Introduction
COASY protein associated neurodegeneration (CoPAN), is a rare, progressive autosomal recessive neuroferritinopathy due to pathogenic mutations in the COASY gene, coding for Coenzyme A Synthase.\cite{1} We present three patients with CoPAN identified on newborn screening with dried bloodspot (DBS) acylcarnitine profiles consistent with carnitine palmitoyltransferase 1a (CPT1a) deficiency, ie an elevated ratio of free carnitine (C0) to the sum of palmitoylcarnitine (C16) and octanoylcarnitine (C18): (C0/C16+C18). 

Case 1
Patient 1 was born at 37 weeks gestation, with drug resistant epilepsy presenting on day 1 of life. Examination demonstrated microcephaly (head circumference 28cm, < 1 centile) and globally brisk deep tendon reflexes. MRI brain identified cerebellar hypoplasia, immature cortical sulcation and parenchymal atrophy (see image 1). DBS acylcarnitine profiles demonstrated a pattern consistent with CPT1a deficiency, however the plasma acylcarnitine profile was normal (See table 1). The patient died on day 42 of life from necrotizing enterocolitis.

Table 1 – Dried blood spot acylcarnitine results of patient 1

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>C0 (8-70 µmol/L)</th>
<th>C18 (0.49-1.55 µmol/L)</th>
<th>C16 (0.7-7.5 µmol/L)</th>
<th>C10/C16+C18 (8-70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 4</td>
<td>96 ↑</td>
<td>0.21 ↓</td>
<td>0.56 ↓</td>
<td>125 ↑</td>
</tr>
<tr>
<td>Day 6</td>
<td>78 ↑</td>
<td>0.16 ↓</td>
<td>0.62 ↓</td>
<td>96 ↑</td>
</tr>
</tbody>
</table>

Image 1 – Patient 1 MRI brain day

T1 sagittal image (left) demonstrating cerebellar atrophy (yellow arrow). T2 axial image (right) demonstrating immature cortical sulcation and parenchymal volume loss.

Case 2
Patient 2 (sibling of patient 1) was born at 36 weeks gestation, with drug resistant epilepsy presenting on day 1 of life. Examination demonstrated microcephaly (head circumference 31.5 cm, < 1 centile) and global deep tendon hyporeflexia. MRI brain identified cerebellar hypoplasia, immature cortical sulcation and parenchymal atrophy (see image 2). DBS acylcarnitine profiles demonstrated a pattern consistent with CPT1a deficiency, however the plasma acylcarnitine profile was normal (See table 2). The patient died aged 18 months from intestinal failure.

Table 2 – Dried blood spot acylcarnitine results of patient 2

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>C0 (8-70 µmol/L)</th>
<th>C18 (0.49-1.55 µmol/L)</th>
<th>C16 (0.7-7.5 µmol/L)</th>
<th>C10/C16+C18 (8-70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3</td>
<td>100 ↑</td>
<td>0.16 ↓</td>
<td>0.5 ↓</td>
<td>151 ↑</td>
</tr>
<tr>
<td>Day 9</td>
<td>108 ↑</td>
<td>0.14 ↓</td>
<td>0.43 ↓</td>
<td>166 ↑</td>
</tr>
</tbody>
</table>

Pathogenic COASY mutations
Patient 1/2: c. [1403_1404dup]; [215A>G]
Patient 3: c. [1403_1404dup]; [1495C>T]

Image 2 – Patient 2 MRI brain day 2 of life

MRI brain performed at day 2 of life. T1 sagittal image (left) demonstrating cerebellar atrophy (yellow arrow). T2 axial image (right) demonstrating immature cortical sulcation.

Case 3
Patient 3 was born at 38 weeks gestation following an unremarkable pregnancy. Developmental delay was evident during infancy, with focal seizures presenting at age 15 months. Examination demonstrated lower limb dystonia and globally brisk deep tendon reflexes. MRI brain demonstrated a diffusely thin corpus callosum and symmetric basal ganglia T2 hyperintensity and diffusion restriction of diffusion weighted imaging (see image 3). DBS acylcarnitine profiles demonstrated a persistent pattern consistent with CPT1a deficiency, however the plasma acylcarnitine profile was normal (See table 3). The patient is now 2 years of age.

Table 3 – Dried blood spot acylcarnitine results of patient 3

<table>
<thead>
<tr>
<th>Age (days)</th>
<th>C0 (8-70 µmol/L)</th>
<th>C18 (0.49-1.55 µmol/L)</th>
<th>C16 (0.7-7.5 µmol/L)</th>
<th>C10/C16+C18 (8-70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 3</td>
<td>135 ↑</td>
<td>0.25 ↓</td>
<td>0.8 ↓</td>
<td>129 ↑</td>
</tr>
<tr>
<td>Day 49</td>
<td>76 µmol/L*</td>
<td>0.21 ↓</td>
<td>0.42 ↓</td>
<td>130 ↑</td>
</tr>
<tr>
<td>2 years</td>
<td>110 µmol/L*</td>
<td>0.1 ↓</td>
<td>0.3 ↓</td>
<td>275 µmol/L*</td>
</tr>
</tbody>
</table>

* Reference ranges for these results is different to neonatal ranges.

Image 3 – Patient 3 MRI brain age 15 months

T1 sagittal image (left) demonstrating diffusely thin corpus callosum (yellow arrow). Diffusion weighted imaging (right, red arrows) demonstrating symmetric diffusion restriction of basal ganglia.

Discussion
Coenzyme A synthase functions in the mitochondria where it regulates the final two steps of Coenzyme A synthesis from panthothenate. CoPAN is a rare disorder with two known phenotypes – pontocerebellar hypoplasia type 12 and neurodegeneration with brain iron accumulation type 6.\cite{3} This CPT1a DBS pattern has been reported previously in two siblings with CoPAN.\cite{3} The pathophysiology accounting for the CPT1a DBS acylcarnitine pattern is unknown.

Conclusion
CoPAN can present with DBS acylcarnitine profiles consistent with CPT1a deficiency.

REFERENCES