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## SIGNIFICANT CHANGE IN BIOMETAL DISTRIBUTION IN BRAINS OF ALZHEIMER'S DISEASE (TGSWDI) MICE

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Abstract 1753

## SIGNIFICANT CHANGE IN BIOMETAL DISTRIBUTION IN BRAINS OF ALZHEIMER'S DISEASE (TGSWDI) MICE

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### Aims

Neuronal demise in Alzheimer's disease (AD) occurs years later than the accumulation of amyloid-beta plaques and neurofibrillary tangles, but the mechanisms underlying neuronal death remain unresolved. Increasing accumulation of biometals (e.g. iron, zinc, copper, and manganese) increases oxidative stress, and their accumulation is worsened by cerebral amyloid angiopathy (CAA) which causes microbleeds with the deposition of iron. We hypothesized that AD studied in a mouse model with CAA (TgSwDI) causes pathological deposition of biometals with resulting dyshomeostasis.

### Methods

Brains of TgSwDI mice, which deposit amyloid plaques and CAA from 3-6 months, and C57Bl/6j control mice, aged 7, 12, and 24 months (n=6-12 per age) were dissected into the cortex, hippocampus, thalamus, and cerebellum. The content of iron, zinc, copper, and manganese was measured using ICP-OES. The hippocampus and thalamus were also examined for gene expression of selected iron-handling proteins using TaqMan qPCR, and the hippocampi from 24 months mice were examined for their protein content using LC-MS/MS.

### Results

The content of biometals varied among different brain regions, ages, and genotype. Combining the biometal content of each brain region revealed that TgSwDI mice had significantly different biometal profiles compared to controls. The gene expression of ferritin light and heavy chains significantly decreased in TgSwDI mice at all ages, while the expression of the transferrin receptor was unaffected. The LC-MS/MS analysis showed that TgSwDI mice had severe gliosis without significant changes in iron-handling proteins.

### Conclusions

Our findings show that the content of biometals is significantly changed in different brain regions of TgSwDI mice with a simultaneous reduction in ferritin expression. The suppressed expression of ferritin isoforms combined with the change in biometal content likely contribute to oxidative stress and neuronal damage in TgSwDI mice.

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