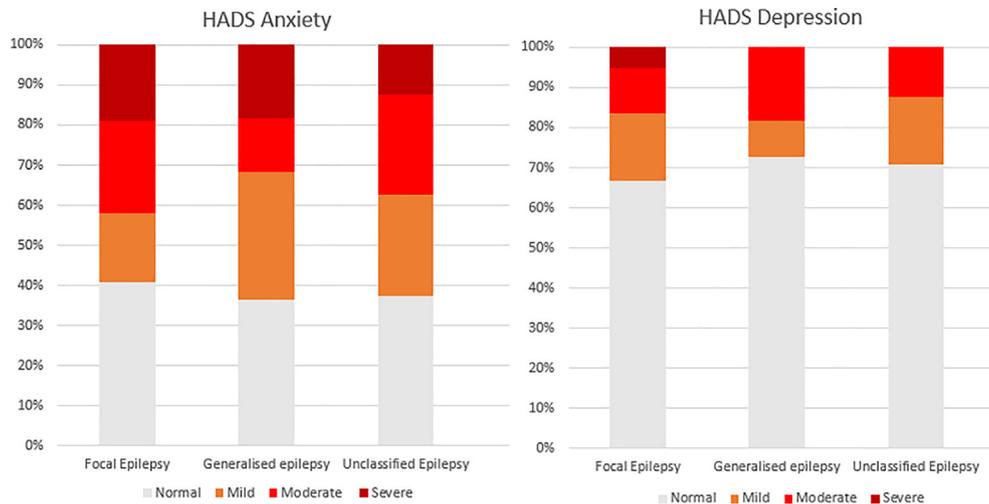


Fig. 2. Distributions of HADS classification scores for anxiety and depression across the 3 epilepsy groups.

Table 2
Logistic regression: Predictors of anhedonia.

		B	S.E.	Wald	df	Sig.	Exp(B)
Step 1 ^a	Age	−0.010	0.013	0.569	1	0.451	0.990
	Sex (Male 1; Female2)	−0.375	0.325	1.326	1	0.250	0.687
	Focal Epilepsy	0.265	0.478	0.308	1	0.579	1.304
	Generalized Epilepsy	1.701	0.786	4.678	1	0.031	5.477
	Verbal Learning	−0.041	0.016	6.816	1	0.009	0.960
	Processing Speed	−0.071	0.060	1.418	1	0.234	0.931
	Constant	1.161	1.191	0.949	1	0.330	3.192

$R^2 =$ Cox & Snell = 0.11, Nagekerke 0.15. Model Chi square 23.1. df 6, $p < 0.001$.

$t = 0.65$, $df = 148$, $p = 0.25$). However, the group with anhedonia had significantly slower processing speed ($t = 2.6$, $df = 194$, $p < 0.004$) and weaker memory skills ($t = 3.0$, $df = 205$, $p = 0.001$) than those who did not report significant anhedonia.

Rating of significant difficulties gaining pleasure on 12 of the 14 items on the SHAPS was associated with cognitive difficulties, with those reporting an inability to feel pleasure on the item scoring significantly lower on tests of cognitive function than those who were able to gain pleasure. Of the three cognitive domains examined (overall intellectual ability, verbal memory, and processing speed), a poor memory had the strongest relationship; with lower memory function associated with an impaired ability to experience pleasure on 9 of the 14 items. See Table 3 for significance and effect sizes.

4. Discussion

We found that anhedonia is a relatively common presentation in people with epilepsy with 35% of people in our mixed sample scoring positively for the presence of anhedonia on the SHAPS. Whilst the prevalence of anhedonia was greatest in our sample in those with unclassified epilepsy (45.8%), differences in the prevalence of anhedonia between the epilepsy groups did not reach statistical significance. The prevalence of anhedonia in all of our groups is greater than the 15% estimated in the general healthy population [29].

As expected, we found that people with a concurrent diagnosis of depression were more likely to report anhedonia than those without. However, 30% of our sample without a formal diagnosis of depression also reported anhedonia. These patients did not differ from those with a diagnosis of depression with respect to sex distribution or their scores on the depression subscale of the HADS,

however, patients with anhedonia who had a concurrent diagnosis of depression reported significantly greater levels of general psychological distress with higher levels of anxiety on the HADS than those reporting anhedonia without a diagnosis of depression.

The dissociation between anhedonia and depression raises some questions given that anhedonia is one of the major criteria for diagnosing clinical depression. This dissociation in our data probably reflects a number of factors including the nature of the clinical diagnosis, the transience of symptoms, the effectiveness of treatment, the reliability/validity of screening measures, and the limitations of record-based research. The impact of treatment on symptoms is of particular interest. The literature examining the PANAS (Positive and Negative Affect Schedule) in patients indicates that a reduction of depressive mood as indicated by the HADS by no means implies the recovery of pleasure; thus, these measures may miss a clinically important aspect of altered affect/motivation, namely anhedonia in the absence of depressive mood [30,31].

All of the patients in this sample are under the care of a multi-disciplinary team including neuropsychiatrists and clinical psychologists who specialize in the care of people with epilepsy. It would be reasonable to surmise that if depression is under-recognized in this specialist setting it is likely to be missed by greater numbers of people who do not have access to this kind of service.

Anhedonia has long been associated with depression but our findings provide support for a substantial link between anxiety and the inability to derive pleasure from everyday activities, consistent with previous studies [11,20]. We found that scores on the SHAPS were highly correlated with the anxiety score on the HADS. Maintaining high levels of anxiety is a significant drain on an individual's mental reserves, so it makes sense that the ability

Table 3

Cognitive function and inability to gain pleasure: Differences in scores on the tests of cognitive function between the groups who reported inability to feel pleasure (scores of 3 or more on the SHAPS) vs ability to feel pleasure (scores of 2 or less) [21] on each item of the SHAPS.

	SHAPS item Endorsed	SHAPS item not endorsed	T-Test	Effect Size: Cohen's d		
				Standardizer	95% Confidence Interval	
					Lower	Upper
Overall Cognitive Reserve	Mean score	Mean score	Group differences			
9. I would enjoy reading a book, magazine or newspaper.	99.1 (8.3)	103.7 (12.1)	$T = 2.0, df 148, p = 0.01$	10.90	0.018	.687
Processing Speed	Mean score	Mean score	Group differences			
4. I would be able to enjoy my favourite meal.	6.9 (2.6)	8.3 (3.1)	$T = 2.2, df 194, p = 0.01$	3.05	0.054	.837
6. I would find pleasure in the scent of flowers or the smell of a fresh sea breeze or freshly baked bread.	7.3 (2.9)	8.3 (3.1)	$T = 1.9, df = 193, p = 0.02$	3.07	-0.003	.677
11. I would find pleasure in small things, e.g. bright sunny day, a telephone call from a friend.	7.3 (3.2)	8.3 (3.0)	$T = 1.78, df 193, p = 0.03$	3.07	-0.034	.693
12. I would be able to enjoy a beautiful landscape or view	6.69 (2.9)	8.31 (3.08)	$T = 2.04, df = 193, p = 0.02$	3.07	0.016	.860
13. I would get pleasure from helping others.	6.25 (3.27)	8.3 (3.04)	$T = 2.55, df 183 p = 0.006$	3.06	0.151	1.185
Memory Function	Mean score	Mean score	Group differences			
3. I would find pleasure in my hobbies and pastimes.	43.0 (12.9)	46.6 (11.7)	$T = 1.68, df 204, p = 0.04$	11.96	-0.050	.649
4. I would be able to enjoy my favourite meal.	41.9 (11.1)	46.6 (12.)	$T = 2.06, df 205, p = 0.02$	11.90	0.017	.775
5. I would enjoy a warm bath or refreshing shower	41.5 (13.9)	46.7 (11.5)	$T = 2.2, df 204 p = 0.01$	11.05	-0.415	.596
7. I would enjoy seeing other people's smiling faces	42.1 (11.9)	46.5 (11.9)	$T = 1.7, df 204, p = 0.04$	11.92	-0.045	.780
8. I would enjoy looking smart when I have made an effort with my appearance	41.7 (13.8)	46.7 (11.5)	$T = 2.1 df 203, p = 0.01$	11.08	-0.560	.346
10. I would enjoy a cup of tea or coffee or my favourite drink.	41.7(11.7)	46.4 (11.9)	$T = 1.71, df = 205, p = 0.04$	11.05	-0.497	.488
11. I would find pleasure in small things, e.g. bright sunny day, a telephone call from a friend.	39.23 (13.7)	47.62 (10.9)	$T = 4.08, df 204, p < 0.001$	11.55	0.369	1.081
13. I would get pleasure from helping others.	37.39 (11.5)	47.3 (11.7)	$T = 3.4, df = 193, p < 0.001$	11.72	0.355	1.339
14. I would feel pleasure when I receive praise from other people.	41.0 (12.8)	47.2 (11.7)	$T = 2.5, df = 193, p = 0.005$	11.87	0.124	.931

Effect size standardizer: The denominator used in estimating the effect sizes. Cohen's d uses the pooled standard deviation.

to enjoy simple things will be impaired in the presence of the significant demands on mental reserve that are associated with clinical levels of anxiety. Our findings suggest that the presence of anhedonia should not just alert the treating clinician to the possible presence of depression in their patients, it should also prompt an investigation of anxiety.

We found a small, but significant association between cognitive function and anhedonia. In our logistic regression model our measure of verbal memory in combination with demographic and clinical factors accounted for a small, but significant amount of the variance in the model, around 15%. A low verbal learning score was a significant predictor of the presence of anhedonia. Although people with anhedonia did not differ from those without on a measure of overall cognitive reserve (Reading IQ) they did score significantly lower on tests of processing speed and memory function. It is also noteworthy that the item endorsed most frequently on the SHAPS in our sample related to a pastime with a significant cognitive component – finding pleasure in reading books, magazines, and papers. In addition, poor memory had the strongest relation with anhedonia with lower memory function associated with an impaired ability to experience pleasure on 9 of 14 items on the SHAPS. Our study design does not allow for causal inferences, we can only note the association but it is likely that anhedonia is mediated to at least some extent by the common impairments in cognitive function experienced by people with epilepsy. These difficulties themselves are multifactorial in nature [32]. However, the findings raise the intriguing possibility that some aspects of anhedonia may be relieved by the implementation of targeted rehabilitation approaches that combine anxiety management techniques with cognitive rehabilitation, to widen access to activities that people may find pleasurable.

Anhedonia is traditionally viewed as the inability to gain pleasure from activities. As a measure of anhedonia, the SHAPS

was primarily developed in healthy subjects and secondarily in people with idiopathic mental illnesses. Its applications in populations with diseases that result in real-life constrictions of pleasurable activities are not well studied, but one could fail to endorse the term 'I would enjoy ...' because this activity is unavailable rather than an inability to feel pleasure when engaged in the activity. A recent longitudinal study of responses on the SHAPS in cannabis users found a significant increase in anhedonia during the COVID-19 lockdowns, possibly reflecting the reduced availability of opportunities to enjoy activities during this period compared to the relative pre-pandemic freedoms [33]. In epilepsy, multiple biopsychosocial barriers may prevent or discourage participation in pleasurable activities in the first place, setting up a negative spiral whereby people are unable to derive pleasure from activities because they no longer participate in them. The ambiguous phrasing in the SHAPS could be modified in future studies with people with epilepsy to make the clear distinction between the inability to feel pleasure when partaking in some activities and the lack of opportunity to feel pleasure due to intrinsic factors associated with the condition.

In addition to the ambiguity in the wording of the SHAPS, this study has a number of other shortcomings. As a pragmatic, clinical sample of people referred for a neuropsychological assessment, those with focal epilepsy were by far the largest group in the sample. Most people with epilepsy are not under the care of a tertiary center and may never undergo a neuropsychological assessment as such, whilst this sample may reflect a typical research population, they may not represent the wider population of people with epilepsy. A related issue is the anti-seizure medications that the people in this sample were taking. We did not control for this in our design and many were on complex regimes, taking multiple medications at different doses. GABAergic mechanisms may be involved in depression [34] with reduced levels reported in the

plasma [35], cerebrospinal fluid [36], and resected cortical tissue [37] of people with depression. It is possible that some antiseizure medications with GABAergic mechanisms may be a protective factor with respect to depression. Having established the increased prevalence of anhedonia in people with epilepsy, we now plan to explore the possibility of a protective impact of antiseizure medications on the presentation of anhedonia in this sample.

5. Conclusions

Anhedonia is common in people with epilepsy and occurs in those without a formal diagnosis of depression. The prevalence of anhedonia is increased in patients with focal, generalized, and unclassified epilepsy. The presence of anhedonia is associated with increased levels of anxiety and impairments in cognitive function, particularly with respect to memory and slowed processing speed. Anxiety and cognitive difficulties may mediate some of the barriers to experiencing pleasure in epilepsy, raising the possibility of targeted treatments for some people with epilepsy.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.yebeh.2022.108966>.

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