Metabolic Changes in ASD

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Methodology

- 12 patients

  3 Autism: Ages 3/3/3.7

  3 PDD: Ages 3/3/6

  3 Asperger: Ages 6/7/15.1

  3 Speech delay and Sensory Problems (SHL): Ages 3/5/5

Methodology

- Complete Medical History
- Past Medical History
- Family Medical History
- Thorough Physical Examination

Methodology

Metabolic Evaluation

Urine Organic Acids

Plasma Lactate

Plasma Pyruvate

Plasma Amino Acids

Plasma Ammonia

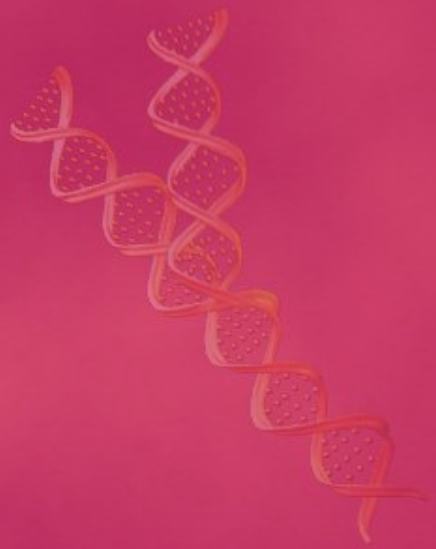
Plasma Carnitine Profile

Plasma Acylcarnitine Profile

Methodology

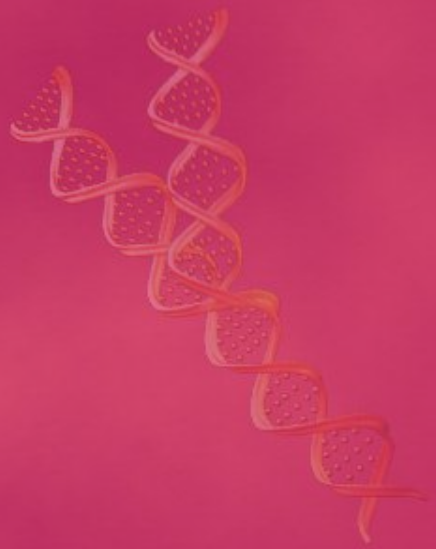
Genetic Evaluation

- Pedigree
- Blood Chromosomes (Karyotype)



Methodology

- Neurologic Evaluation
- Physical Examination
- Electro Encephalogram



Methodology

- Statistical evaluation of results

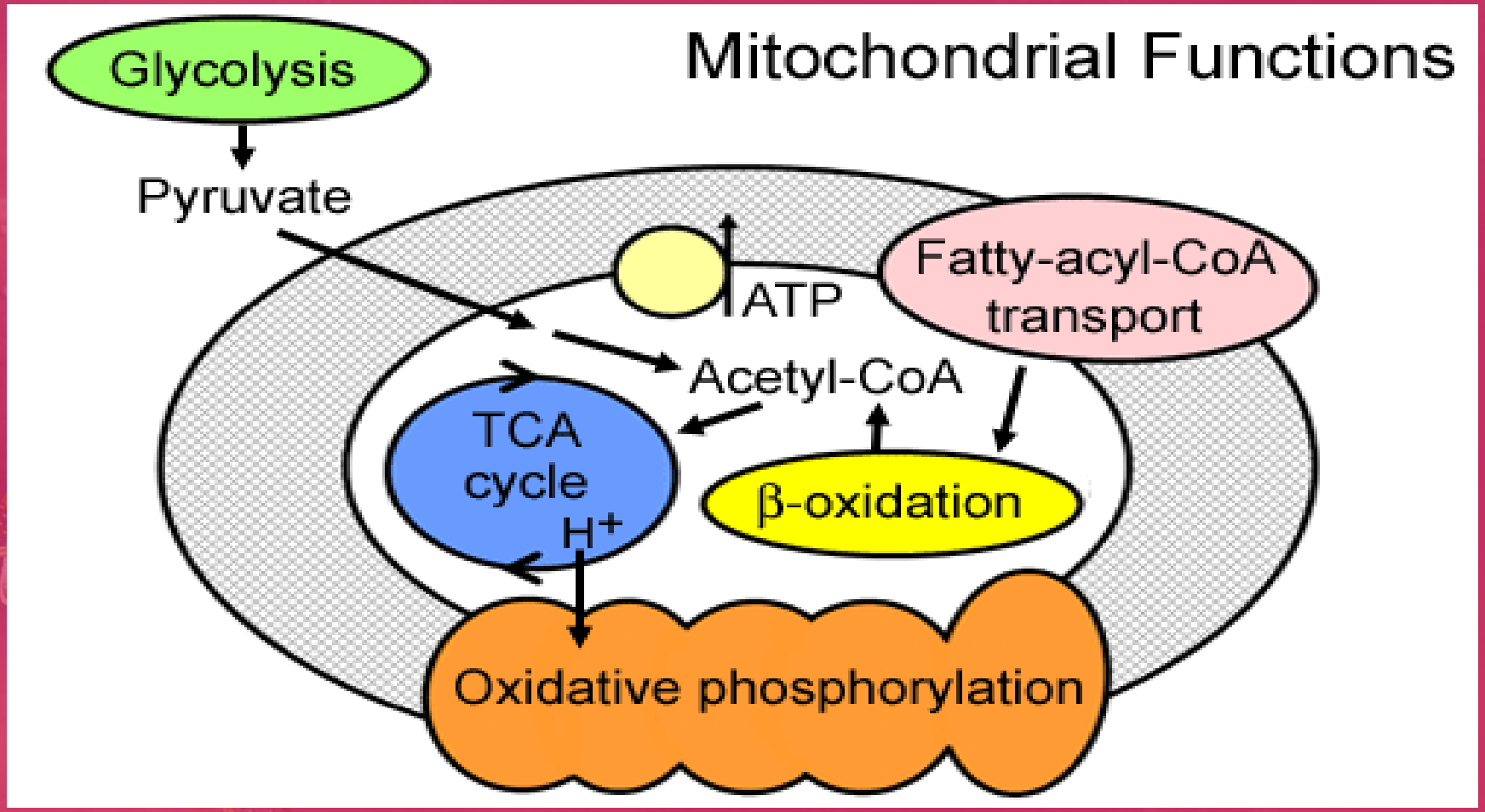
  Dr. Mauricio Cabrera Rios

  Applied Optimization Group

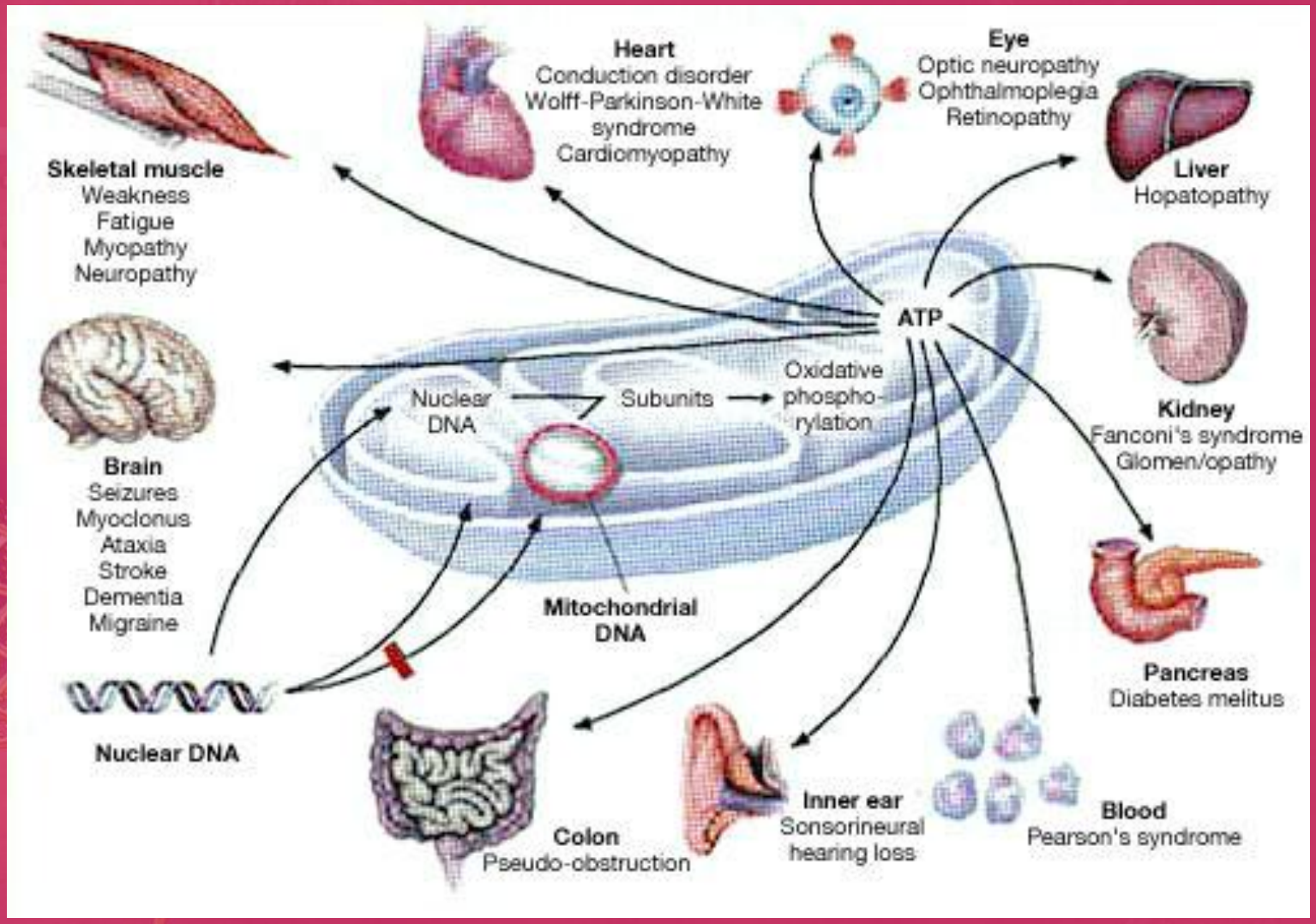
Results

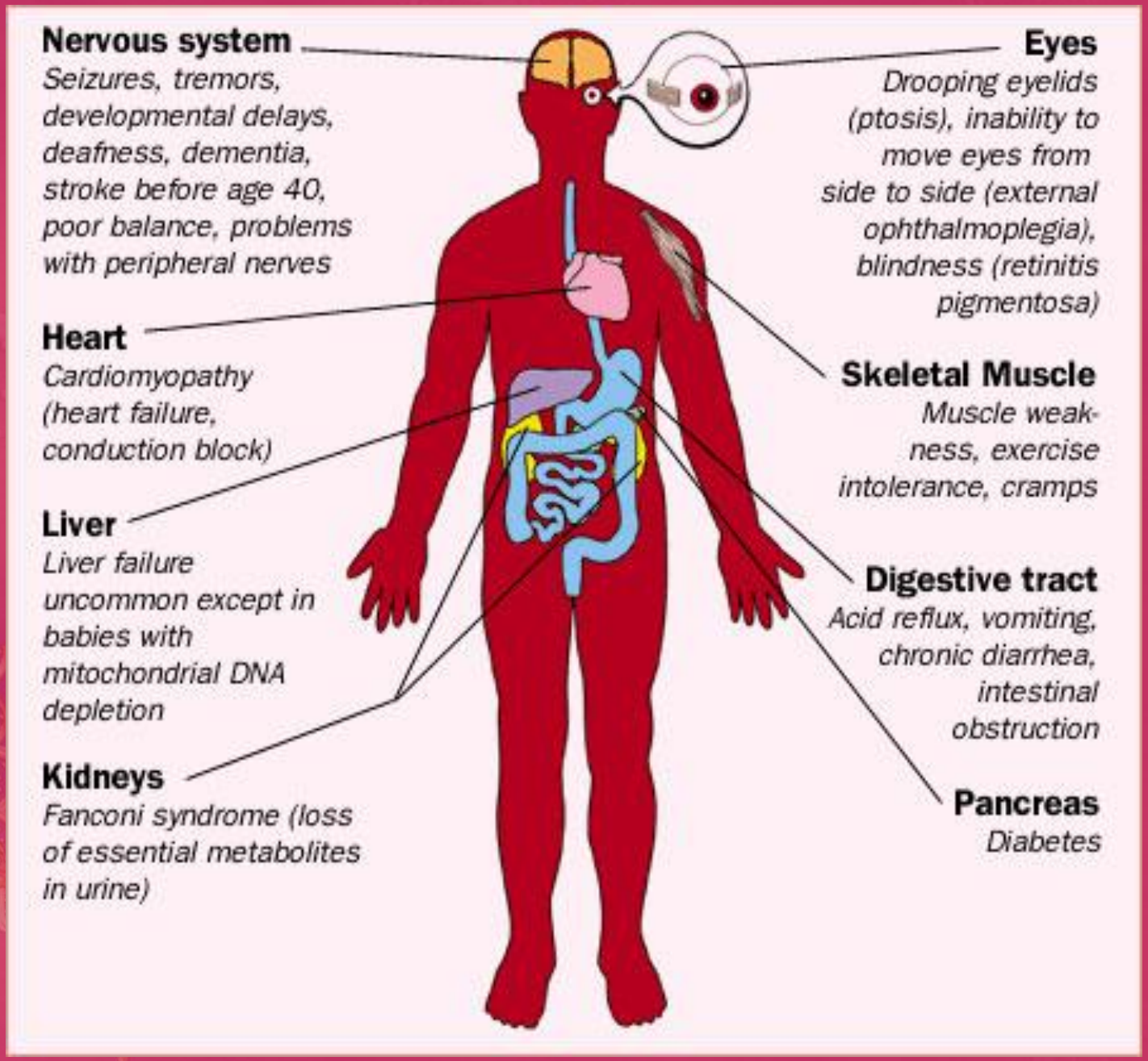
- 3 Females Autism/Asperger/SHL
- 9 Males 2 Autism/3 PDD/2 Asperger/3SHL
- Ratio 3:1

Mitochondria



Mitochondria




Nervous system
Seizures, tremors, developmental delays, deafness, dementia, stroke before age 40, poor balance, problems with peripheral nerves
Heart
Cardiomyopathy (heart failure, conduction block)
Liver
Liver failure uncommon except in babies with mitochondrial DNA depletion
Kidneys
Fanconi syndrome (loss of essential metabolites in urine)
Eyes
Drooping eyelids (ptosis), inability to move eyes from side to side (external ophthalmoplegia), blindness (retinitis pigmentosa)
Skeletal Muscle
Muscle weakness, exercise intolerance, cramps
Digestive tract
Acid reflux, vomiting, chronic diarrhea, intestinal obstruction
Pancreas
Diabetes

Results

Lactate

5.4-80.1 mg/dl

Pyruvate

0.11-0.18 mg/dld

Lactate/Pyruvate Ratio (L/P)

38-728

Results

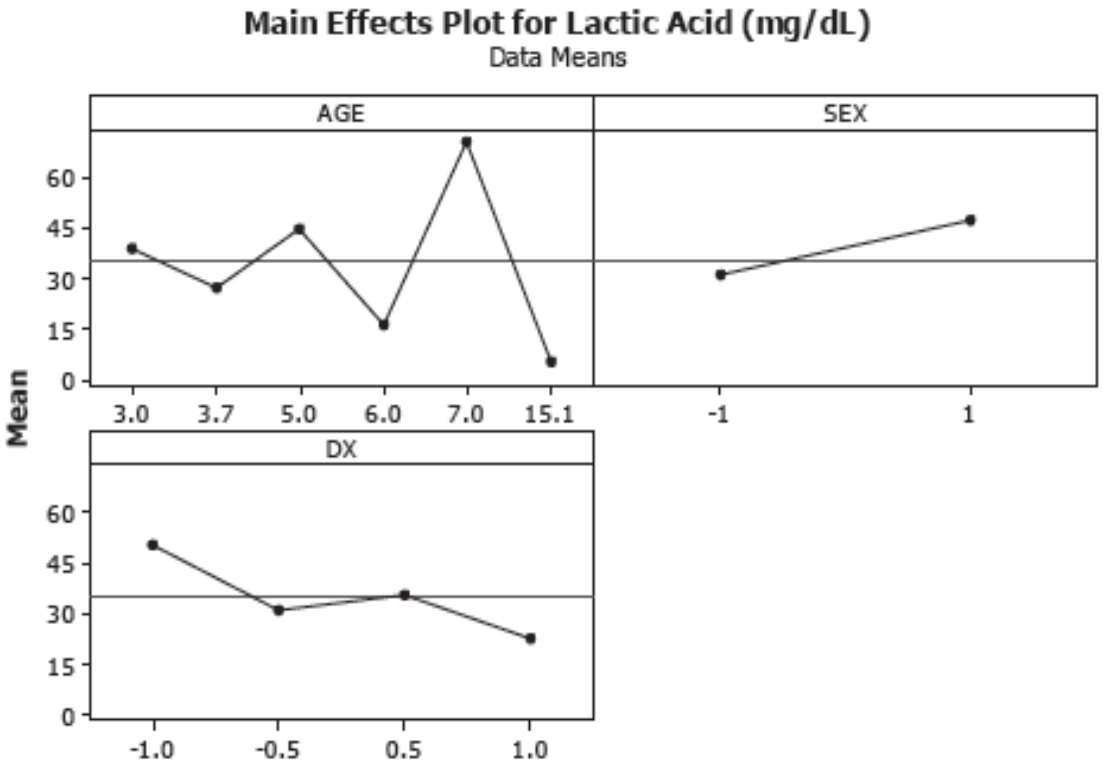


Figure 4. Lactic Acid is higher in females (Sex 1) than in males (Sex -1), higher in ASD (DX -1) and lower in PDD (DX 1). It seems to have larger variation as age progresses.

Results

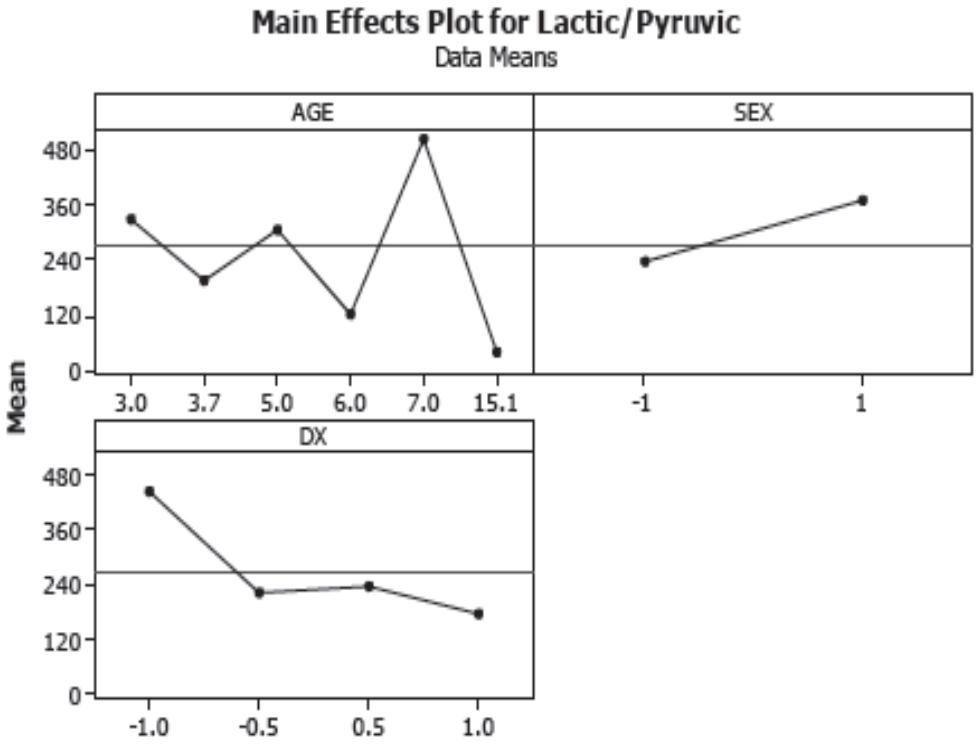


Figure 5. Lactic/Pyruvic Ratio is larger in females (Sex 1) than in males (Sex -1), and higher in ASD (DX -1).

It seems to have larger variation as age progresses.

Results

Carnitine Total

26-94 umol/L

Carnitine Free

23-71 umol/L

Free/Total Carnitine Ratio (F/T)

0.75-0.95

Carnitine

Carnitine (β-hydroxy-γ-trimethylammonium butyrate) is a hydrophilic molecule that plays an essential role in the transfer of long-chain fatty acids inside mitochondria for β oxidation. Carnitine binds acyl residues and help in their elimination. This mechanism is essential in binding/removing abnormal organic acids in several organic acidemias and explains the secondary carnitine deficiency that can result from them. Carnitine conjugation decreases the number of acyl residues attached to CoA and increases the ratio between free and acylated CoA

Results

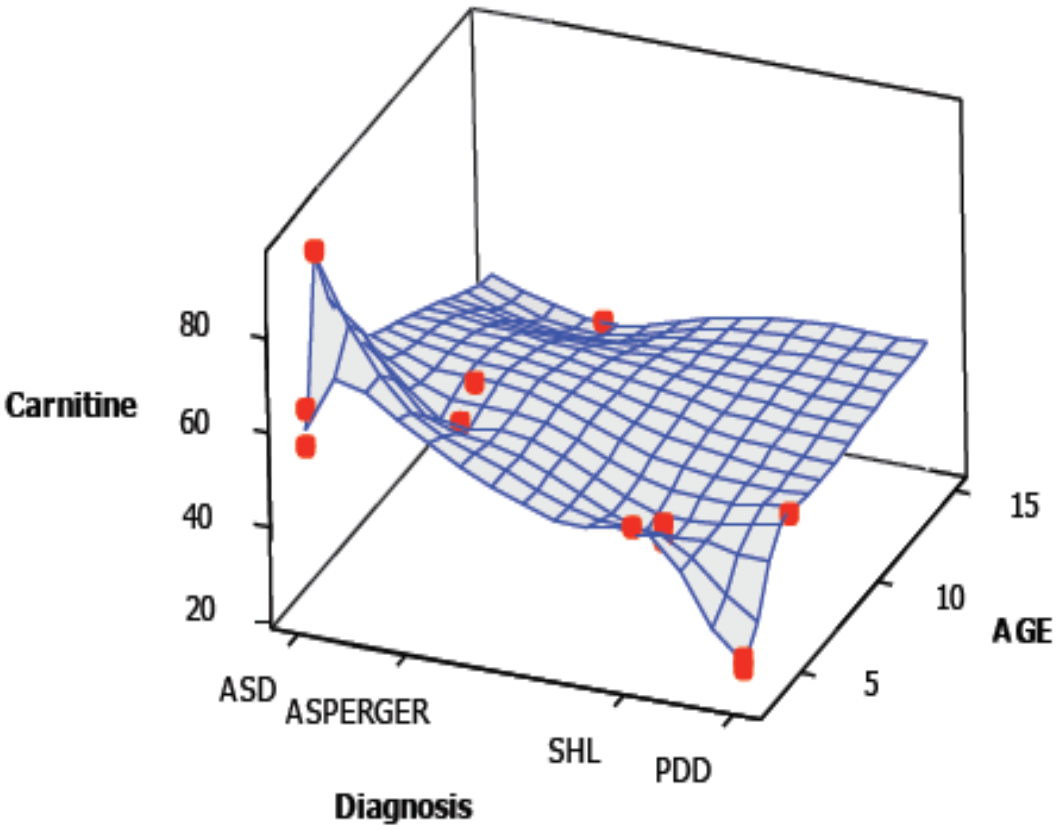


Figure 2. Carnitine tends to be higher in ASD and lower in PDD. It also seems to markedly change (increase or decrease) with age up to 5 years to then plateau.

Results

Acylcarnitine

Elevations of C5DC (gluterylcarnitine) in 3 Patients. 1 with Autism and 2 with SHL

Acylcarnitine

Fatty acid transport and mitochondrial oxidation is a complex pathway that plays a major role in energy production during times of fasting and metabolic stress. Once free acids are released into the blood they are taken up by the liver and muscle cells and activated to coenzyme A esters. Then they are transported into the mitochondria and oxidized in a cyclic fashion by four sequential reactions that are each catalyzed by one of multiple enzymes. The acyl-CoA dehydrogenases are chain-length specific enzymes. Deficiencies or abnormalities in these result VLCAD, LCAD, MCAD, and SCAD. Any illness may lead to a fasting state that can then lead to the depletion of glucose stores. Once this occurs, fatty acid metabolism becomes the dominant energy source. If there is an abnormality in fatty acid metabolism, then life-threatening episodes of metabolic decompensation can ensue.

Results

Urine Organic Acids

Normal in all 12 Patients

Urine Organic Acids

Organic acidemias (*e.g.*, methylmalonic or propionic acidemia, multiple carboxylase

deficiency) are caused by abnormal metabolism of proteins, fats or carbohydrates and are

characterized by marked metabolic acidosis with ketosis, often with elevated lactate and

mild to moderate hyperammonemia. Common signs include vomiting, signs of

encephalopathy, neutropenia and thrombocytopenia.

Results

Plasma Amino Acids

Elevation of Glutamic Acid in 1 Patient and GABA in 1

Plasma Amino Acids

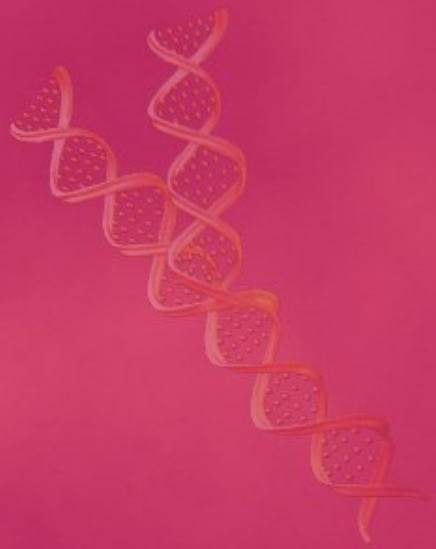
Aminoacidopathies (*e.g.*, phenylketonuria, hereditary tyrosinemia, non ketotic hyperglycinemia (NKH), maple syrup urine disease (MSUD) and homocystinuria) may have similar presentation to the organic acidemias, but are a very heterogeneous group of disorders.

Results

- Plasma Ammonia
  - Mildly elevated in 5 patients

Plasma Ammonia

Urea cycle defects (*e.g.*, citrullinemia, ornithine transcarbamylase deficiency, and arginosuccinic aciduria) result from the inability to detoxify nitrogen and are characterized by severe hyperammonemia and respiratory alkalosis, with a typical onset after 24 hours of age.



Results

Blood Chromosomes

Normal in all 12 Patients

Results

Electro Encephalogram

Abnormal in 1 Patient

Results

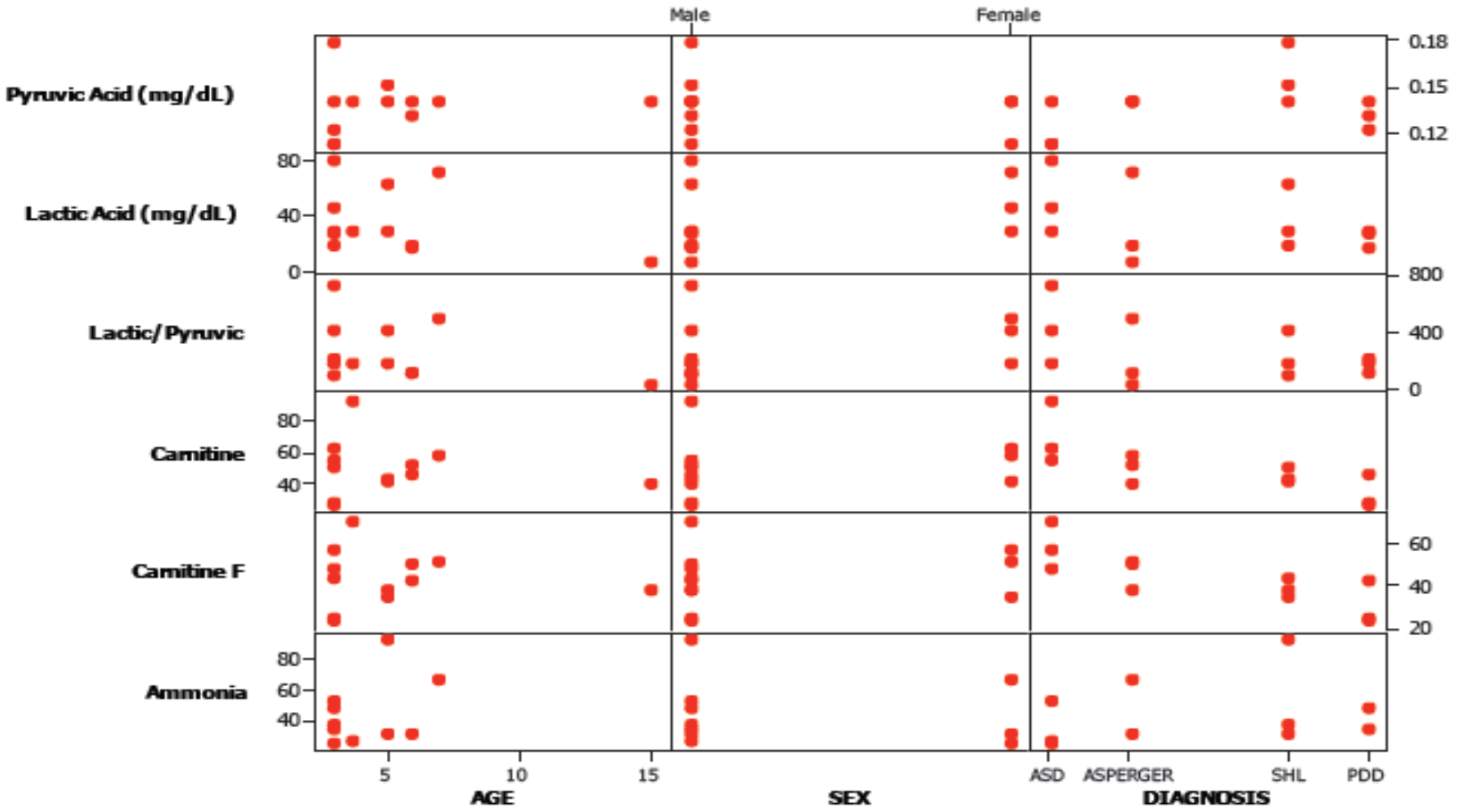


Figure 1. Plot of measurements vs. characteristics

Discussion

Thank You