Greyhound Neuropathy - what lessons to learn?

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Greyhound Hereditary Neuropathy

(also: Hereditary Polyneuropathy)

- Onset: 3 – 9 months of age
- Generalized muscle weakness
- Exercise intolerance
- „bunny-hopping“ gait
- Absence of reflexes
- Laryngeal affection: changes in voice, regurgitation

- Final stage: severe ataxia, muscle atrophy, inability to stand
- **No pain!** general condition not affected!

Greyhound Hereditary Neuropathy

cause: missense mutation in the *NDRG1*-gene

- Undersupply of the peripheric nerve system, leading to nerve degeneration
- Due to the lack of nervous stimulation the muscles degrade gradually
- recessive inheritance
- Resembles human Charcot-Marie-Tooth-Disease type 4D

- DNA test available since 2009
- Percentage of carriers was very high in the population!

What to know about Neuropathy?

- Test your dogs (if they are not free by parentage)
- Never breed two carriers!

	N	**n**
N	NN	Nn
N	NN	Nn

- That‘s it!

Mutations (I)

- **Natural process!**
- Based on faults in DNA duplication
- Somatic cell („body cells“): no impact on the population
- Germline (reproductive cells, sperm/oocytes): passing on to next generation
- Loss of function: recessive inheritance
- Gain of function: dominant inheritance (rare)
- **Mutations aren‘t mandatory negative – they are the motor of evolution!**

Mutations (II)

- Every living creature carries a load of several recessive mutations – most of them unknown
- One intact allele is usually sufficient and can maintain function
- Recessive mutations only become visible if an individual has two defective alleles, inherited from each parent and descending from a common ancestor

Homozygousity (I)

Definition: both alleles on a gene locus are identical

Natural situation:

- Homozygousity is highly undesirable
- Variation in alleles is essential for the adaptability of an organism (or a population) on environmental conditions
- Strong mechanisms to avoid inbreeding
  → homozygousity for mutations is a very unlikely event in wild populations

Homozygousity (II)

Artificial selection:

- Targeted inbreeding is a widely used selection tool to archieve homozygousity for desired traits
- The more homozygous an animal, the more reliably it will inherit its characteristic traits to its offspring
- Inbreeding increases the probability to produce offspring with certain desired traits

Negative aspects of homozygousity

- Also undesired traits will be homozygous → **recessive diseases appear**

- A high genetic variability on DLA alleles is crucial for a functional immune system
  (homozygousity on these gene loci is correlated to a lot of autoimmune diseases like SLO, AIHA, autoimmune meningitis, autoimmune nephritis, hypothyroidism…)

Matador sires

- Definition: a matador sire is a sire who is overrepresented in all matings of his generation
- Cannot be determined by absolute numbers – in a popular breed more than 10 matings can be at an average, whilst in a small breed even 5 litters might be far too many

The charm of matador sires

- Proven sires offer a higher predictability for the future puppies‘ qualities
- Puppies of champion sires might be easier to sell

- „Safety culture“ in breeding is understandable in many ways, but it will ruin every breeds gene pool!

The harm of matador sires (I)

- The smaller the breed population, the higher the risk!
- Every matador sire excludes a lot of other males of his generation from contributing to the gene pool – the alleles of these males are lost
- The frequent use of matador sires accelerates the inbreeding levels within the population enormously
- In worst case, very few single sires are introduced in nearly every bloodline worldwide, to follow an actually fashionable type

The harm of matador sires (II)

Consequences:

- Loss of genetic diversity
- Increasing homozygousity
- Impossibility to avoid linebreeding on these sires (because they appear in nearly every pedigree)

Actual matadors

- Windrock Fernando
  11 litters (2003 – 2016) →13 litters by his F1 offspring
- Boughton Benvoluto
  6 litters (2003 – 2008) → 25 litters by his F1 offspring
- Epic Brave at Sobers
  6 litters (2003 – 2009) → 33 litters by his F1 offspring
- Showline Sporting Trophy at Sobers
  11 litters (2009 - 2013) → 33 litters by his F1 offspring

Presence of historic sires in the pedigrees of today

Treetops Hawk (1951)

12 generations pedigree:

- Windrock Fernando (1999)
  → 507 x (25,7%)
- Boughton Benvoluto (2000)
  → 449 x (29,0%)
- Epic Brave at Sobers (2001)
  → 470 x (25,2%)
- Showline Sporting Trophy at Sobers (2009)
  → 493 x (17,6%)

What caused Neuropathy?

The occurrence of Neuropathy was neither bad luck, nor the fault of a certain dog (or certain breeder) –
it was the direct consequence of our breeding strategies!

What caused neuropathy?

- The mutation happened accidentally and was passed from generation to generation without being detected
- Excessive breeding from a very restricted number of males helped to spread the defect widely within the population
- More and more inbreeding on these great dogs of the past increased the likelihood that descendants inherited the mutated allele from both parents
  → first neuropathy cases occurred
- **Misguided breeding strategies didn‘t cause the mutation, but they lead to an undetected spreading all over the population**

What we should learn:

- We cannot prevent the occurrence of new mutations
- But we should take care that unknown mutations cannot uncontrolledly spread over the population again
- Misleaded breeding strategies of the past (over-use of matador sires, excessive inbreeding and impoverishment of the gene pool) cannot be undone, **but we should not repeat these faults again and again and again!**

What we have learnt…

- **NOTHING!**
- Matador breeding continues
- Breeding programmes all over the world are more and more based on the same dogs
- Unfashionable bloodlines disappear
- Impoverishment of the gene pool is rather accelerated
- Neuropathy was a „warning shot“, which went unheard
- **If we don‘t change our breeding strategies, it‘s not the question IF we will face a new recessive disease - but only which one and when…**

What to do…

- Testing for known recessive traits
- Testing for genetic variability (www.mydogdna.com, www.feragen.at,…)

- **Conservation and enlargement of the gene pool!**

What to do…

- **Strict limitation of stud services !!!!!!!!!!**
  No Show Greyhound male should produce more than 4 litters worldwide!
- Conservation of old, rare and unfashionable bloodlines
- Crossbreeding to working lines
- Change of breeding strategies to population genetic aspects:
  no more „only the best to the best“, but
  „breed from as many different individuals as possible“

Breeding from carriers or not?

- Excluding all neuropathy carriers from breeding would solve the neuropathy problem within one generation
- But it would reduce the gene pool remarkably, reducing genetic diversity and increasing the risk to accumulate new mutations

- **Despite its clinical severity, Neuropathy is the only disease in the breed we can control to 100%!**

  →better take all efforts to fight against the cause (=the lack of genetic variability) instead of the symptom (the disease)!

What could happen…

Rumford S-litter:
mother: tested free
father: unknown

Genetic testing Greyhound Neuropathy

You have contributed samples to our research project “Hereditary Greyhound Neuropathy of Show Greyhounds”. We applied a DNA test that allows the unequivocal diagnosis of carriers for this monogenetic autosomal recessive inherited disease.

Lab ID	Dog	Kennel	ID	Sex	Date of birth	Neuropathy genotype
GY319	Sibelius	Rumford		m	06.06.2010	carrier
GY320	Salvator	Rumford		m	06.06.2010	carrier
GY321	Somersault	Rumford			06.06.2010	carrier
GY322	Souvenir	Rumford			06.06.2010	carrier
GY323	Souvereign	Rumford		m	06.06.2010	carrier
GY324	Silvretta	Rumford		f	06.06.2010	carrier

Kind regards

Prof. Dr. Cord Drögemüller

What also could happen…

Rumford U-litter:
mother: carrier
father: free

Genetic testing Greyhound Neuropathy

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Lab ID	Dog	Kennel	ID	Chip ID	Sex	DOB	Neuropathy genotype
GY417	Ustinov	Rumford		276098106210294	m		free
GY418	Ultravox	Rumford		276098106199817	w		free
GY419	Ultra Violet	Rumford		276098106200497	w		free
GY420	Ultramarin	Rumford		276098106066600	w		free
GY421	Unicum	Rumford		276098106197682	w		free
GY422	Unicorn	Rumford		276098106196334	w		free
GY423	Uppsala	Rumford		276098106198402	w		free
GY424	Umberta	Rumford		276098106209522	w		free

Kind regards

Thank you for your attention!

For further questions:

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