

# Abstract

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## Experimental study of fatigue provoked by biotin deficiency in mice.

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**OBJECTIVE:** We investigated the relationships among behavioral parameters, forced-swimming test parameters, and plasma and organ biotin concentrations in biotin-deficient mice.

**METHODS:** Male ddY mice were divided into four groups: early biotin deficiency group (ED group; biotin-free diet for three weeks), progressive biotin-deficiency group (PD group; biotin-free diet for seven weeks), and two age-matched control groups.

**RESULTS:** The dermatological symptoms of frank biotin deficiency were observed in most mice in the PD groups (72.3%) but in only 27% of ED group mice. The liver biotin level was greatly decreased in ED and PD groups, and the plasma biotin level was also significantly decreased in the PD group, but the biotin levels were quite stable in muscle and brain. There were significant decreases in swimming time in ED and PD groups and in struggling behavior in the PD group, suggesting that biotin-deficient mice become depressed and/or fatigued without biotin deficiency being apparent in brain and muscle. One single-injection biotin administration led to a prompt recovery in swimming time. Biochemical data revealed a decrease in liver glucokinase activity and an increase in ketone bodies in both liver and plasma in biotin-deficient mice. In addition, simultaneous biotin deficiency and forced walking synergistically provoked significant increases in total ketone bodies in both plasma and liver.

**CONCLUSION:** These results suggest that depression and/or fatigue are induced in mice by biotin deficiency.

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