



Dear Doctor,

Greetings from Micro Labs. We are happy to bring you “**EPILEPSY Newsletter**” which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

1. Long-term seizure independence following frontal lobe epilepsy surgery is supported by thalamostriatal disconnection
2. Modified Atkins Diet is Safe, Effective, and Tolerable in Patients with Drug-Resistant Epilepsy
3. Focal epilepsy and Modifiable Cardiovascular Risk Factors and the Risk of Dementia
4. A case report on neurosurgery for pregnancy-related intractable epilepsy



Long-term seizure independence following frontal lobe epilepsy surgery is supported by thalamostriatal disconnection.

A frontal lobe surgery for focal drug-resistant epilepsy results in around 50% of patients being seizure-free after surgery, but only about 30% of patients continue to be seizure-free over the long term.¹ Partially removing the epileptogenic lesion is likely to result in an early seizure recurrence, whilst totally removing the epileptogenic lesion does not guarantee against a later seizure recurrence. This implies a coexisting epileptogenic network that facilitates ictogenesis in nearby or far-off latent epileptic foci. The study proposes that projections from the striatum and the thalamus to the cortex may contribute to this shared epileptogenic network because thalamic and striatal dysregulation can support epileptogenesis and disconnection of cortico-thalamostriatal pathways through hemispherotomy or neuromodulation can improve seizure outcome regardless of focality.²

Retrospective case collection was used by the researchers, who first reviewed the clinical information of 80 patients who had surgery for frontal lobe epilepsy in a row. Patients were initially evaluated for comorbidities, medication resistance, and history of epilepsy, as well as having volumetric MRI, video-EEG telemetry, neuropsychiatric, and cognitive tests. To look at common patterns of disconnection linked to sustained seizure-freedom, the researchers conducted voxel-based and tractography disconnectome studies. The dissociation of the anterior cortico-striatal projections and anterior thalamic radiation was independently correlated with seizure freedom at 3 and 5 years.

Seizure freedom was linked to fibre disconnection at 3 and 5 years, according to a non-parametric two-sample t-test (Fig. 1). The atlas-based analysis showed that disconnecting anterior cortico-thalamostriatal projections was related to better seizure outcomes after three years: only 2/16 (12%) of patients with disconnected anterior thalamic radiation experienced seizure recurrence, as opposed to 20/31 (64%) of patients with preserved anterior thalamic radiation [$2(1) = 11.468$, $P_{corrected} 0.001$, respectively]. (Fig 2). Analysis of tractography using normative Data revealed that disconnection of the anterior thalamic radiation was significantly associated with seizure outcome after 3 years [85% versus 64% streamlines resected in seizure-free/seizure-recurrence groups; $t(45) = 3.125$; $P 0.003$] and after 5 years [87% versus 61% streamlines resected in seizure-free/seizure-recurrence groups; $t(31) = 3$.

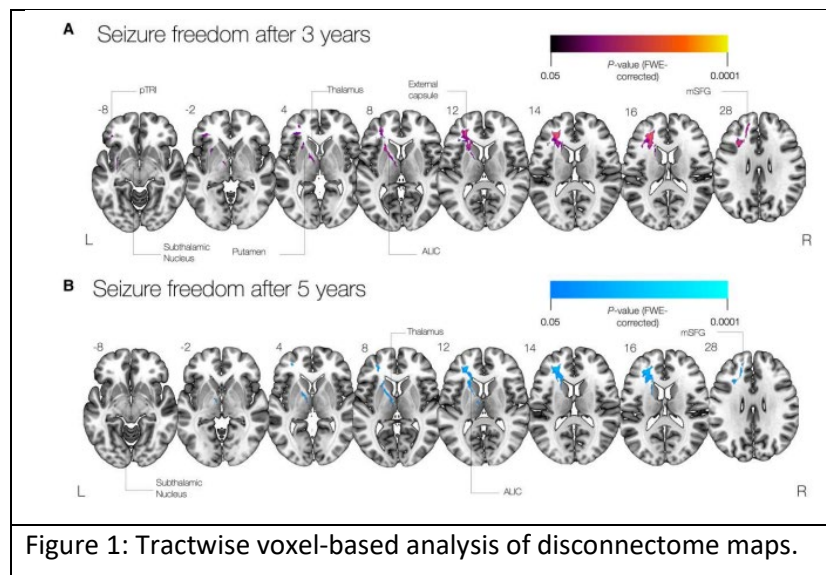


Figure 1: Tractwise voxel-based analysis of disconnectome maps.

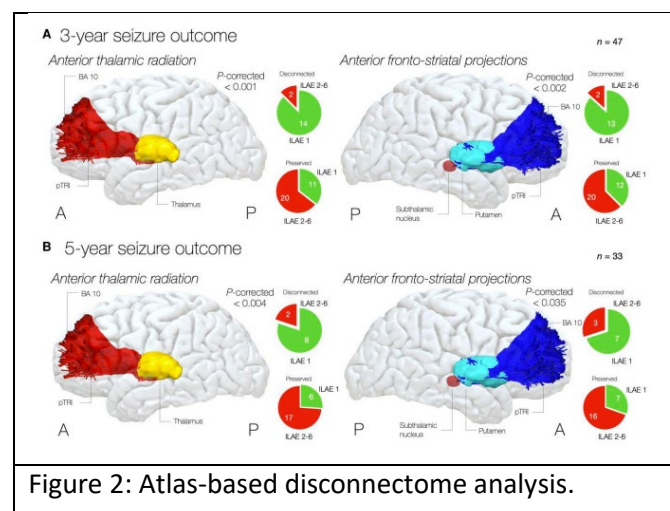


Figure 2: Atlas-based disconnectome analysis.

In the current investigation, disconnection patterns that may be important for long-term seizure independence were examined using retrospective data from 47 patients who had frontal lobe epilepsy surgery. According to the study's disconnectome analyses, anterior thalamic and corticostriatal projections being disconnected is substantially related with seizure independence at 3 and 5 years, indicating that these white matter pathways may be important in avoiding delayed seizure recurrence.² These findings are consistent with prior research and stimulation studies³, which imply that these fibres may influence epileptogenesis, and they also suggest that cortico-thalamostriatal separation may be related to long-term seizure freedom. With immediate implications for corrective epilepsy surgery and long-term seizure



freedom2, the current findings provide a fresh paradigm to comprehend delayed seizure recurrence in focal frontal lobe epilepsy.

The study's findings suggest that disconnection beyond epileptogenic zone ablation may prevent delayed seizure recurrence, and cortico-thalamic and cortico-striatal disconnection may be crucial in maintaining seizure freedom in patients with epileptogenic lesion complete resection. Regardless of the location of the lesion, these connections may make up an epileptogenic network that all frontal lobe epilepsy sufferers share. Improved seizure outcomes may result from targeted disconnection of this network, which takes into account each person's functional level and cognitive reserve in addition to current surgical resection techniques.

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2. Giampiccolo D, Binding LP, Caciagli L, Rodionov R, Foulon C, de Tisi J, Granados A, Finn R, Dasgupta D, Xiao F, Diehl B, Torzillo E, Van Dijk J, Taylor PN, Koepp M, McEvoy AW, Baxendale S, Chowdhury F, Duncan JS, Miserocchi A. Thalamostriatal disconnection underpins long-term seizure freedom in frontal lobe epilepsy surgery. *Brain.* 2023 Jun 1;146(6):2377-2388.
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Modified Atkins Diet is Safe, Effective, and Tolerable in Patients with Drug-Resistant Epilepsy

The modified Atkins diet (MAD) is a KDT that is most frequently adopted by adults. It generally consists of a liberal fat consumption, a modest protein intake, and a daily net carbohydrate limit of 20 g (total carbohydrate minus fibre) per day. The standard ketogenic diet, which calls for a ratio of grammes of fat to grammes of mixed carbohydrate and protein, is more stringent than the MAD.¹ Drug-resistant epilepsy (DRE) has led to the development of the modified Atkins diet (MAD) as an adjuvant treatment. There is little evidence for DRE in adults; the majority of research are in youngsters.² The purpose of this research was to determine if conventional medication therapy (SDT) with MAD reduced seizure frequency and improved psychosocial outcomes in adolescents and adults with DRE (nonsurgical) at 6 months compared to SDT alone.



Participants with DRE between the ages of 10 and 55 who attended outpatient epilepsy clinics between August 2015 and April 2019 and experienced more than two seizures per month despite taking at least three appropriate antiseizure medications (ASMs) at the highest tolerated doses and who had not used any type of diet therapy in the previous year were included in the study. Following eligibility verification, patients were randomised to either SDT with MAD (intervention arm) or SDT alone (control arm). Quality of life (QOL), behaviour, adverse events, and withdrawal rate after 6 months were the secondary goals in addition to a >50% reduction in seizure frequency, which was the primary goal. A goal-to-treat analysis was carried out.

160 patients (80 adults and 80 adolescents) who passed the eligibility screening out of a total of 243 were randomly assigned to the intervention or control arm. Both groups' baseline demographic and clinical traits were equivalent. At 6 months, 26.2% of the intervention group saw a >50% seizure reduction compared to 2.5% of the control group (95% CI 13.5-33.9; $p < 0.001$) (Table 1). The intervention group saw an improvement in QOL of 52.1 17.6 vs. 42.5 16.4 in the control group (mean difference, 9.6; 95% CI 4.3 to 14.9, $p < 0.001$). However, 49 patients were able to participate in behaviour assessments, and at the conclusion of the trial, improvements were seen between the intervention and control groups (65.6 7.9 vs. 71.4 8.1, $p = 0.015$). Two patients developed diarrhoea, and one patient lost weight.

Table 1: Efficacy of Diet in Seizure Frequency at the End of Treatment (6 Months) in All Patients						
Seizure reduction	Intervention group	Control group	Proportion difference (95% CI)		RR (95% CI)	Value
A) ITT analysis [SDT plus MAD group (n = 80) and SDT group (n = 80)]						
'More than 50%	21 (26.2%)	2 (2.5%)	23.7 (13.5, 33.9)	10 (2.54,43.3)		<0.001
More than 90%	6(7.5%)	0	7.5 (1.7, 13.3)	Undefined		0.0285
Complete seizure-free	4 (5%)	0	5.0 (0.2, 9.7)	Undefined		0.116
B) PP analysis [SDT plus MAD group (n = 46) and SDT group (n = 62)]						
'More than 50%	21 (45.7%)	2 (3.2%)	42.0 (27.3,57.4)	14.2(3.94,57.35)		<0.001
More than 90%	6 (13%)	0	13 (3.3, 22.7	-		0.005b



Complete seizure-free	4 (8.7%)	0	8.7 (0.5, 16.8)			0.03b
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In the intervention group of adults and adolescents, there was a substantial reduction in seizure frequency, and QOL improved for the entire population. Significantly better non-seizure domains (QOL) were seen in the intervention group when compared to the control group ($r = 0.17$, $p = 0.027$). There may be fewer and less frequent seizures, which would obviously improve quality of life. Without the use of any benchmark scales, several additional researchers, including more recent dietary studies, have observed greater QOL.³

It's interesting to note that, contrary to what has been observed in other research, there was no significant difference in weight reduction ($>10\%$) in the diet group. However, according to some reports, adults tend to lose weight more often. When compared to the baseline, most biochemical indicators in this research did not alter after six months on the diet. One patient did not have hyperuricemia. However, one research found that the lipid profile increased during the first three months of the diet; these levels returned to normal following a year of therapy, even in individuals who had been on the MAD for more than three years.²

At the conclusion of the trial, the MAD group showed improvement in all areas (reduced seizure frequency and behavioural issues) compared to the control group. Although MAD is a useful tool for reducing seizures, more study is needed to evaluate its effectiveness in terms of biomarkers and descriptive metabolomics investigations.

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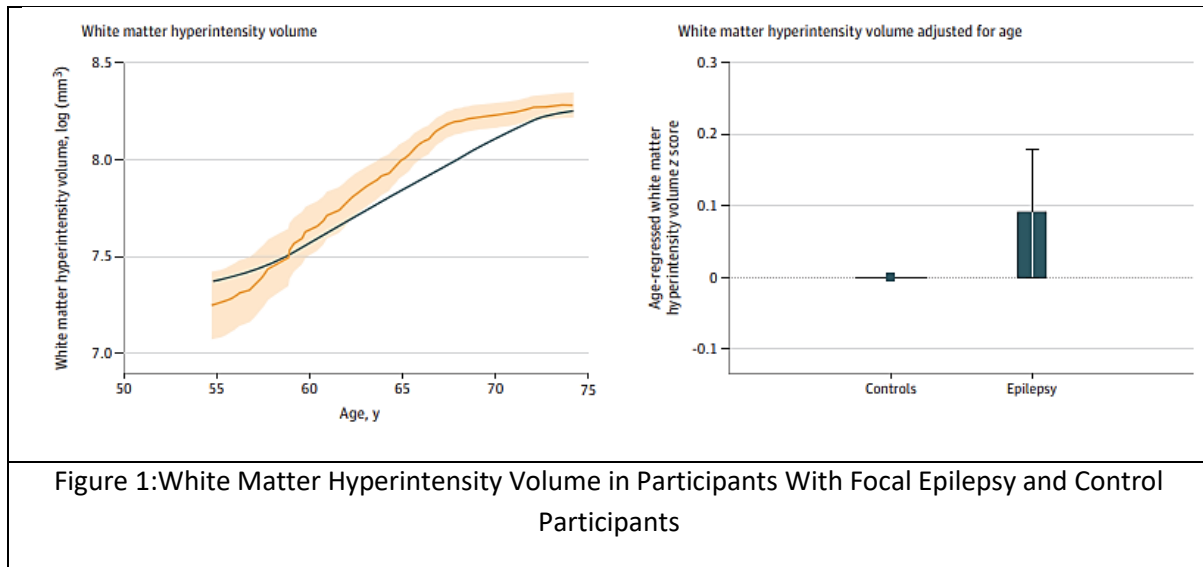
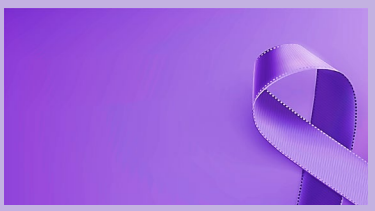
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Focal epilepsy and Modifiable Cardiovascular Risk Factors and the Risk of Dementia

There have been reports of connections between epilepsy and dementia, two frequent neurological illnesses, and endocrine or immunological markers. Endocrine and immune system abnormalities may have a role in the development of dementia and epilepsy. Hormones are one of the primary physiological regulators of brain development.¹ In elderly people, epilepsy has been linked to dementia and perhaps cognitive decline. However, it is yet unknown how much epilepsy may raise the risk of dementia, how this relates to the risk of other neurological disorders, and how modifiable cardiovascular risk factors may alter this risk.² Therefore, the comparison of the varied risks of later dementia for focal epilepsy, stroke, migraine, and healthy controls, stratified by cardiovascular risk, was the goal.

The UK Biobank, a population-based cohort of more than 500 000 adults aged 38 to 72 who underwent physiological measures, cognitive tests, and donated biological samples, provided the data for this cross-sectional study. Based on variables such as waist to hip ratio, history of hypertension, hypercholesterolemia, diabetes, and smoking pack-years, people were assigned to low, moderate, or high cardiovascular risk categories. Measures of executive function, total hippocampus, grey, and white matter hyperintensity volumes, and incident all-cause dementia are also included.

A diagnosis of focal epilepsy alone accounted for 3864 of the 495 149 individuals (225 481 [45.5%] males; mean [SD] age, 57.5 [8.1] years), stroke alone accounted for 6397, and migraine alone accounted for 14 518. Participants who had epilepsy and stroke had executive function that was equivalent to or worse than that of the control and migraine group. In comparison to stroke (HR, 2.56, 95% CI, 2.28 to 2.87; $P < .001$), or migraine (HR, 1.02; 95% CI, 0.85 to 1.21; $P = .94$), focal epilepsy was linked to a greater risk of dementia (hazard ratio [HR], 4.02; 95% CI, 3.45 to 4.68; $P < .001$). Participants with focal epilepsy and high cardiovascular risk were more than 13 times more likely than controls with low cardiovascular risk to acquire dementia (HR, 13.66; 95% CI, 10.61 to 17.60; $P < .001$). 42 353 individuals were included in the imaging subsample. In contrast to controls, focal epilepsy was linked to lower hippocampal volume (mean difference, 0.17; 95% CI, 0.02 to 0.32; $t = 2.18$; $P = .03$) and lower total grey matter volume (mean difference, 0.33; 95% CI, 0.18) than usual. White matter hyperintensity volume did not change significantly (mean difference, 0.10; 95% CI, 0.07 to 0.26; $t = 1.14$; $P = .26$) (Figure 1).



This study shown that, as compared to controls, people with focal epilepsy had lower cognitive performance in their mid- to late-life. Widespread structural brain changes, as seen by decreased hippocampus and grey matter volumes, were linked to focal epilepsy. In the Framingham Heart research, 43 patients with epilepsy were shown to have an elevated risk of dementia (HR, 1.9; 95% CI, 1.11-3.57), which was slightly lower than the findings. Cardiovascular risk factors may be taken into account in these investigations, or they may not be at all. The researchers used a previously published cardiovascular risk score²² to categorise people in order to look into the potential impact of cardiovascular burden. The study discovered that people with high cardiovascular risk and epilepsy have a more than 13-fold higher risk of dementia than people without epilepsy and low cardiovascular risk. The risk of dementia was now higher than the chance of stroke.

In this investigation, focal epilepsy was significantly linked to a higher risk of dementia than stroke, which was amplified significantly in those with high cardiovascular risk. Further research indicates that reducing the incidence of dementia in people with epilepsy by focusing on modifiable cardiovascular risk factors may be a beneficial strategy.

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A case report on neurosurgery for pregnancy-related intractable epilepsy

The fourth most common non-communicable disease affecting years lived with disability worldwide, epilepsy is a dangerous neurological condition that is characterised as experiencing at least two unprovoked seizures in a 24-hour period. Worldwide, epilepsy affects more than 52 million individuals, leading to 18.3 million YLD.¹ Around 600,000 pregnancies every year, or 0.3% to 0.5% of all pregnancies globally, include pregnant women with epilepsy. Without clinical standards, intracranial diseases needing urgent neurosurgery treatment in the obstetric environment continue to offer a challenge for doctors despite rapidly developing diagnostic and therapeutic tools.² In this report, the treatment of a 40-year-old lady with intractable focal epilepsy who needed urgent neurosurgery when her condition worsened during pregnancy was detailed.

After getting pregnant, a 40-year-old right-handed lady with documented focal epilepsy saw a 500-fold increase in daily seizures and a shift in seizure semiology, according to a research published in G3P2ab1. At the age of 7, the patient's epilepsy was discovered. Early on in the second trimester, seizures changed into 3- to 4-times-per-night hyperkinetic episodes. Daytime activities with a risk of injury and accompanying falls started to appear. An increase in ASMs had no effect on these seizures. Lamotrigine 250 mg BID and Levetiracetam were the two medications she was taking at the time; her ASM levels were therapeutic. When compared to the results of the MRI Brain 1.5 T, the grey matter of the right frontal lobe remained unaltered and likely represented a centre of gliosis or cortical dysplasia because of the high signal abnormalities within the subcortical white matter (Fig. 1). Every day, EEG samples were examined. As needed, interim reports were produced. Each time, the right anterior quadrant of the EEG signature appeared, suggesting a right frontal signature (Fig. 2).

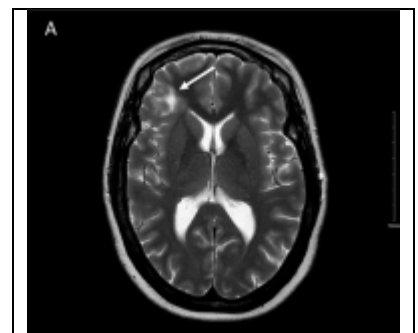
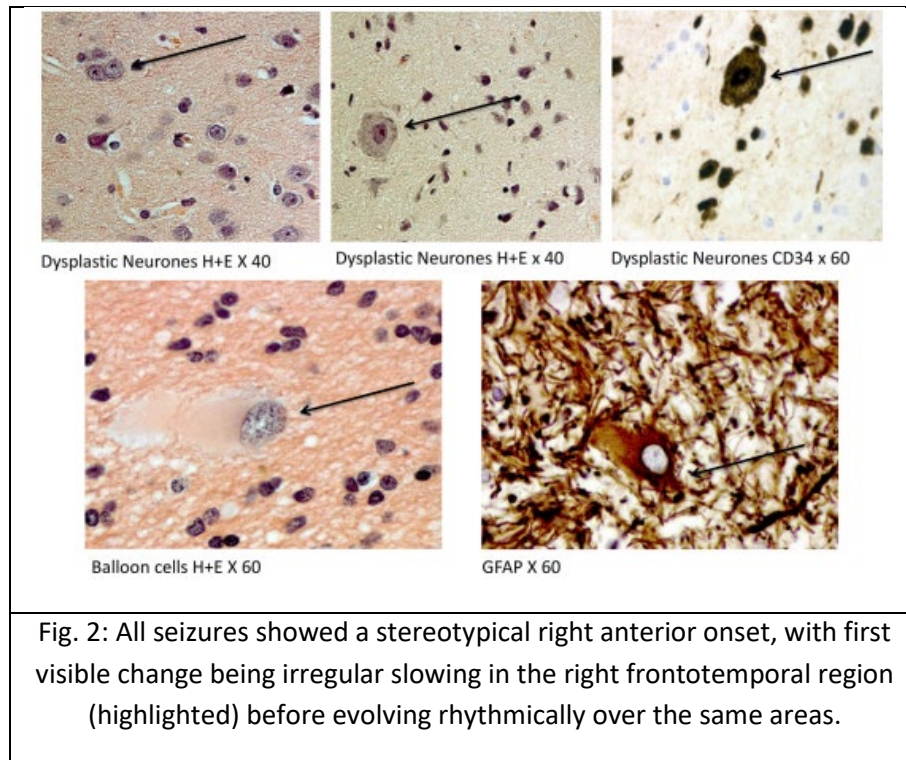
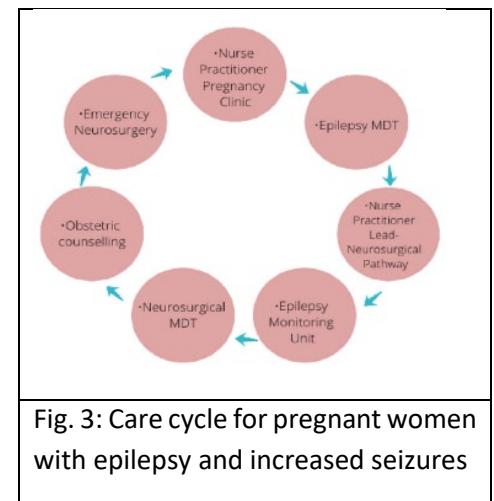


Fig.1 : Pre-Op MRI (Axial FSE T2W) Right Fronto -lateral dysplasia(arrow)



With the help of the Obstetrical Epilepsy Service and anaesthesia, the dangers to the mother and the unborn child during the pregnancy were reviewed at the ESRM. At 24 weeks pregnant, the patient underwent a successful focal frontal lobe resection. Neither phase II cortical EEGs nor cortical mapping were done during the reconstructive operation. Six weeks post-op, she reported two auras but seizure independence otherwise. Complete lesion eradication is shown in post-op imaging. The resected specimen had architectural anomalies, dysmorphic neurones, and balloon cells indicative of Cortical Dysplasia Palmini Type 2B, according to histopathology examination (Fig. 3).

At full term, a daughter was delivered vaginally without incident. At 28 months, the patient is still seizure-free.



Focal cortical dysplasias (FCDs) are frequent and highly epileptogenic causes of medically intractable epilepsy. Patients who had resective epilepsy surgery and had FCD II showed extremely favourable results for both the first year and the long-term seizure-free outcomes. The use of anaesthetic was the biggest worry in terms of the surgery's hazards. Due to the potential for laryngeal oedema and changes in the mother's position during pregnancy, regional anaesthesia is thought to be safer in pregnancy than general anaesthesia, however the mode of anaesthesia was selected with the goal of achieving the best surgical results. During



anaesthesia, the mother's medicines are frequently transferred to the unborn through the placenta. However, neither general anaesthesia nor regional anaesthesia have been linked to any significant negative effects on the foetus.³

Preconception counselling is necessary for women who have epilepsy in order to maximise the chances of a healthy pregnancy.

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