Enzyme and Sulphur Oxidation Deficiencies in Autistic Children with Known Food/Chemical Intolerances

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We are currently carrying out studies to determine whether children with autism and known food/chemical intolerances have a deficiency of phenol-sulphotransferase-P enzyme and/or a low capacity to oxidize sulphur compounds. These studies are being carried out by Dr. R. H. Waring, Biochemistry Department, Birmingham University, United Kingdom.

On the results obtained so far, all 18 children have a low enzyme level, and some have a low capacity to oxidize sulphur compounds (see Table 1). We have now tested approximately 40 children for just the enzyme deficiency (unpublished results) and this is very low in every child. This enzyme metabolizes phenols and amines.[1,2] Therefore with a reduced level, these children will be unable to fully metabolize foods and chemicals which contain phenols. Many drugs are also metabolized on this pathway!, and these children do have adverse reactions to various medications. Courses of antibiotics result in a worsening of autistic behaviour, sedatives have the reverse effect, and anaesthesia is known to cause difficulties. Amines are also metabolized with this enzyme, and a deficiency would cause a build-up of substances such as serotonin, dopamine and noradrenaline. It is well documented that some persons with autism have high levels of serotonin.[3] If, as a result of this build-up, serotonin, dopamine, noradrenaline, and other body chemicals are being further metabolized this may produce substances similar to phytotoxins (toxins produced by plants), for example. This could happen due to phenolics competing for and inhibiting amine oxidase. Inert neurotransmitters could also be manufactured, such as octopamine, which is the phenol analogue of noradrenaline.

Dr. Waring has also carried out blood tests on 14 children in this category (unpublished results), and has found that they all have low levels of sulphate, which is the substrate which is used by phenol-sulphotransferase-P enzyme. These results indicate that there may be a fault either in manufacture of sulphate or that sulphate is being used up dramatically on an unknown toxic substance these children may be producing. This may indicate that more than one sulphotransferase enzyme may be affected, and requires further investigation to determine that it may not be strictly an enzyme deficiency, but appears to be such, due to low levels of substrate.

The test for level of enzyme is done by administering paracetamol (acetaminophen), and collecting urine for the following eight hours (see Appendix 1). When these tests were carried out, parental reports showed that most of the children had a reduced level of urine output over the eight hour collection period, and they were also feverish and generally "off-colour".

This became apparent because we were trying to collect urine, and many children did not urinate until the very end of the eight hour period. Parents should be made aware that administering paracetamol may give this effect which may be masked during illness, but that they need to be aware of the effects of this drug on these particular children, which is given relatively freely during minor illness.

The majority of children in this category - autistic-like children who were perfectly normal up until a certain age (mainly between 18 months to two years, although this varies) -have allergy to or intolerance of many foods/ chemicals, the main offenders being wheat, cow's milk and salicylates. This may manifest as a true "allergic" reaction, for example urticaria or asthma, but in the majority of these children the only effect is a worsening of their

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Table 1
Enzyme Deficiencies in Autistic Children with Known Food/Chemical Intolerances Carried Out by Dr. R. H. Waring at Birmingham University, UK.

	Sample No	SI*	PS/PG*
AOR	1	2.0	0.17 +
BN	2	>80	1.3
LD	3	>80	1.5
JS	4	>80	0.23
JP	5	3.2	1.1
JSw	6	2.1	0.8
DM	7	>80	0.6
DMo	8	>80	0.6
MS	9	8.7	0.08
RB	10	5.0	0.76
SB	11	7.1	1.0
SH	12	3.6	0.83
AP	13	2.1	1.4
DMc	14	>80	1.9
MP	15	>80	0.65
MS	16	-	0.55
MT	17	2.0	0.43
DW	18	3.5	0.32

* SI - Sulphoxidation Index PS - Paracetamol Sulphate
PG - Paracetamol Glucuronide
+ The figure here reflects the deficiency level of the enzyme, done by measuring the metabolites of paracetamol.

Children with an S.I. (sulphoxidation index) of >80 (greater than 80) have a very low capacity to oxidize sulphur compounds. Age matched children have a sulphoxidation index between 0.5 and 6.60. This problem is strongly associated with chemical/food allergies, but the cause for this is not clear.

Children with a low (1.5 or below) sulphotransferase level (PS/PG) are unable to fully metabolize phenols/amines. Age matched children have values of between 2.1 and 11.6.

These results show that some children are unable to oxidize sulphur compounds, some have a very low sulphotransferase level, and some have both problems.

autistic-like behaviour. The reaction may be apparent within hours, or it may take a few days. When the behaviour worsens, it is usually accompanied by red face and/or ears, and an excessive thirst, the latter possibly due to the children trying to keep the toxic substances as dilute as possible, as they are unable to excrete them normally.[4]

The children's family histories show asthma, eczema, migraine (particularly in mothers), hay fever, plus many other "allergy"-related conditions. Their siblings may display learning difficulties, dyslexia, etc. and the affected children have a strong tendency towards changing handedness or becoming ambidextrous, when they transfer from being normal to their autistic-like state.[5]

Many metabolic processes can be disturbed by phenolic compounds, and so cause many physical problems which are only slightly noticeable in childhood, such as excessive thirst, night sweats, facial flushing, increased pulse rate, abdominal disturbances, etc.,[6] but nevertheless are present, but not investigated as a part of these children's mental disturbance. The children display cravings for the very substances which do them damage, which are not only contained in foods, but also in the non-food items they mouth, suck, chew and ingest, eg. plastics, rubber, paper, metal, cement, soap, perfume, food colourings, and at the onset of autism, their diet changes completely. They become picky eaters, only eating very few foods, avoiding some foods and craving others, and start to eat non-foods to great excess.

The results so far have proved that there is a metabolic disturbance in these children. However, as this disturbance of sulphate metabolism may well be an end result of some other biochemical fault which remains to be discovered, we now hope to continue with further studies on more children and different biochemical pathways to determine whether there may be other factors contributing to this condition.

References

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APPENDIX I

Methodology of Testing

Carbocisteine/SCMC

Two tablets of SCMC (750mg) (1 for children) are taken at 8 am and all urine is collected for the next 8 hours. The total volume is measured and an aliquot (approximately 10ml) sent for analysis. Urine samples (0.12ml) are applied to paper chromatograms, with standard compounds. Descending paper chromatography is used for separation (n - butanol / acetic acid / butyl acetate / water, 120 / 25 / 10 / 50) overnight. The chromatogram is then dried and dipped in the chloroplatinate reagent. Sulphur compounds appear as yellow/ cream spots and are measured (planimetric densitometry) and compared with standard values.

Ref: Biochem. Pharmacol. 1982 31 (3151-4)

Paracetamol (Acetaminophen)

One tablet (500mg) (or equivalent child dose) is taken at approximately 8 am and an aliquot of urine collected as above. Samples (10 ul) are injected into a high pressure liquid chromotography machine, with a C18 column (Techopak, 25 cm) pressure 150 bar and mobile phase 1% (v/v) acetic acid / methanol / ethyl acetate (90 / 15/0.1 by volume) and a flow rate of 1.6 ml/min. Detection is by ultra violet spectrophotometry at 250 nm. Conjugate formation is detected by incubation with glucuronidase or sulphatase, and results are expressed as milligram equivalent of paracetamol.

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