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### Literature search results

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#### Search details

Children, autism and secondary dysautonomia. Etiology.

#### Resources searched

NHS Evidence; TRIP Database; Cochrane Library; CINAHL; EMBASE; MEDLINE

**Database search terms:**
- exp AUTISTIC DISORDER, (autism OR autistic), (child* OR "young person" OR "young people" OR paediatric* OR pediatric*), exp CHILD, exp ADOLESCENT, adolescen*, "young adult*", exp YOUNG ADULT, exp PEDIATRICS, infant*, etiolog*, aetiology*, exp ETIOLOGY, dysautonomia, exp DYSAUTONOMIA, "autonomic dysfuntion", "autonomic nervous system", malfunction, dysfunction

#### Guidelines and Policy

Nothing found

#### Evidence-based reviews

Nothing found

#### Published research – Databases

**Abnormal autonomic and associated brain activities during rest in autism spectrum disorder.**

**Author(s)** Eilam-Stock T, Xu P, Cao M, Gu X, Van Dam NT, Anagnostou E.
Autism spectrum disorders are associated with social and emotional deficits, the aetiology of which are not well understood. A growing consensus is that the autonomic nervous system serves a key role in emotional processes, by providing physiological signals essential to subjective states. We hypothesized that altered autonomic processing is related to the socio-emotional deficits in autism spectrum disorders. Here, we investigated the relationship between non-specific skin conductance response, an objective index of sympathetic neural activity, and brain fluctuations during rest in high-functioning adults with autism spectrum disorder relative to neurotypical controls. Compared with control participants, individuals with autism spectrum disorder showed less skin conductance responses overall. They also showed weaker correlations between skin conductance responses and frontal brain regions, including the anterior cingulate and anterior insular cortices. Additionally, skin conductance responses were found to have less contribution to default mode network connectivity in individuals with autism spectrum disorders relative to controls. These results suggest that autonomic processing is altered in autism spectrum disorders, which may be related to the abnormal socio-emotional behaviours that characterize this condition.

Source: Medline
Available in fulltext from Brain at Free Access Content

Atypical pupillary light reflex and heart rate variability in children with autism spectrum disorder.

Author(s) Daluwatte C, Miles JH, Christ SE, Beversdorf DQ, Takahashi TN, Yao G

Citation: Journal of Autism & Developmental Disorders, August 2013, vol./is. 43/8(1910-25), 0162-3257;1573-3432 (2013 Aug)

Publication Date: August 2013

Abstract: We investigated pupillary light reflex (PLR) in 152 children with ASD, 116 typically developing (TD) children, and 36 children with non-ASD neurodevelopmental disorders (NDDs). Heart rate variability (HRV) was measured simultaneously to study potential impairments in the autonomic nervous system (ANS) associated with ASD. The results showed that the ASD group had significantly longer PLR latency, reduced relative constriction amplitude, and shorter constriction/redilation time than those of the TD group. Similar atypical PLR parameters were observed in the NDD group. A significant age effect on PLR latency was observed in children younger than 9 years in the TD group, but not in the ASD and NDD groups. Atypical HRV parameters were observed in the ASD and NDD groups. A significant negative correlation existed between the PLR constriction amplitude and average heart rate in children with an ASD, but not in children with typical development.

Source: Medline

Investigating the autonomic nervous system response to anxiety in children with autism spectrum disorders.

Author(s) Kushki A, Drumm E, Pla Mobarak M, Tanel N, Dupuis A, Chau T, Anagnostou E

Citation: PLoS ONE [Electronic Resource], 2013, vol./is. 8/4(e59730), 1932-6203;1932-6203 (2013)

Publication Date: 2013
Abstract: Assessment of anxiety symptoms in autism spectrum disorders (ASD) is a challenging task due to the symptom overlap between the two conditions as well as the difficulties in communication and awareness of emotions in ASD. This motivates the development of a physiological marker of anxiety in ASD that is independent of language and does not require observation of overt behaviour. In this study, we investigated the feasibility of using indicators of autonomic nervous system (ANS) activity for this purpose. Specially, the objectives of the study were to 1) examine whether or not anxiety causes significant measurable changes in indicators of ANS in an ASD population, and 2) characterize the pattern of these changes in ASD. We measured three physiological indicators of the autonomic nervous system response (heart rate, electrodermal activity, and skin temperature) during a baseline (movie watching) and anxiety condition (Stroop task) in a sample of typically developing children (n = 17) and children with ASD (n = 12). The anxiety condition caused significant changes in heart rate and electrodermal activity in both groups, however, a differential pattern of response was found between the two groups. In particular, the ASD group showed elevated heart rate during both baseline and anxiety conditions. Elevated and blunted phasic electrodermal activity were found in the ASD group during baseline and anxiety conditions, respectively. Finally, the ASD group did not show the typical decrease in skin temperature in response to anxiety. These results suggest that 1) signals of the autonomic nervous system may be used as indicators of anxiety in children with ASD, and 2) ASD may be associated with an atypical autonomic response to anxiety that is most consistent with sympathetic over-arousal and parasympathetic under-arousal.

Source: Medline
Available in fulltext from PLoS ONE at EBSCOhost
Available in fulltext at PLoS One; Collection notes: On first login to a ProQuest journal you will need to select 'Athens (OpenAthens Federation)' from Select Region, and then 'NHS England' from Choose your Library.

Highlights in clinical autonomic neuroscience: new insights into autonomic dysfunction in autism.
Author(s) Cheshire WP
Citation: Autonomic Neuroscience-Basic & Clinical, November 2012, vol./is. 171/1-2(4-7), 1566-0702;1872-7484 (2012 Nov 2)
Publication Date: November 2012
Abstract: Investigations of autonomic nervous system biomarkers in autism have been sparse relative to its prevalence. Recent studies of children with autism spectrum disorders (ASD) have increasingly drawn correlations between autonomic findings and psychosocial behavior. Studies of heart rate variability, pupil size, salivary alpha-amylase, and electrodermal responsiveness have shown that children with ASD differ from normally developing children in their autonomic responsiveness to visualizing human faces and other mental tasks. While some results have conflicted, much of the data appears to support the theory of a hypersympathetic state in autism insufficiently attenuated by vagal parasympathetic influences. To what degree these differences in autonomic physiology might influence cognitive processing and behavior rather than simply being epiphenomena of a pervasive disorder of brain development is as yet unclear.
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Source: Medline

Author(s) Ming X, Bain JM, Smith D, Brimacombe M, Gold von-Simson G, Axelrod FB
Abstract: As a screening tool to identify symptoms of autonomic dysfunction, the Pediatric Autonomic Symptoms Scale was administered to parents of children with familial dysautonomia, autism spectrum disorders, and age-matched controls. The total scores for the presence of symptoms were compared among the 3 groups for each section and overall. The Pediatric Autonomic Symptoms Scale distinguished controls from children with familial dysautonomia and autism spectrum disorders with scores from each section and overall scores. Familial dysautonomia children scored significantly higher in visceral symptoms, while children with autism spectrum disorders scored significantly higher in psychosocial symptoms. In familial dysautonomia, the concordance for the presence of symptoms within sections and overall scores ranged from 71% to 100%. The concordance for absence of autonomic dysfunction symptoms in controls ranged from 75% to 87.5%. The Pediatric Autonomic Symptoms Scale is comprehensive and can profile autonomic dysfunction in the 2 neurodevelopmental disorders. Its usefulness in other pediatric disorders remains to be studied.

Source: Medline

Assessing autonomic dysfunction symptoms in children: A pilot study
Author(s) Ming X., Bain J.M., Smith D., Brimacombe M., Gold Von-Simson G., Axelrod F.B.
Citation: Journal of Child Neurology, April 2011, vol./is. 26/4(420-427), 0883-0738;1708-8283 (April 2011)
Publication Date: April 2011
Abstract: As a screening tool to identify symptoms of autonomic dysfunction, the Pediatric Autonomic Symptoms Scale was administered to parents of children with familial dysautonomia, autism spectrum disorders, and age-matched controls. The total scores for the presence of symptoms were compared among the 3 groups for each section and overall. The Pediatric Autonomic Symptoms Scale distinguished controls from children with familial dysautonomia and autism spectrum disorders with scores from each section and overall scores. Familial dysautonomia children scored significantly higher in visceral symptoms, while children with autism spectrum disorders scored significantly higher in psychosocial symptoms. In familial dysautonomia, the concordance for the presence of symptoms within sections and overall scores ranged from 71% to 100%. The concordance for absence of autonomic dysfunction symptoms in controls ranged from 75% to 87.5%. The Pediatric Autonomic Symptoms Scale is comprehensive and can profile autonomic dysfunction in the 2 neurodevelopmental disorders. Its usefulness in other pediatric disorders remains to be studied. 2011 The Author(s).
Source: EMBASE

Dysautonomia in autism spectrum disorder: case reports of a family with review of the literature.
Author(s) Lonsdale D, Shamberger RJ, Obrenovich ME
Citation: Autism Research & Treatment Print, 2011, vol./is. 2011/(129795), 2090-1933;2090-1933 (2011)
Publication Date: 2011
Abstract: Case histories of a mother and her two children are reported. The mother was a recovered alcoholic. She and her two children, both of whom had symptoms that are typical of autistic spectrum disorder, had dysautonomia. All had intermittently abnormal erythrocyte transketolase studies indicating abnormal
thiamine pyrophosphate homeostasis. Both children had unusual concentrations of urinary arsenic. All had symptomatic improvement with diet restriction and supplementary vitamin therapy but quickly relapsed after ingestion of sugar, milk, or wheat. The stress of a heavy metal burden, superimposed on existing genetic or epigenetic risk factors, may be important in the etiology of autism spectrum disorder when in combination. Dysautonomia has been associated with several diseases, including autism, without a common etiology. It is hypothesized that oxidative stress results in loss of cellular energy and causes retardation of hard wiring of the brain in infancy, affecting limbic system control of the autonomic nervous system.

**Source:** Medline
Available in fulltext from Autism Research and Treatment at Directory of Open Access Journals

**Autism from a biometric perspective.**

**Author(s)** Kostyuk N, Rajnarayanan RV, Isokpehi RD, Cohly HH

**Citation:** International Journal of Environmental Research & Public Health [Electronic Resource], May 2010, vol./is. 7/5(1984-95), 1660-4601; 1660-4601 (2010 May)

**Publication Date:** May 2010

**Abstract:** PURPOSE: The aim of this pilot study was to test autistic children, siblings and their parents using a biometric device based on the gas discharge visualization (GDV) technique in order to assess their psycho-emotional and physiological functional state based on the activity of the autonomic nervous system.HYPOTHESIS: We hypothesize that the biometric assessment based on GDV will enable us: (1) to evaluate some specific features associated with autism spectrum disorder (ASD) as well as to compare autistic children to their siblings and to controls; (2) to analyze the differences in individual values of parents of autistic children versus parents of normal children.RESULTS: Out of total of 48 acupuncture points present on ten fingertips of both hands and associated to organs/organ systems, autistic children differed significantly from controls (p < 0.05) in 36 (images without filter) and 12 (images with filter), siblings differed significantly from controls (p < 0.05) in 12 (images without filter) and seven (images with filter), autistic children differed significantly (p < 0.05) from siblings in eight (images without filter) and one (images with filter), fathers of autistic children differed significantly (p < 0.05) from controls in 14 (images without filter) and three (images with filter) and mothers of autistic children differed significantly (p < 0.05) from controls in five (images without filter) and nine (images with filter) acupuncture points.CONCLUSIONS: All compared groups have shown significant difference on both psycho-emotional (images without filter) and physiological (images with filter) levels. However, the differences between autistic children and controls expressed on psycho-emotional level were the most significant as compared to the other groups. Therefore, the activity of the sympathetic autonomic nervous system is significantly altered in children with autism. The biometric method based on GDV is a promising step in autism research that may lead towards creating a disease profile and identify unique signature/biomarker for autism. Further work should involve more participants in order to augment our findings.

**Source:** Medline
Available in fulltext from International Journal of Environmental Research and Public Health at National Library of Medicine

Available in fulltext from International Journal of Environmental Research & Public Health at EBSCOhost

Available in fulltext at International Journal of Environmental Research and Public
Health: Collection notes: On first login to a ProQuest journal you will need to select 'Athens (OpenAthens Federation)' from Select Region, and then 'NHS England' from Choose your Library.

Larger tonic pupil size in young children with autism spectrum disorder.
Author(s) Anderson CJ, Colombo J
Citation: Developmental Psychobiology, March 2009, vol./is. 51/2(207-11), 0012-1630;1098-2302 (2009 Mar)
Publication Date: March 2009
Abstract: The symptoms of Autism Spectrum Disorder (ASD) have been suggested to manifest from atypical functioning of the autonomic nervous system (ANS), leading to altered arousal and atypical processing of salient stimuli. Coherent with this, persons with ASD show heightened autonomic activity, sleep difficulties, and structural and neurochemical alterations within the ANS. Recently, we observed decreased pupil responses to human faces in children with ASD. In the current study, we found differences in baseline (tonic) pupil size, with the ASD group exhibiting a larger pupil size than age-matched controls. Pupil responses are sensitive and reliable measures of ANS functioning, thus, this finding highlights the role of the ANS, and may provide clues about underlying neuropathology.
Source: Medline
Available in fulltext from Developmental Psychobiology at EBSCOhost

Pediatric autonomic disorders.
Author(s) Axelrod FB, Chelimsky GG, Weese-Mayer DE
Citation: Pediatrics, July 2006, vol./is. 118/1(309-21), 0031-4005;1098-4275 (2006 Jul)
Publication Date: July 2006
Abstract: The scope of pediatric autonomic disorders is not well recognized. The goal of this review is to increase awareness of the expanding spectrum of pediatric autonomic disorders by providing an overview of the autonomic nervous system, including the roles of its various components and its pervasive influence, as well as its intimate relationship with sensory function. To illustrate further the breadth and complexities of autonomic dysfunction, some pediatric disorders are described, concentrating on those that present at birth or appear in early childhood.
Source: Medline
Available in fulltext from Pediatrics at Free Access Content
Available in fulltext from Pediatrics at Highwire Press
Available in print at Lincoln County Hospital Professional Library
Available in fulltext from Pediatrics at American Academy of Pediatrics

Autonomic responses of autistic children to people and objects.
Author(s) Hirstein W, Iversen P, Ramachandran VS
Citation: Proceedings of the Royal Society of London - Series B: Biological Sciences, September 2001, vol./is. 268/1479(1883-8), 0962-8452;0962-8452 (2001 Sep 22)
Publication Date: September 2001
Abstract: Several recent lines of inquiry have pointed to the amygdala as a potential lesion site in autism. Because one function of the amygdala may be to produce autonomic arousal at the sight of a significant face, we compared the responses of autistic children to their mothers’ face and to a plain paper cup. Unlike normals, the autistic children as a whole did not show a larger response to the person than to the cup. We also monitored sympathetic activity in autistic children as they engaged in a wide range of everyday behaviours. The children tended to use
self-stimulation activities in order to calm hyper-responsive activity of the sympathetic ('fight or flight') branch of the autonomic nervous system. A small percentage of our autistic subjects had hyporesponsive sympathetic activity, with essentially no electrodermal responses except to self-injurious behaviour. We sketch a hypothesis about autism according to which autistic children use overt behaviour in order to control a malfunctioning autonomic nervous system and suggest that they have learned to avoid using certain processing areas in the temporal lobes.

**Source:** Medline

Available in fulltext from *Proceedings of the Royal Society B: Biological Sciences* at [National Library of Medicine](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1011173/).