Plural ‘autisms’ and the promises of autism metabolomics.

Paul Whiteley PhD, ESPA Research, UK

paul.whiteley@espa-research.org.uk

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Content

1. The increasing moves towards **the pluralisation of autism** (**‘the autisms’**),
2. **Many routes** to a diagnosis of autism or autism spectrum disorder (ASD),
3. What studying dietary intervention for autism has taught me,
4. **Enter metabolomics** & **the bigger picture of individualised / phenotype-based autism science**.

Based on **peer-reviewed science** (many links provided, happy to provide additional scientific references).

- Apologies for the blatant self-promotion throughout this talk (I’m not nearly as important as I make out).
- ‘*Standing on the shoulders of giants*’ and ‘*No man is an island*’. PS, KC, MH, LT, CS and lots of others to mention.
- Very grateful to the Robert Luff Foundation for their financial support down the years.
- Focus is on **the biology-behaviour nexus** (not necessarily of great interest to everyone).
- COI: Employed by ESPA Research. A director of Analutos Ltd (providing various mass spectrometric analytical services)

The pluralisation of autism

- "*To describe ASD [autism spectrum disorder] as **a heterogeneous label** does not do justice to the wide range of presentations that the condition entails*"[1].
- Syndromic and non-syndromic autism represent good starting points but still underplay **the massive heterogeneity included under the diagnostic label**.
- The bigger picture: **autism rarely appears in some sort of diagnostic vacuum**[2].
- **Prevalence estimates for autism are still increasing**[3,4]. Arguments solely about 'better awareness' or 'better surveillance' are **becoming less and less relevant** (particularly in pædiatric cohorts).
- Presentation of autism or traits of autism are **typically dynamic** (sensitive to environment, maturation, adaptation, intervention, *etc.*). Questions whether, for some, they are universally present lifelong…

1.Whiteley P, Marlow B, Kapoor RR, Blagojevic-Stokic N, Sala R. Autoimmune Encephalitis and Autism Spectrum Disorder. Front Psychiatry. 2021 Dec 17;12:775017. doi: 10.3389/fpsyt.2021.775017.
2.Gillberg C, Fernell E. Autism plus versus autism pure. J Autism Dev Disord. 2014 Dec;44(12):3274-6. doi: 10.1007/s10803-014-2163-1.
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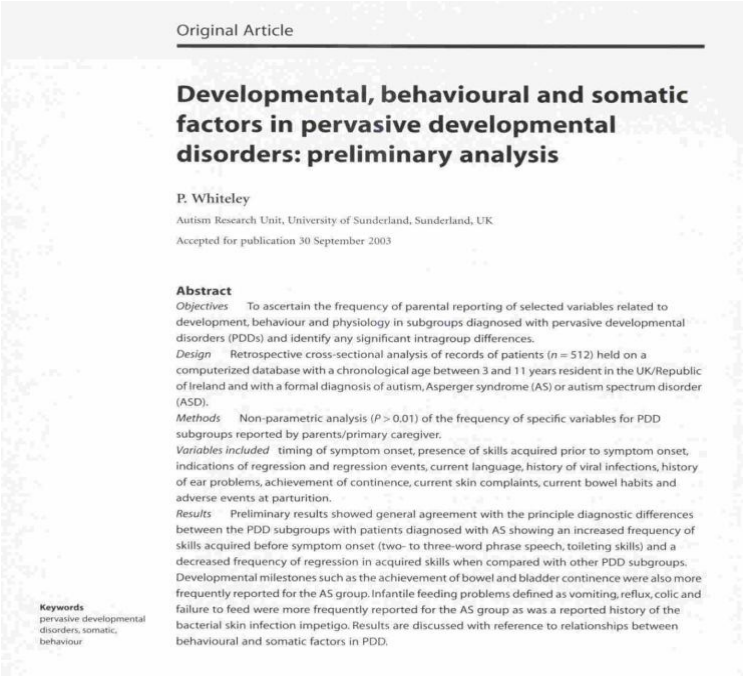
Autism rarely appears in a diagnostic vacuum…



Original Article

Developmental, behavioural and somatic factors in pervasive developmental disorders: preliminary analysis

P. Whiteley

Autism Research Unit, University of Sunderland, Sunderland, UK

Accepted for publication 30 September 2003

Abstract

Objectives To ascertain the frequency of parental reporting of selected variables related to development, behaviour and physiology in subgroups diagnosed with pervasive developmental disorders (PDDs) and identify any significant intragroup differences.

Design Retrospective cross-sectional analysis of records of patients ($n = 512$) held on a computerized database with a chronological age between 3 and 11 years resident in the UK/Republic of Ireland and with a formal diagnosis of autism, Asperger syndrome (AS) or autism spectrum disorder (ASD).

Methods Non-parametric analysis ($P > 0.01$) of the frequency of specific variables for PDD subgroups reported by parents/primary caregiver.

Variables included timing of symptom onset, presence of skills acquired prior to symptom onset, indications of regression and regression events, current language, history of viral infections, history of ear problems, achievement of continence, current skin complaints, current bowel habits and adverse events at parturition.

Results Preliminary results showed general agreement with the principle diagnostic differences between the PDD subgroups with patients diagnosed with AS showing an increased frequency of skills acquired before symptom onset (two- to three-word phrase speech, toileting skills) and a decreased frequency of regression in acquired skills when compared with other PDD subgroups. Developmental milestones such as the achievement of bowel and bladder continence were also more frequently reported for the AS group. Infantile feeding problems defined as vomiting, reflux, colic and failure to feed were more frequently reported for the AS group as was a reported history of the bacterial skin infection impetigo. Results are discussed with reference to relationships between behavioural and somatic factors in PDD.

Keywords
pervasive developmental disorders, somatic, behaviour

Neuropsychiatric Disease and Treatment

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REVIEW

Bridging the Gap Between Physical Health and Autism Spectrum Disorder

This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment

Regina Sala[1]
Lorene Amet[2]
Natasa Blagojevic-Stokic[3]
Paul Shattock[4]
Paul Whiteley[5]

[1]Centre for Psychiatry, Wolfson Institute, Barts & The London School of Medicine & Dentistry Queen Mary University of London, London, UK; [2]Autism Treatment Plus, Edinburgh, UK; [3]Thinking Autism, London, UK; [4]Education & Services for People with Autism, Sunderland, UK; [5]Education & Services for People with Autism Research, Sunderland, UK

Abstract: Autism spectrum disorder (ASD) is a highly complex and heterogeneous developmental disorder that affects how individuals communicate with other people and relate to the world around them. Research and clinical focus on the behavioural and cognitive manifestations of ASD, whilst important, have obscured the recognition that ASD is also commonly associated with a range of physical and mental health conditions. Many physical conditions appear with greater frequency in individuals with ASD compared to non-ASD populations. These can contribute to a worsening of social communication and behaviour, lower quality of life, higher morbidity and premature mortality. We highlight some of the key physical comorbidities affecting the immune and the gastrointestinal systems, metabolism and brain function in ASD. We discuss how healthcare professionals working with individuals with ASD and parents/carers have a duty to recognise their needs in order to improve their overall health and wellbeing, deliver equality in their healthcare experiences and reduce the likelihood of morbidity and early mortality associated with the condition.

Keywords: autism spectrum disorder, ASD, physical health, comorbidity, inequality

Plain Language Summary

A diagnosis of autism spectrum disorder (ASD) is based on the presence of impairments with social communication and repetitive or restricted patterns of behaviour. Much of the scientific interest has focused on the behaviours and cognitive functioning that define ASD and how they can affect a person's day-to-day quality of life. However, ASD does not typically appear as a stand-alone condition. Various other health conditions affecting physical and mental wellbeing are also commonly reported. These can have an important impact on daily living, social communication and behaviour. We highlight some of the conditions affecting the immune and gastrointestinal systems, metabolism and brain function, and how they can influence a person's quality of life and increase the risk of early mortality. We discuss how professionals, working with those with ASD and their parents and carers can recognise the impact such conditions may have on individuals with ASD.

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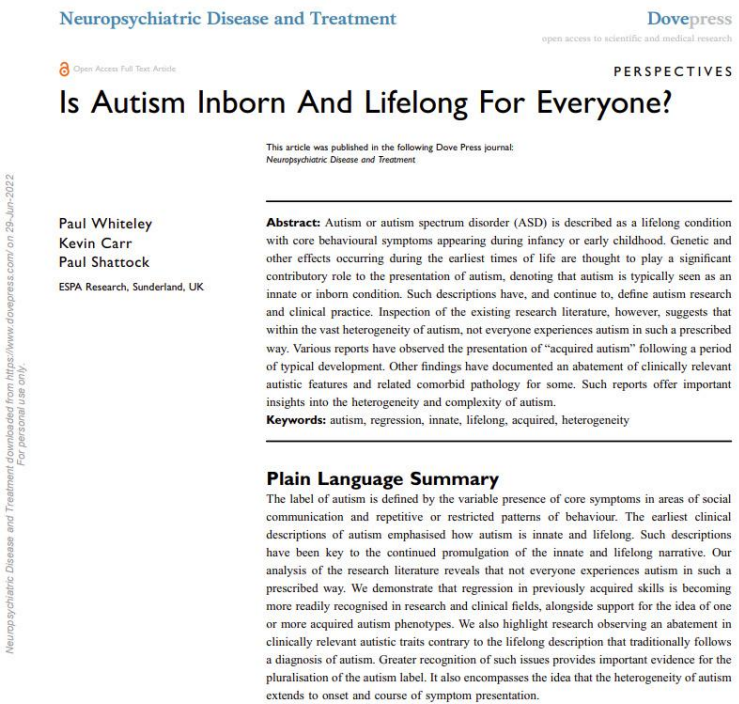
2.Sala R, Amet L, Blagojevic-Stokic N, Shattock P, Whiteley P. Bridging the Gap Between Physical Health and Autism Spectrum Disorder. Neuropsychiatr Dis Treat. 2020 Jun 30;16:1605-1618. doi: 10.2147/NDT.S251394.

Some important (not universally popular) questions

- **(Autistic) Regression is real**. Parent/caregiver observations were correct.
- Estimates of regression accompanying autism range from 30-50% in scientific texts.
- Regression "*the rule, not the exception*"?
- **Autism as 'lifelong' might not be as universal a concept as many people think**.
- Loss of autism (diagnosis) is currently estimated to occur in about 10% of people. More data needed.
- Yes, some misdiagnosis but not always.
- Loss of autism diagnosis observed to occur alongside loss of other psychiatric comorbidity too.
- **More (objective/longitudinal) study required**.



Neuropsychiatric Disease and Treatment

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PERSPECTIVES

Is Autism Inborn And Lifelong For Everyone?

This article was published in the following Dove Press journal:
Neuropsychiatric Disease and Treatment

Paul Whiteley
Kevin Carr
Paul Shattock

ESPA Research, Sunderland, UK

Abstract: Autism or autism spectrum disorder (ASD) is described as a lifelong condition with core behavioural symptoms appearing during infancy or early childhood. Genetic and other effects occurring during the earliest times of life are thought to play a significant contributory role to the presentation of autism, denoting that autism is typically seen as an innate or inborn condition. Such descriptions have, and continue to, define autism research and clinical practice. Inspection of the existing research literature, however, suggests that within the vast heterogeneity of autism, not everyone experiences autism in such a prescribed way. Various reports have observed the presentation of "acquired autism" following a period of typical development. Other findings have documented an abatement of clinically relevant autistic features and related comorbid pathology for some. Such reports offer important insights into the heterogeneity and complexity of autism.

Keywords: autism, regression, innate, lifelong, acquired, heterogeneity

Plain Language Summary

The label of autism is defined by the variable presence of core symptoms in areas of social communication and repetitive or restricted patterns of behaviour. The earliest clinical descriptions of autism emphasised how autism is innate and lifelong. Such descriptions have been key to the continued promulgation of the innate and lifelong narrative. Our analysis of the research literature reveals that not everyone experiences autism in such a prescribed way. We demonstrate that regression in previously acquired skills is becoming more readily recognised in research and clinical fields, alongside support for the idea of one or more acquired autism phenotypes. We also highlight research observing an abatement in clinically relevant autistic traits contrary to the lifelong description that traditionally follows a diagnosis of autism. Greater recognition of such issues provides important evidence for the pluralisation of the autism label. It also encompasses the idea that the heterogeneity of autism extends to onset and course of symptom presentation.

1.Whiteley P, Carr K, Shattock P. Is Autism Inborn And Lifelong For Everyone? Neuropsychiatr Dis Treat. 2019 Oct 7;15:2885-2891. doi: 10.2147/NDT.S221901.

Many routes to a diagnosis of autism

- Contrary to some discussions, **the aetiology of <u>some</u> autism is not a complete mystery**.
- **Syndromic autism** - appearing as part of a genetic condition - is a well-recognised path to a diagnosis of autism *e.g.* BCKDK (Branched Chain Ketoacid Dehydrogenase Kinase).[1]
- Offspring risk of autism is heightened following **prenatal exposure to sodium valproate**. The UK Government acknowledges this science and has for nearly a decade (3-5 fold increased risk).[2]
- **'MAR autism'** (maternal autoantibodies to foetal brain proteins) becoming more widely researched[3].
- Various infections have been linked to the onset/presentation of autism either peripherally (prenatal rubella, cytomegalovirus (CMV) exposure) or more directly (following various types of encephalitis including AE)[4,5].

1. Novarino G, El-Fishawy P, Kayserili H, Meguid NA, Scott EM, Schroth J, Silhavy JL, Kara M, Khalil RO, Ben-Omran T, Ercan-Sencicek AG, Hashish AF, Sanders SJ, Gupta AR, Hashem HS, Matern D, Gabriel S, Sweetman L, Rahimi Y, Harris RA, State MW, Gleeson JG. Mutations in BCKD-kinase lead to a potentially treatable form of autism with epilepsy. Science. 2012 Oct 19;338(6105):394-7. doi: 10.1126/science.1224631.
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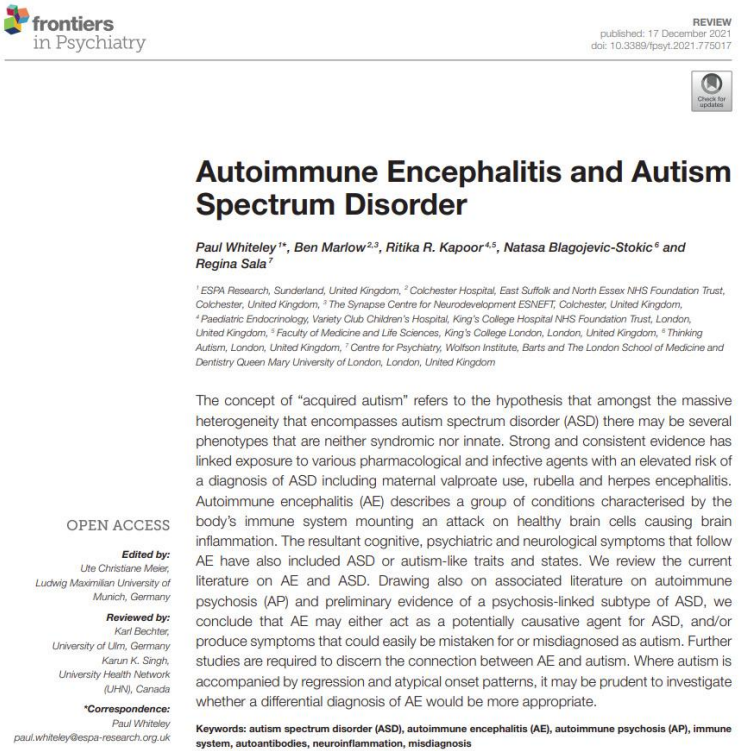
Can specific infections manifest as autism? Probably.

- Adds to the notion of ‘acquired autism’ for some.
- Autoimmune encephalitis (AE) = the body's immune system mounting an attack on healthy brain cells causing brain inflammation.
- ‘Brain on fire’ is required reading.
- **Various case reports on autism or autistic symptoms appearing as part of AE**.
- Lots of symptom overlaps: AE linked to OCD, psychosis, *etc*.
- **Some abatement of autism / autistic symptoms following medical treatment of AE**.
- Not exactly a popular topic among some people.



frontiers in Psychiatry

REVIEW
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Autoimmune Encephalitis and Autism Spectrum Disorder

Paul Whiteley[1], Ben Marlow[2,3], Ritika R. Kapoor[4,5], Natasa Blagojevic-Stokic[6] and Regina Sala[7]*

[1] ESPA Research, Sunderland, United Kingdom, [2] Colchester Hospital, East Suffolk and North Essex NHS Foundation Trust, Colchester, United Kingdom, [3] The Synapse Centre for Neurodevelopment ESNEFT, Colchester, United Kingdom, [4] Paediatric Endocrinology, Variety Club Children's Hospital, King's College Hospital NHS Foundation Trust, London, United Kingdom, [5] Faculty of Medicine and Life Sciences, King's College London, London, United Kingdom, [6] Thinking Autism, London, United Kingdom, [7] Centre for Psychiatry, Wolfson Institute, Barts and The London School of Medicine and Dentistry Queen Mary University of London, London, United Kingdom

The concept of “acquired autism” refers to the hypothesis that amongst the massive heterogeneity that encompasses autism spectrum disorder (ASD) there may be several phenotypes that are neither syndromic nor innate. Strong and consistent evidence has linked exposure to various pharmacological and infective agents with an elevated risk of a diagnosis of ASD including maternal valproate use, rubella and herpes encephalitis. Autoimmune encephalitis (AE) describes a group of conditions characterised by the body’s immune system mounting an attack on healthy brain cells causing brain inflammation. The resultant cognitive, psychiatric and neurological symptoms that follow AE have also included ASD or autism-like traits and states. We review the current literature on AE and ASD. Drawing also on associated literature on autoimmune psychosis (AP) and preliminary evidence of a psychosis-linked subtype of ASD, we conclude that AE may either act as a potentially causative agent for ASD, and/or produce symptoms that could easily be mistaken for or misdiagnosed as autism. Further studies are required to discern the connection between AE and autism. Where autism is accompanied by regression and atypical onset patterns, it may be prudent to investigate whether a differential diagnosis of AE would be more appropriate.

Keywords: autism spectrum disorder (ASD), autoimmune encephalitis (AE), autoimmune psychosis (AP), immune system, autoantibodies, neuroinflammation, misdiagnosis

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Ute Christiane Meier, Ludwig Maximilian University of Munich, Germany

Reviewed by:
Karl Bechter, University of Ulm, Germany
Karun K. Singh, University Health Network (UHN), Canada

****Correspondence:***
Paul Whiteley
paul.whiteley@espa-research.org.uk

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What studying dietary intervention for autism has taught me (1)

- Studying a possible connection between autism and **foodstuffs containing gluten and/or casein** has been a focus of my (25+ years) career.
- Gluten found in various cereal and grain-based products.
- Casein found in mammalian dairy sources.
- Lots of references to gluten and casein in autism peer-reviewed science.
- Not every reference to ‘milk and autism’ advocates for a ‘deleterious’ relationship.
- For example: our SR/MA on breastfeeding rates and offspring autism → ‘mothers milk’ *might* be protective… (with caveats)

Maternal breastfeeding and autism spectrum disorder in children: A systematic review and meta-analysis

Ping-Tao Tseng[1†], Yen-Wen Chen[2†], Brendon Stubbs[3,4,5], Andre F. Carvalho[6,7], Paul Whiteley[8], Chia-Hung Tang[9], Wei-Cheng Yang[10], Tien-Yu Chen[11], Dian-Jeng Li[12,13], Che-Sheng Chu[14], Wei-Chieh Yang[15], Hsin-Yi Liang[16], Ching-Kuan Wu[1], Cheng-Fang Yen[17,18], Pao-Yen Lin[19,20]

[1]Department of Psychiatry, Tsyr-Huey Mental Hospital, Kaohsiung Jen-Ai's Home, Taiwan, [2]Department of Neurology, E-Da Hospital, Kaohsiung, Taiwan, [3]Physiotherapy Department, South London and Maudsley NHS Foundation Trust, London, UK, [4]Health Service and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience (IoPPN), King's College London, De Crespigny Park, London, UK, [5]Faculty of Health, Social Care and Education, Anglia Ruskin University, Chelmsford, UK, [6]Translational Psychiatry Research Group and Department of Clinical Medicine, Federal University of Ceará, Fortaleza, CE, Brazil, [7]Department of Clinical Medicine, Faculty of Medicine, Federal University of Ceará, Rua Prof. Costa Mendes, 1608, 4º andar, 60430-040, Fortaleza, CE, Brazil, [8]ESPA Research, 2A Hylton Park Road, Sunderland SR5 3HD, UK, [9]Department of Psychiatry, Tainan hospital, Ministry of Health and Welfare, Taiwan, [10]Department of Adult Psychiatry, Kaohsiung Municipal Kai-Syuan Psychiatric Hospital, Kaohsiung City, Taiwan, [11]Department of Psychiatry, Tri-Service General Hospital; School of Medicine, National Defense Medical Center, Taipei, Taiwan, [12]Department of Addiction Science, Kaohsiung Municipal Kai-Syuan Psychiatric Hospital, Kaohsiung City, Taiwan, [13]Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung City, Taiwan, [14]Department of Psychiatry, Puli Branch, Taichung Veterans General Hospital, Nantou County, Taiwan, [15]Department of Pediatrics, DA-AN Women and Children Hospital, Tainan City, Taiwan, [16]Department of Child Psychiatry, Chang Gung Memorial Hospital at Taoyuan and Chang Gung University, Taoyuan, Taiwan, [17]Department of Psychiatry, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan, [18]Department of Psychiatry, School of Medicine, and Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan, [19]Department of Psychiatry, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, Kaohsiung, Taiwan, [20]Institute for Translational Research in Biomedical Sciences, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung City, Taiwan

Objectives: Autism spectrum disorder (ASD) refers to a group of conditions variably affecting communicative and social interactive abilities presenting alongside behaviors with various restricted and repetitive patterns. In addition to genetic factors that influence the onset of the symptoms, there is growing interest in the potential involvement of non-genetic environmental factors. Some aspects of breastfeeding practices, including rates, timing, or optimality, have been put forward as environmental risk factors for autism. However, previous studies showed a controversial relationship between ASD and breastfeeding.

Methods: A meta-analysis on the association between maternal breastfeeding and ASD in children was conducted. We also explored potential moderating factors which might influence this association. Articles reporting the association between breastfeeding and a diagnosis of ASD were included.

Results: Seven articles were included in the meta-analysis. Cumulatively, children with ASD ($n = 1463$), either in the form of clinical diagnosis or self-report, were significantly less likely to have been breastfed than children without ASD ($n = 1180$) (OR = 0.61, 95% CI = 0.45–0.83, $P = 0.002$). Subgroup analyses revealed that results remained significant for children who were breastfed with additional supplementation.

Discussion: This meta-analysis provides evidence that breastfeeding (exclusively or including additional supplements) may protect against ASD. Prospective longitudinal research is required to disentangle the complex relationships and to explore potential pathophysiological mechanisms.

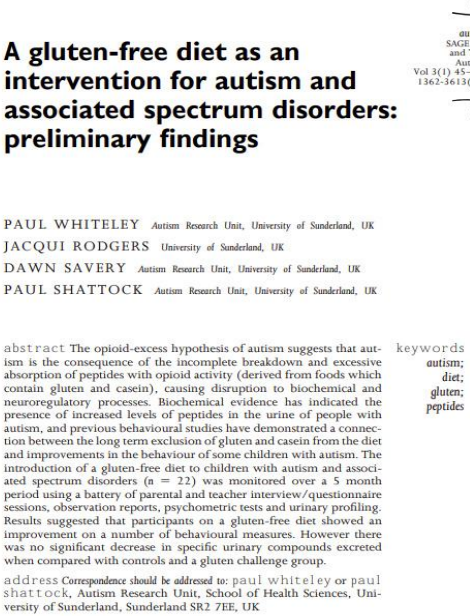
Correspondence to: Cheng-Fang Yen, Department of Psychiatry, Kaohsiung Medical University Hospital, 100, Ziyou first Road, Sanmin District, Kaohsiung City 807, Taiwan. Email: p03132006@gmail.com; Pao-Yen Lin, Department of Psychiatry, Kaohsiung Chang Gung Memorial Hospital and Chang Gung University College of Medicine, 123, Dapi Road, Niaosong District, Kaohsiung City 833, Taiwan. Email: paoyenlin@gmail.com

†Contribute equally as first authors.

Keywords: Autism, Breastfeeding, Protective effect, Systemic review

1.Tseng PT, Chen YW, Stubbs B, Carvalho AF, Whiteley P, Tang CH, Yang WC, Chen TY, Li DJ, Chu CS, Yang WC, Liang HY, Wu CK, Yen CF, Lin PY. Maternal breastfeeding and autism spectrum disorder in children: A systematic review and meta-analysis. Nutr Neurosci. 2019 May;22(5):354-362. doi: 10.1080/1028415X.2017.1388598.

What studying dietary intervention for autism has taught me (2)



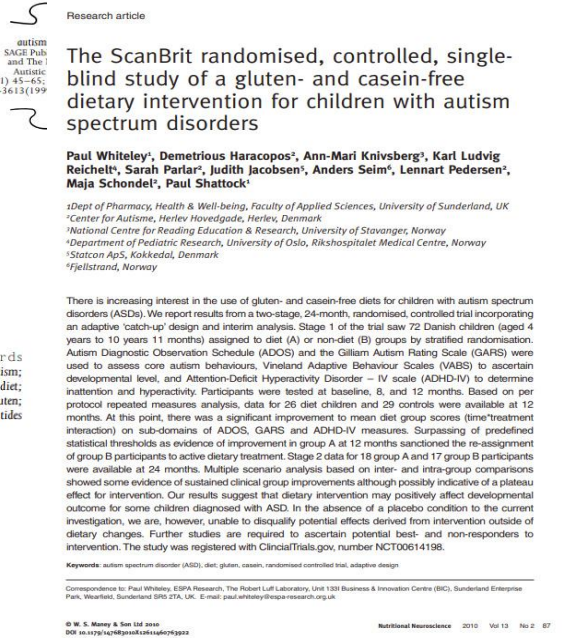
A gluten-free diet as an intervention for autism and associated spectrum disorders: preliminary findings

PAUL WHITELEY Autism Research Unit, University of Sunderland, UK
JACQUI RODGERS University of Sunderland, UK
DAWN SAVERY Autism Research Unit, University of Sunderland, UK
PAUL SHATTOCK Autism Research Unit, University of Sunderland, UK

abstract The opioid-excess hypothesis of autism suggests that autism is the consequence of the incomplete breakdown and excessive absorption of peptides with opioid activity (derived from foods which contain gluten and casein), causing disruption to biochemical and neuroregulatory processes. Biochemical evidence has indicated the presence of increased levels of peptides in the urine of people with autism, and previous behavioural studies have demonstrated a connection between the long term exclusion of gluten and casein from the diet and improvements in the behaviour of some children with autism. The introduction of a gluten-free diet to children with autism and associated spectrum disorders (n = 22) was monitored over a 5 month period using a battery of parental and teacher interview/questionnaire sessions, observation reports, psychometric tests and urinary profiling. Results suggested that participants on a gluten-free diet showed an improvement on a number of behavioural measures. However there was no significant decrease in specific urinary compounds excreted when compared with controls and a gluten challenge group.

keywords autism; diet; gluten; peptides

address Correspondence should be addressed to: paul whiteley or paul shattock, Autism Research Unit, School of Health Sciences, University of Sunderland, Sunderland SR2 7EE, UK



Research article

autism
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Autistic
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The ScanBrit randomised, controlled, single-blind study of a gluten- and casein-free dietary intervention for children with autism spectrum disorders

Paul Whiteley[1], Demetrious Haracopos[2], Ann-Mari Knivsberg[3], Karl Ludvig Reichelt[4], Sarah Parlar[2], Judith Jacobsen[5], Anders Seim[6], Lennart Pedersen[2], Maja Schondel[2], Paul Shattock[1]

[1]Dept of Pharmacy, Health & Well-being, Faculty of Applied Sciences, University of Sunderland, UK
[2]Center for Autisme, Herlev Hovedgade, Herlev, Denmark
[3]National Centre for Reading Education & Research, University of Stavanger, Norway
[4]Department of Pediatric Research, University of Oslo, Rikshospitalet Medical Centre, Norway
[5]Statcon ApS, Kokkedal, Denmark
[6]Fjellstrand, Norway

There is increasing interest in the use of gluten- and casein-free diets for children with autism spectrum disorders (ASDs). We report results from a two-stage, 24-month, randomised, controlled trial incorporating an adaptive 'catch-up' design and interim analysis. Stage 1 of the trial saw 72 Danish children (aged 4 years to 10 years 11 months) assigned to diet (A) or non-diet (B) groups by stratified randomisation. Autism Diagnostic Observation Schedule (ADOS) and the Gilliam Autism Rating Scale (GARS) were used to assess core autism behaviours, Vineland Adaptive Behaviour Scales (VABS) to ascertain developmental level, and Attention-Deficit Hyperactivity Disorder – IV scale (ADHD-IV) to determine inattention and hyperactivity. Participants were tested at baseline, 8, and 12 months. Based on per protocol repeated measures analysis, data for 26 diet children and 29 controls were available at 12 months. At this point, there was a significant improvement to mean diet group scores (time*treatment interaction) on sub-domains of ADOS, GARS and ADHD-IV measures. Surpassing of predefined statistical thresholds as evidence of improvement in group A at 12 months sanctioned the re-assignment of group B participants to active dietary treatment. Stage 2 data for 18 group A and 17 group B participants were available at 24 months. Multiple scenario analysis based on inter- and intra-group comparisons showed some evidence of sustained clinical group improvements although possibly indicative of a plateau effect for intervention. Our results suggest that dietary intervention may positively affect developmental outcome for some children diagnosed with ASD. In the absence of a placebo condition to the current investigation, we are, however, unable to disqualify potential effects derived from intervention outside of dietary changes. Further studies are required to ascertain potential best- and non-responders to intervention. The study was registered with ClinicalTrials.gov, number NCT00614198.

Keywords: autism spectrum disorder (ASD), diet, gluten, casein, randomised controlled trial, adaptive design

Correspondence to: Paul Whiteley, ESPA Research, The Robert Luff Laboratory, Unit 133I Business & Innovation Centre (BIC), Sunderland Enterprise Park, Wearfield, Sunderland SR5 2TA, UK. E-mail: paul.whiteley@espa-research.org.uk

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frontiers in
HUMAN NEUROSCIENCE

REVIEW ARTICLE

Gluten- and casein-free dietary intervention for autism spectrum conditions

Paul Whiteley[1]*, Paul Shattock[1], Ann-Mari Knivsberg[2], Anders Seim[3], Karl L. Reichelt[4], Lynda Todd[1], Kevin Carr[1] and Malcolm Hooper[1]

[1] ESPA Research, The Robert Luff Laboratory, Unit 133I Business and Innovation Centre, Sunderland, UK
[2] National Centre for Reading Education & Research, University of Stavanger, Stavanger, Norway
[3] Fjellstrand, Norway
[4] Department of Pediatric Research, Rikshospitalet Medical Centre, University of Oslo, Oslo, Norway

Edited by:
Mohsen Sharifi, Northumbria University, UK

Reviewed by:
Emily Severance, Johns Hopkins University School of Medicine, USA
Jennifer Daley, University of Phoenix, USA

****Correspondence:***
Paul Whiteley, ESPA Research, The Robert Luff Laboratory, Unit 133I Business and Innovation Centre, Wearfield, Sunderland SR5 2TA, UK.
e-mail: paul.whiteley@espa-research.org.uk

Dietary intervention as a tool for maintaining and improving physical health and wellbeing is a widely researched and discussed topic. Speculation that diet may similarly affect mental health and wellbeing particularly in cases of psychiatric and behavioral symptomatology opens up various avenues for potentially improving quality of life. We examine evidence suggestive that a gluten-free (GF), casein-free (CF), or gluten- and casein-free diet (GFCF) can ameliorate core and peripheral symptoms and improve developmental outcome in some cases of autism spectrum conditions. Although not wholly affirmative, the majority of published studies indicate statistically significant positive changes to symptom presentation following dietary intervention. In particular, changes to areas of communication, attention, and hyperactivity are detailed, despite the presence of various methodological shortcomings. Specific characteristics of best- and non-responders to intervention have not been fully elucidated; neither has the precise mode of action for any universal effect outside of known individual cases of food-related co-morbidity. With the publication of controlled medium- and long-term group studies of a gluten- and casein-free diet alongside more consolidated biological findings potentially linked to intervention, the appearance of a possible diet-related autism phenotype seems to be emerging supportive of a positive dietary effect in some cases. Further debate on whether such dietary intervention should form part of best practice guidelines for autism spectrum conditions (ASCs) and onward representative of an autism dietary-sensitive enteropathy is warranted.

It's difficult and complicated but…

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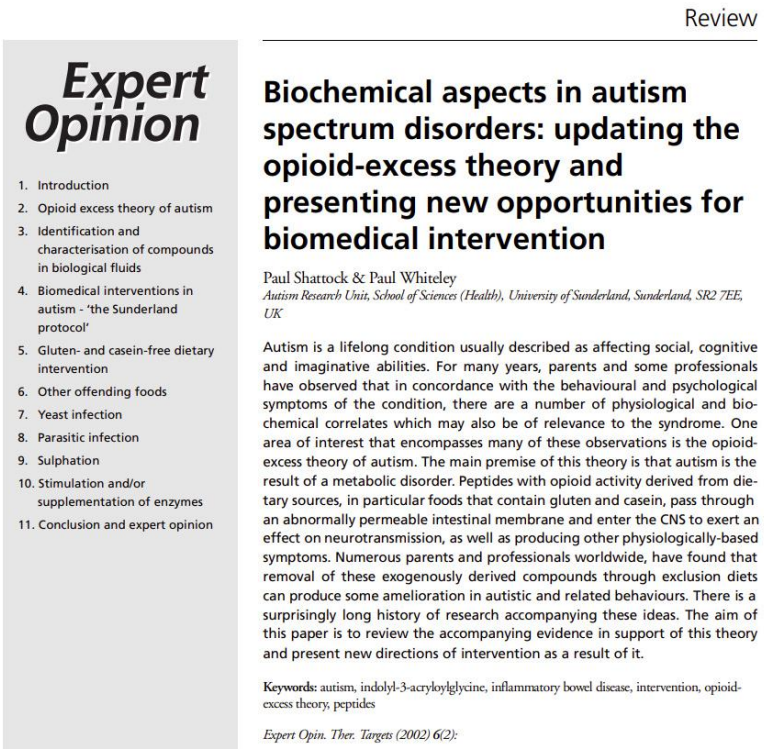
3. Whiteley P, Shattock P, Knivsberg AM, Seim A, Reichelt KL, Todd L, Carr K, Hooper M. Gluten- and casein-free dietary intervention for autism spectrum conditions. Front Hum Neurosci. 2013 Jan 4;6:344. doi: 10.3389/fnhum.2012.00344.

What studying dietary intervention for autism has taught me (3)

- The idea that dietary changes might, for some, affect the presentation of core and/or peripheral signs and symptoms means **we should also focus on functional biology / biochemistry not just genes**…
- **The 'gut-brain' axis** might be particularly important (add in **gut bacteria, yeasts & viruses** and **immune system** too).
- Various mechanisms are probably at work. Moves to 'affect' identified mechanisms might one day mean that removal of dietary components is not required.



Review

Expert Opinion

1. Introduction
2. Opioid excess theory of autism
3. Identification and characterisation of compounds in biological fluids
4. Biomedical interventions in autism - 'the Sunderland protocol'
5. Gluten- and casein-free dietary intervention
6. Other offending foods
7. Yeast infection
8. Parasitic infection
9. Sulphation
10. Stimulation and/or supplementation of enzymes
11. Conclusion and expert opinion

Biochemical aspects in autism spectrum disorders: updating the opioid-excess theory and presenting new opportunities for biomedical intervention

Paul Shattock & Paul Whiteley
Autism Research Unit, School of Sciences (Health), University of Sunderland, Sunderland, SR2 7EE, UK

Autism is a lifelong condition usually described as affecting social, cognitive and imaginative abilities. For many years, parents and some professionals have observed that in concordance with the behavioural and psychological symptoms of the condition, there are a number of physiological and biochemical correlates which may also be of relevance to the syndrome. One area of interest that encompasses many of these observations is the opioid-excess theory of autism. The main premise of this theory is that autism is the result of a metabolic disorder. Peptides with opioid activity derived from dietary sources, in particular foods that contain gluten and casein, pass through an abnormally permeable intestinal membrane and enter the CNS to exert an effect on neurotransmission, as well as producing other physiologically-based symptoms. Numerous parents and professionals worldwide, have found that removal of these exogenously derived compounds through exclusion diets can produce some amelioration in autistic and related behaviours. There is a surprisingly long history of research accompanying these ideas. The aim of this paper is to review the accompanying evidence in support of this theory and present new directions of intervention as a result of it.

Keywords: autism, indolyl-3-acryloylglycine, inflammatory bowel disease, intervention, opioid-excess theory, peptides

Expert Opin. Ther. Targets (2002) 6(2):

1.Shattock P, Whiteley P. Biochemical aspects in autism spectrum disorders: updating the opioid-excess theory and presenting new opportunities for biomedical intervention. Expert Opin Ther Targets. 2002 Apr;6(2):175-83. doi: 10.1517/14728222.6.2.175.

What studying dietary intervention for autism has taught me (4)

Proceedings of the Nutrition Society, Page 1 of 6 doi:10.1017/S0029665117002798

The Joint Winter Meeting between the Nutrition Society and the Royal Society of Medicine held at The Royal Society of Medicine, London on 6–7 December 2016

Conference on 'Diet, nutrition and mental health and wellbeing' Optional symposium

Food and the gut: relevance to some of the autisms

Paul Whiteley
ESPA Research, 2A Hylton Park, Hylton Park Road, Sunderland SR5 3HD, UK

Complex, diverse and rarely appearing without comorbidity, the autism spectrum disorders continue to be a source of research interest. With core symptoms variably impacting on social communication skills, the traditional focus of many research efforts has centred on the brain and how genetic and environmental processes impact on brain structure, function and/or connectivity to account for various behavioural presentations. Alongside emerging ideas on autistic traits being present in various clinical states, the autisms, and the over-representation of several comorbid conditions impacting on quality of life, other research avenues have opened up. The central role of the brain in relation to autism may be at least partially influenced by the functions of other organs. The gastrointestinal (GI) tract represents an important biological system pertinent to at least some autism. The notion of a gut–brain–behaviour axis has garnered support from various findings: an overrepresentation of functional and pathological bowel states, bowel and behavioural findings showing bidirectional associations, a possible relationship between diet, GI function and autism and recently, greater focus on aspects of the GI tract such as the collected gut microbiota in relation to autism. Gaps remain in our knowledge of the functions of the GI tract linked to autism, specifically regarding mechanisms of action onward to behavioural presentation. Set however within the context of diversity in the presentation of autism, science appears to be moving towards defining important GI-related autism phenotypes with the possibility of promising dietary and other related intervention options onward to improving quality of life.

Autism: The autisms: Brain: Comorbidity: Gastrointestinal (GI) tract: Bowel: diet: Gluten: Casein: Milk

Proceedings of the Nutrition Society, Page 1 of 6 doi:10.1017/S0029665114001475

The Nutrition Society Summer Meeting 2014 was held at the University of Glasgow on 14–17 July 2014

Nutritional management of (some) autism: a case for gluten- and casein-free diets?

Paul Whiteley
ESPA Research, 2A Hylton Park, Hylton Park Road, Sunderland SR5 3HD, UK

Autism spectrum disorders represent a diverse and heterogeneous array of conditions unified by the variable presence of specific behaviours impacting social and communicative functions (social affect) alongside other presentation. Common overt characteristics may come about as a consequence of several different genetic and biological processes differentially manifesting across different people or groups. The concept of plural 'autisms' is evolving, strengthened by an increasingly important evidence base detailing different developmental trajectories across the autism spectrum and the appearance of comorbidity variably interacting with core symptoms and onwards influencing quality of life. Reports that dietary intervention, specifically the removal of foods containing gluten and/or casein from the diet, may impact on the presentation of autism for some, complement this plural view of autism. Evidence suggestive of differing responses to the use of a gluten- and casein-free diet, defined as best- and non-response, has combined with some progress on determining the underlying genetic and biological correlates potentially related to such dietary elements. The preliminary suggestion of a possible diet-related autism phenotype is the result. This review will highlight several pertinent aspects onwards to an effect of food in some cases of autism including research on the pharmacological activity of food metabolites, immune response, issues with gut barrier function and some contribution from the gut microbiota. These represent promising areas in need of far greater research inspection in order to potentially define such a diet-related subgroup on the autism spectrum.

Autism spectrum disorder: Diet: Gluten: Casein: Intervention

Food-related phenotypes of autism?

1.Whiteley P. Food and the gut: relevance to some of the autisms. Proc Nutr Soc. 2017 Nov;76(4):478-483. doi: 10.1017/S0029665117002798.
2.Whiteley P. Nutritional management of (some) autism: a case for gluten- and casein-free diets? Proc Nutr Soc. 2015 Aug;74(3):202-7. doi: 10.1017/S0029665114001475.

What studying dietary intervention for autism has taught me (5)

- ‘Best’ & ‘non’ responders to dietary intervention for autism means that **the umbrella label of autism doesn’t necessarily confer universally shared biology**…
- There may be ways to determine **individual response** to intervention through examination of behaviour or…
- Through **the application of metabolomics**.
- “*If you’ve met [the biology of] one autistic person, you’ve met [the biology of] one autistic person*”.
- Oh and dietary intervention ‘for autism’, <u>with the right support</u>, is not inherently unsafe.

Data mining the ScanBrit study of a gluten- and casein-free dietary intervention for children with autism spectrum disorders: Behavioural and psychometric measures of dietary response

Lennart Pedersen[1], Sarah Parlar[1], Kajsa Kvist[2], Paul Whiteley[3], Paul Shattock[3]

[1]Center for Autisme, Herlev Hovedgade 199, 2730 Herlev, Denmark, [2]PFA Pension, Sundkrogsgade 4, 2100 København, Denmark, [3]ESPA Research, The Robert Luff Laboratory, Unit 133i, Business & Innovation Centre (BIC), Sunderland Enterprise Park, Wearfield, Sunderland SR5 2TA, UK

We previously reported results based on the examination of a gluten- and casein-free diet as an intervention for children diagnosed with an autism spectrum disorder as part of the ScanBrit collaboration. Analysis based on grouped results indicated several significant differences between dietary and non-dietary participants across various core and peripheral areas of functioning. Results also indicated some disparity in individual responses to dietary modification potentially indicative of responder and non-responder differences. Further examination of the behavioural and psychometric data garnered from participants was undertaken, with a view to determining potential factors pertinent to response to dietary intervention. Participants with clinically significant scores indicative of inattention and hyperactivity behaviours and who had a significant positive changes to said scores were defined as responders to the dietary intervention. Analyses indicated several factors to be potentially pertinent to a positive response to dietary intervention in terms of symptom presentation. Chronological age was found to be the strongest predictor of response, where those participants aged between 7 and 9 years seemed to derive most benefit from dietary intervention. Further analysis based on the criteria for original study inclusion on the presence of the urine compound, *trans*-indolyl-3-acryloylglycine may also merit further investigation. These preliminary observations on potential best responder characteristics to a gluten- and casein-free diet for children with autism require independent replication.

Keywords: Autism spectrum disorder, Dietary intervention, Gluten, Casein

1.Pedersen L, Parlar S, Kvist K, Whiteley P, Shattock P. Data mining the ScanBrit study of a gluten- and casein-free dietary intervention for children with autism spectrum disorders: behavioural and psychometric measures of dietary response. Nutr Neurosci. 2014 Sep;17(5):207-13. doi: 10.1179/1476830513Y.0000000082.

What studying dietary intervention for autism has taught me (6)

- Not our work but PROSPERO reviews (2022) say yes (x2)…
- "*The results of a meta-analysis suggest that diet therapies can significantly ameliorate core symptoms of ASD, and GFD diets are conducive to improving social behaviors*".
- "*The current meta-analysis showed that a GFCF diet can reduce stereotypical behaviors and improve the cognition of children with ASD*".

SYSTEMATIC REVIEW article

Front. Neurol., 14 March 2022
Sec. Pediatric Neurology
https://doi.org/10.3389/fneur.2022.844117

Efficacy and Safety of Diet Therapies in Children With Autism Spectrum Disorder: A Systematic Literature Review and Meta-Analysis

Yuping Yu[1,2†], Jinyue Huang[2,3†], Xiaofang Chen[1,2†], Jia Fu[1,2†], Xinhui Wang[1,2], Linjie Pu[1,2], Chunyu Gu[1,2] and Chunquan Cai[2,3,4,5*]

[1] Graduate College of Tianjin Medical University, Tianjin, China
[2] Tianjin Children's Hospital (Children's Hospital of Tianjin University), Tianjin, China
[3] Tianjin Pediatric Research Institute, Tianjin, China
[4] Tianjin Key Laboratory of Birth Defects for Prevention and Treatment, Tianjin, China
[5] Department of Neurosurgery, Tianjin Children's Hospital, Tianjin, China

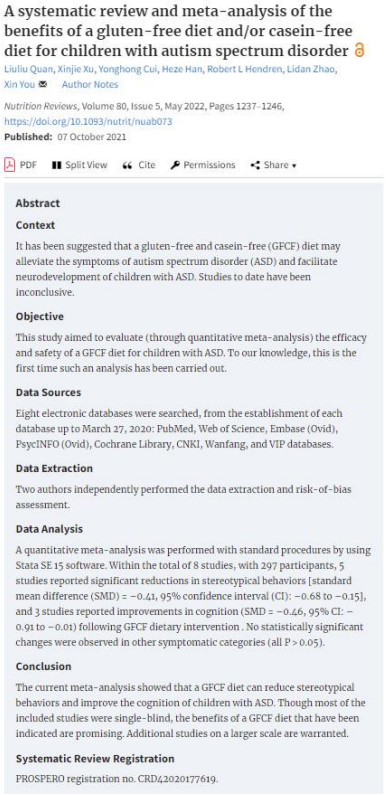
Objective: Autism Spectrum Disorder is a neurodevelopmental disorder, with a rapid increase in recognition over the past decade. Interest in alternative therapies is growing annually, such as dietary therapies including gluten-free and/or casein-free diet, and the ketogenic diet. However, there is no consensus on the efficacy and safety of dietary therapy in children with ASD up to now. This study aimed to assess the efficacy and safety of these diet interventions for children with ASD based on a meta-analysis of global data.

Methods: Seven databases (Cochrane Library, PubMed, EMBASE, Web of Science, VIP, CNKI, and Wanfang) were searched according to the established inclusion criteria, from the inception of the databases to August 18, 2021. The Cochrane Bias risk assessment tool was intended to assess the quality of the included studies. Review Manager 5.4 software was used as an efficacy analysis tool of the included studies, taking the core autistic symptoms and scales of ASD as therapeutic efficacy evaluations.

Results: In total, 7 RCTs with 338 participants were finally obtained. All studies assessed the association between core autistic symptoms and therapeutic diet, showing a statistically significant effect (standard mean difference (SMD) of −0.51, 95% confidence interval (CI): −0.81 to −0.21), in which two studies which followed the GFD diet reported significant reductions in social behaviors (SMD of−0.41, 95% CI: −0.75 to −0.06), showing no correlation with the length of the interventions ($P < 0.05$). Two studies were performed in KD diet suggested a significant effect in core symptoms (SMD of −0.67, 95% CI: −1.04 to −0.31). No statistically significant changes were observed in the GFCF diet, GFD diet, cognition, communication, and stereotypical behaviors subgroups (all $P > 0.05$).

Conclusion: The results of a meta-analysis suggest that diet therapies can significantly ameliorate core symptoms of ASD, and GFD diets are conducive to improving social behaviors. Although the results suggest the effectiveness of dietary therapy for ASD, limited by the small sample size of RCTs, more well-designed, and high-quality clinical trials are needed to validate the above conclusions.

Systematic Review Registration: https://www.crd.york.ac.uk/PROSPERO/, identifier: CRD42021277565.



A systematic review and meta-analysis of the benefits of a gluten-free diet and/or casein-free diet for children with autism spectrum disorder

Liuliu Quan, Xinjie Xu, Yonghong Cui, Heze Han, Robert L Hendren, Lidan Zhao, Xin You ✉ Author Notes

Nutrition Reviews, Volume 80, Issue 5, May 2022, Pages 1237–1246,
https://doi.org/10.1093/nutrit/nuab073
Published: 07 October 2021

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Abstract

Context

It has been suggested that a gluten-free and casein-free (GFCF) diet may alleviate the symptoms of autism spectrum disorder (ASD) and facilitate neurodevelopment of children with ASD. Studies to date have been inconclusive.

Objective

This study aimed to evaluate (through quantitative meta-analysis) the efficacy and safety of a GFCF diet for children with ASD. To our knowledge, this is the first time such an analysis has been carried out.

Data Sources

Eight electronic databases were searched, from the establishment of each database up to March 27, 2020: PubMed, Web of Science, Embase (Ovid), PsycINFO (Ovid), Cochrane Library, CNKI, Wanfang, and VIP databases.

Data Extraction

Two authors independently performed the data extraction and risk-of-bias assessment.

Data Analysis

A quantitative meta-analysis was performed with standard procedures by using Stata SE 15 software. Within the total of 8 studies, with 297 participants, 5 studies reported significant reductions in stereotypical behaviors [standard mean difference (SMD) = −0.41, 95% confidence interval (CI): −0.68 to −0.15], and 3 studies reported improvements in cognition (SMD = −0.46, 95% CI: −0.91 to −0.01) following GFCF dietary intervention . No statistically significant changes were observed in other symptomatic categories (all $P > 0.05$).

Conclusion

The current meta-analysis showed that a GFCF diet can reduce stereotypical behaviors and improve the cognition of children with ASD. Though most of the included studies were single-blind, the benefits of a GFCF diet that have been indicated are promising. Additional studies on a larger scale are warranted.

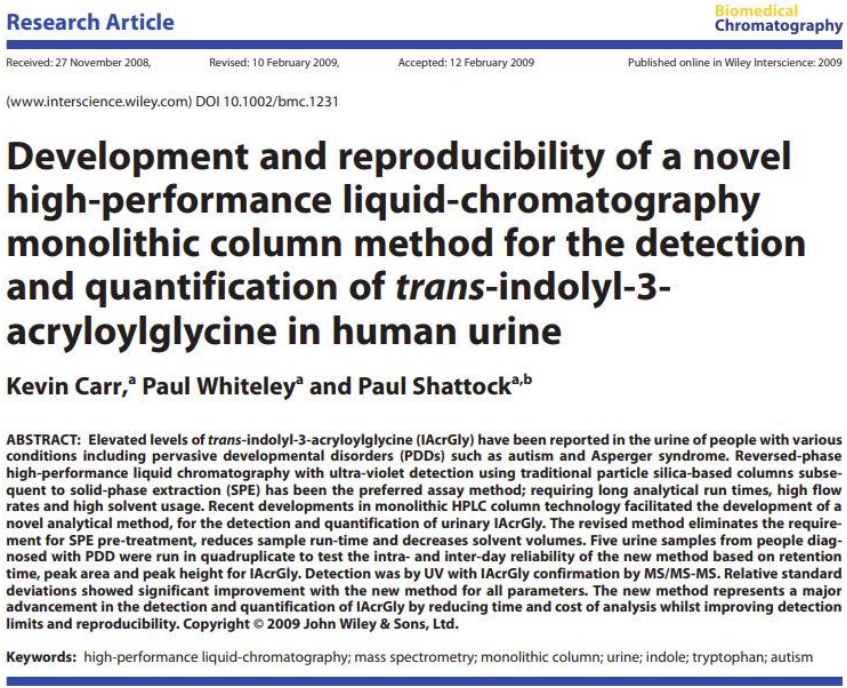
Systematic Review Registration

PROSPERO registration no. CRD42020177619.

1.Yu Y, Huang J, Chen X, Fu J, Wang X, Pu L, Gu C, Cai C. Efficacy and Safety of Diet Therapies in Children With Autism Spectrum Disorder: A Systematic Literature Review and Meta-Analysis. Front Neurol. 2022 Mar 14;13:844117.
2.Quan L, Xu X, Cui Y, Han H, Hendren RL, Zhao L, You X. A systematic review and meta-analysis of the benefits of a gluten-free diet and/or casein-free diet for children with autism spectrum disorder. Nutr Rev. 2022 Apr 8;80(5):1237-1246.

Enter metabolomics & individualised autism science (1)

- Metabolomics: **the study of low molecular weight metabolites** (in urine and/or blood for example), **their changes over time** and **their relevance to health and wellbeing**.
- Kinda started with ‘sweet urine disease’: ants tasting urine to measure urinary sugar content.
- Fast forward a few thousand years: **technology is key** (separation, detection, identification, data mining). Mass spec / NMR = gold standards.
- Autism is ripe for metabolomics study: *e.g.* **potential biomarkers for early diagnosis** and/or **predicting intervention responses**.



Research Article

Biomedical Chromatography

Received: 27 November 2008, Revised: 10 February 2009, Accepted: 12 February 2009 Published online in Wiley Interscience: 2009

(www.interscience.wiley.com) DOI 10.1002/bmc.1231

Development and reproducibility of a novel high-performance liquid-chromatography monolithic column method for the detection and quantification of *trans*-indolyl-3-acryloylglycine in human urine

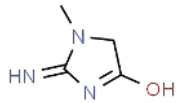
Kevin Carr,[a] Paul Whiteley[a] and Paul Shattock[a,b]

ABSTRACT: Elevated levels of *trans*-indolyl-3-acryloylglycine (IAcrGly) have been reported in the urine of people with various conditions including pervasive developmental disorders (PDDs) such as autism and Asperger syndrome. Reversed-phase high-performance liquid chromatography with ultra-violet detection using traditional particle silica-based columns subsequent to solid-phase extraction (SPE) has been the preferred assay method; requiring long analytical run times, high flow rates and high solvent usage. Recent developments in monolithic HPLC column technology facilitated the development of a novel analytical method, for the detection and quantification of urinary IAcrGly. The revised method eliminates the requirement for SPE pre-treatment, reduces sample run-time and decreases solvent volumes. Five urine samples from people diagnosed with PDD were run in quadruplicate to test the intra- and inter-day reliability of the new method based on retention time, peak area and peak height for IAcrGly. Detection was by UV with IAcrGly confirmation by MS/MS-MS. Relative standard deviations showed significant improvement with the new method for all parameters. The new method represents a major advancement in the detection and quantification of IAcrGly by reducing time and cost of analysis whilst improving detection limits and reproducibility. Copyright © 2009 John Wiley & Sons, Ltd.

Keywords: high-performance liquid-chromatography; mass spectrometry; monolithic column; urine; indole; tryptophan; autism

1.Carr K, Whiteley P, Shattock P. Development and reproducibility of a novel high-performance liquid-chromatography monolithic column method for the detection and quantification of trans-indolyl-3-acryloylglycine in human urine. Biomed Chromatogr. 2009 Oct;23(10):1108-15.

Enter metabolomics & individualised autism science (2)



- Already some clues emerging about what sort of metabolites might be important to autism.
- 'Details' are key. Our findings related to **urinary creatinine measurements in autism** suggested even basic measures might show important differences[1].
- Creatinine = key metabolite used to correct for urinary concentration (among other things).
- We, and others[2], reported **a significantly lower creatinine concentration** in the urine of those with autism vs. non-autistic controls.

Pediatrics International (2006) **48**, 292–297 doi: 10.1111/j.1442-200X.2006.02207.x

Original Article

Spot urinary creatinine excretion in pervasive developmental disorders

PAUL WHITELEY,[1] ROSEMARY WARING,[2] LEE WILLIAMS,[3] LIBUSE KLOVRZA,[2] FRANCES NOLAN,[4] SUSAN SMITH,[4] MALCOLM FARROW,[5] KALLIOPI DODOU,[3] W. JOHN LOUGH[3] AND PAUL SHATTOCK[1]

[1]*Autism Research Unit, School of Health, Natural & Social Sciences and* [3]*The Sunderland Pharmacy School, University of Sunderland, Sunderland,* [2]*School of Biosciences, University of Birmingham, Birmingham,* [4]*Green Lanes Surgery, Winchmore Hill, London and* [5]*School of Mathematics & Statistics, University of Newcastle Upon Tyne, Newcastle Upon Tyne, UK*

Abstract

Background: Excretion of creatinine in urine represents the end-point of endogenous energy transfer from stored adenosine triphosphate in skeletal and cardiac muscle. Measurement of urinary creatinine is commonly used to correct for total urine concentration. Various quantitative measures of compounds suspected to be either pathological to, or indicative of, possible therapeutic interventions for Pervasive Developmental Disorders (PDD) have relied extensively on spot creatinine as a ratio quantity, although this important metabolite has not been exclusively studied within this population.

Methods: Levels of urinary creatinine in spot urine samples were analyzed for a group of children diagnosed with PDD ($n = 24$; median age, 75 months; range, 39–137 months) and a control group ($n = 50$; median age, 109 months; range, 59–140 months). Diagnosis of PDD was confirmed using the Autism Diagnostic Interview–Revised. Samples were collected and analyzed blind for creatinine content using an improved Jaffe's reaction method.

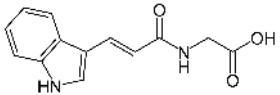
Results: Controlling for sample pH and body mass index, a significant decrease in urinary creatinine concentration was found in the PDD group compared to controls using a Mann–Whitney two-tailed ranks test ($P = 0.001$).

Conclusion: Further studies of protein catabolism and renal function in autism are required to ascertain the relevance of decreased spot urinary creatinine excretion identified in this preliminary study. Issues regarding the use of single urine creatinine measurements and associated confounding variables are discussed in light of the findings, together with recommendations to use other internal or external standards for the quantification of urinary compounds in PDD research.

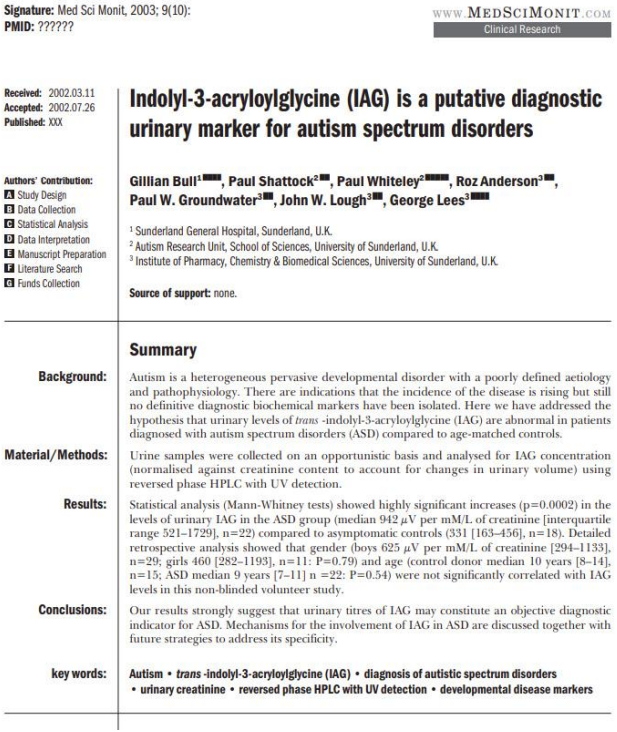
Key words adenosine triphosphate, autism, body mass index, creatinine, pervasive developmental disorder, renal function, urine.

1. Whiteley P, Waring R, Williams L, Klovrza L, Nolan F, Smith S, Farrow M, Dodou K, Lough WJ, Shattock P. Spot urinary creatinine excretion in pervasive developmental disorders. Pediatr Int. 2006 Jun;48(3):292-7. doi: 10.1111/j.1442-200X.2006.02207.x.
2. Lussu M, Noto A, Masili A, Rinaldi AC, Dessì A, De Angelis M, De Giacomo A, Fanos V, Atzori L, Francavilla R. The urinary 1 H-NMR metabolomics profile of an italian autistic children population and their unaffected siblings. Autism Res. 2017 Jun;10(6):1058-1066. doi: 10.1002/aur.1748.

Enter metabolomics & individualised autism science (3)



- But the research road is bumpy.
- Some initial ‘excitement’ that IAG (a metabolite of the amino acid tryptophan) might have some biomarker potential for autism[1].
- Alas, independent studies were not totally confirmatory (although did stress **a possible connection between ‘GI-autism’[2] and levels of IAG**).
- IAG still may have a role to play in relation to **intestinal hyperpermeability (‘leaky gut’)** in autism and other labels and response to GF diet.



Signature: Med Sci Monit, 2003; 9(10):
PMID: ??????

WWW.MEDSCIMONIT.COM
Clinical Research

Received: 2002.03.11
Accepted: 2002.07.26
Published: XXX

Indolyl-3-acryloylglycine (IAG) is a putative diagnostic urinary marker for autism spectrum disorders

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

Gillian Bull[1], Paul Shattock[2], Paul Whiteley[2], Roz Anderson[2], Paul W. Groundwater[3], John W. Lough[3], George Lees[3]

[1] Sunderland General Hospital, Sunderland, U.K.
[2] Autism Research Unit, School of Sciences, University of Sunderland, U.K.
[3] Institute of Pharmacy, Chemistry & Biomedical Sciences, University of Sunderland, U.K.

Source of support: none.

Summary

Background: Autism is a heterogeneous pervasive developmental disorder with a poorly defined aetiology and pathophysiology. There are indications that the incidence of the disease is rising but still no definitive diagnostic biochemical markers have been isolated. Here we have addressed the hypothesis that urinary levels of *trans* -indolyl-3-acryloylglycine (IAG) are abnormal in patients diagnosed with autism spectrum disorders (ASD) compared to age-matched controls.

Material/Methods: Urine samples were collected on an opportunistic basis and analysed for IAG concentration (normalised against creatinine content to account for changes in urinary volume) using reversed phase HPLC with UV detection.

Results: Statistical analysis (Mann-Whitney tests) showed highly significant increases (p=0.0002) in the levels of urinary IAG in the ASD group (median 942 μV per mM/L of creatinine [interquartile range 521–1729], n=22) compared to asymptomatic controls (331 [163–456], n=18). Detailed retrospective analysis showed that gender (boys 625 μV per mM/L of creatinine [294–1133], n=29; girls 460 [282–1193], n=11: P=0.79) and age (control donor median 10 years [8–14], n=15; ASD median 9 years [7–11] n =22: P=0.54) were not significantly correlated with IAG levels in this non-blinded volunteer study.

Conclusions: Our results strongly suggest that urinary titres of IAG may constitute an objective diagnostic indicator for ASD. Mechanisms for the involvement of IAG in ASD are discussed together with future strategies to address its specificity.

key words: **Autism • *trans* -indolyl-3-acryloylglycine (IAG) • diagnosis of autistic spectrum disorders • urinary creatinine • reversed phase HPLC with UV detection • developmental disease markers**

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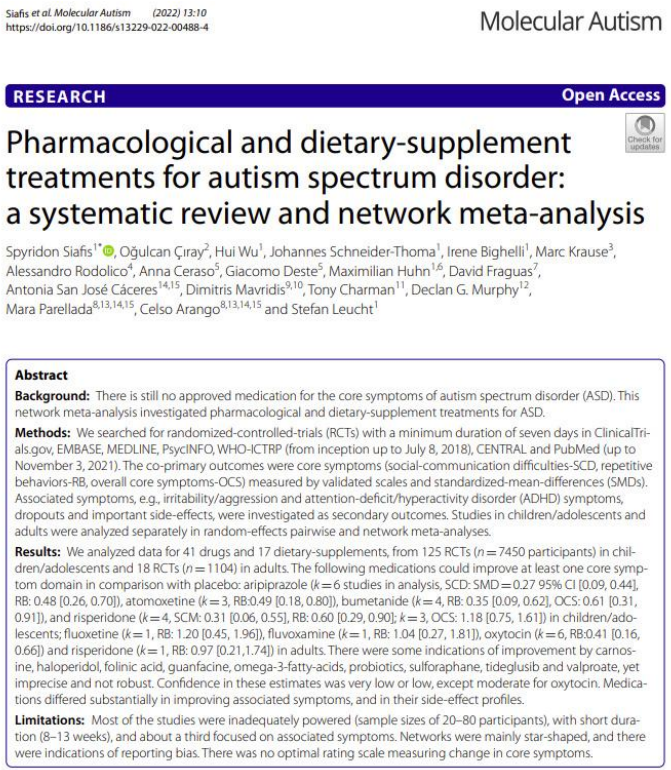
2. Wang L, Angley MT, Gerber JP, Young RL, Abarno DV, McKinnon RA, Sorich MJ. Is urinary indolyl-3-acryloylglycine a biomarker for autism with gastrointestinal symptoms? Biomarkers. 2009 Dec;14(8):596-603. doi: 10.3109/13547500903183962. PMID: 19697973.

Enter metabolomics & individualised autism science (4)

- The research journey is still continuing.
- Focus on the use of q-ToF (quadrupole Time of Flight) mass spectrometry (gold standard).
- Currently screening multiple candidate compounds across hundreds of biological samples.
- Results pending with more projects planned (subject to funding). And if you wish to donate…

Enter metabolomics & individualised autism science (5)

- Another ‘not our work paper’.
- More PROSPERO registered evidence.
- “*Some medications could improve core symptoms, although this could be likely secondary to the improvement of associated symptoms.*”
- Whole slew of different compounds *e.g.* “*... some indications of improvement by carnosine,... folinic acid, guanfacine, omega-3-fatty-acids, probiotics, sulforaphane.*”
- **Personalised testing to determine which compound is for which person / ‘autisms’**.
- Not every compound will be helpful for everyone.



Siafis et al. Molecular Autism (2022) 13:10
https://doi.org/10.1186/s13229-022-00488-4

Molecular Autism

RESEARCH Open Access

Pharmacological and dietary-supplement treatments for autism spectrum disorder: a systematic review and network meta-analysis

Spyridon Siafis[1*], Oğulcan Çıray[2], Hui Wu[1], Johannes Schneider-Thoma[1], Irene Bighelli[1], Marc Krause[3], Alessandro Rodolico[4], Anna Ceraso[5], Giacomo Deste[5], Maximilian Huhn[1,6], David Fraguas[7], Antonia San José Cáceres[14,15], Dimitris Mavridis[9,10], Tony Charman[11], Declan G. Murphy[12], Mara Parellada[8,13,14,15], Celso Arango[8,13,14,15] and Stefan Leucht[1]

Abstract

Background: There is still no approved medication for the core symptoms of autism spectrum disorder (ASD). This network meta-analysis investigated pharmacological and dietary-supplement treatments for ASD.

Methods: We searched for randomized-controlled-trials (RCTs) with a minimum duration of seven days in ClinicalTrials.gov, EMBASE, MEDLINE, PsycINFO, WHO-ICTRP (from inception up to July 8, 2018), CENTRAL and PubMed (up to November 3, 2021). The co-primary outcomes were core symptoms (social-communication difficulties-SCD, repetitive behaviors-RB, overall core symptoms-OCS) measured by validated scales and standardized-mean-differences (SMDs). Associated symptoms, e.g., irritability/aggression and attention-deficit/hyperactivity disorder (ADHD) symptoms, dropouts and important side-effects, were investigated as secondary outcomes. Studies in children/adolescents and adults were analyzed separately in random-effects pairwise and network meta-analyses.

Results: We analyzed data for 41 drugs and 17 dietary-supplements, from 125 RCTs ($n = 7450$ participants) in children/adolescents and 18 RCTs ($n = 1104$) in adults. The following medications could improve at least one core symptom domain in comparison with placebo: aripiprazole ($k = 6$ studies in analysis, SCD: SMD = 0.27 95% CI [0.09, 0.44], RB: 0.48 [0.26, 0.70]), atomoxetine ($k = 3$, RB:0.49 [0.18, 0.80]), bumetanide ($k = 4$, RB: 0.35 [0.09, 0.62], OCS: 0.61 [0.31, 0.91]), and risperidone ($k = 4$, SCM: 0.31 [0.06, 0.55], RB: 0.60 [0.29, 0.90]; $k = 3$, OCS: 1.18 [0.75, 1.61]) in children/adolescents; fluoxetine ($k = 1$, RB: 1.20 [0.45, 1.96]), fluvoxamine ($k = 1$, RB: 1.04 [0.27, 1.81]), oxytocin ($k = 6$, RB:0.41 [0.16, 0.66]) and risperidone ($k = 1$, RB: 0.97 [0.21,1.74]) in adults. There were some indications of improvement by carnosine, haloperidol, folinic acid, guanfacine, omega-3-fatty-acids, probiotics, sulforaphane, tideglusib and valproate, yet imprecise and not robust. Confidence in these estimates was very low or low, except moderate for oxytocin. Medications differed substantially in improving associated symptoms, and in their side-effect profiles.

Limitations: Most of the studies were inadequately powered (sample sizes of 20–80 participants), with short duration (8–13 weeks), and about a third focused on associated symptoms. Networks were mainly star-shaped, and there were indications of reporting bias. There was no optimal rating scale measuring change in core symptoms.

1. Siafis S, Çıray O, Wu H, Schneider-Thoma J, Bighelli I, Krause M, Rodolico A, Ceraso A, Deste G, Huhn M, Fraguas D, San José Cáceres A, Mavridis D, Charman T, Murphy DG, Parellada M, Arango C, Leucht S. Pharmacological and dietary-supplement treatments for autism spectrum disorder: a systematic review and network meta-analysis. Mol Autism. 2022 Mar 4;13(1):10. doi: 10.1186/s13229-022-00488-4.

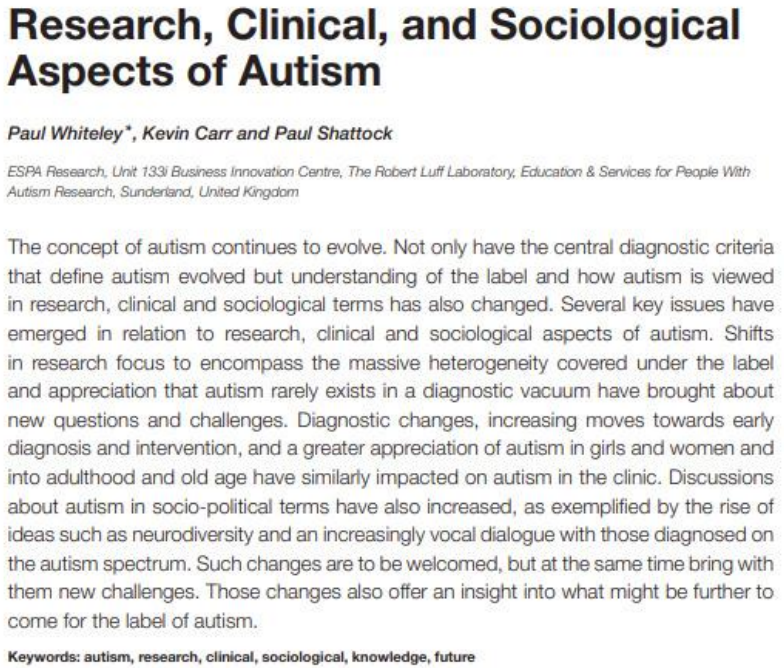
Conclusions

1. The concept of the **plural ‘autisms’** is starting to become a clinical reality.
2. There are seemingly **many routes to a diagnosis of autism or ‘autisms’**.
3. There are **complicated relationships between autism and diet**.
    a. GF/CF diets can seemingly affect the presentation of autism for some people.
    b. Biology can therefore affect psychology and behaviour.
    c. Best and non-responders to diet means different biology within autism too.
4. **Metabolomics offers a way to study that (individual/phenotype) biology**.
5. Promising biomarker candidates for autism already identified.
6. More study = more results to come.

And finally: science doesn't happen in a vacuum…

- Not everyone will be enamoured by this kind of research agenda and that's OK.
- Evidence-based science is the key.
- **A diagnosis of autism is not the finishing line** (lessons from the plural 'autisms').
- Stay curious: ask 'why?' and 'how?'
- "***If you've met [the biology of] one autistic person, you've met [the biology of] one autistic person***".

Thank you.



Research, Clinical, and Sociological Aspects of Autism

Paul Whiteley*, Kevin Carr and Paul Shattock

ESPA Research, Unit 133i Business Innovation Centre, The Robert Luff Laboratory, Education & Services for People With Autism Research, Sunderland, United Kingdom

The concept of autism continues to evolve. Not only have the central diagnostic criteria that define autism evolved but understanding of the label and how autism is viewed in research, clinical and sociological terms has also changed. Several key issues have emerged in relation to research, clinical and sociological aspects of autism. Shifts in research focus to encompass the massive heterogeneity covered under the label and appreciation that autism rarely exists in a diagnostic vacuum have brought about new questions and challenges. Diagnostic changes, increasing moves towards early diagnosis and intervention, and a greater appreciation of autism in girls and women and into adulthood and old age have similarly impacted on autism in the clinic. Discussions about autism in socio-political terms have also increased, as exemplified by the rise of ideas such as neurodiversity and an increasingly vocal dialogue with those diagnosed on the autism spectrum. Such changes are to be welcomed, but at the same time bring with them new challenges. Those changes also offer an insight into what might be further to come for the label of autism.

Keywords: autism, research, clinical, sociological, knowledge, future

1. Whiteley P, Carr K, Shattock P. Research, Clinical, and Sociological Aspects of Autism. Front Psychiatry. 2021 Apr 29;12:481546. doi: 10.3389/fpsyt.2021.481546.

Plural ‘autisms’ and the promises of autism metabolomics.

Paul Whiteley PhD, ESPA Research, UK

paul.whiteley@espa-research.org.uk

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