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The role of obesity in cognitive dysfunction in people with epilepsy

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ABSTRACT

Objective: In the general population, obesity is associated with accelerated age-related cognitive decline. The impact of obesity on cognitive function in neurological populations who already have a heightened risk of cognitive decline is unknown. This study explored the relationship between obesity and cognitive underfunction in people with medically intractable epilepsy.
Methods: Eighty-one consecutive patients admitted for evaluation for medically intractable epilepsy (36 females and 45 males) underwent tests of memory and intellectual function. Optimal level of function was assessed using the National Adult Reading Test — Revised. Measures of underfunction were calculated by subtracting current measures of intellectual ability from the NART IQ. Body mass index (BMI) was used as an index of obesity.
Results: Twenty-nine people had a BMI in the healthy range (36%), 31 were overweight (38%), and 21 were obese (26%). The healthy weight, overweight, and obese groups did not differ in age at the time of assessment, age at seizure onset, or optimal level of function (NART IQ). The obese group had a greater degree of suboptimal processing speed and demonstrated a greater degree of underfunction on the Full Scale IQ (FSIQ) measure compared to the healthy weight group. Body mass index accounted for 14% of the variance in underfunction in processing speed and 10% of the variance in underfunction in FSIQ. Controlling for the effects of age, all measures of memory function were significantly correlated with BMI, with poorer scores associated with higher BMIs.
Significance: A small but significant proportion of the variance in memory function and intellectual underfunction in people with epilepsy is explained by BMI. Further work is needed to establish whether a reduction in BMI to within healthy limits is associated with improvements in cognitive function in this group.

1. Introduction

In the general population, obesity is associated with accelerated age-related cognitive decline from middle age onwards [1]. Adults without dementia who are obese perform more poorly on standardized memory tests compared to individuals who are of healthy weight [2,3]. They also have smaller hippocampi [4], particularly those with central obesity [5]. Central obesity in middle age is also associated with an increased risk of developing dementia in old age [5]. The mechanisms underlying this relationship are complex and multifactorial. Obesity is a biomarker for the cardiovascular risk factors and diseases that have a direct impact on cognitive function, including diabetes and insulin resistance, elevated triglyceride levels, white matter disease, hypertension, and hypercholesterolemia [6].

The impact of obesity on cognitive function in younger neurological populations who have preexisting, heightened risks of cognitive dysfunction is unknown. The mechanisms of cognitive dysfunction in epilepsy are complex. The underlying pathology, antiepileptic medications, and psychological factors all interact with the functional reserve of an individual to shape their cognitive profile. Cognitive functions change over time, with progressive deterioration associated with frequent generalized seizures and stepwise deteriorations following episodes of status epilepticus or seizure-related injuries [7,8].

A recent review found that the rates of obesity in people with epilepsy are similar to those found in the general population [9]. While there are no associations between obesity and epilepsy type, duration, or etiology, obesity rates are higher in patients with refractory than nonrefractory epilepsy (36.9% vs. 24.6%). Obesity is also more common in patients treated with polytherapy than those treated with monotherapy (37.7% vs. 25%). Some antiepileptic medications, particularly sodium valproate and pregabalin, have weight gain as a significant side effect [10].

This study explored the relationship between obesity and cognitive function and measures of decline on standardized indices of intellectual and memory function in people with medically intractable epilepsy. The prevalence of memory deficits in this population is already high because

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of a combination of the underlying pathology, treatment effects, and psychiatric morbidities associated with the condition [6,7]. We hypothesized that the effects of obesity on cognitive function seen in the general population would be evident in this neurological population. This study was designed to examine the variance in measures of intellectual decline and memory function that is explained by BMI in people with intractable epilepsy.

2. Methods

2.1. Design

This was a cohort study of 81 consecutive adult patients who were referred for a neuropsychological assessment at our specialist epilepsy assessment service in 2013–2014.

2.2. Participants

All participants had a clinical diagnosis of epilepsy and were taking at least one antiepileptic medication at the time of assessment, at which point they all had medically intractable epilepsy, i.e., they continued to experience seizures despite taking antiepileptic medications. All participants in this study spoke English as a first language. Patients who had a diagnosis of nonepileptic attack disorder (NEAD) or who were unable to complete the neuropsychological assessment because of sensory deficits or psychiatric disturbance were excluded from the study. The majority of the participants had focal epilepsy (n = 77), 36 had a temporal lobe focus, 41 had an extratemporal focus or difficult-to-localize epilepsy, and four had generalized epilepsy. All participants underwent a 3-T structural MRI scan (see Table 1).

The clinical and demographic characteristics of the sample are presented in Table 2. All participants underwent a medical interview at the time of their admission to the ward which documented their medical history and all previous diagnoses. None of the participants had been given a diagnosis of sleep apnea at the time of their assessment, but sleep studies to investigate this possibility were not conducted during their admission. One participant had a diagnosis of type 1 diabetes; none had developed type 2 diabetes. Sixteen participants had evidence of white matter disease on MRI. In 5 of the 16, the white matter lesions were the only abnormalities evident on MRI.

2.3. Neuropsychological tests

The IQs derived from the National Adult Reading Test — Revised [11] were used to provide a measure of each participant's optimal level of intellectual function (5.8 points were subtracted to allow for the restandardization of the Wechsler Adult Intelligence Scale — IV (WAIS-IV)).

All participants completed the WAIS-IV UK Edition [12]. The Verbal Comprehension, Perceptual Reasoning, Working Memory, and Processing Speed indices were used as measures of intellectual function. The list learning and list retention scores from the BIRT Memory and Information Processing Battery (BMIPB) [13] were used as measures of verbal learning and recall, respectively. In the list learning task, the patient is aurally presented with a list of 15 words to learn over trials and is then required to recall them following exposure to a distractor list. The design learning and design recall measures from the BMIPB were used as measures of visual learning and recall, respectively. In the design learning task, the patient is exposed for 10 s to a design that has nine features and is required to reproduce it over five trials. Recall is tested following exposure to a distractor design. These tests have been described previously and have been shown to be sensitive to hippocampal pathology [14,15].

A measure of cognitive underfunction was calculated for each index of intellectual function by subtracting the index score from the NART IQ. In the general population, BMI is negatively correlated with measures of intellectual function [16]; those with lower IQs are more likely to become obese than those with higher IQs [17]. In addition to underlying genetic factors, people with lower intellectual reserves, in particular deficits in executive functions, may make poorer diet choices than those with stronger intellectual abilities [17–19]. We controlled for this pattern in our study by creating individual measures of cognitive underfunction for each participant. By subtracting each patient's current level of function from reliable measures of their optimal level of ability, we ensured that the measures of intellectual underfunction that we used in the analyses were relative to each patient's optimal level of function rather than the norms in the general population.

Reliable estimates of an individual's optimal memory function are not available. Measures of underfunction can only be inferred using standardized neuropsychological tests. The memory scores were converted to z-scores using the means and standard deviations from published age-referenced norms for each test to allow statistical comparisons [12,13].

Seventy-six of the participants completed the Hospital Anxiety and Depression Scale, yielding scores for anxiety and depression.

Table 1
MRI pathology.

	Frequency	Percent
Normal: no abnormality detected	35	43.2
Hippocampal sclerosis	12	14.8
Cortical dysplasia	11	13.6
Dysembryoplastic neuroepithelial tumor	2	2.5
Structural lesion	8	9.9
Hyperintense lesion	2	2.5
White matter disease	5	6.2
Surgery	2	2.5
Infarct	4	4.9
Total	81	100.0

Table 2
Clinical and demographic characteristics of the participants.

		Normal weight, N = 29	Overweight, N = 31	Obese, N = 21
Epilepsy type	Focal	n = 28 (n = 17 temporal)	n = 30 (n = 6 temporal)	n = 19 (n = 5 temporal)
	Generalized	n = 1	n = 1	n = 2
No. of AEDs	1	n = 7	n = 3	n = 2
	2	n = 13	n = 12	n = 7
	>2	n = 9	n = 16	n = 12
Age at assessment		32.0 (10.5)	35.6 (11.0)	36.5 (10.0)
Age at epilepsy onset		18.2 (6.9)	18.2 (12.5)	15.8 (12.3)

2.4. Body mass index

All patients undergo a general health screen when they are admitted to the hospital, and their weight and height are recorded. Body mass index was calculated using the following formula: BMI = mass (kg) / (height (m))^2. Participants with a BMI of less than or equal to 18.4 were classified as underweight. Participants with a BMI of between 18.5 and 24.9 were classified as having healthy weight. Participants with a BMI of between 25 and 29.9 were classified as overweight. Participants with a BMI of 30 or over were classified as obese.

2.5. Statistical methods

Partial correlations, controlling for age at the time of assessment, were used to examine the relationship between BMI and neuropsychological test scores. To examine the differences between the healthy, overweight, and obese groups on the neuropsychological measures, ANOVAs were used.