Original article

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Obesity and its association with generalised epilepsy, idiopathic syndrome, and family history of epilepsy

Lady D Ladino [1,2], Lizbeth Hernández-Ronquillo [1], José F. Téllez-Zenteno [1]

[1] Department of Medicine, Division of Neurology, University of Saskatchewan, Saskatoon, Canada
[2] Department of Neurology, Hospital Pablo Tobón Uribe, Medellín, Colombia

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ABSTRACT – *Aim*. Previous studies support the concept that obesity is a common comorbid condition in patients with epilepsy (PWE). In this study, we present the body mass index (BMI) and data from a survey to assess physical activity in a sample of PWE from an epilepsy clinic. *Methods*. Between June of 2011 and January of 2013, 100 PWE from an adult epilepsy clinic were included. We obtained BMI, waist circumference, and information regarding physical activity using a standardised questionnaire. Clinical, demographic, electrographic, and imaging parameters were collected from charts. *Results*. Mean age of patients was 40±14 (18-77) years. The BMI distribution was as follows: 2 patients (2%) underweight, 26 (26%) normal weight, 34 (34%) overweight, 25 (25%) obese, and 13 (13%) with morbid obesity. In our study, obesity was defined as having a BMI ≥30. We found 38 (38%) patients in this range. There was no difference in the rate of drug-resistant epilepsy between obese and non-obese patients (55 *vs*. 55%; *p*=0.05). Leisure time habit was reported in 82% of obese patients and 79% of patients without obesity. Overall, the most frequent activity was walking (70%). Factors associated with obesity were generalised epilepsy (OR: 2.7, 1.1-6.6; *p*=0.012), idiopathic syndrome (OR: 2.7, 1.04-7; *p*=0.018), and family history of epilepsy (OR: 6.1, 1.5-24.2; *p*=0.002). *Conclusion*. Our study suggests an association between obesity, idiopathic generalised epilepsy, and family history of epilepsy. Our study shows that PWE are physically active and there is no clear relation between exercise and obesity. We could not identify any association between drug-resistant epilepsy and obesity. Absence of direct comparison with a control non-epileptic population; a cross-sectional design not allowing evaluation of a causal association among variables; and reliance on self-reported physical activity are to be considered as limitations of the present study.

Key words: body mass index, genetic syndrome, leisure activity, overweight, physical activity and waist circumference

Correspondence:
José F. Téllez Zenteno
Department of Medicine,
Division of Neurology Royal University Hospital,
Saskatoon, SK,
S7N 0W8 Canada
<jose.tellez@usask.ca>

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Obesity is one of the greatest scourges of modern health in the industrialised world and now in many developing countries. In some developed countries, such as USA and Canada, the prevalence of overweight and obese subjects is 68 and 62%, respectively (Statistics Canada, 2010; Flegal *et al*., 2012;). There are potential reasons to consider that patients with epilepsy (PWE) have a higher risk of developing obesity than the general population. First, epilepsy itself may cause progressive weight gain through central nervous system (CNS) pathways. The regulation of food intake is a complex process involving interactions between brain regions responsible for behavioural control; a dysfunction in these centres may result in increased appetite and weight gain. This interaction has been demonstrated through hypothalamic-mediated mechanisms in rat models with epilepsy (St-Pierre *et al*., 2009), amygdala-mediated mechanisms in kindled rats (Hum *et al*., 2009), and hippocampus and fornix-mediated mechanisms in rats (Davidson *et al*., 2009) and humans (Metzler-Baddeley *et al*., 2013).

Bodyweight gain is a common and frequent side effect associated with the use of AEDs. This association has been reported for many years with the use of valproic acid and carbamazepine, and more recently, with some of the new drugs such as vigabatrin, gabapentin and pregabalin (Jallon and Picard, 2001; Ben-Menachem, 2007). Valproic acid enhances GABA transmission within the hypothalamic axis, causing appetite stimulation, hyperinsulinaemia and hyperleptinaemia, and decreased concentrations of ghrelin and adiponectin. All these phenomena can be prompted by insulin and leptin resistance and by becoming overweight. Carbamazepine can cause overeating, fat deposition, water retention, and oedema which also can result in overweight (Hamed, 2007). While many metabolic changes may occur as a consequence of epilepsy or AEDs usage, a paediatric study detected obesity as a common comorbidity in children with newly-diagnosed untreated epilepsy (Daniels *et al*., 2009), suggesting that obesity may prime the CNS for seizures (Lee and Mattson, 2014).

Finally, some studies have found that PWE participate less frequently in physical activities than the general population (Steinhoff *et al*., 1996; Hinnell *et al*., 2010). This restriction has been explained, partly due to fears of either injury during seizures or the possibility of exercise-induced seizures (Gordon *et al*., 2010). Few studies have addressed the prevalence of obesity in epilepsy clinics and its relation with drug-resistant epilepsy. This study has the following objectives: a) to determine the prevalence of obesity in a cohort of patients referred to an epilepsy centre; b) to evaluate the association between obesity and drug-resistant epilepsy; and c) to assess the amount of physical activity in PWE. Our initial hypothesis was that obesity was more frequent in patients with drug-resistant epilepsy, and physical activity was more frequent in non-obese PWE.

Materials and methods

Type of study and sample of PWE

This was a cross-sectional study performed at the Royal University Hospital in Saskatoon, Saskatchewan, Canada. The Institutional Review Board of the University of Saskatchewan approved the study. Adult PWE were identified from the epilepsy clinic of the previously mentioned hospital. All patients were recruited consecutively from outpatients attending our epilepsy clinic. After their clinical appointment, PWE were approached and asked to voluntarily participate in the study. A full explanation of the nature of the study was provided to the patients. Informed consent was obtained from every patient before interviews and measures. Exclusion criteria were as follows: patients with non-confirmed diagnosis of epilepsy or patients with non-epileptic seizures; patients in a wheelchair with severe disability that prevents appropriate body measurements; pregnancy; and history of bariatric surgery. The medical history of each patient was obtained from the hospital charts. Family history of epilepsy was considered positive when the patient had a first-degree relative (a parent or sibling) with a confirmed diagnosis of epilepsy regardless of the electroclinical syndrome. Epilepsy syndrome and seizures types were classified according to recommendations of the International League Against Epilepsy (ILAE). Drug-resistant epilepsy was defined with the new consensus-definition of the ILAE (Kwan *et al*., 2010).

Physical activity survey

A trained physician conducted a standardised questionnaire to assess physical activity that was part of the Canadian Community Health Survey 2000-2001 cycle 1.1 (CCHS) (Canadian Community Health Survey 2000-2001 cycle 1.1., 2003). The questionnaire assesses physical activity in the previous six months of the interview. It includes questions about physical activity that is not related to work. Respondents are asked to report physical activity from a list of up to 18 leisure-time activities (walking, swimming, dance, gardening, *etc*.). For each activity, the patient is asked about the frequency of participation (number of occasions per week in the past six months) and duration of participation on each occasion (1 to 15 minutes, 16 to 30 minutes, 31 to 60 minutes, or more than one hour). The survey also addresses an

estimation of one's own physical activity (usually sitting, standing or walking, lifting light or heavy loads). Additionally, we included the season when the questionnaire was completed (winter, from November to April, and other periods, from May to October) due to potential variations in physical activity patterns.

Anthropometric data

Height and weight were measured while subjects were wearing light clothing and no shoes. They were measured with a wall-mounted stadiometer and calibrated scale. Index BMI was calculated with the following formula: bodyweight in kilograms divided by the square of standing height in metres, reported in units of kg/m^2. Waist circumference (WC) was measured using an inelastic and flexible tape measure, with the individual in a standing position, and assessed at the approximate midpoint between the lower margin of the last palpable rib and the top of the iliac crest (World Health Organization, 2008). The measurements were made with the tape held snugly, but not constricting, and at a level parallel to the floor. The subject stood in a relaxed posture, with arms at the sides, feet positioned close together, and weight evenly distributed across the feet. We defined five categories of BMI according to the WHO (World Health Organization, 1995) as follows: underweight (<18.5), normal weight (18.5-24.9), overweight (25-29.9), obese (30-34.9), and morbidly obese (>35). WC was also classified using the criteria of the WHO and Health Canada with regards to risk to health, as follows: low risk (men: 93.9 or less; women: 79.9 or less), increased risk (men: 94-101.9; women: 80-87.9), and high risk (men: 102 or more; women: 88 cm or more). On the basis of the criteria for metabolic syndrome, women with a WC >80 cm and men with a WC >94 cm were classified with an abnormal WC (effectively increasing the associated health risk in this group) (Grundy *et al*., 2004).

Analysis

A descriptive analysis was used to assess frequencies and distributions. As appropriate, a comparison was made with either the T test or Fisher's exact test. All analyses were performed using SPSS version 20 (SPSS Inc., Chicago, Ill., USA) with a type I error set at $p<0.05$.

Results

General characteristics of the cohort

One hundred PWE were evaluated. The clinical characteristics of the sample are displayed in *table 1*. In this cohort, the mean BMI was 29±8 (16-60). The BMI distribution was as follows: 2 patients (2%) underweight, 26 (26%) normal weight, 34 (34%) over-weight, 25 (25%) obese, and 13 (13%) with morbid obesity. Overall, 38 patients (38%) were obese and 72% were over-weight or obese (abnormal weight) (*figure 1*). No difference in BMI was found between genders. Seventy-nine percent of patients had focal epilepsy and 21% had generalised epilepsy. In the focal cases, the most common location was temporal in 70% of cases, frontal in 22%, and parieto-occipital in 8%. Twelve patients (12%) had a positive family history of epilepsy. Two patients had two relatives with epilepsy. In total, there were 14 relatives affected, 12 (86%) had idiopathic generalised epilepsy, and two (14%) had mesial temporal sclerosis. In the medical records, there was no information about family history of obesity. A complete neuropsychological evaluation showed developmental delay (DD) in 16% of patients and psychiatric comorbidity in 37%. At the time of the study, 50% of patients were taking lamotrigine, 39% levetiracetam, 35% clobazam, 24% carbamazepine, 14% topiramate, 14% valproic acid, 12% lacosamide, and 10% phenytoin. Seven (7%) patients were taking other drugs, such as clonazepam, oxcarbazepine, primidone, ethosuximide, and zonisamide. The most frequent physical activities in the group were walking and home exercise. Sixty-six patients considered themselves to be sedentary (*table 2*).

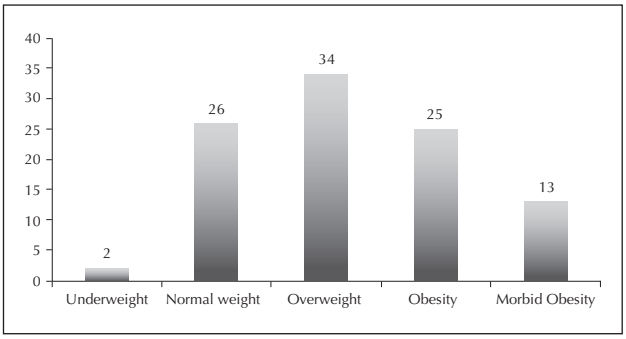

Figure 1. BMI (based on the World Health Organization) distribution of patients with epilepsy (*n*=100).

Obese *vs* non-obese patients

Clinical features

There was no difference in the frequency of drug-resistant epilepsy between obese and non-obese patients (55 *vs*. 55%; $p=0.48$). Factors associated with obesity in this study were as follows: generalised epilepsy (OR 2.7; CI: 1.1-6.6; $p=0.01$), idiopathic syndrome (OR: 2.7; CI: 1.04-7; $p=0.02$), family history of epilepsy (OR: 6.1; CI: 1.5-24.2; $p=0.002$), and a longer history of epilepsy (19 *vs*. 17 years; $p=0.005$) (*table 3*). Obese patients with epilepsy had a higher rate of

Table 1. Clinical and anthropometric characteristics of the sample (*n*=100).

Variable ***n*=100**		**Mean** ***n* (%)**	**+/- SD**	**Range**
Gender (male)		56 (56%)	-	-
Age		40	14	18-77
Age at epilepsy diagnosis		22	17.5	1-74
Years of evolution		18	14.2	1-61
Frequency of seizures per month		5	19.1	0-162
Weight (kg)		86	23.2	46-170
Height (m)		1.7	0.11	1.5-1.9
BMI		29	8	16-60
Waist circumference (cm)		100	18	65-162
AEDs in the past		4	2	1-11
Actual number of AEDs		2	1	1-5
Polytherapy		66 (66%)	-	-
Drug-resistant epilepsy		55 (55%)	-	-
Epilepsy surgery		27 (27%)	-	-
Aetiology	Unknown	34 (34%)	-	-
	MTS	26 (26%)		
	Tumour	12 (12%)		
	FCD	9 (9%)		
	Trauma	6 (6%)		
	Congenital malformation	5 (5%)		
	Stroke	3 (3%)		
	AVM	3 (3%)		
	Infection	2 (2%)		
Genetic Syndrome*	JME Lennox-Gastaut syndrome JAE	6 (6%) 5 (5%) 1 (1%)	-	-

BMI: body mass index, AEDs: antiepileptic drugs, MTS: mesial temporal sclerosis, FCD: focal cortical dysplasia, AVM: Arteriovenous malformation, JME: juvenile myoclonic epilepsy, JAE: juvenile absence epilepsy.
*Recognized genetic syndrome by the ILAE.

Table 2. Physical activity in the sample, based on the survey of the Canadian Community Health Survey 2000-2001 cycle 1.1 (*n*=100).

Variable		Mean (%)
Leisure activity		80 (80%)
Walking		70 (70%)
Home exercise		21 (21%)
Weight training		18 (18%)
Bicycling		16 (16%)
Gardening		16 (16%)
Swimming		15 (15%)
Jogging		12 (12%)
Bowling		8 (8%)
Volleyball		7 (7%)
Insight of physical activity	Sit	25 (25%)
	Stand-walk	41 (41%)
	Lift light loads	22 (22%)
	Lift heavy loads	12 (12%)
Season survey time	Winter	60 (60%)
	No winter	40 (40%)

cognitive impairment (21%), compared to non-obese patients (13%). Also, a clearly recognised genetic epileptic syndrome (18%) was more frequent in obese patients with epilepsy compared to non-obese patients (8%). Both differences were not statistically significant. When we compared patients with normal and abnormal weight (overweight and obese), we did not find any difference between the groups (*table 4*).

Antiepileptic drugs

All patients were taking AEDs. Patients with obesity received a higher number of AEDs during their lifetime, compared to non-obese patients (p=0.02) (*table 3*). When we compared patients with and without obesity, we found some trends but without statistical significance. Valproic acid was used more commonly as a previous treatment (47 *vs*. 40%; OR 1.3; CI: 0.6-3; p=0.05) and as a current treatment (18 *vs*. 11%; OR 1.8; CI: 0.6-5.5; p=0.05). Topiramate was also more commonly used in the past (34 *vs*. 22.5%; OR 1.8; CI: 0.7-4.4; p=0.05) in patients with obesity. No other differences were found between doses of AEDs or duration of treatment.

Physical activity

Approximately 80% of patients in both groups (obese *vs*. not obese) reported at least one physical activity every week. The number of leisure activities per week was lower in obese (1.8±1.7), compared to non-obese patients (2.3±2.1), but this was not statistically significant. Overall, the most common reported activity was walking (70%). There were similar rates for the majority of physical activities in both groups of patients. Home exercise and jogging were significantly less frequent in obese patients, compared to non-obese patients. Finally, there was a trend for weight training to be less frequent in obese patients (10 *vs*. 22%; p=0.05) (*table 5*).

Waist circumference analysis

The WC in the whole group was 100±18 cm. In males, the WC was 100±16 cm and in females was 99±20 cm. The difference between genders was not statistically significant. The WC was abnormal (increased or high risk) in 77% of patients. Regarding the comparison of all clinical and socio-demographic variables in patients with normal and abnormal WC, two variables were statistically significant. Patients with abnormal WC were younger at diagnosis (20±14 *vs*. 23±18; p=0.04) and also had longer evolution of epilepsy (19±15 *vs*. 16±10; p=0.04), compared to patients with normal WC. Patients with abnormal WC, compared to those with normal WC, reported a higher number of activities per week (3.0±2.7 *vs*. 1.9±1.7; p=0.002), and two specific activities were performed less frequently in patients with abnormal WC: walking (31 *vs*. 52%; p>0.05) and jogging (4 *vs*. 39%; p=0.001).

Discussion

Epidemiological studies have shown that PWE have higher rates of somatic comorbid conditions, compared to people without epilepsy. This comorbidity profile indicates the need for a more integrated approach for these patients (Gaitatzis *et al*., 2004). In recent decades, obesity has become a worldwide health problem, and some studies have demonstrated that epilepsy and obesity could be comorbid (Steinhoff *et al*., 1996; Gilliam *et al*., 2005; Daniels *et al*., 2009; Hinnell *et al*., 2010). Understanding the comorbidity of epilepsy is important because it can influence treatment. Few studies have investigated the underlying mechanisms behind the association between weight gain and epilepsy (Hum *et al*., 2009; St-Pierre *et al*., 2009). To the best of our knowledge, this is one of the few studies demonstrating an association between obesity, idiopathic epilepsy, and family history of epilepsy, suggesting a common genetic pathway for both diseases.

According to data from the 2007-2009 Canadian Health Measures Survey (CHMS), the prevalence of obesity combined with being overweight in the Canadian population was 62% (Public Health Agency of Canada, 2011). Our study showed a higher rate (72%), which

Table 3. Demographic and clinical variables in patients with and without obesity (*n*=100).

Variable *n*=100	**Obese n=38**		**Non-obese n=62**		**P value**	**OR**	**CI**
	Mean *n* (%)	**+/- SD**	**Mean *n* (%)**	**+/- SD**			
Gender (male)	20 (53%)		36 (58%)		0.29	1.2	0.5-2.8
Age at study time (yr.)	39.4	14.6	40.7	13.8	0.32	-	-
Age at the diagnosis (yr.)	20	18	23.5	17.3	0.45	-	-
Years of evolution	19.4	17.4	17.2	11.8	0.005	-	-
Febrile seizures	4 (10%)		3 (5%)		0.13	2.3	0.5-10.9
Family history of epilepsy	9 (24%)		3 (4.8%)		0.002	6.1	1.5-24.2
Status epilepticus	7 (18.4%)		14 (22.6%)		0.31	0.7	0.3-2.1
Frequency of seizures per month	3.6	11.5	6.1	22.6	0.14	-	-
≥1 seizure per month	15 (39.5%)		29 (46.8%)		0.24	0.7	0.3-1.7
Focal findings in the neurological exam	1 (2.6%)		9 (14.5%)		0.02	0.16	0.02-1.3
Developmental Delay	8 (21%)		8 (13%)		0.14	1.8	0.6-5.3
Psychiatric comorbidity	12 (31.6%)		25 (40.3%)		0.18	0.7	0.3-1.6
Idiopathic syndrome	13 (34.2%)		10 (16.1%)		0.01	2.7	1.04-7
Recognized genetic syndrome	7 (18.4%)		5 (8%)		0.06	2.6	0.7-8.8
EEG generalized discharges	16 (42%)		13 (21%)		0.01	2.7	1.1-6.6
Total number of AEDs	4.3	2.6	3.9	2.08	0.02	-	-
Polytherapy	26 (68%)		40 (64%)		0.34	1.2	0.5-2.8
Drug-resistant epilepsy	21 (55%)		34 (55%)		0.48	1.01	0.4-2.3
Epilepsy surgery	7 (18%)		20 (32%)		0.06	0.5	0.2-1.3
Ongoing AEDs							
Valproic Acid	7 (18.4%)		7 (11.3%)		0.16	1.8	0.6-5.5
Carbamazepine	9 (23.7%)		15 (24.1%)		0.5	0.1	0.3-2.5
Topiramate	5 (13.1%)		9 (14.1%)		0.42	0.9	0.3-2.9
Previous use of AEDs							
Valproic Acid	18 (47.3%)		25 (40.3%)		0.24	1.3	0.6-3
Carbamazepine	17 (44.7%)		31 (50%)		0.3	0.8	0.4-1.8
Topiramate	13 (34.2%)		14 (22.6%)		0.1	1.8	0.7-4.4

For the analysis, patients with obesity and morbid obesity were added (*n*=38).
Obesity is considered as BMI more than 30.

Table 4. Demographic and clinical variables in patients with and without abnormal weight (*n*=100).

Variable *n*=100	Abnormal weight *n*=72		Normal weight *n*=28		*P* value	OR	CI
	Mean *n* (%)	+/-SD	Mean *n* (%)	+/-SD			
Gender (male)	40 (55.5%)		16 (57.1%)		0.44	0.94	0.38-2.26
Age at study time (yr.)	41.3	14.4	37.5	13.1	0.11	-	-
Age at the diagnosis (yr.)	22.5	19.1	21.2	12.8	0.37	-	-
Years of evolution	18.7	15.5	16.3	10.1	0.22	-	-
Febrile seizures	5 (6.9%)		2 (7.1%)		0.48	0.97	0.17-5.31
Family history of epilepsy	9 (12.5%)		3 (10.7%)		0.4	1.19	0.29-4.76
Status epilepticus	13 (18%)		8 (28.6%)		0.12	0.55	0.19-1.52
Frequency of seizures per month	4.1	12.1	7.9	30.7	0.18	-	-
≥1 seizure per month	31 (43%)		13 (46.4%)		0.38	0.87	0.36-2.09
Focal findings in the neurological exam	6 (8.3%)		4 (14.3%)		0.18	0.54	0.14-2.1
Developmental Delay	13 (18%)		3 (10.7%)		0.18	1.8	0.48-7.01
Psychiatric comorbidity	24 (33.3%)		13 (46.4%)		0.11	0.57	0.23-1.4
Idiopathic syndrome	17 (23.6%)		6 (21.4%)		0.41	1.13	0.39-3.25
Recognized genetic syndrome	8 (11.1%)		4 (14.3%)		0.33	0.75	0.2-2.72
EEG (generalized discharges)	22 (30.5%)		7 (25%)		0.29	1.32	0.49-3.6
Total number of AEDs	4.1	2.5	4	1.6	0.42	-	-
Polytherapy	45 (62.5%)		21 (75%)		0.11	0.55	0.2-1.48
Drug resistant epilepsy	40 (55.5%)		15 (53.5%)		0.43	1.08	0.45-2.6
Epilepsy surgery	20 (27.8%)		7 (25%)		0.39	1.2	0.44-3.2
Ongoing AEDs							
Valproic Acid	10 (13.8%)		4 (14.3%)		0.48	0.96	0.27-3.38
Carbamazepine	18 (25%)		6 (21.4%)		0.35	1.22	0.42-3.48
Topiramate	10 (13.8%)		4 (14.3%)		0.48	0.96	0.27-3.38
Previous AEDs							
Valproic Acid	29 (40.2%)		14 (50%)		0.19	0.67	0.28-1.6
Carbamazepine	33 (45.8%)		15 (53.6%)		0.24	0.73	0.3-1.76
Topiramate	21 (29.1%)		6 (21.4%)		0.21	1.5	0.53-4.25

The abnormal weight group is the patient's group with overweight and obesity.
Patients with abnormal weight (*n*=72) were defined as those who were overweight, obese, or morbidly obese.

Table 5. Physical activity in obese and non-obese patients in the last six months (*n*=100).

Variable *n*=100	**Obese n=38**		**Non-obese *n*=62**		***P* value**
	Mean *n* (%)	**+/-SD**	**Mean *n* (%)**	**+/-SD**	
Leisure activity[a]	31 (82%)		49 (79%)		0.37
Number of activities per week	1.8	1.7	2.4	2.2	0.08
≥3 activities per week	12 (31.6%)		24 (38.7%)		0.23
Walking	28 (73.6%)		42 (67.7%)		0.26
Home exercise	4 (10.5%)		17 (27.4%)		0.02
Weight training	4 (10.5%)		14 (22.6%)		0.06
Bicycling	4 (10.5%)		12 (19.3%)		0.27
Gardening	5 (13.1%)		11 (17.7%)		0.37
Swimming	5 (13.1%)		10 (16.1%)		0.7
Jogging	1 (2.6%)		11 (17.7%)		0.01
Feeling active	13 (34.2%)		21 (33.9%)		0.49

[a] Self-reported physical activity in last six months.

is consistent with the Canadian National Population-based survey of health status and health-related behaviours of Canadian adolescents and adults, where a higher rate of obesity was found in PWE (19%; 95% CI: 16.6-21.6), compared to the general population (15%; 95% CI: 15.3-15.6) (Hinnell *et al*., 2010). Our findings could also be explained by potential regional variation. Saskatchewan is the province in Canada with the highest estimates of obesity, which is potentially explained due to the large component of First Nation populations in the north of the province and their very well-known high prevalence of obesity (Public Health Agency of Canada, 2011).

Our study did not show a correlation between obesity and drug-resistant epilepsy. This observation contrasts with the recent study by Janousek *et al*. (2013) in which more patients with drug-resistant epilepsy were overweight and obese, compared to those with non-drug-resistant epilepsy. Nevertheless, Janousek *et al*. did not use the current ILAE criteria for drug-resistant epilepsy, which was used in this study (Kwan *et al*., 2010). They defined drug-resistant epilepsy as the persistence of ≥one seizure per six months regardless of treatment with ≥ three AEDs. Further studies exploring this aspect should be performed in the future.

Some studies have described that epilepsy is significantly associated with less physical activity, compared to the general population. According to some studies, PWE participate less in sports and have lower levels of fitness (Steinhoff *et al*., 1996; Arida *et al*., 2003; Wong and Wirrell, 2006; Hinnell *et al*., 2010). These studies suggest that the stigma associated with epilepsy may limit participation in physical activities (Arida *et al*., 2003), but also the use of AEDs can produce lethargy, thereby contributing to decreased activity (Wong and Wirrell, 2006; Ben-Menachem, 2007). Some studies have shown that the rates of physical activity between patients with and without epilepsy is the same (Nakken, 1999; Elliott *et al*., 2008; Gordon *et al*., 2010). Our study shows that PWE have a high rate of physical activity regardless of being obese (81%) or non-obese (79%). One third of our population reported more than three leisure activities per week and one third felt active. This prevalence is higher than the reported regular physical activity in Canadians studies. Chen and Mao (2006) reported that overall, 47% of men and 43% of women were physically active; in obese men and women, the corresponding rates were 40 and 29%, respectively. According to the results from the Canadian Community Health Survey Cycle 2.2 (2004-2005), only less than half of Canadians (44% males and 42% females) aged >25 years were physically active (Liu *et al*., 2008). The high rate of physical activity identified in our study could be related to more positive attitudes

toward leisure activities in PWE and the desire and willingness to incorporate the health benefits of exercise into their lives. However, it may also be related to a bias of our methodology (self-reported physical activity).

Walking is the most popular activity among adult Canadians, regardless of age, gender, BMI, or income group (Bryan and Katzmarzyk, 2009). Seventy percent of the Canadian population walks every week according to the 2005 CCHS (Gilmour, 2007). Interestingly, walking was also the exercise of choice for the majority of our PWE. Overall, in our sample, 70% of patients walk every week, this finding is consistent with other studies exploring physical activity in PWE (Elliott *et al*., 2008; Ablah *et al*., 2009; Gordon *et al*., 2010). This trend may be explained by the increased need to walk for PWE due to driving restrictions. Although exercise patterns were very similar between obese and non-obese patients, home exercise, jogging, and weight training were performed less frequently in the obese group. Weight training and home exercise was not performed frequently in our group of PWE, similar to the study of Gordon *et al*. (2010), however, this is in contrast to a Norwegian study in which PWE reported weight training as one of their preferred activities (Nakken, 1999).

Interestingly, our study shows an association between idiopathic syndrome, DD, and obesity. This relationship has been described before in a study of untreated children with newly diagnosed epilepsy (Daniels *et al*., 2009). The basis of this association remains unclear and some hypotheses have been generated. First, paediatric genetic epilepsy has been linked to different phenotypes, including variable degrees of intellectual disability (Pandolfo, 2013). People with DD are more vulnerable than the general population to overweight (Grondhuis and Aman, 2014) and some potential reasons for this association have been described. DD has been associated with sedentary behaviour and physical inactivity (Maiano, 2011). Sedentary lifestyle patterns, such as playing digital games, using computers, and especially watching television, have been associated with obesity and described in the normal population but also in people with DD (Rey-Lopez *et al*., 2008). For example, watching television reduces energy expenditure and has been associated with higher intake of unhealthy food (Epstein *et al*., 2005; Maiano, 2011). Also, patients with moderate-to-severe intellectual disabilities can have some restrictions of physical activities (Chen *et al*., 2010). Finally, the use of psychotropic medications that are commonly used for children with DD to treat aggression, self-injuring behaviour, depression, and anxiety can lead to being overweight (Grondhuis and Aman, 2014).

In addition to indirect environmental factors, some of the main risk factors for being overweight are probably genetically determined (Grondhuis and Aman, 2014). In our study, the main risk factors associated with obesity were: seizure onset at young age, a positive family history of epilepsy, and a confirmed idiopathic syndrome. These findings could be related to an underlying genetic abnormality. Although the evidence is scanty, some researchers have identified a genetic role for weight gain and food intake in mutant epileptic mice, mediated by serotoninergic receptors (Heisler *et al*., 1998). Heisler *et al*. (1998) demonstrated that the serotonin 5ht2c receptor null mutant in mice is associated with epilepsy and obesity. Even though only certain epilepsy genetic syndromes in humans, such as Prader-Willi syndrome, are related to obesity, there are some reports in the literature describing an association between early onset of obesity, DD, and epilepsy in children (Vauthier *et al*., 2012). It is possible that an unknown genetic dysfunction of neural pathways in humans may trigger an increased susceptibility for seizure disorders and secondary obesity. On the other hand, obesity, DD, and primary generalised epilepsy could be a consequence of the same global brain dysfunction mediated by a particular genetic mutation (Pandolfo, 2013). More research is needed in this area, considering that an association between obesity and epilepsy type, duration, or aetiology was not found in recent studies exploring obesity in PWE (Janousek *et al*., 2013).

As expected, valproic acid has more commonly been used in the past (47 *vs*. 40%) and is commonly used today (18 *vs*. 11%) in obese patients. This observation contrasts with a recent study (Janousek *et al*., 2013) in which one of the lowest rates of obesity was reported in patients treated with valproic acid ($p<0.005$). In our study, obese patients received more AEDs throughout their lifetime and topiramate was also more commonly used in obese PWE, probably due to the inclination of epileptologists to treat obese patients with this drug for a potential effect on weight reduction. Janousek *et al*. (2013) reported a similar finding to our study in 554 PWE, and described a lower prevalence of obesity in patients with monotherapy, compared to polytherapy (25 *vs*. 38%; $p=0.005$), as well as a common use of topiramate in patients with obesity, compared to other monotherapies ($p=0.002$).

Our study has some limitations. We did not perform a direct comparison with a group of healthy people. Second, the study design was cross-sectional, therefore no causal association among variables could be inferred. A third limitation was the reliance on self-reported physical activity. Some PWE may have over-reported their leisure activities to reflect a socially desirable profile. It is known that healthy people often underestimate sedentary activities and overestimate aerobic activities (Klesges *et al*., 1990), hence we recognise that our collection method may have provided inaccurate estimates of physical activity.

Conclusion

Obesity is highly prevalent in PWE but is not related to drug-resistant epilepsy. We could not find a clear association between obesity and physical activity in PWE. The most salient observation was the association between generalised epilepsy, young age at diagnosis, epilepsy family history, and idiopathic syndrome with obesity. This information can help physicians to choose medications but also identify potential risk factors for obesity. Longitudinal studies using other methodologies could help to understand the potential association between obesity and epilepsy. □

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