HNF1B research update

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HNF1B support day, September 2018

UNIVERSITY OF EXETER | MEDICAL SCHOOL

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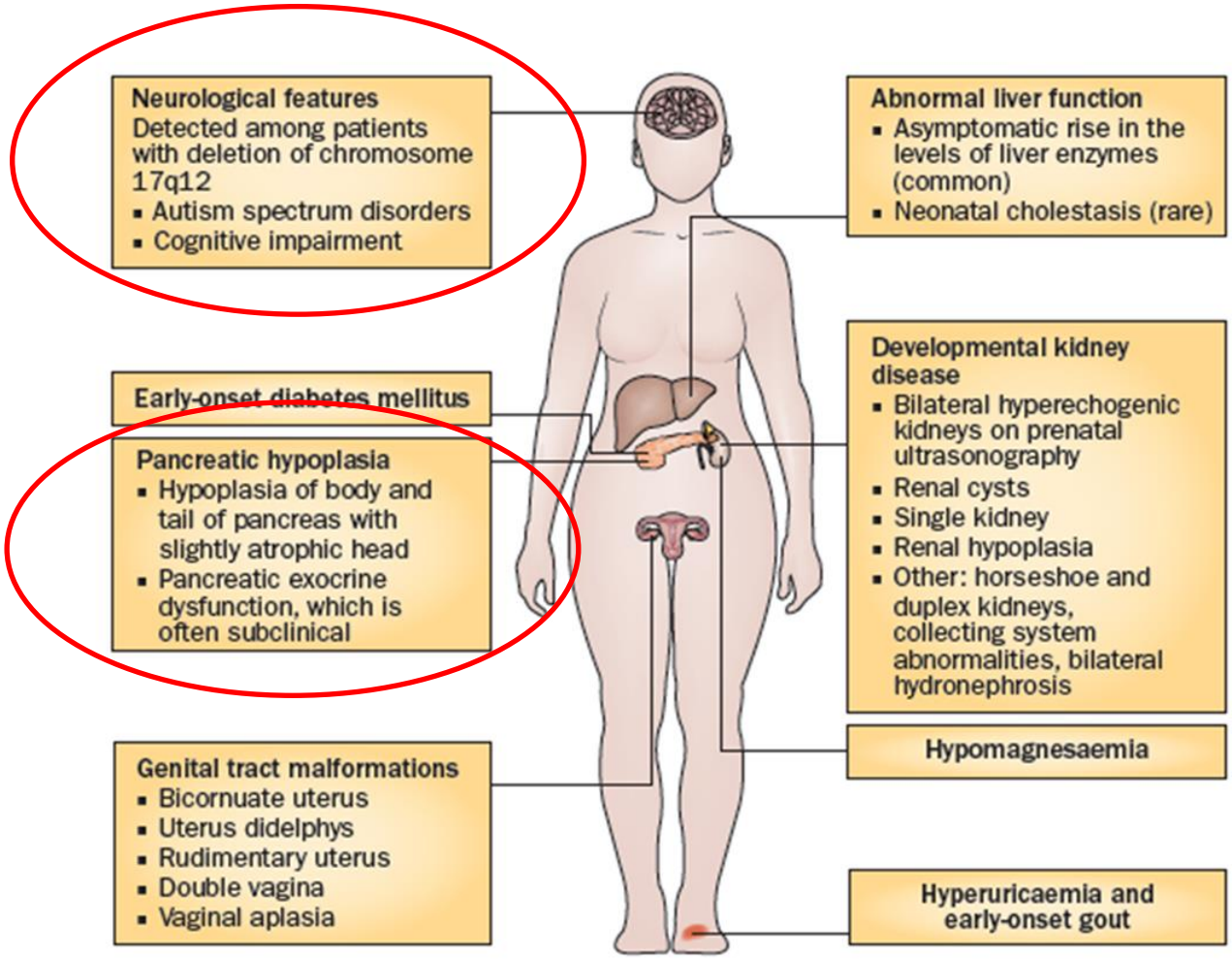
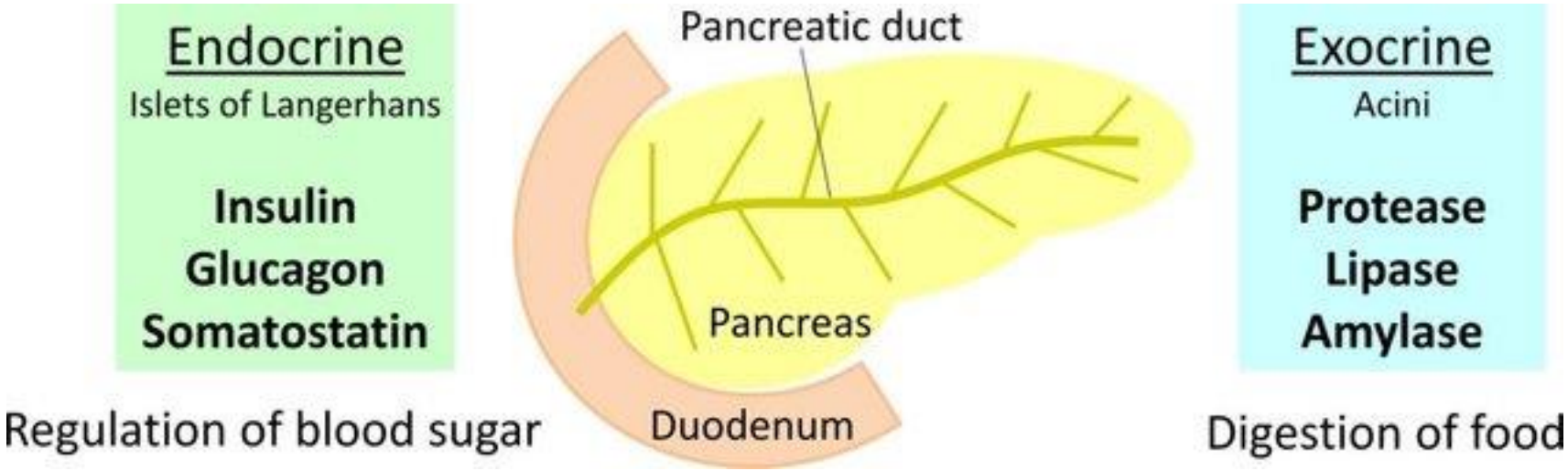
Overview


Neurological features
Detected among patients with deletion of chromosome 17q12
▪ Autism spectrum disorders
▪ Cognitive impairment
Early-onset diabetes mellitus
Pancreatic hypoplasia
▪ Hypoplasia of body and tail of pancreas with slightly atrophic head
▪ Pancreatic exocrine dysfunction, which is often subclinical
Genital tract malformations
▪ Bicornuate uterus
▪ Uterus didelphys
▪ Rudimentary uterus
▪ Double vagina
▪ Vaginal aplasia
Abnormal liver function
▪ Asymptomatic rise in the levels of liver enzymes (common)
▪ Neonatal cholestasis (rare)
Developmental kidney disease
▪ Bilateral hyperechogenic kidneys on prenatal ultrasonography
▪ Renal cysts
▪ Single kidney
▪ Renal hypoplasia
▪ Other: horseshoe and duplex kidneys, collecting system abnormalities, bilateral hydronephrosis
Hypomagnesaemia
Hyperuricaemia and early-onset gout

HNF1B and the pancreas



Aim of our study

- To measure faecal elastase in people with HNF1B-associated disease
  - Regardless of diabetes status

- To assess symptoms

What did we find?

- Faecal elastase was low in 18/29 (62%)
- 8/29 (28%) had a measurement suggestive of exocrine pancreatic insufficiency
- 3 suffered with symptoms and improved with treatment

What did we conclude?

- Faecal elastase deficiency is a common feature of the condition
- May be more symptomatic than previously thought
- Measure faecal elastase if people have long-standing abdominal pain, loose stools or unintended weight loss

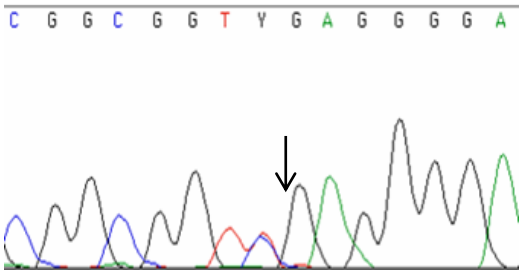
HNF1B and the brain

- ~15,000 people with autism, delayed development or learning difficulties

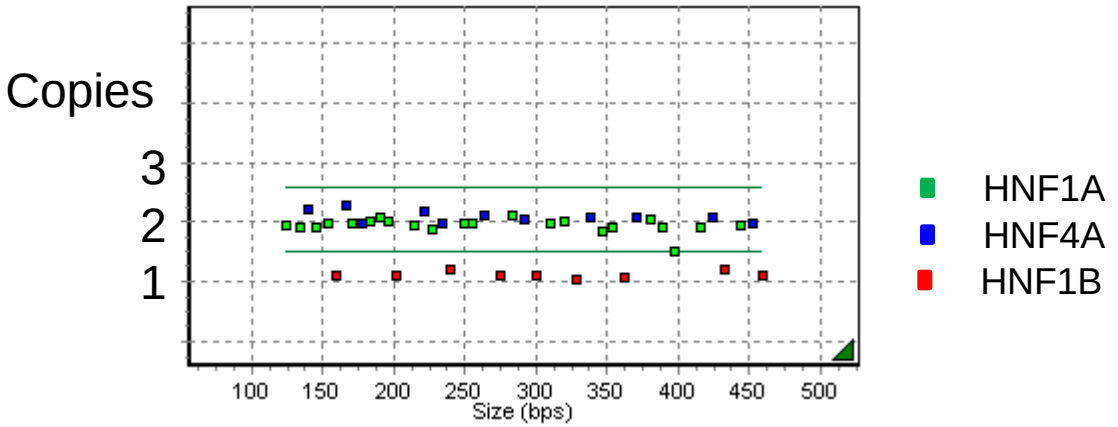
- Large deletion (including *HNF1B*) found in 18 individuals

Genetics

- Genetic “spelling mistake” = mutation



- Gene is missing = deletion



Aim of our study

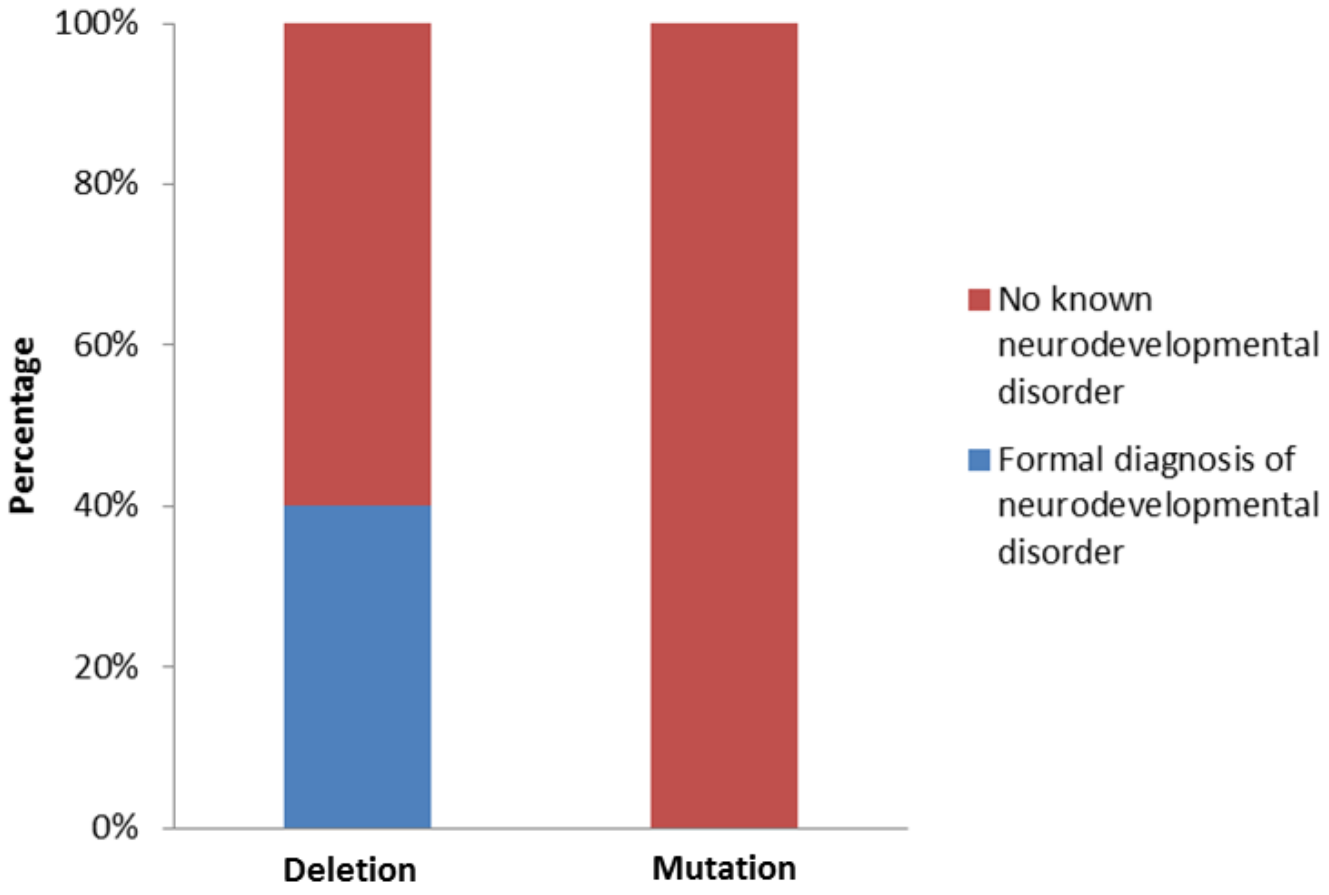
- To assess neuropsychological disorders in people with *HNF1B* mutations or deletions under follow-up with renal or diabetes services

What did we do?

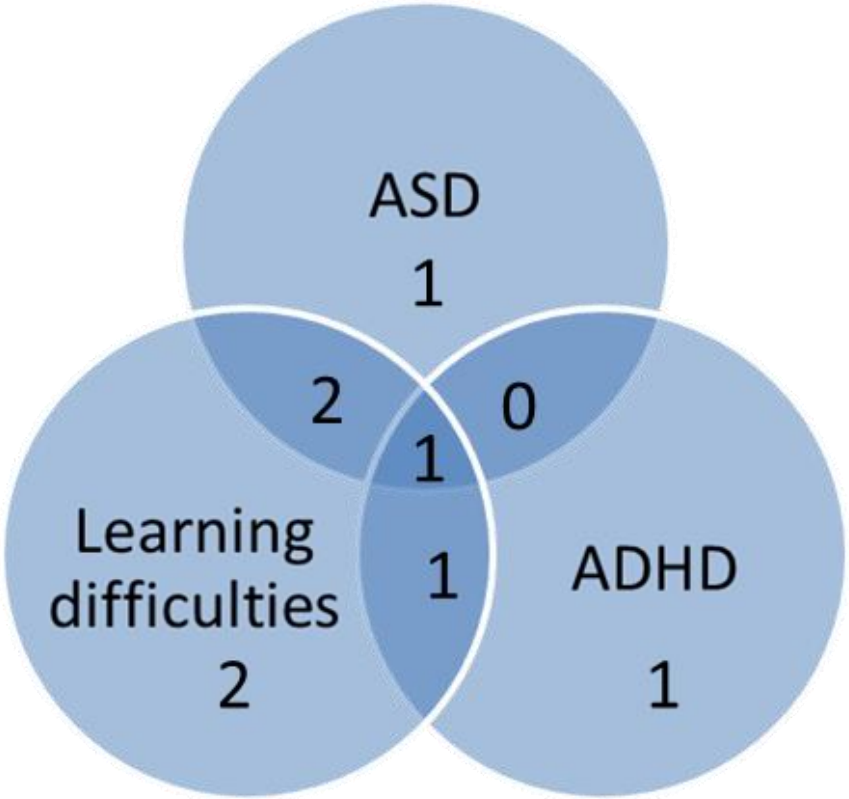
- 38 children and adults from 4 UK sites visited
  - 20 with deletion
  - 18 with mutation

Assessments:
Brief behavioural screening (SDQ)
Clinical diagnosis (review of medical notes)
Autistic traits (AQ)
IQ (KBIT2)

8/20 individuals with a deletion had a clinical diagnosis



Overlap of diagnoses



What did we conclude?

- Neurodevelopmental features only seen in people with a deletion
- *HNF1B* gene unlikely to be the cause
- Important for renal/diabetes teams to be aware of this increased risk

Future research

- Thank you to everyone that took part in my study

- **www.rarerenal.org** for future research opportunities

RareRenal
Information on rare kidney diseases