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Case report

The impact of cannabis use on intracarotid amobarbital testing

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ABSTRACT

Chronic cannabis use impacts memory functioning, even while users are not acutely intoxicated. The impact of cannabis use on Wada or intracarotid amobarbital testing (IAT) has not previously been described. We reviewed cannabis consumption in epilepsy patients undergoing IAT during pre-surgical work-up. Of 58 patients reviewed, 16 patients (28%) indicated regular use. During IAT, five regular cannabis users with suspected temporal lobe epilepsy exhibited poor memory while testing their presumptively healthy temporal lobe (i.e., the side opposite that targeted for epilepsy surgery), indicating the potential for an amnestic syndrome post-operatively. It was suspected that the pattern of IAT results for these patients was attributable to the deleterious impact of cannabis use on cognition. Thus, three of the five underwent repeat IAT after a period of enforced abstinence. On repeat IAT, each of the three patients exhibited improved memory performance while testing their healthy temporal lobe, suggesting that the healthy temporal lobe of each mediated sufficient memory ability to allow for epilepsy surgery. These findings raised concerns that frequent cannabis use may alter IAT results, leading to incorrect assessments regarding potential post-operative cognitive deficits, and led to a mandate at our institution that patients must stop cannabis use before IAT.

1. Introduction

The Wada test or intracarotid amobarbital test (IAT) is used for language lateralization and to assess memory function in patients with drug-resistant epilepsy who are considering anterior temporal lobectomy with hippocampal resection as treatment [1]. During the test, amobarbital is injected into the internal carotid artery and inactivates brain function in the dependent vascular territory, typically including hippocampal function. It is intended to mimic the effect of removing the epileptogenic temporal lobe and its medial structures, and assesses whether the remaining, contralateral temporal lobe can provide sufficient memory function to compensate for the loss of the ipsilateral hippocampus. If a patient exhibits poor memory performance while testing the presumptively healthy side, an anterior temporal resection with removal of mesial structures cannot be recommended as the results indicate that the patient may have inadequate memory function post-operatively. Conceivably, systemic factors that impair memory, such as medications or drugs like cannabis, can interfere with IAT performance and cause misleading results.

Colorado legalized "medical marijuana" after voter approval in November 2000 and the use of cannabis for personal, recreational consumption after elections in November 2012. Epilepsy was considered by legislators, not physicians, as one of the statewide-approved medical indications for "medical marijuana." Despite the lack of rigorous scientific data, some patients, particularly those with drug-resistant epilepsy, use it frequently. Indeed, a survey of epilepsy patients in Denver conducted immediately prior to legalization of recreational cannabis found that 33% of patients consumed plant-derived cannabis [2].

Chronic cannabis users with no known neurological disease exhibit mild deficits in learning and memory, as well as other cognitive domains, even while not acutely intoxicated [3]. However, no differences on cognitive testing are detected between cannabis users and non-users after an abstinence period of about four weeks, though individuals who began using in adolescence may exhibit more persistent cognitive deficits [4,5]. The mild cognitive deficits observed among chronic users early on during a period of abstinence are thought to possibly represent the effects of persistent low levels of tetrahydrocannabinol (THC), abstinence phenomena, or both [3].

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The use of cannabis products with higher ratios of cannabidiol (CBD) to THC may attenuate cognitive effects, but findings in this regard are limited and mixed [6,7].

We noted that there have been no studies evaluating the effects of cannabis use on IAT. Given the above-mentioned use of cannabis in patients with epilepsy and its negative impact on cognition, this study

Table 1
Patient and IAT data for all cannabis users who failed IAT with respect to planned resection site

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age	47	24	57	45	38
Gender	M	M	M	M	M
Epilepsy Duration [years]	9	6	2	5	1
AEDs tried [#]	4	6	6	2	2
Focus	L temporal	L temporal	L temporal	L temporal	L temporal
MRI Findings	L HS and status post L occipital tumor resection	Non-lesional	Non-lesional	L inferior temporal cavernous malformation	L lateral temporal cavernous hemangioma
Pre-Surgical Neuropsychology Test Results-Confrontation Naming [Boston Naming Test]	Moderately impaired [T-score = 27]	Mildly impaired [T-score = 39]	Within Normal Limits [T-score = 57]	Moderately Impaired [T-score = 27]	Within Normal Limits [T-score = 40]
Pre-Surgical Neuropsychology Test Results-Verbal Memory [California Verbal Learning Test-2nd Edition]	Moderately impaired [Total Learning T-score = 27; Delayed Free Recall T-score = 25]	Mildly impaired [Total Learning T-score = 46; Delayed Free Recall T-score = 35]	Within Normal Limits [Total Learning T-score = 31; Delayed Free Recall T-score = 45]	Within Normal Limits [Total Learning T-score = 48; Delayed Free Recall T-score = 50]	Within Normal Limits [Total Learning T-score = 46; Delayed Free Recall T-score = 40]
Pre-Surgical Neuropsychology Test Results-Visual Memory [Figure Memory Test[a]/Brief Visual Memory Test-Revised Edition[b]/Wechsler Memory Scale-4th Edition Visual Reproduction[c]]	Severely impaired [[b]Total Learning T-score = <20; Delayed Free Recall T-score = <20]	Within Normal Limits [[a]Total Learning T-score = 46; Delayed Free Recall T-score = 56]	Within Normal Limits [[c]Total Learning T-score = 43; Delayed Free Recall T-score = 49]	Within Normal Limits [[a]Total Learning T-score = 51; Delayed Free Recall T-score = 81]	Within Normal Limits [[b]Total Learning T-score = 38; Delayed Free Recall T-score = 46]
Frequency cannabis consumption	Daily	Daily	Daily	Daily	3-4x/week
Duration cannabis consumption	>2 years	>2 years	>2 years	>2 years	>2 years
Method of cannabis consumption	Smoking/ combustion of the plant flower	Smoking/ combustion of the plant flower	Smoking/ combustion of the plant flower	Smoking/ combustion of the plant flower	Smoking/ combustion of the plant flower
1st IAT Dosing†	100 mg b/l	100 mg b/l	150 mg b/l	100 mg b/l	100 mg b/l
Radiology comment 1st IAT	Crossover filling of the left anterior cerebral artery from the right anterior circulation. A fetal PCA is noted	Mild anterior cross flow with left-sided injection, not present with right-sided injection	With fast injection speed (4 ml/sec) on either side cross-filling of the contralateral middle and anterior cerebral arteries was demonstrated. Cross-filling was not observed with slow injection speed of 1 mL/sec	With L injection mild cross-filling into the contralateral right middle cerebral artery territory as well as across the anterior communicating artery	With R injection filling of a posterior communicating artery and the posterior cerebral artery, however the P1 segment only flash fills minimally and does not fill the basilar artery
1st IAT Results	Injection L: -2/ 7 Injection R: 1/ 7 Language: L	Injection L: 0/ 7 Injection R: 6/ 7 Language: L	Injection L: -1/ 7 Injection R: 1/ 7 Language: L	Injection L: 3/ 7 Injection R: 7/ 7 Language: L	Injection L: 1/ 7 Injection R: 6/ 7 Language: L
2nd IAT Dosing†	100 mg b/l	80 mg b/l	150 mg b/l	N/A	N/A
Radiology comment 2nd IAT	The left A1 is dominant and fills both anterior cerebral arteries. A fetal PCA is noted	Crossover filling of the right anterior cerebral artery from the left anterior circulation	Unremarkable	N/A	N/A
2nd IAT Results	Injection L: 4.5/ 7 Injection R: -1/ 7 Language: L	Injection L: 5/ 7 Injection R: 7/ 7 Language: L	Injection L: 6/ 7 Injection R: 0/ 7 Language: L	N/A	N/A
Interval between 1st IAT and 2nd IAT [days]	68	503	91	N/A	N/A
Surgery	No - Concerns about complications	No - Seizure free with added lacosamide	Yes - L temporal lobectomy	Yes - Lesionectomy without resection of the L hippocampus	No - Patient had no seizures captured during scalp VEEG
Seizure Outcome	N/A	N/A	Reduction in seizure frequency	Seizure free for 11 months, then recurrent seizures	N/A
Neuropsychology Test Outcome	N/A	N/A	Decline on test of confrontation naming [Boston Naming T-score = 29] but stable performance on tests of verbal and visual memory	Stable performance on tests of confrontation naming and verbal and visual memory functioning	N/A

b/l: bilateral; HS: hippocampal sclerosis; IAT: intracarotid amobarbital testing; L: Left; R: Right.
† The standard protocol at our institution is 100 mg amobarbital, per side. For patients 2 and 3, dosing varied based on initial clinical response (e.g., because patient 2 was overly sedated when administered 100 mg, the dose was reduced).

aimed to retrospectively analyze whether cannabis use has impacted IAT results. This may have significant clinical implications as the test carries a 0.6% risk of stroke and may provide erroneous "pass" or "fail" data that could impact the decision to pursue resective surgery [8].

2. Methods

This is a retrospective study assessing the impact of cannabis use and IAT approved by the Colorado Multiple Institutional Review Board. The hospital electronic medical record system was searched for patients 18 years or older who underwent IAT between January 2012 and December 2013. The time frame was chosen as it coincided with more consistent documentation of cannabis use in the charts, but before abstinence became mandatory prior to IAT at our institution (see Section 5). In addition to IAT results and cannabis use information, clinical data examined included age, gender, duration of epilepsy, number of anticonvulsant drugs, type of epilepsy, radiological comments, neuropsychological test results, and surgical outcomes (if applicable).

3. Results

Of 58 patients that underwent IAT, sixteen (28%) reported cannabis use; all were patients with drug- resistant temporal lobe epilepsy undergoing work-up for epilepsy surgery. Of these, nine indicated daily use, three used cannabis at least twice per week, one reported once monthly use, and frequency was not recorded for the remaining three patients. Of the 12 frequent cannabis users (defined as at least twice weekly use), six passed IAT with expected results permitting the intended temporal resection. The other six patients had unexpected results. More specifically, while one patient unexpectedly passed IAT with sufficient memory scores after injections in each hemisphere, five of these patients failed either bilaterally (two patients) or when testing the healthy hemisphere (three patients). The data was reviewed in conference and a negative impact from these five patients' cannabis consumption was suspected. Subsequently, two patients who had failed bilaterally and one with unilateral failure were asked to stop using cannabis for at least four weeks and then repeat IAT. Table 1 shows that for these three patients (patients 1, 2, and 3), results of the second IAT were different compared to the first IAT, and indicated that the healthy hemisphere was indeed able to support memory adequately. Radiological comments regarding cross-flow are presented in Table 1. There were no recorded adverse events associated with the first or second IAT. There were no significant issues identified attributable to other causes, such as incomplete anesthesia of one hemisphere that would have been considered reason for different IAT results. It was thusly felt that the second IAT was more representative of the true memory functioning of each patient. The remaining two patients did not repeat IAT (patients 4 and 5 in Table 1), as they had lateral vascular malformations and were considered surgical candidates because mesial structures could be spared with a resection. Of the six patients with unexpected IAT results, three patients underwent a resection (anterior temporal lobectomy in two cases and lesionectomy in one). Unfortunately, one experienced word-finding difficulties with measurable decline on a test of confrontation naming, but otherwise there were no unexpected postoperative deficits.

4. Discussion

Self-reported consumption of cannabis is relatively common in patients with epilepsy, found in 21–33% of patients [2,9], and chronic cannabis use may impact cognition in the absence of acute intoxication for brief period, though more persistent deficits may occur among individuals who began using in adolescence [3–5]. In this context, there is a need to be prepared for side-effects that may interfere with pre-surgical testing. Indeed, our case review demonstrated that 25% of patients who used cannabis at least twice weekly had unexpected IAT results that improved following abstinence.

Intracarotid amobarbital testing has variable reliability with respect to memory testing. In one study, up to 63% of repeat bilateral IATs had information on memory lateralization that was not exactly reproduced [10]. In light of the variability in the test, our retrospectively analyzed cases do not prove that cannabis is responsible for the negative impact on cognition and IAT testing. In fact, they highlight that the effect of cannabis during IAT testing may also be variable. However, the fact that three patients who underwent repeat IAT exhibited improved memory function, rather than some improvement and some deterioration, supports the hypothesis that cannabis may have influenced performance adversely.

Our retrospectively analyzed case series demonstrates a need for prospective studies that more formally assess the impact of cannabis use on IAT. Of particular interest may be the varying impact of cannabis products with different ratios of CBD to THC. In recent years, there has been growing interest in the use of CBD containing products for the management of epilepsy, especially with recently published randomized controlled trials of pharmaceutically prepared CBD that demonstrated efficacy in both Lennox–Gastaut and Dravet Syndromes and approval of Epidiolex by the FDA in 2018 [11,12]. Unlike THC, CBD is not psychoactive and is presumed to have little or no impact on cognition. In fact, CBD may attenuate the cognitive, as well as psychomimetic, effects of THC, though findings in this regard are limited and mixed [6,7]. Notably, it is assumed that none of the three patients who underwent repeat IAT were using a high CBD content product, as artisanal CBD products were not widely available in 2013 and because they reported chronic consumption for many years prior.

5. Conclusions

Based on our limited experience, we recommend inquiring about cannabis use in all patients scheduled for IAT and to consider delaying the procedure until they demonstrate abstenance from using cannabis products containing THC. This process may spare the patient an invalid test and risks associated with repeat angiography. We have introduced a protocol at our own facility in which patients are screened for use of cannabis, and are informed that they must stop consuming cannabis products for four weeks prior to IAT. On the day of the procedure, the patients are again asked whether they have consumed cannabis and, if they confirm recent use (e.g., within the week preceding IAT), the procedure is canceled and rescheduled.

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Declaration of Competing Interest

The authors affirm that they do not have conflicts of interest.

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