SLC19A1—Double Homozygous (rs3788200 and rs1051266) Report

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Pathophysiology and Clinical Significance

The SLC19A1 gene (also known as the Reduced Folate Carrier 1, or RFC1) is responsible for the active transport of active folates from the blood into the interior of the cell. The rs1051266 (80G>A) and rs3788200 variants impair the structural integrity and binding affinity of this transport protein. **A homozygous state severely reduces the rate of intracellular folate absorption.**

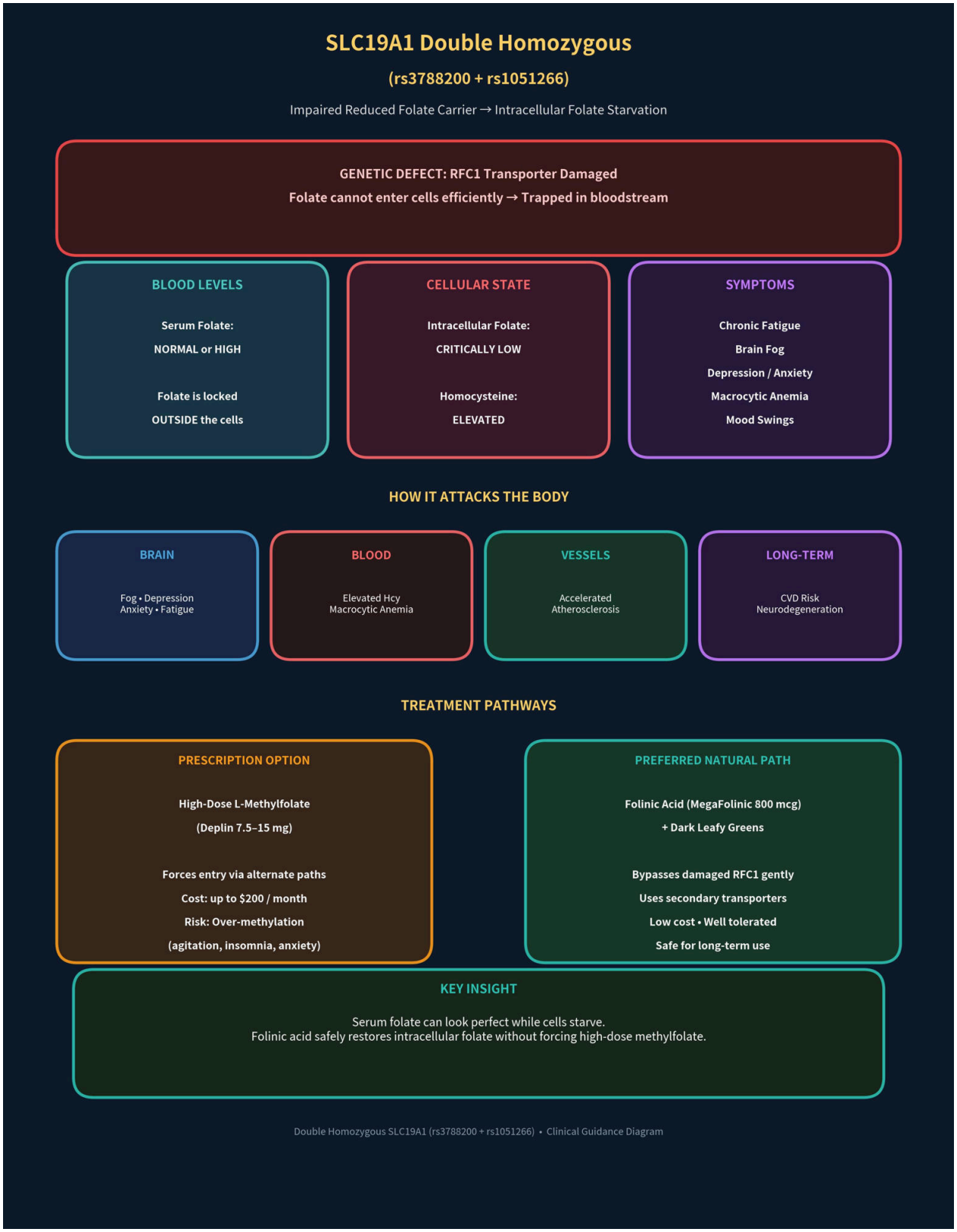
Signs, Symptoms, and Associated Diseases

Despite normal or even high serum folate levels (as the folate is trapped outside the cells), the patient suffers from intracellular folate deficiency. This leads to elevated homocysteine levels. **Symptoms include chronic fatigue, brain fog, mood disturbances (depression/anxiety), and macrocytic anemia. Long-term risks include accelerated atherosclerosis, cardiovascular disease, and neurodegenerative disorders.**

Treatment, Biologics, and Natural Options

- **Referral/Allopathic:** Cardiology referral for a baseline cardiovascular workup due to elevated homocysteine risks.
- **Biologics/Medical:** While prescription high-dose L-methylfolate (e.g., Deplin 7.5 mg or 15 mg) is often prescribed to force folate into the cells via alternative transport pathways, it can cost up to $200 per month and frequently causes severe over-methylation side effects, including agitation, insomnia, anxiety, and muscle aches if titrated too quickly.
- **Natural/Adjuvant (Preferred):** Stand-alone natural therapy requires bypassing synthetic folic acid entirely (which competes for the already impaired receptors). To achieve cellular saturation without the side effects or high costs of methylfolate, the patient should utilize over-the-counter **Folinic Acid**. A highly recommended, cost-effective option is **Source Naturals MegaFolinic (800mcg)**. (Or even Leucovorin but at 15mg it is usually too much folinic acid for a small child (or even a large child or adult) so lesser options usually re safer and work better. **The patient can safely take multiple doses of MegaFolinic daily as directed to saturate the blood plasma, forcing the active folinic acid into the cells through secondary transport pathways**. This should be implemented alongside a diet heavy in organic, dark leafy greens (spinach, kale) which provide natural folate co-factors.

Diagram


SLC19A1 Double Homozygous
(rs3788200 + rs1051266)
Impaired Reduced Folate Carrier → Intracellular Folate Starvation
GENETIC DEFECT: RFC1 Transporter Damaged
Folate cannot enter cells efficiently → Trapped in bloodstream
BLOOD LEVELS
Serum Folate:
NORMAL or HIGH
Folate is locked
OUTSIDE the cells
CELLULAR STATE
Intracellular Folate:
CRITICALLY LOW
Homocysteine:
ELEVATED
SYMPTOMS
Chronic Fatigue
Brain Fog
Depression / Anxiety
Macrocytic Anemia
Mood Swings
HOW IT ATTACKS THE BODY
BRAIN
Fog • Depression
Anxiety • Fatigue
BLOOD
Elevated Hcy
Macrocytic Anemia
VESSELS
Accelerated
Atherosclerosis
LONG-TERM
CVD Risk
Neurodegeneration
TREATMENT PATHWAYS
PRESCRIPTION OPTION
High-Dose L-Methylfolate
(Deplin 7.5–15 mg)
Forces entry via alternate paths
Cost: up to $200 / month
Risk: Over-methylation
(agitation, insomnia, anxiety)
PREFERRED NATURAL PATH
Folinic Acid (MegaFolinic 800 mcg)
+ Dark Leafy Greens
Bypasses damaged RFC1 gently
Uses secondary transporters
Low cost • Well tolerated
Safe for long-term use
KEY INSIGHT
Serum folate can look perfect while cells starve.
Folinic acid safely restores intracellular folate without forcing high-dose methylfolate.
Double Homozygous SLC19A1 (rs3788200 + rs1051266) • Clinical Guidance Diagram

References

1. Purser D. *SLC19A1—Double Homozygous (rs3788200 and rs1051266)*. Clinical Reference Manuscript. 2026.
2. Chango A, Emery-Fillon N, de Courcy GP, et al. A polymorphism (80G->A) in the reduced folate carrier gene and its associations with folate status and homocysteinemia. *Mol Genet Metab*. 2000;70(4):310-315.
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4. Gellekink H, den Heijer M, Heil SG, Blom HJ. The A80G polymorphism in the reduced folate carrier gene and its associations with folate status. *Eur J Hum Genet*. 2004;12(1):8-14.