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REFERRALS

Seizures - Beyond Benzodiazepines

27.03.2024

Jos Bongers, MSc, MVM, Dipl. ECVN, MRCVS

Emergency seizure management

Goals:

1. **Stop seizures**
2. **Systemically stabilize and protect the brain**
3. **Treat the underlying causes**
4. **Prevent further seizures**

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STOP SEIZURES

BACK TO BASICS

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What is an epileptic seizure?

- Disturbance of neuronal environment lowering the threshold for electrical activity
- Excessive and/or hypersynchronous electrical activity in the cerebral cortex
- Results in paroxysmal episodes of abnormal consciousness, motor activity, sensory input and/or autonomic function
- Epilepsy occurs in between 0.5 to 5.7% of dogs and 0.5 to 1% of cats

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How do epileptic seizures arise?

Inadequate Neuronal Inhibition:

- Abnormality of inhibitory neurotransmitters
  - GABA (γ-aminobutyric acid) = major inhibitory neurotransmitter
- Primary loss of inhibitory neurons
- Decreased neuromodulation by serotonin, dopamine or noradrenaline

Excessive Neuronal Excitation:

- Abnormality of excitatory neurotransmitters
  - L-glutamate = major excitatory neurotransmitter
- Increased acetycholine

Combination of the above

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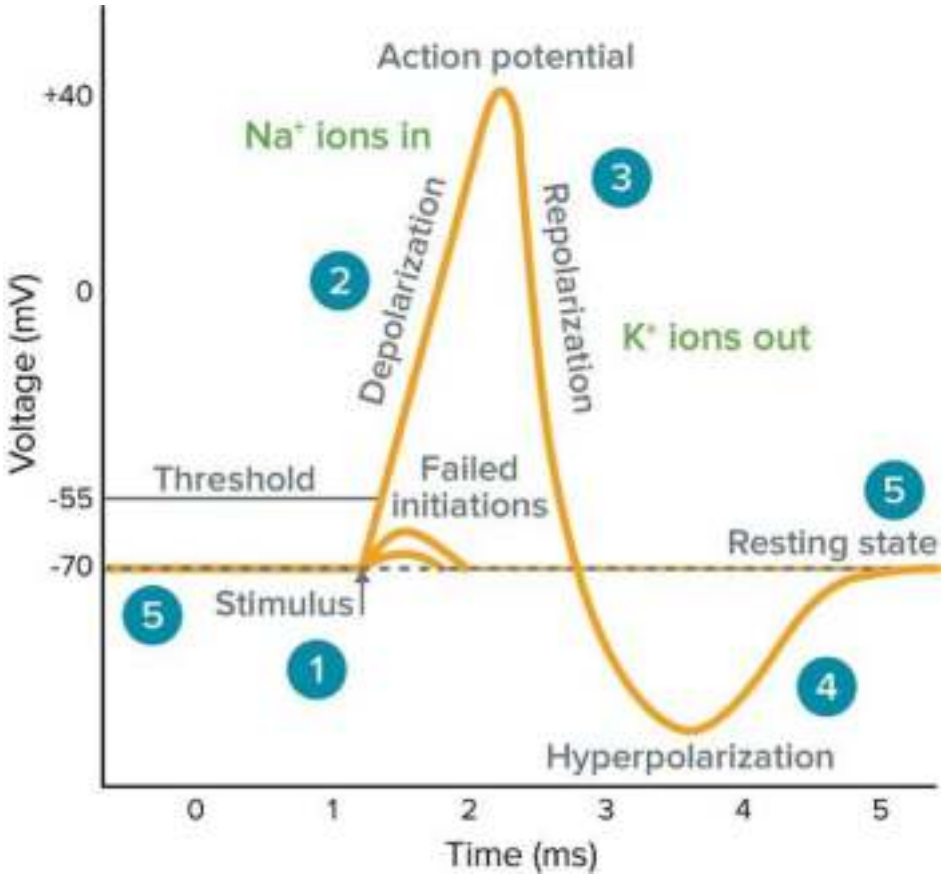
Normal neuronal cell physiology

- Membrane potential is determined by influx/efflux of ions through voltage gated channels:
  - Extracellular sodium >>> than intracellular
  - Extracellular potassium <<< than intracellular
- Action potentials are created by a reduction in the cell membrane potential
- An increased permeability of voltage gated channels to sodium results in depolarisation (sodium flows into cell)
- At the axon terminal this depolarisation results in opening of calcium channels
- Calcium enters the cell resulting in release of neurotransmitters



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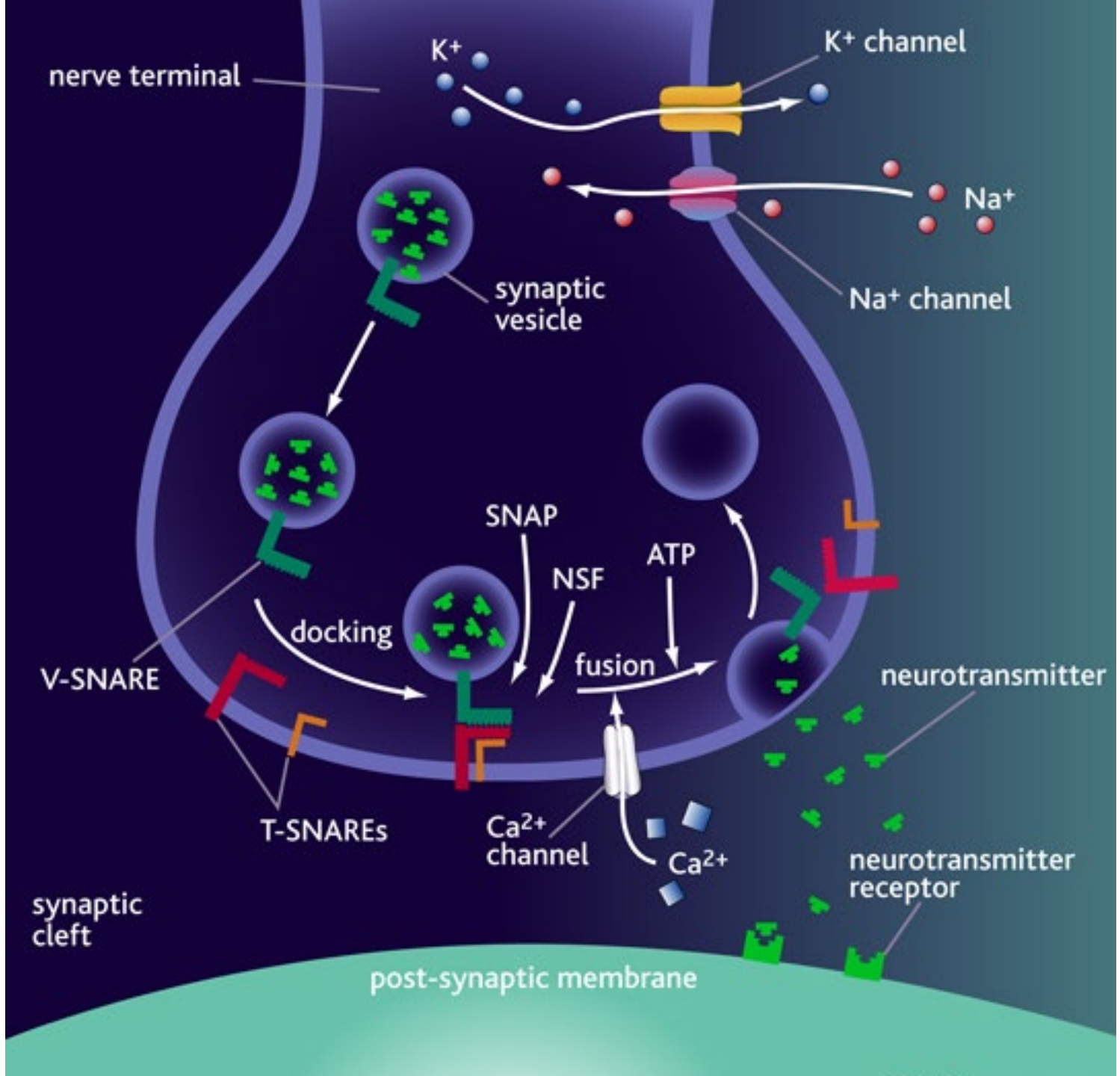
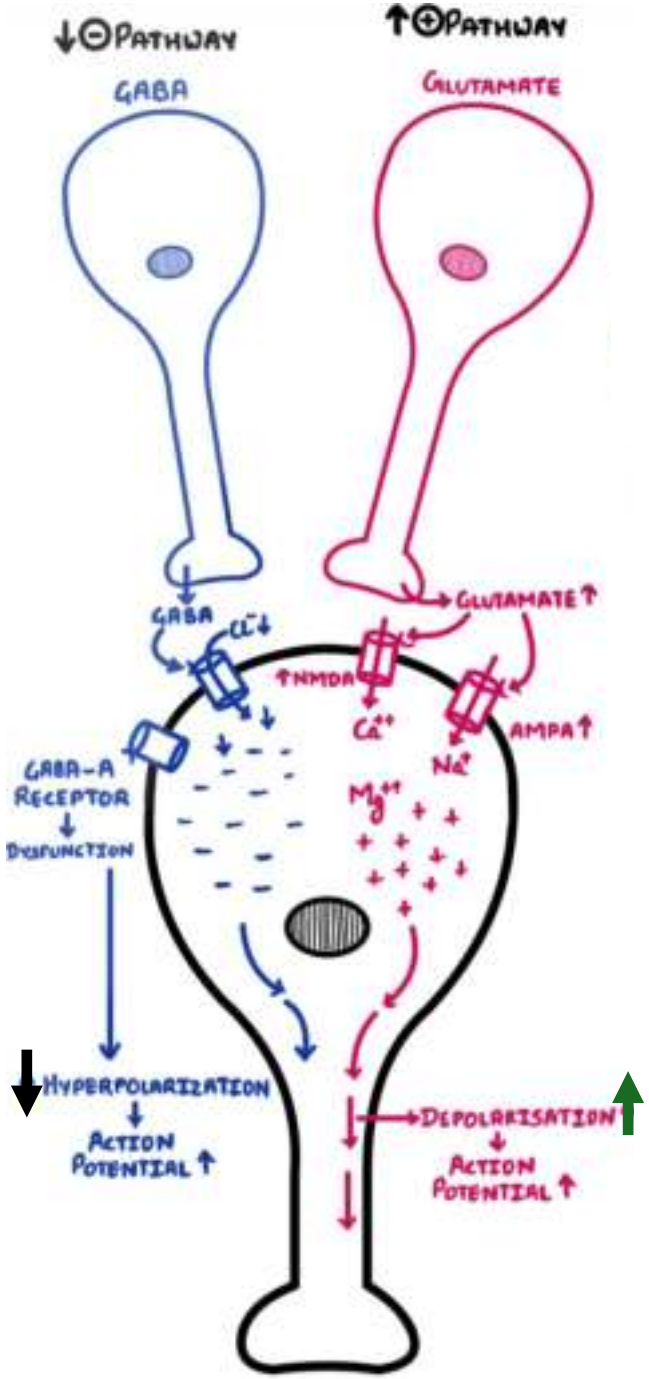

nerve terminal
K+
K+ channel
Na+
Na+ channel
synaptic vesicle
SNAP
NSF
ATP
docking
fusion
V-SNARE
T-SNAREs
Ca2+ channel
Ca2+
neurotransmitter
neurotransmitter receptor
synaptic cleft
post-synaptic membrane

Change in seizure threshold



What is an epileptic seizure?

Terminology

- **Seizure**
- **Epileptic seizure**
- **Reactive seizure**
- **Epilepsy**
- **Cluster seizures**
- **Status epilepticus**

International veterinary epilepsy task force consensus report on epilepsy definition, classification and terminology in companion animals

Mette Berendt[1*], Robyn G. Farquhar[2], Paul J. J. Mandigers[3], Akos Pakozdy[4], Sofie F. M. Bhatti[5], Luisa De Risio[6], Andrea Fischer[7], Sam Long[8], Kaspar Matiasek[9], Karen Muñana[10], Edward E. Patterson[11], Jacques Penderis[12], Simon Platt[13], Michael Podell[14], Heidrun Potschka[15], Marti Batlle Pumarola[16], Clare Rusbridge[17,18], Veronika M. Stein[19], Andrea Tipold[19] and Holger A. Volk[20]

Seizure ≠ Epilepsy

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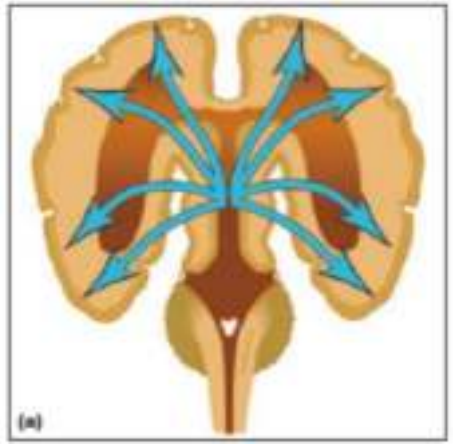
Epileptic seizure type

Generalised epileptic seizures

Involves both hemispheres

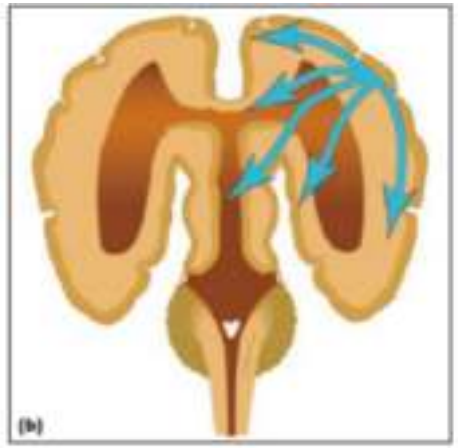
- Clonic seizure
- Tonic seizure
- Tonic-clonic seizure
- Myoclonic seizure



Focal epileptic seizures

Restricted to one area in the cortex of one hemisphere

- Motor
- Autonomic
- Behavioural



BSAVA Manual of Canine and Feline Neurology (2013)

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Seizure mimics

- Syncope
- Narcolepsy
- Vestibular attacks
- Compulsive disorder
- Pain associated behavior
- Idiopathic head tremor
- Movement disorder

Trigger
Duration
Level of consciousness
Post-episodic changes
Autonomic signs
Muscle tone

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Is it a seizure?

- ✓ Tonic (limb rigidity)
- ✓ Clonic (jerking)
- ✓ Involving all 4 limbs
- ✓ Loss of consciousness
- ✓ Salivation
- ✓ Jaw clenching

https://www.youtube.com/watch?v=D-0bAeAsSFY

GENERALISED TONIC-CLONIC SEIZURE (GTCS)

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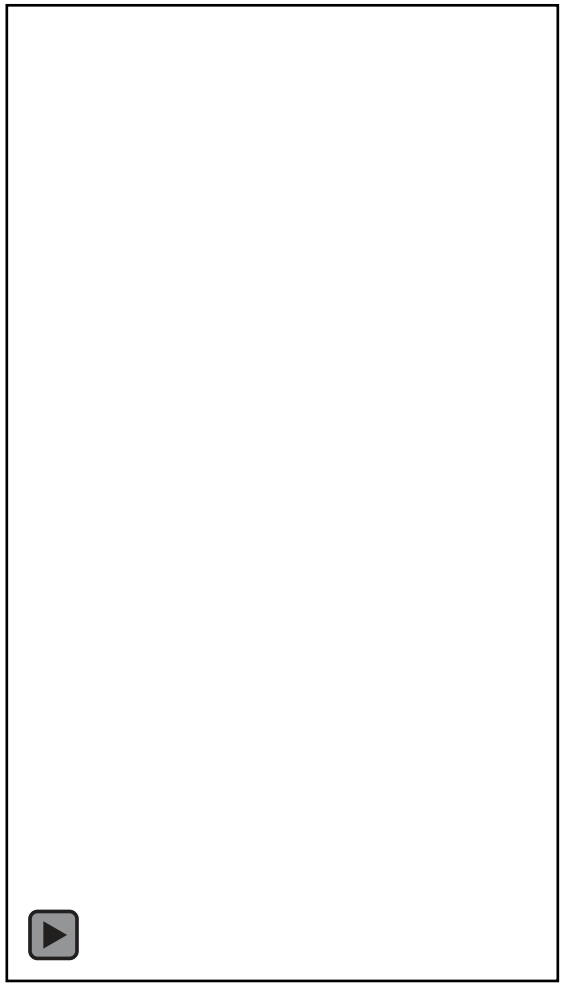
Is it a seizure?

- ✓ Repeated jerking head movements
- ✓ Jaw clenching
- ✓ Consciouss



FOCAL SEIZURE

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Is it a seizure?

- ✓ Uncontrolled side-to-side ('no') head tremors at rest
- ✓ Remains alert and responsive
- ⇒ Normally can be stopped when dog is focussed on goal-orientated task (e.g. food, ball), opposite to intention tremor

CANINE IDIOPATHIC HEAD TREMOR SYNDROME (IHTS)

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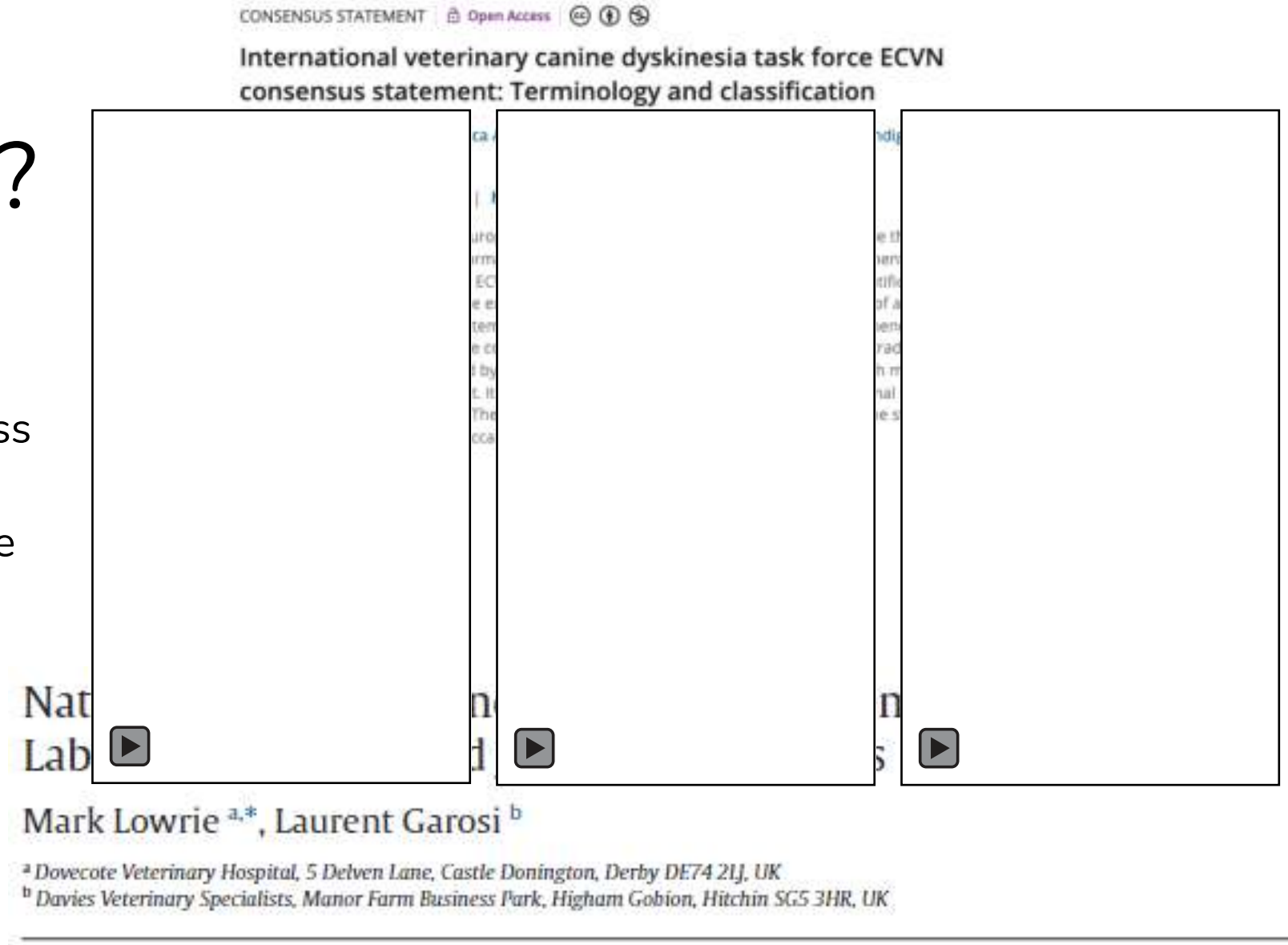
Is it a seizure?

- ✓ Involvement of all 4 limbs without loss of consciousness
- ✓ Dystonia (persistent muscle stiffness and delayed muscle relaxation)



CONSENSUS STATEMENT | Open Access

International veterinary canine dyskinesia task force ECVN consensus statement: Terminology and classification

Mark Lowrie [a,*], Laurent Garosi [b]

[a] Dovecote Veterinary Hospital, 5 Delven Lane, Castle Donington, Derby DE74 2LJ, UK
[b] Davies Veterinary Specialists, Manor Farm Business Park, Higham Gobion, Hitchin SG5 3HR, UK

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Diazepam
rectal solution
5 mg
For rectal use
DESITIN
5 tubes
STOP SEIZURES

STOP SEIZURES – why?

- Insufficiency of seizure termination mechanisms and imbalance between excitatory and inhibitory activity ➔ **status epilepticus (16.5%)**
- Status epilepticus ➔ permanent brain damage (e.g. neuronal cell necrosis, network reorganization, gliosis) and severe systemic complications (e.g. cardiorespiratory collapse, shock, acidosis, electrolyte imbalances)
  - Occurrence & severity proportionally related to duration seizure activity
  - Short-term mortality (29.8%)
    - ↑ patient age, ↓ duration hospitalization, development of SE before arrival & SE caused by potentially fatal etiology
  - SE recurrence (27%)
    - Prior hx of pharmacoresistant epilepsy, predominance of a focal seizure phenotype

Management starts at home

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3 yo FN Border collie. Previous hx of IE and on maintenance 5 mg/kg phenobarbital BID. Presented with status epilepticus for the last 30 min.

A High dose (2 mg/kg) rectal diazepam bolus 2-3 x + place IV and monitor

0%

B Intramuscular/intranasal midazolam bolus 2-3 x + place IV and monitor

0%

C Intramuscular/intranasal midazolam bolus + place IV + 60 mg/kg levetiracetam bolus IV

0%

D Intramuscular/intranasal midazolam bolus + place IV + 60 mg/kg levetiracetam bolus IV + 2-3 mg/kg ph…

0%

E Intramuscular/intranasal midazolam bolus + place IV + ketamine CRI 0.1-0.5 mg/kg/hr

0%

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E Intramuscular/intranasal midazolam bolus + place IV + ketamine CRI 0.1-0.5 mg/kg/hr

0%

Major classes of veterinary anti-epileptic drugs (AEDs)

- Barbiturates: **phenobarbital**
- Benzodiazepines: **diazepam, midazolam**, clonazepam, clorazepate
- Imepitoin - **Pexion**
- Bromide: **potassium bromide**
- Fatty acids: sodium valproate
- Fructose derivatives: topiramate
- GABA analogs: gabapentin, pregabalin
- Hydantoins: phenytoin
- Pyrimidinediones; primidone
- Pyrrolidines: **levetiracetam**

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Suitable Medications for Emergency Therapy

Medication	Dose
Diazepam	0.5 to 1 mg/kg IV bolus, repeated 2 to 3 times (onset of anticonvulsant effect is 2 to 3 minutes) Constant IV infusion: dogs 1 to 2 mg/kg/h, cats: 0.5 to 1 mg/kg/h (NB: adsorbs to plastic)
Midazolam	0.2 mg/kg IV bolus (can be used with diazepam) Constant IV infusion: 0.3 mg/kg/h added to IV fluids (but not fluids containing calcium)
Levetiracetam (particularly cluster seizures)	60 mg/kg IV bolus Constant IV infusion: 5-10 mg/kg/hour to effect
Phenobarbital loading dose (rapidly increase blood levels)	Phenobarbital naïve animals: total load of 18-24 mg/kg Animals currently on Pb: total load of 6 to 8 mg/kg
Pentobarbitone (no longer available in UK)	Only used with continued seizures despite treatment as above. Dogs and cats: 3-15 mg/kg given slowly IV to effect
Propofol infusion (where seizures continue)	Only used with continued seizures despite treatment as above. 0.1 to 0.4 mg/kg/min to clinical effect
Potassium Bromide loading dose	200 mg/kg/day for 5-days, divided into multiple daily doses, OR 1000 mg/kg over 24-hours. Then onto maintenance dose.

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Acute seizure management of seizures at home

First aid for any seizure

- STAY calm, keep calm, begin timing seizure
- Keep your pet SAFE, remove harmful objects, don't restrain, protect their heads
- Keep the airway clear and don't put your hands or any objects in mouth
- Administer anticonvulsive tx
- STAY until your pet has fully recovered and at least an hour after
- Update your seizure diary

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Delivery routes of Diazepam and Midazolam
At home

Administration route	Advantages	Limitations
Transdermal	Painless Easy to use Suitable for home No requirement for medical training Avoidance of first-pass hepatic metabolism	Subject to blood-brain barrier Slow release not suitable for emergency
Buccal	Painless Ease to administer Suitable for home No requirement for medical training Avoidance of first-pass hepatic metabolism	Subject to blood-brain barrier Potentially unfavourable pharmacokinetics Delivery of limited drug amount If swallowed, functions as oral Dog's compliance is needed Incorrect administration during seizures
Sublingual	Similar to buccal	Similar to buccal
Oral	Painless Easy to use No requirement for medical training Suitable for home	Subject to blood-brain barrier Potentially unfavourable pharmacokinetics Slow absorption not suitable for emergency Potential for gastrointestinal degradation Subject to first-pass hepatic metabolism Dog's compliance is needed
Rectal	Minimal pain/discomfort Relatively easy to use No requirement for medical training Suitable for home	Subject to blood-brain barrier Variability in effectiveness (clinical evidence) Variability in pharmacokinetics Partially subject to first-pass hepatic metabolism Likely slow onset of action Socially unacceptable
Intranasal	Likely effective (clinical evidence) Likely rapid onset of action (clinical evidence) Likely favourable pharmacokinetics Avoidance of first-pass hepatic metabolism Avoidance of blood-brain barrier No requirement for medical training Relatively easy to use Painless Suitable for home	Need for high concentration drug Potentially affected by mucosal factors Potentially affected by drug formulation Need for a veterinary nasal device

Charalambous et al. (2021)

Cluster seizures

2 or more generalized epileptic seizures in 24 hours

In severe clusters, then in addition to maintenance therapy can use additional pulse therapy during the cluster with:

- Levetiracetam (Keppra™) (treatment of choice)
- IR diazepam, (IN midazolam)
- Gabapentin (Neurontin)

J Vet Intern Med 2012;26:334–340

Double-Masked, Placebo-Controlled Study of Intravenous Levetiracetam for the Treatment of Status Epilepticus and Acute Repetitive Seizures in Dogs

B.T. Hardy, E. E. Patterson, J.M. Cloyd, R.M. Hardy, and I.E. Leppik

Background: Status epilepticus (SE) and acute repetitive seizures (ARS) are common canine neurologic emergencies. No evidence based studies are available to guide treatment in veterinary patients. Parenteral levetiracetam (LEV) has many favorable properties for the emergency treatment of seizures, but its safety and efficacy in dogs for SE and ARS are unknown.

Hypothesis: Intravenous LEV is superior to placebo in controlling seizures in dogs with SE or ARS after treatment with IV diazepam.

Animals: Nineteen client-owned dogs admitted for SE or ARS.

Methods: Randomized, placebo-controlled, double-masked study. Dogs with SE or ARS were randomized to receive IV LEV (30 or 60 mg/kg using an adaptive dose-escalation approach) or placebo, in addition to standard of care treatment. They were monitored for at least 24 hours after admission for additional seizures.

Results: The responder rate (defined as dogs with no additional seizures after administration of the study medication) after LEV was 56% compared with 10% for placebo ($P = .06$). Dogs in the placebo group required significantly more boluses of diazepam compared with the LEV group ($P < .05$). Seizure etiologies identified were idiopathic epilepsy (n = 10), inflammatory central nervous system disease (n = 4), intracranial neoplasia (n = 2), hepatic encephalopathy (n = 1), and 2 dogs had no cause determined. No serious adverse effects were attributable to LEV administration.

Conclusions and Clinical Importance: LEV was safe and potentially effective for the treatment of SE and ARS in these client owned dogs. Larger, controlled clinical trials are needed to confirm this preliminary observation.

Key words: Canine; Cluster seizures; Epilepsy; Pharmacokinetics.

Cluster seizures

Aim is to reduce the number of seizures in a cluster

Levetiracetam (Keppra™) – at 20 to 30mg/kg TID to QID for the duration of the cluster only (preferably QID).

- At the end of the cluster stop the additional drug.
- All the time the dog remains on its normal maintenance therapy.
- Most clusters typically last between 24 to 72 hours.
- May need to reduce the dose if the dog appears too sedated, especially large/giant breed dogs

Status epilepticus

Specific Short-Acting Anticonvulsant Therapy

- Diazepam 0.5 - 1.0 mg/kg IV or 0.5 - 2.0 mg/kg rectally
- Midazolam 0.1-0.5 mg/kg IV or 0.2 mg/kg IN

- 2 to 3 minutes to clinical effect
- repeat up to three times

Remember in cats the half-life of diazepam is longer: dose more carefully

Pharmacokinetics of Diazepam and Midazolam

Diazepam

- Wide margin of safety
- Anticonvulsant effect of diazepam following IV administration is 2-3 minutes, but despite half life of over 3 hours, the CNS concentrations decline rapidly and anticonvulsant effect only lasts around 20 minutes in dogs. The treatment will therefore need to be repeated.

Midazolam

- Wide margin of safety and broad therapeutic index
- Time to seizure cessation:
  - intranasal: 33 sec and seizure control in 70-75% of dogs
  - Intravenous: 64 sec and seizure control in 61% of dogs
- Rapid elimination (half-life around 53-77 minutes)

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Delivery routes of Diazepam and Midazolam - *In hospital*

Administration route	Advantages	Limitations
Intravenous	Likely effective (clinical evidence) Likely rapid onset of action (clinical evidence) Precise control of the administered dose Avoidance of first-pass hepatic metabolism	Subject to blood-brain barrier Requirement for hospitalisation Requirement for medically-trained staff Hard to establish during seizures Not for at-home use
Intramuscular	Likely favourable pharmacokinetics Avoidance of first-pass hepatic metabolism	Subject to blood-brain barrier Requirement for training or medical staff Needle/syringe misuse by non-trained caregivers Less suitable for at-home use Soft tissue or nerve damage risk Infection risk Painful

Charalambous et al. (2021)

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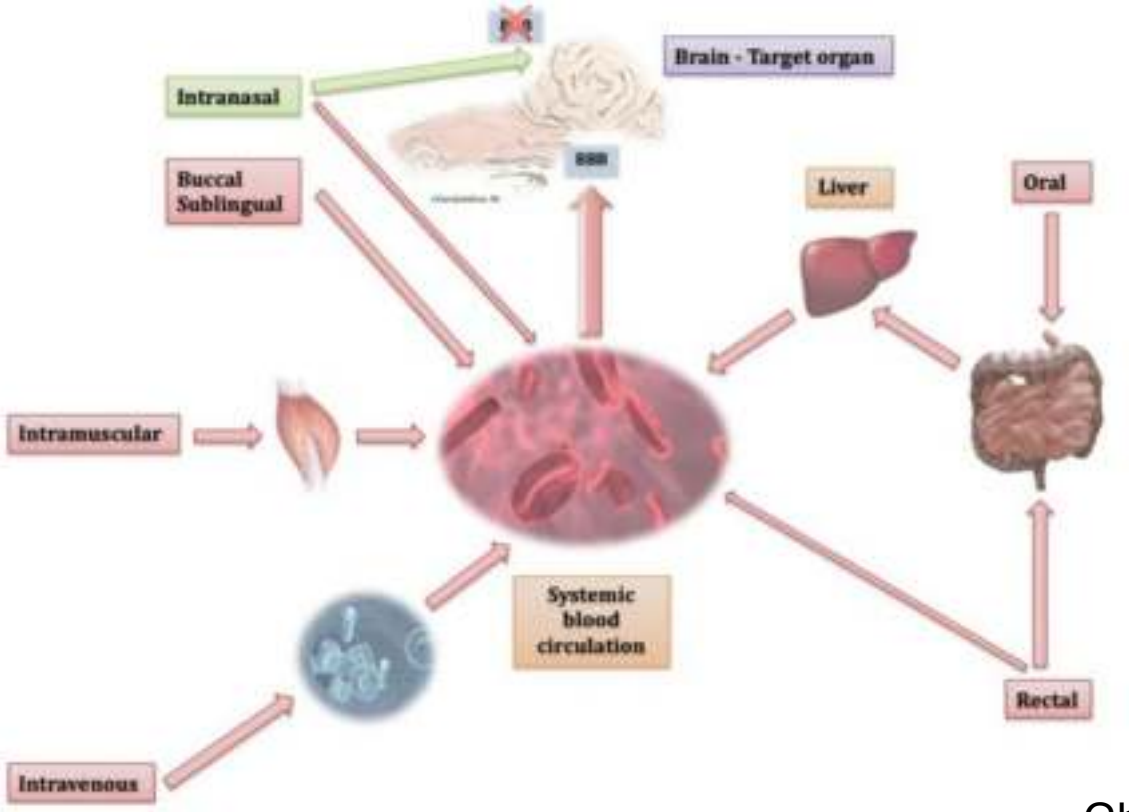
Delivery routes of Midazolam

Intranasal: direct (via olfactory and trigeminal nerves) & indirect (via blood circulation ➔ BBB)



Charalambous et al. (2021)

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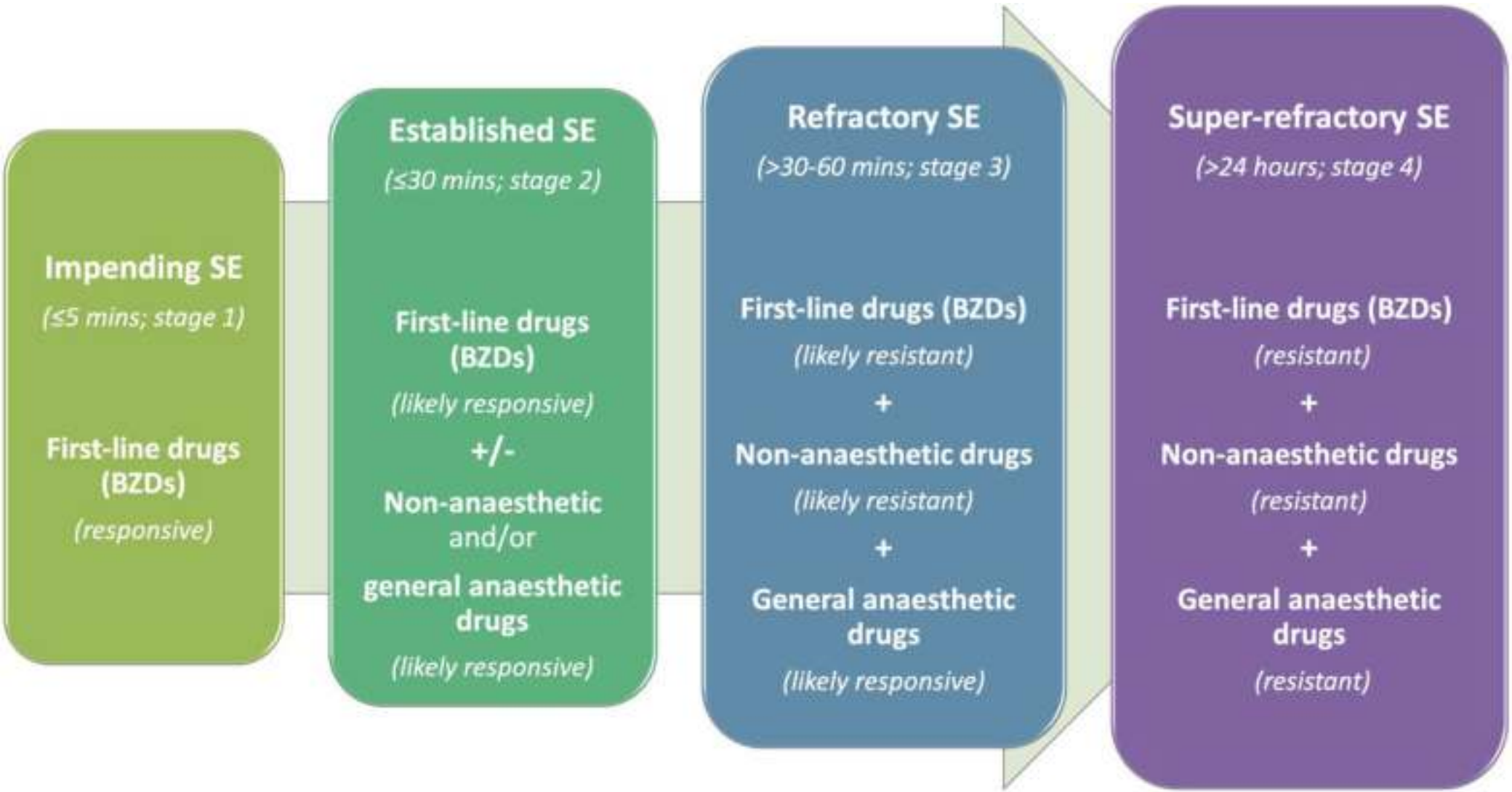
Therapeutic considerations in status epilepticus (SE)

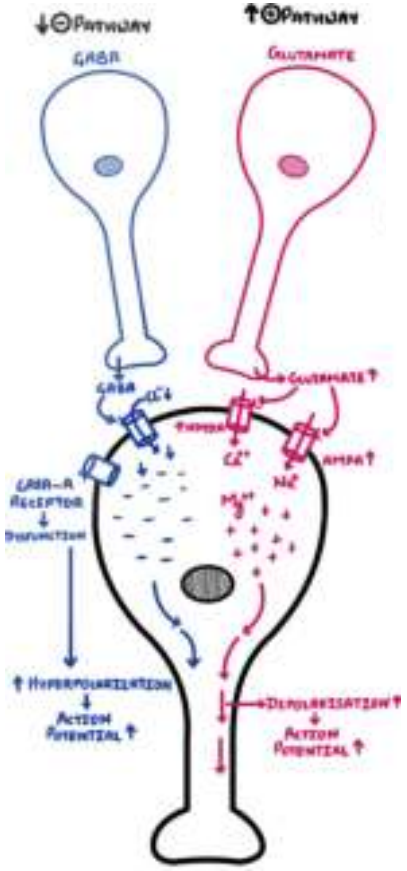
Four stages:

1. **Impending SE**
   - < 5 min of continuous seizure activity
   - Likely respond to first-line antiseizure therapy
2. **Established SE**
   - < 30 min of continuous seizure activity
   - Likely less responsive to first-line line antiseizure activity
   - Adjunctive non-GA or GA antiseizure tx may be needed
3. **Refractory SE**
   - 30-60 min of continuous seizure activity
   - Resistant to first-line and non-GA antiseizure therapy
   - Adjunctive GA therapy is needed
4. **Super-refractory SE**
   - > 24h continuous seizure activity or seizure recurrence or seizure recurrence after initiation of tx with GA antiseizure therapy
   - Seizures likely resistant to any antiseizure therapy

M. Charalambous et al. (2021)

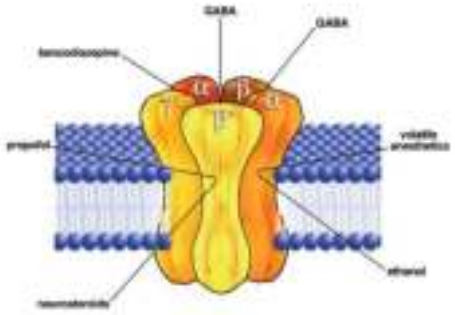


Why does SE progress to refractory stages?



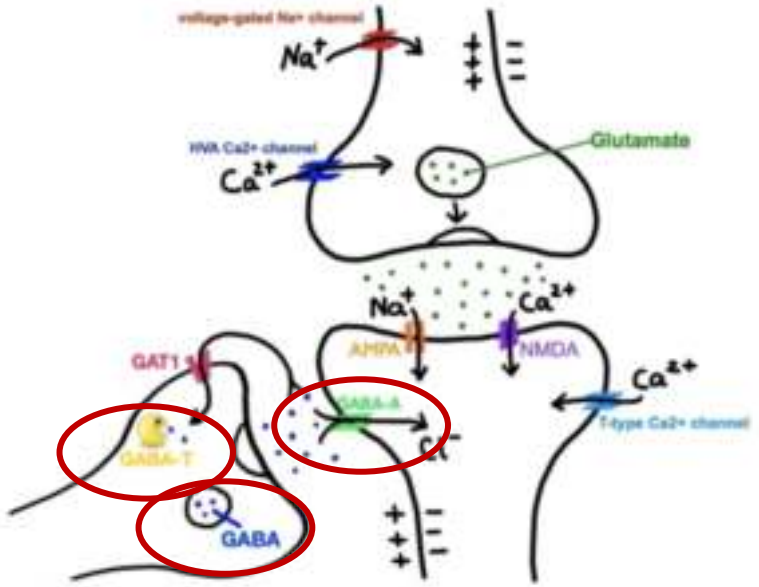
Stage 1 (< 5 min):

- **Loss of GABA-induced inhibition**
- Upregulation excitation induced by NMDA and AMPA receptors for glutamate
- BBB transporters overexpression



Tx:

- BZD: Binds to $GABA_A$ y-units



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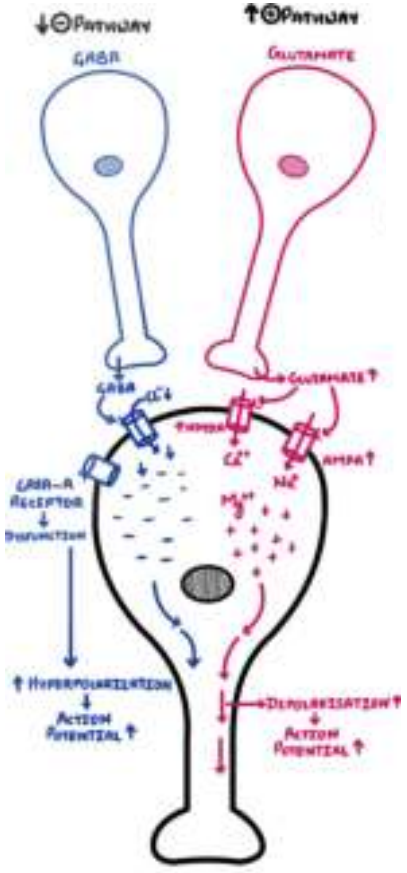


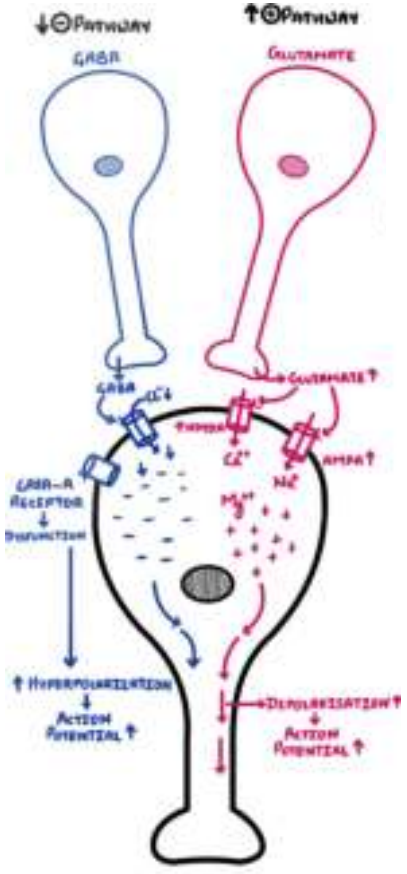
Stage 1 (< 5 min):

- Loss of GABA-induced inhibition
- Upregulation excitation induced by NMDA and AMPA receptors for glutamate
- **BBB transporters overexpression**

Tx:

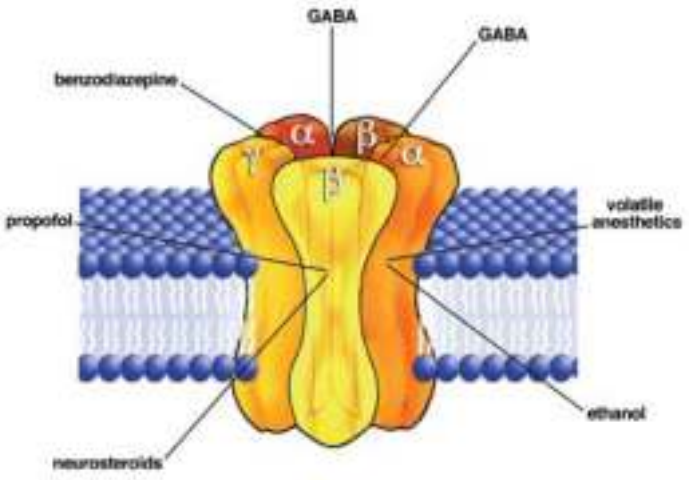
- Administration routes bypassing BBB ➔ intranasal route

Why does SE progress to refractory stages?



Stage 2,3 (30-60 min):

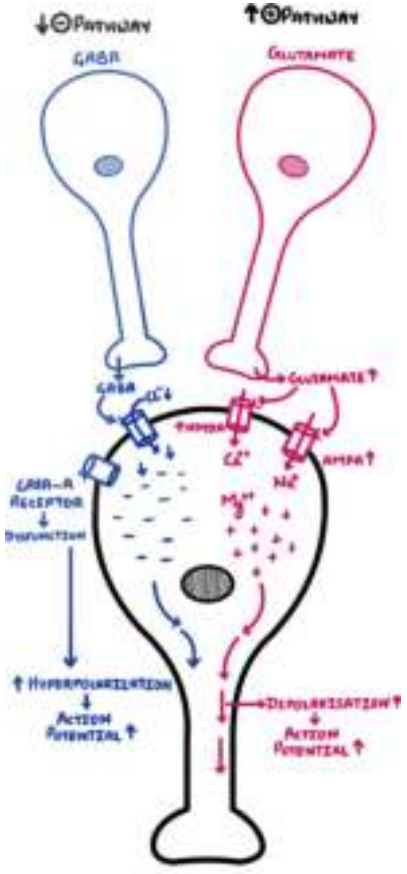
- Reduced synaptic targets (change in $GABA_A$ γ subunits and chloride homeostasis)
- Refractory to BZD's



Tx:

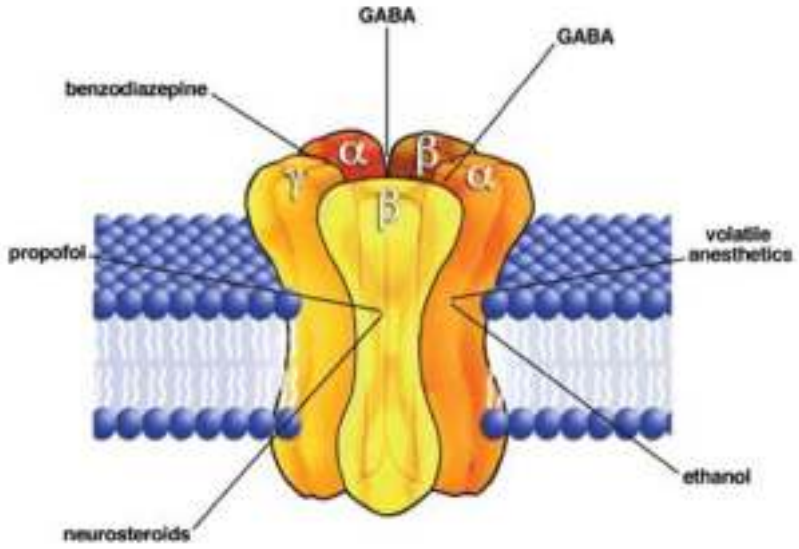
- Phenobarbital, propofol, inhalation anaesthetics: Medication acting on other external subunits (α,β)

Why does SE progress to refractory stages?



Stage 3,4 (>60 min):

- Resistance to most $GABA_A$ acting drugs, ↓ AMPA, ↑ NMDA)



Tx:

- Ketamine = glutamate receptor (NMDA) antagonist
- May even help preventing resistance if administered in early stage

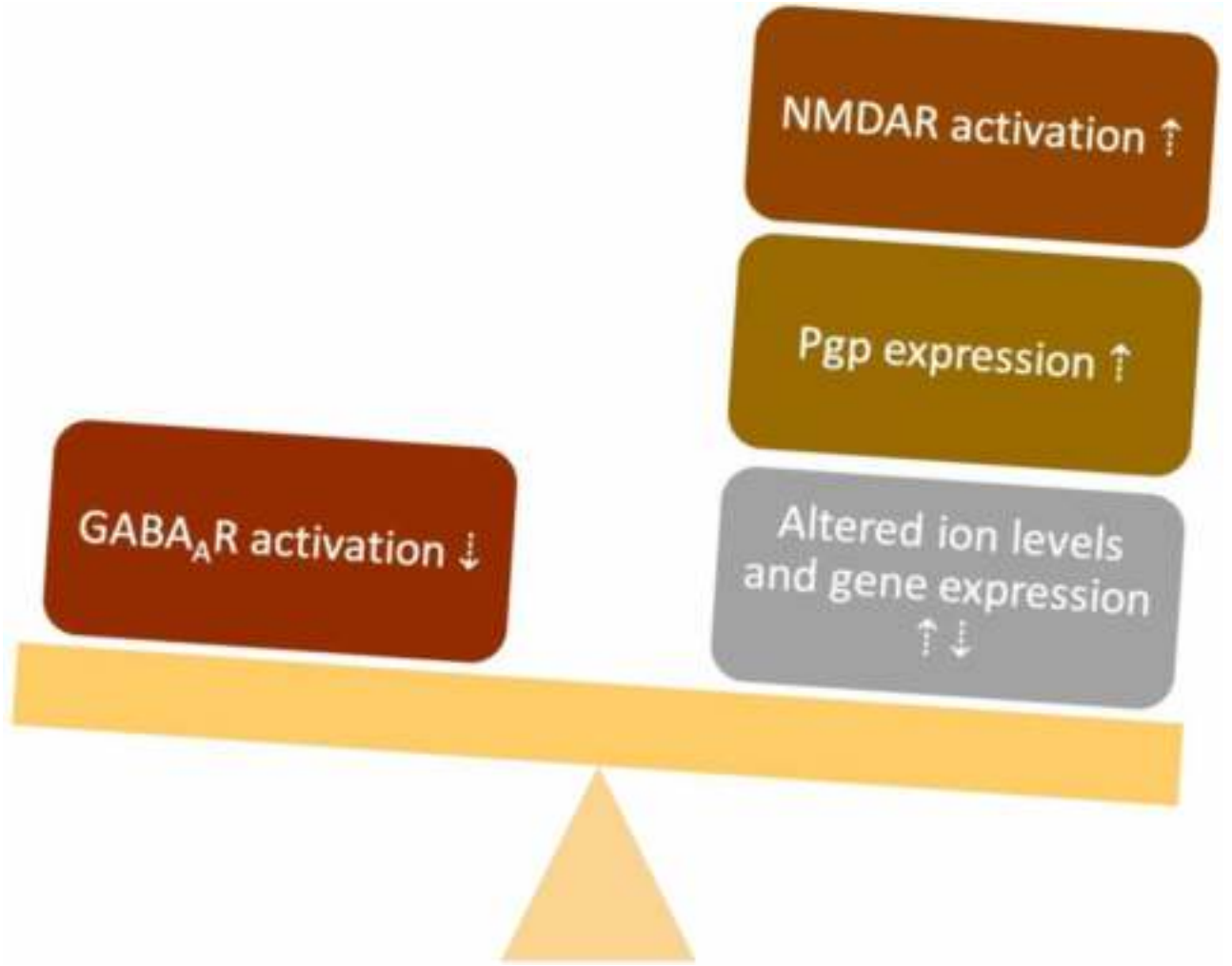


Illustration of the imbalance between inhibitory and excitatory mechanisms occurring during SE. GABA$_A$R, γ-aminobutyric acid A; NMDAR, N-methyl-D-aspartate receptor; PgP, P-glycoprotein. M.Charalambous et al. (article in press)

Status epilepticus

Rapidly achieving effective phenobarbital Blood Levels

Phenobarbital naïve animals:

- Initial loading dose of 12 mg/kg IV
- Blood concentration of 65 - 100umol/l
- Clinical effect in 20 minutes
- If animal not too sedated: further boluses at 3 mg/kg to take total dose to 18 – 24 mg/kg

Animals presently on Pb therapy:

- Already have blood levels: large bolus will result in toxic levels.
- Single bolus of 3 mg/kg to slightly increase levels (blood sample for Pb level first)
- Potassium bromide loading dose

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Status epilepticus

Bromide Loading Regime

Dogs going into Status Epilepticus in the presence of therapeutic levels of phenobarbital or in cases with severe liver impairment

Oral or rectal loading dose:

- Rectal loading may cause severe diarrhoea
- 200mg/kg daily for 5 days, divided into 4 to 6 doses
- Single loading dose of 600 to 1000mg/kg, divided into multiple doses

Monitor level post-load and one month later

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Status epilepticus – ongoing seizure activity

May need to sedate or GA for 12 to 36 hours

- Constant diazepam infusion: 0.5-2.0 mg/kg/hour
- Constant midazolam infusion: 0.1-0.3mg/kg/hour
- Propofol infusion: 0.1-0.5 mg/kg/min
- Ketamine infusion: 0.1-0.5 mg/kg/hr
- Fosphenytoin: 15 mg/kg IV bolus


frontiers | Frontiers in Veterinary Science

OPEN ACCESS

Isoflurane treatment for refractory and super-refractory status epilepticus in dogs

Eirini Sarpekidou*, Georgios Polyzois, Virginia Papageorgiou, Ioannis Savvas, Zoe Polizopoulou and George Kazakos

- 73.1% ISO administration resulted in successful RSE/SRSE treatment and poor outcome in 26.9%
- Median time of anesthetic cycles with ISO was 12.67h
- Side effects occurred in 88.5% of episodes (hypothermia, hypotension).

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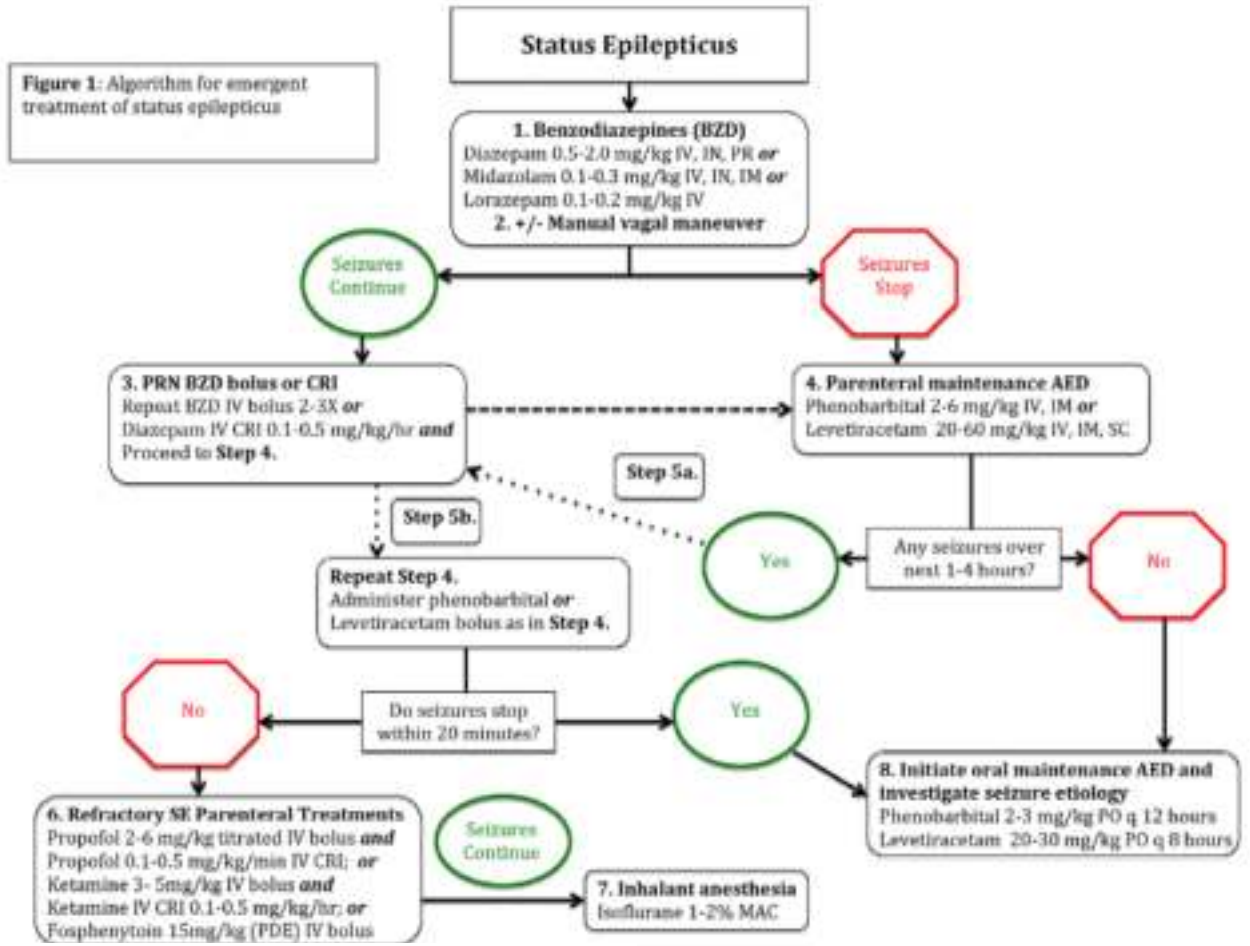
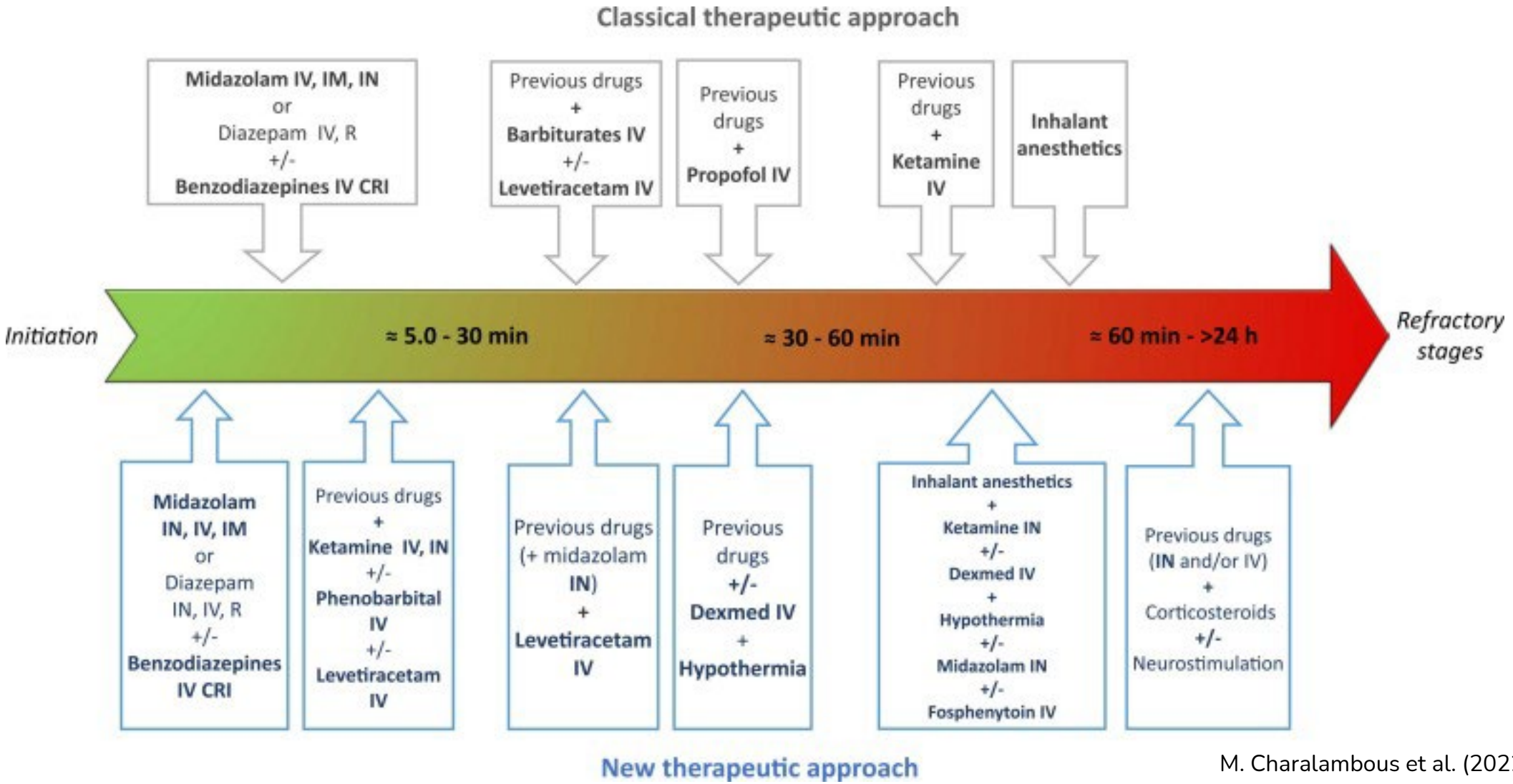
Status epilepticus: when to give what?



S.B. Golubovic & J.H. Rossmeisl Jr.

Status epilepticus – future considerations



M. Charalambous et al. (2022)

Drug targets

Table 1
Current drugs used in the management of canine status epilepticus (SE) and their potential targets for addressing the therapeutic obstacles.

Drugs	Administration route	Number of SE obstacles which are potentially addressed	Potential mechanisms of actions	Other possible effects
Midazolam	IN	2	$GABA_AR$ agonist, partial BBB bypass	N/A
	IV	1	$GABA_AR$ agonist	
Diazepam	IN	2	$GABA_AR$ agonist, partial BBB bypass	N/A
	IV	1	$GABA_AR$ agonist	
Ketamine	IN	2–3	NMDAR antagonist + /- prevention of $GABA_AR$ downregulation, partial BBB bypass	Neuroprotection (prevention of excitotoxicity), antioxidant and anti-inflammatory effects
	IV	1–2	NMDAR antagonist + /- prevention of $GABA_AR$ downregulation	
Ketamine and midazolam	IV	2	NMDAR antagonist + /- prevention of $GABA_AR$ downregulation, $GABA_AR$ agonist	Neuroprotection (prevention of excitotoxicity), antioxidant and anti-inflammatory effects
	IN	3	NMDAR antagonist + /- prevention of $GABA_AR$ downregulation, $GABA_AR$ agonist, partial BBB bypass	
Dexmedetomidine	IV	N/A	N/A	a2 adrenoreceptor agonist, neuroprotection (prevention of excitotoxicity, decrease in metabolic demand)
Levetiracetam	IV	1	Interference with gene expression and protein synthesis, decrease in intracellular Ca^{2+}	Decrease in neurotransmitters release, neuroprotection (prevention of excitotoxicity)
Barbiturates	IV	1	$GABA_AR$ agonist (non-BZD site), decrease in intracellular Na^+ and Ca^{2+},	Decrease in glutamate release
Propofol	IV	1	$GABA_AR$ agonist (non-BZD site)	Glycine receptor agonist + /- NMDAR antagonist
Inhalant anaesthetics	Inhalant	1	$GABA_AR$ agonist (non-BZD site)	Decrease in neurotransmitters release
Corticosteroids	IV	2	Prevention of $GABA_AR$ downregulation and Pgp upregulation	Anti-inflammatory effect, decrease in brain oedema and intracranial pressure

BBB, blood-brain barrier; BZD, benzodiazepine; GABAAR, γ-aminobutyric acid A receptor; N/A, not applicable or available; NMDAR, N-methyl-D-aspartate receptor; Pgp, P-glycoprotein
Figure legends

M. Charalambous et al. (2022)

SYSTEMICALLY PROTECT AND STABILISE THE BRAIN

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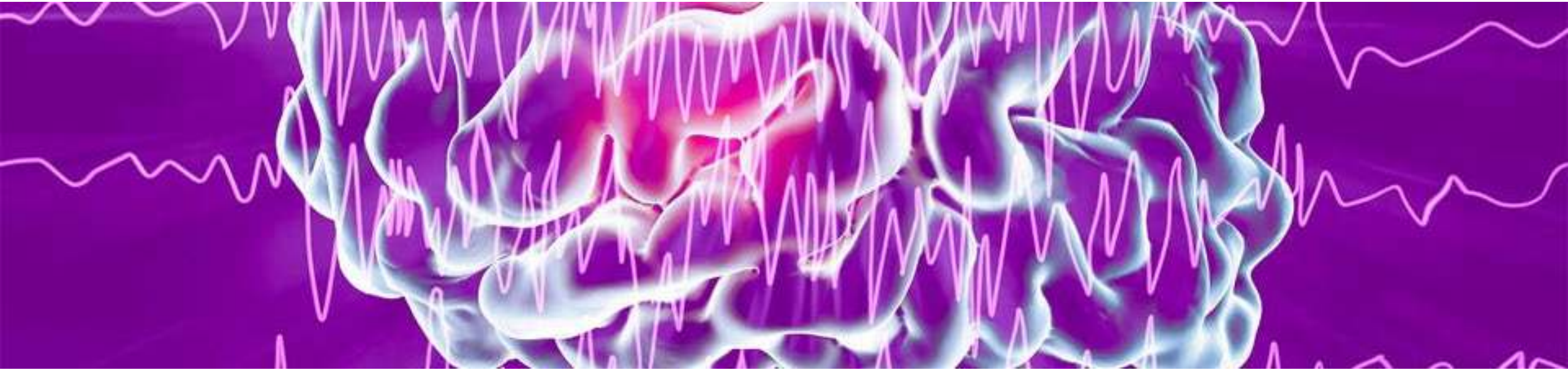
Brain damage

> 30 min: ‘decompensation phase’ ➔ systemic hypotension, ↓ cerebral blood flow, disruption BBB, cerebral oedema, neuronal cell death
> 60 min: severe and potentially fatal systemic complications incl cardiac arrhythmias, ↑ ICP and multiple organ failure



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TREAT THE UNDERLYING CAUSES

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Differential diagnoses

VITAMIN D

inflammatory (infectious), trauma, anomaly, metabolic (PSS)

idiopathic **(majority of cases)**, inflammatory (MUO)

Vascular (ischemic or haemmorhagic stroke), neoplasia, degenerative

Reactive seizures

Dogs

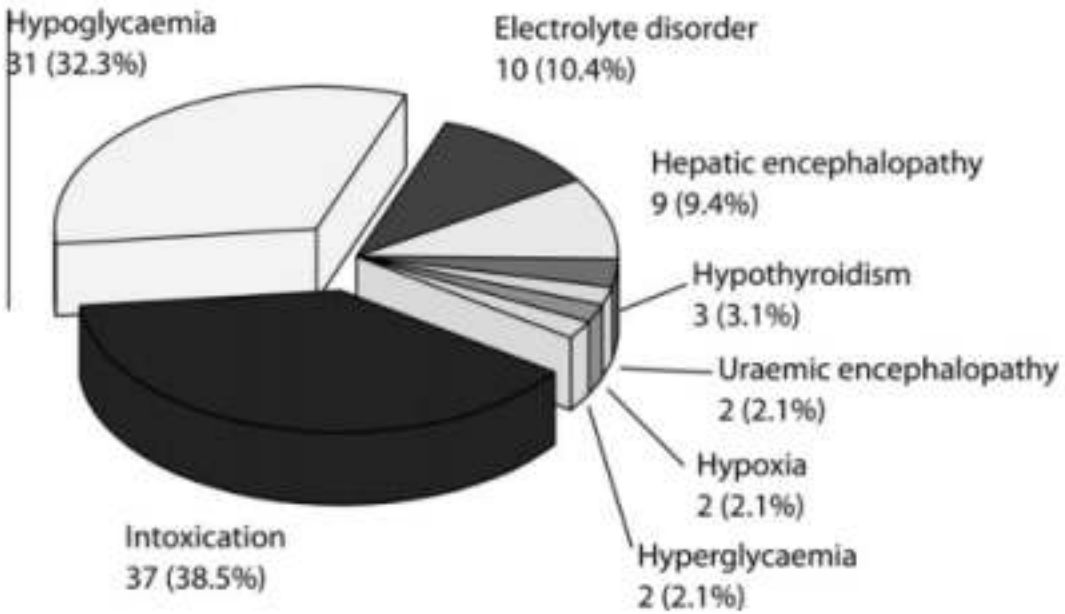


Fig. 1. Occurrence of seizures due to metabolic and toxic disturbances ($n = 96$). Proven and presumptive intoxications (37 dogs) and hypoglycaemia (31 dogs) were the most frequent extracranial causes for seizures.

Cats

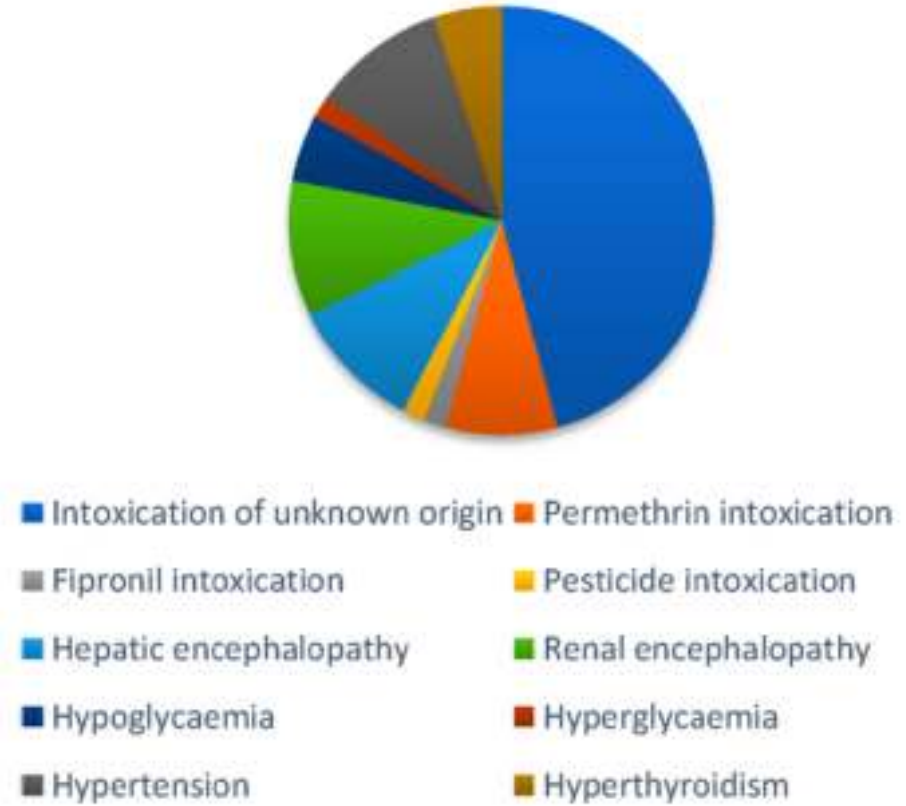
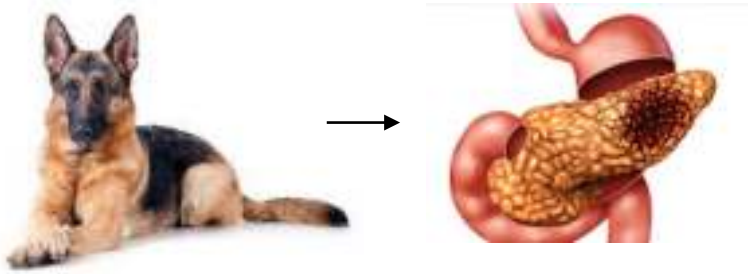
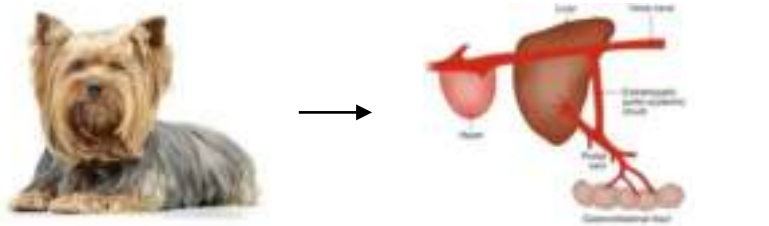
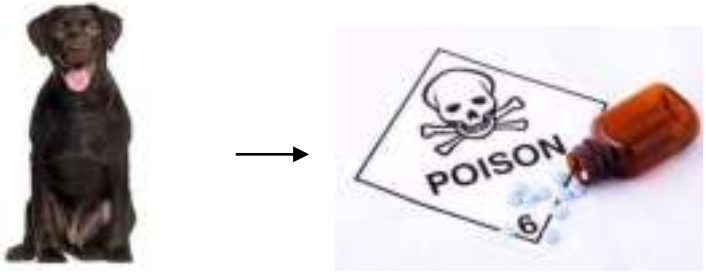


Fig. 2. Occurrence of seizures due to metabolic and toxic disturbances ($n = 64$). Proven and presumptive intoxications were the most common causes, followed by renal encephalopathy and portosystemic shunts. CKD, chronic kidney disease; PSS, portosystemic shunt.

Basic work-up







- Breed, age & clinical history
  - How long has the animal been seizing?
  - Previous hx of seizures
  - Clinical signs prior to the seizures?
  - Access to toxins? Scavenger?
  - On any medication? Any emergency intervention started at home?
- Complete clinical & neurological examination
- Blood work including CBC, serum biochemistry

(sodium, potassium, chloride, calcium, phosphate, alanine aminotransferase (ALT), alkaline phosphatase (ALP), total bilirubin, urea, creatinine, total protein, albumin, glucose, cholesterol, triglycerides, and fasting bile acids and/or ammonia)(De risio et al. 2015)

- MRI brain and CSF analysis? When to refer?

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When to perform an MRI & CSF?

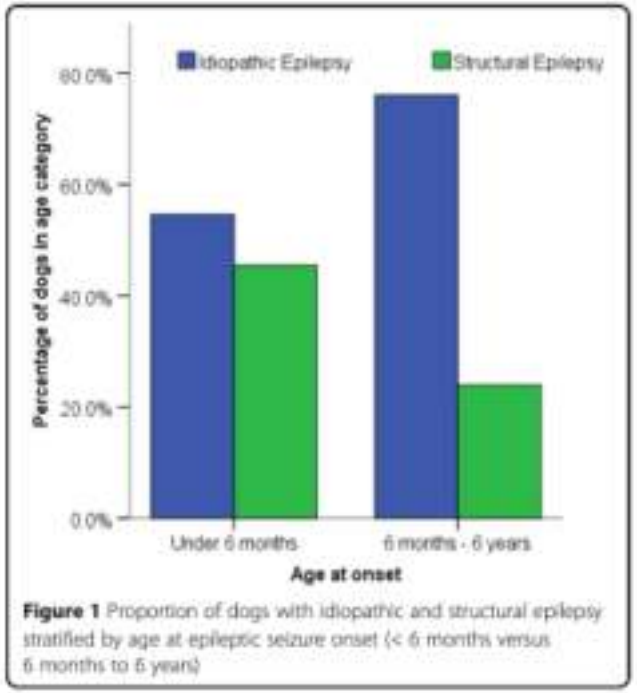

Figure 1 Proportion of dogs with idiopathic and structural epilepsy stratified by age at epileptic seizure onset (< 6 months versus 6 months to 6 years)

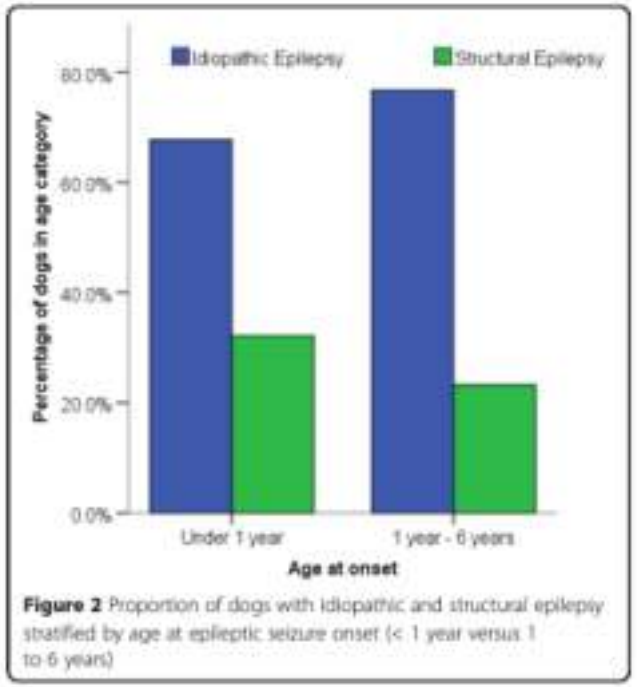

Figure 2 Proportion of dogs with idiopathic and structural epilepsy stratified by age at epileptic seizure onset (< 1 year versus 1 to 6 years)

De Risio et al. BMC Veterinary Research (2015)

After exclusion of reactive seizures in dogs with:

- Age at epileptic seizure onset < 6 months or > 6 years
- Interictal neurological abnormalities consistent with intracranial neurolocalisation
- Status epilepticus or cluster seizure
- A previous presumptive diagnosis of IE and drug-resistance with single AED titrated to the highest tolerable level

- Cats under < 3 years or > 6 years?
  - Most frequently diagnosed in adult to middle-aged cats.
  - Cats aged 3.0 to <6.0 years had 3.32 times higher odds of epilepsy diagnosis compared to cats <3.0 years of age.

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PREVENT FURTHER SEIZURES

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REFERRALS

Maintenan

Do not forget to conti

	Dog dose
Phenobarbital	2–3 mg/kg PO q 12 h
Potassium bromide (for oral use only)	20–40 mg/kg PO q 24 h (sodium bromide can be use
Levetiracetam	20–30 mg/kg PO q 8 h
Zonisamide	5 mg/kg PO q 12 h (if receiving phenobarbital increas

A retrospective study of the efficacy of zonisamide in controlling seizures in 57 cats

Dylan M. Djani[1] | Michael Liou[2] | Srikanth Aravamuthan[2] | Vivian Lau[3] | Starr Cameron[1]

[1]School of Veterinary Medicine, Department of Medical Sciences, University of Wisconsin–Madison, Madison, Wisconsin, USA

[2]School of Veterinary Medicine, Department of Statistics, University of Wisconsin–Madison, Madison, Wisconsin, USA

[3]SAGE Veterinary Centers, Redwood City, California, USA

Correspondence
Starr Cameron, School of Veterinary Medicine, University of Wisconsin–Madison, 2015 Linden Drive, Madison, WI 53706, USA.
Email: starr.cameron@wisc.edu

Abstract

Background: Evidence-based recommendations for antiepileptic drug selection in cats beyond phenobarbital are limited, and additional studies are needed for cats where seizures remain inadequately controlled by administration of phenobarbital alone or for cats that cannot safely receive phenobarbital.

Objective: To compare seizure frequency in cats before and after oral administration of zonisamide and describe adverse clinical or clinicopathologic effects in this cohort.

Animals: Fifty-seven cats with a history of seizures.

Methods: Multicenter, retrospective study. Median number of seizures per month and number of seizure days per month were compared before and after administration of zonisamide in all cats, a subgroup of cats with idiopathic epilepsy (IE), and a subgroup of cats receiving zonisamide as sole therapy. Clinical and clinicopathologic adverse effect data were also reported.

Results: A median decrease of 1 ($P = .001$, 95% confidence interval (CI) [−1.0, −0.5]) seizure per month, and 1 ($P = .003$, 95% CI [−1.5, −0.2]) seizure days per month was found across all cats after oral administration of zonisamide. The subgroup with IE showed median decreases of 1 ($P = .03$, 95% CI [−2.0, −0.5]) and 2 ($P = .01$, 95% CI [−2.5, −1.0]), respectively. The most common clinical adverse effects were sedation (17%), ataxia (11%), hyporexia (17%), and emesis (5%). One cat developed mild nonregenerative anemia, 2 cats developed mild metabolic acidosis, and 6 cats showed mild increases in ALT and ALP.

Conclusion: Zonisamide was well tolerated and efficacious in controlling seizure activity in most cats.

KEYWORDS
epilepsy, feline, antiepileptic drugs, antiseizure drugs

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Emergency seizure management

Summary:

1. **Stop seizures**
2. **Systemically stabilize and protect the brain**
3. **Treat the underlying causes**
4. **Prevent further seizures**

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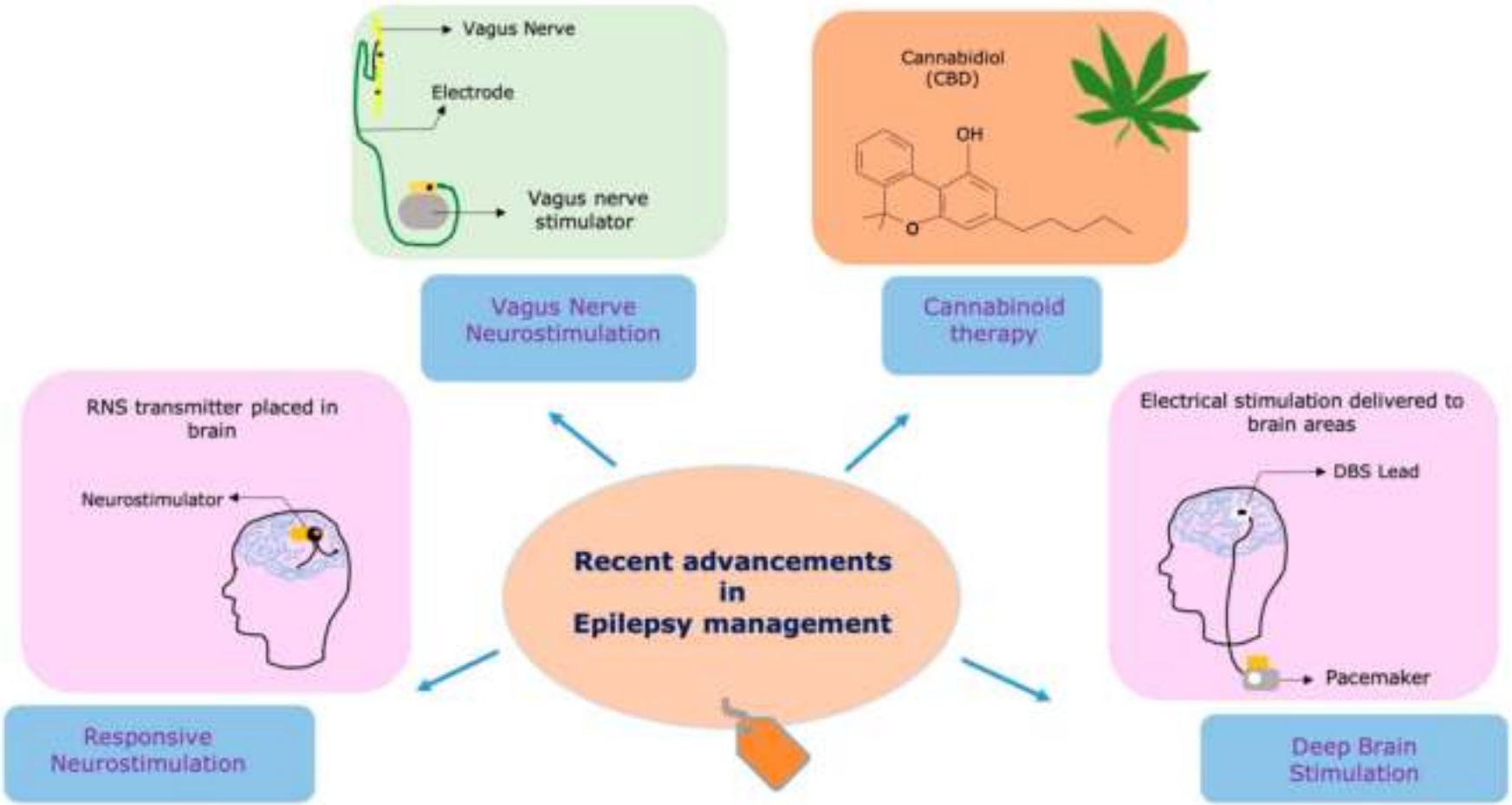
Need for alternative epilepsy management in drug resistant patient



Gosh et al. 2023

2 yo Labrador Retriever with history of single seizures controlled with 20 mg/kg levetiracetam. Normal interictally. Presented with 4 GTC cluster seizures (2-3 min) over the last 24 hrs. Presented post-ictal. Which tx?

A High dose (2 mg/kg) rectal diazepam + place IV and monitor

B Place IV + IV diazepam/midazolam and monitor

C Place IV + 40-60 mg/kg levetiracetam IV and monitor

D Place IV + 40-60 mg/kg levetiracetam IV + start loading (6-12 mg/kg) phenobarbital IV/PO

E Place IV + midazolam CRI 0.1-0.3 mg/kg/min

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D Place IV + 40-60 mg/kg levetiracetam IV + start loading (6-12 mg/kg) phenobarbital IV/PO 0%

E Place IV + midazolam CRI 0.1-0.3 mg/kg/min 0%

Same Labrador as previous however now presented in status epilepticus for the last 45 min.

A IM/IN midazolam bolus + place IV + 40-60 mg/kg levetiracetam bolus IV

B IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV +/- 40-60 mg/kg l...

C IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV + ketamine bolus...

D IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV + midazolam CRI...

E IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital + ketamine CRI 0.1-...

Same Labrador as previous however now presented in status epilepticus for the last 45 min.

A IM/IN midazolam bolus + place IV + 40-60 mg/kg levetiracetam bolus IV

0%

B IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV +/- 40-60 mg/kg levetiracetam bolus IV

0%

C IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV + ketamine bolus 3-5 mg/kg IV

0%

D IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV + midazolam CRI 0.1-0.3 mg/kg/min

0%

E IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital + ketamine CRI 0.1-0.5 mg/kg/hr

0%

Same Labrador as previous however now presented in status epilepticus for the last 45 min.

A IM/IN midazolam bolus + place IV + 40-60 mg/kg levetiracetam bolus IV

0%

B IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV +/- 40-60 mg/kg levetiracetam bolus IV

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C IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV + ketamine bolus 3-5 mg/kg IV

0%

D IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital IV + midazolam CRI 0.1-0.3 mg/kg/min

0%

E IM/IN midazolam bolus + place IV + 12 mg/kg phenobarbital + ketamine CRI 0.1-0.5 mg/kg/hr

0%

6 month old F Yorkshire Terrier presented with acute cluster seizures, develop seizure after admittence. Previous history of stunted growth, behavioral abnormalities and pu/pd. Which tx?

A High dose diazepam IR bolus and monitor, give 2-3x if necessary

B High dose midazolam IN/IM/IV and monitor, give 2-3 x if necessary

C Low dose midazolam IN/IM/IV + 60 mg/kg levetiracetam IV bolus and monitor

D Low dose midazolam IN/IM/IV + 60 mg/kg levetiracetam IV bolus + 12 mg/kg ph…

E Low dose midazolam IN/IM/IV + 60 mg/kg levetiracetam IV bolus + maintenance…

6 month old F Yorkshire Terrier presented with acute cluster seizures, develop seizure after admittence. Previous history of stunted growth, behavioral abnormalities and pu/pd. Which tx?

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0%

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0%

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0%

D Low dose midazolam IN/IM/IV + 60 mg/kg levetiracetam IV bolus + 12 mg/kg phenobarbital IV loading …

0%

E Low dose midazolam IN/IM/IV + 60 mg/kg levetiracetam IV bolus + maintenance 20 mg/kg levetiraceta…

0%

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0%

E Low dose midazolam IN/IM/IV + 60 mg/kg levetiracetam IV bolus + maintenance 20 mg/kg levetiraceta…

0%

1 yo MN Labradoodle, no previous hx, after a walk developped acute vomiting, tremors and displayed two GTCS. Acute seizure activity on presentation. Which tx?

A BDZ IR/IN 2-3 x + place IV and monitor

B BDZ IR/IN + place IV + 60 mg/kg levetiracetam bolus IV

C BDZ IR/IN + place IV + 12 mg/kg phenobarbital IV loading dose

D BDZ IR/IN + place IV + 60 mg/kg levetiracetam bolus IV + maintenance 20 mg/kg…

E BDZ IR/IN + place IV + inhalant anaesthetics

1 yo MN Labradoodle, no previous hx, after a walk developped acute vomiting, tremors and displayed two GTCS. Acute seizure activity on presentation. Which tx?

A BDZ IR/IN 2-3 x + place IV and monitor 0%

B BDZ IR/IN + place IV + 60 mg/kg levetiracetam bolus IV 0%

C BDZ IR/IN + place IV + 12 mg/kg phenobarbital IV loading dose 0%

D BDZ IR/IN + place IV + 60 mg/kg levetiracetam bolus IV + maintenance 20 mg/kg levetiracetam TID 0%

E BDZ IR/IN + place IV + inhalant anaesthetics 0%

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C BDZ IR/IN + place IV + 12 mg/kg phenobarbital IV loading dose 0%

D BDZ IR/IN + place IV + 60 mg/kg levetiracetam bolus IV + maintenance 20 mg/kg levetiracetam TID 0%

E BDZ IR/IN + place IV + inhalant anaesthetics 0%

5 yo FN Greyhound, previously diagnosed with IE. On top end poly therapy incl phenobarbital, bromide, zonisamide, lEV and topiramate but despite cluster seizures every 4-6 weeks. Presented SE. Which tx?

A IN midazolam + Place IV + BDZ IV bolus + 2-3 mg/kg phenobarbital bolus IV and …

B IN midazolam + place IV + BDZ IV bolus + 3-5 mg/kg IV ketamine bolus and moni…

C IN midazolam + place IV + BDZ IV bolus + midazolam CRI 0.1-0.3 mg/kg/min

D IN midazolam + place IV + BDZ IV bolus + ketamine CRI 0.1-0.5 mg/kg/hr

E IN midazolam + place IV + BDZ IV bolus + GA

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D IN midazolam + place IV + BDZ IV bolus + ketamine CRI 0.1-0.5 mg/kg/hr
0%

E IN midazolam + place IV + BDZ IV bolus + GA
0%


WE'VE GOT
EXCITING
NEWS!!

Seizure Clinic

NEW SERVICE

COMING SOON!

What is it?

- Specialised ECVN diplomate lead centre which aims:
  - To classify epileptic seizures OR other neurological episodes
  - To help owners and their pets give a more accurate view of what they can expect by providing a holistic approach to seizure management.

How can we help?

- Ongoing seizure activity despite primary medication
- Alternative treatment option in refractory cases
- Utilization of an online secured veterinary seizure diary with remote diagnosis, management and decision-making (v-Create software is for research only at this stage)
- Help with seizure preparedness including the development of a seizure action plan and how to keep your pet safe

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THANK YOU

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