Bardet-Biedl syndrome

Bardet-Biedl syndrome (BBS) is a rare syndromic ciliopathy, resulting from genetic variants within the BBS family of genes.

This condition presents with a variety of clinical features, some of which are present from birth, while others evolve over time. These manifestations are attributed to impairments in the melanocortin-4 receptor (MC4R) pathway.[1]

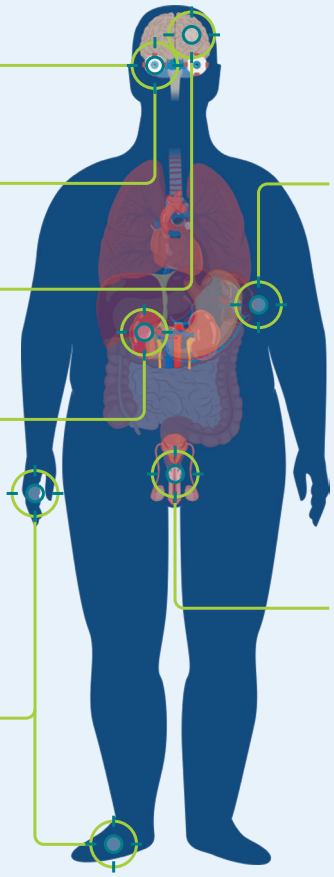
Solomon, living with BBS

Prevelance:

~ 1/125 000[2]

Prevalence estimates may increase as more healthcare providers become aware of the clinical features of BBS and genetically test to aid in clinical diagnosis[3]

Key clinical features of BBS[1,4,15]



Hyperphagia
(pathological, insatiable hunger)

93%
Rod-cone dystrophy

61%
Learning difficulties

53%
Renal anomalies

63% to 81%
Polydactyly

72% to 92%
Obesity

59% to 98%
Genital anomalies

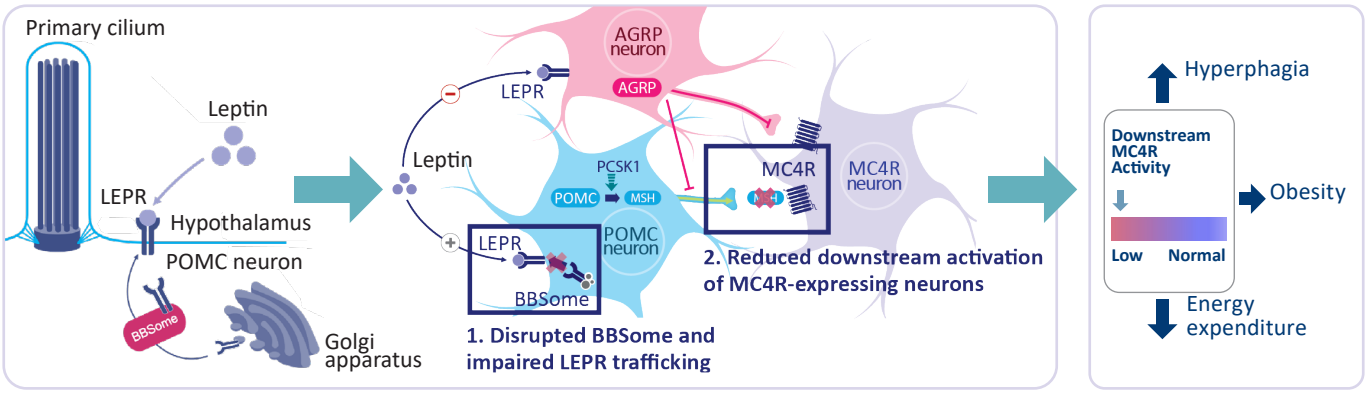
Percentages represent frequency of feature appearance among individuals diagnosed with BBS. The clinical features vary greatly in presence and severity.[1]

More than 20 genes associated with BBS are involved in the MC4R pathway.[1,5]

Eight BBS proteins form a stable complex, the BBSome, which contributes to cilia development and function by trafficking intracellular proteins to ciliary membranes and potentially to other membrane compartments.[5]

Variants in BBS genes disrupt the BBSome, resulting in ciliary defects and impaired signalling of receptors that regulate body weight, such as LEPR.[5-9]

This disrupts LEPR signalling, reducing activation of MC4R-expressing neurons, and can lead to hyperphagia and early-onset, severe obesity.[5-9]



Abbreviations: AGRP, agouti-related protein; LEPR, leptin receptor; MC4R, melanocortin-4 receptor; MSH, melanocyte-stimulating hormone; NPY, neuropeptide Y; PCSK1, proprotein convertase subtilisin/kexin type 1; POMC, proopiomelanocortin.

How is BBS diagnosed?

Diagnosis of BBS is based on clinical findings; diagnosis confirmed by genetic testing.[4]

Primary features[1]

- Genital anomalies
- Learning difficulties
- Obesity
- Polydactyly
- Renal anomalies
- Rod-cone dystrophy

Secondary features[10]

- Anosmia or hyposmia
- Ataxia or poor coordination
- Brachydactyly or syndactyly
- Dental anomalies
- Developmental delay
- Diabetes mellitus
- Hepatic fibrosis
- Left ventricular hypertrophy or congenital heart disease
- Mild spasticity (especially lower limbs)
- Polyuria or polydipsia
- Speech delay or speech impairments
- Strabismus, cataracts, astigmatism

Despite the urgent need for early diagnosis to reduce the impact of future comorbidities, significant delays exist in BBS diagnosis due to lack of awareness and the slow emergence of certain clinical features.[3,11]

Genetic confirmation[12-14]

A genetic diagnosis of BBS can make a significant difference to an individual's life by:

Improving access to appropriate care

Reducing the social stigma of obesity and providing coping strategies for managing stigmatisation

Empowering the individual and carers to understand the root cause of their condition and make informed decisions about their care

Allowing for preventive or prophylactic screening of associated conditions

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