



An Australian nationwide survey on medicinal cannabis use for epilepsy: History of antiepileptic drug treatment predicts medicinal cannabis use



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ABSTRACT

Epilepsy Action Australia conducted an Australian nationwide online survey seeking opinions on and experiences with the use of cannabis-based products for the treatment of epilepsy. The survey was promoted via the Epilepsy Action Australia's main website, on their Facebook page, and by word of mouth. The survey consisted of 39 questions assessing demographics, clinical factors, including diagnosis and seizure types, and experiences with and opinions towards cannabis use in epilepsy. A total of 976 responses met the inclusion criteria. Results show that 15% of adults with epilepsy and 13% of parents/guardians of children with epilepsy were currently using, or had previously used, cannabis products to treat epilepsy. Of those with a history of cannabis product use, 90% of adults and 71% of parents reported success in reducing seizure frequency after commencing cannabis products. The main reasons for medicinal cannabis use were to manage treatment-resistant epilepsy and to obtain a more favorable side-effect profile compared to standard antiepileptic drugs. The number of past antiepileptic drugs tried was a significant predictor of medicinal cannabis use in both adults and children with epilepsy. Fifty-six percent of adults with epilepsy and 62% of parents/guardians of children with epilepsy expressed willingness to participate in clinical trials of cannabinoids. This survey provides insight into the use of cannabis products for epilepsy, in particular some of the likely factors influencing use, as well as novel insights into the experiences of and attitudes towards medicinal cannabis in people with epilepsy in the Australian community.

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1. Introduction

Despite the availability of more than 20 prescription anti-epileptic drugs (AEDs), conventional treatment approaches prove ineffective in approximately 25–30% of people with epilepsy [1,2]. Treatment resistance has a well-defined trajectory: seizure freedom is typically achieved with the first two appropriate AEDs tried, with the probability of achieving “sustained” seizure-freedom declining significantly with each successive drug treatment [3,4].

Uncontrolled epilepsy is associated with an increased risk of morbidity including neuropsychological impairment, psychiatric and behavioural disturbances, and psychosocial difficulties [5–7]. Use of multiple AEDs, in an attempt to overcome treatment-resistance, can also cause impairment, with individuals taking two or more AEDs self-reporting greater cognitive, emotional, and behavioral side effects than those on

a single drug regimen [8]. Failure of conventional treatments, coupled with intolerable side effects during polypharmacy, may lead patients to embrace untested treatment options, such as cannabis and its derivatives, to try to manage seizures.

The endogenous cannabinoid system (ECS) is a complex neuromodulatory system that consists of lipid-like signalling molecules (endocannabinoids) that interact with cannabinoid CB1 and CB2 receptors and other targets in the central and peripheral nervous system [9]. The ECS plays a major role in regulating neuronal excitability, neuroinflammation, and excitotoxicity within the brain [10,11]. Abnormalities in the ECS have been identified in people with various forms of epilepsy [12,13], and genetic and pharmacological modulation of the ECS in rodents causes major effects on seizure susceptibility [10]. Cannabinoids have also been shown to have actions at a range of epilepsy-relevant targets including GABA-A and TRPV receptors in preclinical models [10, 14–16]. These observations have contributed to a growing realization that cannabinoid ligands could be novel therapeutic agents for epilepsy.

The use of plant-derived cannabinoids for seizure reduction has been described for centuries [17], while the last decade has witnessed

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an unprecedented media and community interest in cannabinoids in the management of epilepsy centered around high-profile case studies (e.g. Charlotte Figi) [18]. Past systematic reviews have concluded that there is insufficient evidence to support or refute the use of cannabinoids in treating people with epilepsy [19,20]. More recently, one open-label, one expanded access, and a small number of yet-to-be published placebo-controlled clinical trials have reported positive outcomes with cannabidiol (CBD), a major non-intoxicating cannabinoid found in some strains of the cannabis plant, in various forms of severe pediatric epilepsy [21,22]. However, CBD is not yet available as a registered medicine, and the use of artisanal cannabis-based oil and liquid extracts continues, with an increasing number of anecdotal reports of perceived success. This increasing use of untested cannabis-based products raises some concerns as, in addition to the uncontrolled nature in which some of these products are manufactured, the short- and long-term safety profile of cannabinoid use in humans, particularly in children and in combination with AEDs, is unclear and requires stronger scientific evaluation [2].

A number of recent surveys of cannabis extract use in treating childhood treatment-resistant epilepsy suggest a possible role for cannabis extracts in reducing seizure frequency [23–27]. A large cross-sectional survey of medicinal cannabis users in the United States indicated that the majority of people surveyed (61.2%) were using medicinal cannabis to treat chronic pain, with only 55 (3.8%) of the total cohort using medicinal cannabis for epilepsy or other seizure disorders [28]. However, compared to the other disorders, those using cannabis for epilepsy had among the highest proportion of self-reported perceived efficacy.

Recent regulatory changes and high profile scientific initiatives focused on medicinal cannabis in Australia have intensified community debate and the desire for information on this topic [29,30]. Accordingly, the current study aimed to survey frequency of cannabis extract use for epilepsy in the Australian community, reasons for and against use, and possible factors contributing to trying cannabis extracts to manage epilepsy. Our two targets for the survey were: (1) adults with epilepsy, and (2) parents/guardians of a person with epilepsy.

2. Methods

2.1. Survey

An on-line survey was developed, consisting of 39 questions that measured demographic factors, clinical factors (including diagnosis and seizure types), past treatment history for epilepsy, and attitudes and opinions of cannabis use in epilepsy. Study data were collected by online survey software, Survey Monkey®. The survey link was posted for ten days, and promoted through Epilepsy Action Australia (EAA), a national non-profit organization that provides education and services to people with epilepsy and their families, via their website and emailing list, the EAA Facebook page, and word of mouth.

The study population was any individual who has, or knows someone who has, epilepsy. All responses captured were anonymous and the automatic IP address capture feature on the software was deactivated to maintain confidentiality. The survey's preamble advised participants not to include any identifying information (e.g., names, locations) in questions allowing unlimited free script. Overall, there were 1275 respondents in the survey. Respondents' answers were excluded if they: 1) identified themselves as grandparents, siblings, or "other" of the person with epilepsy ($n = 208$), and 2) failed to respond to Question 15: "Have you or the person with epilepsy tried any form of medicinal cannabis for seizures?" ($n = 91$). The former was to limit the degree of separation between the respondent to the survey and the person with epilepsy. Question 15 referred to both past and present use of medicinal cannabis for treatment of epilepsy. This resulted in 976 eligible responses, consisting of respondents who identified themselves as "self with epilepsy" (45.5%, 444/976) or a "parent and/or guardian" of an individual with epilepsy (54.5%, 532/976).

Table 1
Demographic information of respondents to the Epilepsy Action Australia: cannabis use in epilepsy survey.

	N (%)
Total respondents	976
Age of person with epilepsy	
Children	389 (39.9)
0–5	91 (9.3)
6–12	192 (19.7)
13–17	106 (10.9)
Adults	587 (60.1)
18–24	119 (12.2)
25–64	448 (45.9)
65+	20 (2.0)
Geographical location	
NSW	376 (38.5)
QLD	215 (22.0)
VIC	148 (15.2)
WA	133 (13.6)
SA	44 (4.5)
TAS	35 (3.6)
ACT	15 (1.5)
NT	10 (1.0)

Perceived efficacy was assessed with a dichotomous question: "Do you consider medicinal cannabis successful in managing seizures for you or the person with epilepsy? Yes/No." Two-thirds of the survey questions were dichotomous or multiple-choice options, while the remaining permitted free-text responses (see Data S1). Pre-existing survey data-set was accessed, used, and published in non-identifiable form, and did not require ethics approval according to University of Sydney Human Research Ethics¹.

2.2. Data analysis

Responses were uploaded onto an electronic spreadsheet and tabulated. Data were analysed using SPSS 19.0 (SPSS Inc., Chicago, IL, USA). Thirty-four variables, including demographics and medical history relating to the epilepsy, were tested as potential predictors for medicinal cannabis use. The dependent variable (whether the individual had used medicinal cannabis or not) was dichotomous, and the independent (predictor) variables were a mix of dichotomous and continuous variables. Each independent variable was first entered into a univariate binary logistic regression analysis. Variables that predicted medicinal cannabis use with a degree of significance of $p < 0.1$ were entered into a multivariate forward conditional binary logistic regression analysis [31,32]. Two multivariate analyses were conducted, one for children (<18 years) and one for adults (≥ 18 years) with epilepsy. The regression analysis included 65.5% (255/389) children with epilepsy and 57.5% (338/587) adults with epilepsy.

3. Results

3.1. Demographic information

The survey yielded 976 responses; with 60.1% of the overall sample involving adults with epilepsy, while the remaining were children with epilepsy (Table 1). Geographically, responses were from across Australia: New South Wales (38.5%), Queensland (22%), Victoria (15.2%), Western Australia (13.6%), and South Australia (4.5%), with the remainder forming 6.1%. Epilepsy syndrome of unknown type was the most frequently reported type of epilepsy across both children (41%) and adults (46%) with epilepsy (see Data S2). The second highest frequency syndrome type was structural brain abnormality (4.6%) in

¹ Using existing data collections in research: Guidelines for researchers 2014. The University of Sydney [29/10/16] Available from: <https://intranet.sydney.edu.au/content/dam/intranet/documents/research-support/ethics/ethics-existing-data-guidelines.pdf>

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