



autism research centre

ARC Newsletter 2011

We are delighted to send you our Newsletter that highlights some of the autism research conducted by the ARC published during 2011. It provides a snapshot of the varied kinds of research projects underway at Cambridge University, and gives us an opportunity to thank those who generously gave time to help science, and to thank the agencies and charities that funded the research. Thank you for all your support.

Professor Simon Baron-Cohen (Director)

ARC News

Congratulations on the following new PhDs:

Dr Meng-Chuan Lai obtained his PhD entitled 'How is sex related to autism?' (funded by the Ministry of Education, Taiwan). Dr Teresa Tavassoli obtained her PhD entitled 'Sensory processing in autism' (funded by Autistica and the Pinsent Darwin Trust). Dr Jillian Sullivan obtained her PhD entitled 'Head circumference and autistic traits' (funded by the Gates Foundation).



Dr Meng-Chuan Lai



Dr Teresa Tavassoli



Dr Jillian Sullivan

Dr Owen Churches was awarded his PhD entitled 'ERP studies of face perception in autism' (funded by the Australian MRC). Dr Rick Griffin obtained his PhD entitled 'Social cognition in toddlers' (funded by the MRC).



Dr Owen Churches



Dr Rick Griffin



Ms Donnie Johnson

Congratulations on the following new MPhils:

Donielle Johnson obtained her MPhil entitled 'Autism and synaesthesia: is there a link?' (funded by the Gates Foundation).

Congratulations on the following new Post Doctoral Awards:

Dr Mike Lombardo was awarded a British Academy postdoctoral fellowship for his research entitled 'Autism and social neuroscience'. Dr Meng-Chuan Lai was awarded a postdoctoral grant from the Waterloo Foundation entitled 'Differentiating high-functioning autism and Asperger Syndrome using MRI'. Dr Teresa Tavassoli was awarded a postdoc at the Seaver Center, Mount Sinai Hospital, New York. Dr Jillian Sullivan was awarded a postdoc at the Star Center in Denver conducting research into sensory sensitivity.



Dr Mike Lombardo



Dr Bonnie Auyeung

Congratulations on the following new Grants:

Drs Mike Lombardo and Bonnie Auyeung, and Professors Simon Baron-Cohen and Ed Bullmore were awarded a Wellcome Trust grant entitled 'Foetal testosterone and neuroimaging'. Professor Simon Baron-Cohen is collaborating on a grant from the EU (FP7) entitled 'Autism Inclusion: new technologies for intervention'. Professors Simon Baron-Cohen, John Suckling, and Ed Bullmore are collaborating on a grant from the EU (EME) entitled 'EU AIMS' (Autism Imaging Multicentre Study). Drs Sophia Sun and Carrie Allison, and Professors Simon Baron-Cohen and Carol Brayne were awarded a grant from the Waterloo Foundation entitled 'Screening for autism in China'. Dr Michael Spencer, and Professors John Suckling and Ed Bullmore were awarded an Isaac Newton Trust Grant; entitled 'Developing connections in the adolescent brain'.



Dr Carrie Allison



Dr Sophia Sun



Dr Mike Spencer

Farewell and thanks:

Gaenor Moore, our ARC Administrator, has taken up a position as Senior Administrator in the Law Faculty, Cambridge University. Paula Naimi, our CLASS Clinic Administrator, has taken up a position in the Department of Paediatrics in the Clinical School, Cambridge University. Georgina Woods has left the Q-CHAT project to work as an assistant psychologist in NHS Warwickshire. Francesca Cabedo and Leanne Swain completed their internships on the Autism Family Study. Martine Roelfsema has gone back to Holland following a six month stay at the ARC as a visiting researcher.

Welcome:

Chloe Gayer-Anderson, Ann Spicer, and Carol Farmer, have joined as the Admin Team in Douglas House (Department of Psychiatry, Cambridge University) and provide support to the ARC. Liliana Ruta joined the Q-CHAT project as research associate in January 2011. Emma Robson moved from the Q-CHAT project to start her MPhil in mirror neuron synaesthesia. Dorothea Floris started her MPhil examining handedness and how it relates to global brain volume, asymmetry and the corpus callosum. Following completion of her MPhil in Genetics at Imperial College London, Laura Murphy took up a research assistant post supporting the various genetics projects at the ARC. Debbie Heptonstall has taken up the post of CLASS Clinic Administrator. Philippa Lewington and Renee Soufer are new research assistants working on the Q-CHAT project. Pia Thiemann and Jamal Sipple are visiting research students supporting the oxytocin study. Richard Bethlehem is an intern working on the AIMS study during his Masters in the Netherlands.

Peer-Reviewed Research published in 2011

Full PDFs of the articles below are available at www.autismresearchcentre.com

1. Psychometric analysis of the Empathy Quotient (EQ)

Allison, C., Baron-Cohen, S., Wheelwright, S., Stone, M. and Muncer, S. (2011) *Personality and Individual Differences*, 51, 829–835

This study assessed the dimensionality of the Empathy Quotient (EQ) using two statistical approaches: Rasch and Confirmatory Factor Analysis (CFA). Participants included N = 658 with an autism spectrum condition diagnosis (ASC), N = 1375 family members of this group, and N = 3344 typical controls. Data were applied to the Rasch model (Rating Scale) using WINSTEPS. The Rasch model explained 83% of the variance. Reliability estimates were greater than .90. Analysis of differential item functioning (DIF) demonstrated item invariance between the sexes. Principal Components Analysis (PCA) of the residual factor showed separation into Agree and Disagree response subgroups. CFA suggested that 26-item model with response factors had the best-fit statistics (RMSEA.05, CFI .93). A shorter 15-item three-factor model had an omega (α) of .779, suggesting a hierarchical factor of empathy underlies these sub-factors. The EQ is an appropriate measure of the construct of empathy and can be measured along a single dimension.

PubMedID: not yet listed

Funding: MRC, CLAHRC.

2. Effects of Fetal Testosterone on Visuospatial Ability

Auyeung, B., Knickmeyer, R., Ashwin, E., Taylor, K., Hackett, G. and Baron-Cohen, S. (2011) *Archive of Sexual Behaviour*

This study investigated whether fetal testosterone (FT) measured from second trimester amniotic fluid was related to specific aspects of visuospatial ability, in children aged 7–10 years (35 boys, 29 girls). A series of tasks were used: the children's Embedded Figures Test (EFT) (a test of attention to detail), a ball targeting task (measuring hand-eye coordination), and a computerized mental rotation task (measuring rotational ability). FT



was a significant predictor for EFT scores in both boys and girls, with boys also showing a clear advantage for this task. No significant sex differences were observed in targeting. Boys scored higher than girls on mental rotation. However, no significant relationships were observed between FT and targeting or mental rotation. Girls' performance on the mental rotation and targeting tasks was significantly related to age, indicating that these tasks may have been too difficult for the younger children. These results indicate that FT has a significant role in some aspects of cognitive development but that further work is needed to understand its effect on the different aspects of visuospatial ability.

PubMedID: 22033667

Funding: MRC; The Nancy Lurie-Marks Family Foundation; Trinity College, Cambridge; NIHR CLAHRC.

3. The Big Picture: Storytelling Ability in Adults with Autism Spectrum Conditions

Barnes, J. and Baron-Cohen, S. (2011) *Journal of Autism and Developmental Disorders*

Previous work on story-telling ability in autism spectrum conditions (ASC) has found a pattern of relatively intact use of story grammar in ASC narratives; however, prior analysis has concentrated primarily on whether specific story components are included, rather than how they are included. The present study analyses an existing narrative dataset, concentrating on the kind of information that individuals with and without high functioning autism or Asperger syndrome include about story elements such as setting, character, conflict, and resolution. This analysis showed that individuals with ASC are biased toward providing local over global details about each element, regardless of whether the element involved mental content. These results are discussed in terms of the Weak Central Coherence and Hyper-Systemizing theories.

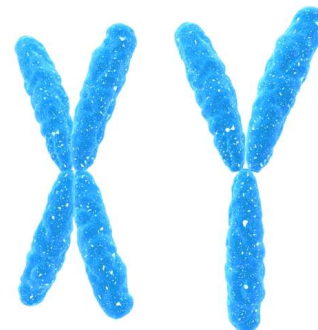
PubMed ID: 22042307

Funding: Fulbright Fellowship; MRC.

4. Why Are Autism Spectrum Conditions More Prevalent in Males?

Baron-Cohen, S., Lombardo, M. V., Auyeung, B., Ashwin, E., Chakrabarti, B. and Knickmeyer, R. (2011) *PloS Biology*, Volume 9, Issue 6. Also see **Supplementary Material to Why Are Autism Spectrum Conditions More Prevalent in Males? Sex Differences in Empathy and Systemizing and the EMB theory**

Autism Spectrum Conditions (ASC) are much more common in males, a bias that may offer clues to the etiology of this condition. Although the cause of this bias remains a mystery, we argue that it occurs because ASC is an extreme manifestation of the male brain. The extreme male brain (EMB) theory, first proposed in 1997, is an extension of the Empathizing-Systemizing (E-S) theory of typical sex differences that proposes that females on average have a stronger drive to empathize while males on average have a



a stronger drive to systemize. In this first major update since 2005, we describe some of the evidence relating to the EMB theory of ASC and consider how typical sex differences in brain structure may be relevant to ASC. One possible biological mechanism to account for the male bias is the effect of fetal testosterone (fT). We also consider alternative biological theories, the X and Y chromosome theories, and the reduced autosomal penetrance theory. None of these theories has yet been fully confirmed or refuted, though the weight of evidence in favor of the fT theory is growing from converging sources (longitudinal amniocentesis studies from pregnancy to age 10 years old, current hormone studies, and genetic association studies of SNPs in the sex steroid pathways). Ultimately, as these theories are not mutually exclusive and ASC is multi-factorial, they may help explain the male prevalence of ASC.

PubMed ID: 21695109

Funding: MRC, Wellcome Trust, Nancy Lurie Marks Foundation, NIHR CLAHRC.

5. Atypical EEG complexity in autism spectrum conditions: A multiscale entropy analysis

Catarino, A., Churches, O., Baron-Cohen, S., Andrade, A. and Ring, H. (2011) *Clinical Neurophysiology*, 122, 2375–2383

Objective: Intrinsic complexity subserves adaptability in biological systems. One recently developed measure of intrinsic complexity of biological systems is multiscale entropy (MSE).



Autism spectrum conditions (ASC) have been described in terms of reduced adaptability at a behavioural level and by patterns of atypical connectivity at a neural level. Based on these observations we aimed to test the hypothesis that adults with ASC would show atypical intrinsic complexity of brain activity as indexed by MSE analysis of electroencephalographic (EEG) activity. Methods: We used MSE to assess the complexity of EEG data recorded from 15 participants with ASC and 15 typical controls, during a face and chair-matching task. Results:

Results demonstrate a reduction of EEG signal complexity in the ASC group, compared to typical controls, over temporo-parietal and occipital regions. No significant differences in EEG power spectra were observed between groups, indicating that changes in complexity values are not a reflection of changes in EEG power spectra. Conclusions: The results are consistent with a model of atypical neural integrative capacity in people with ASC. Significance: Results suggest that EEG complexity, as indexed by MSE measures, may also be a marker for disturbances in task-specific processing of information in people with autism.

PubMed ID: 21641861

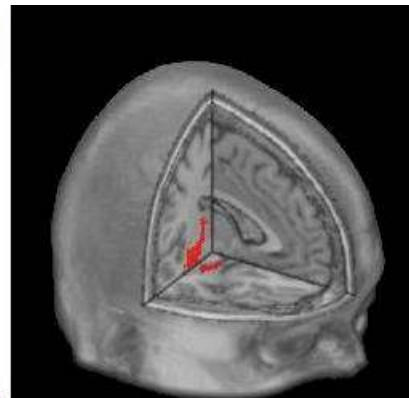
Funding: NIHR CLAHRC; National Alliance for Autism Research (USA); MRC; The Fundação para a Ciência e Tecnologia (Foundation for Science and Technology), Portugal; The Cambridge Australia Trust.

6. Variation in the human cannabinoid receptor CNR1 gene modulates gaze duration for happy faces

Chakrabarti, B. and Baron-Cohen, S. (2011) *Molecular Autism*, 2: 10

Background: From an early age, humans look longer at preferred stimuli and also typically look longer at facial expressions of emotion, particularly happy faces. Atypical gaze patterns towards social stimuli are

common in autism spectrum conditions (ASC). However, it is unknown whether gaze fixation patterns have any genetic basis. In this study, we tested whether variations in the cannabinoid receptor 1 (CNR1) gene are associated with gaze duration towards happy faces. This gene was



selected because CNR1 is a key component of the endocannabinoid system, which is involved in processing reward, and in our previous functional magnetic resonance imaging (fMRI) study, we found that variations in CNR1 modulate the striatal response to happy (but not disgust) faces. The striatum is involved in guiding gaze to rewarding aspects of a visual scene. We aimed to validate and extend this result in another sample using a different technique (gaze tracking). Methods: A total of 30 volunteers (13 males and 17 females) from the general population observed dynamic emotional expressions on a screen while their eye movements were recorded. They were genotyped for the identical four single-nucleotide polymorphisms (SNPs) in the CNR1 gene tested in our earlier fMRI study. Results: Two SNPs (rs806377 and rs806380) were associated with differential gaze duration for happy (but not disgust) faces. Importantly, the allelic groups associated with a greater striatal response to happy faces in the fMRI study were associated with longer gaze duration at happy faces. Conclusions: These results suggest that CNR1 variations modulate the striatal function that underlies the perception of signals of social reward, such as happy faces. This suggests that CNR1 is a key element in the molecular architecture of perception of certain basic emotions. This may have implications for understanding neurodevelopmental conditions marked by atypical eye contact and facial emotion processing, such as ASC.

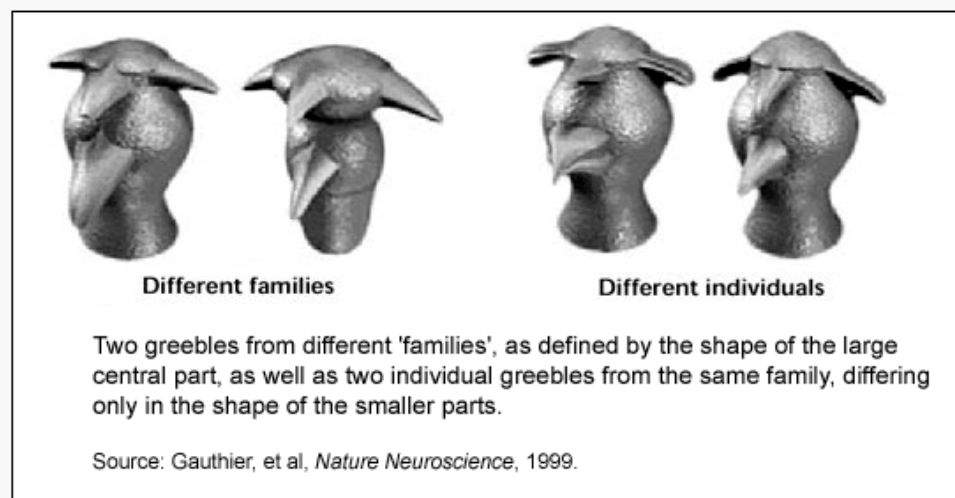
PubMedID: 21714860

Funding: Trinity College Cambridge; Darwin College Cambridge; Target Autism Genome; Nancy Lurie Marks Family Foundation; MRC; NIHR CLAHRC.

7. The development of perceptual expertise for faces and objects in autism spectrum conditions

Damiano, C., Churches, O., Ring, H. and Baron-Cohen S. (2011) *Autism Research*, Aug; 4(4): 297-301.

Previous research indicates that individuals with autism spectrum conditions (ASC) do not develop face expertise to the same extent as typical individuals. Yet it remains unclear whether this atypicality is specific to faces or related to more pervasive perceptual or cognitive deficits involved in the actual process of gaining expertise. To address this question, we examined the extent to which adults with ASC were capable of developing expertise with non-face objects. To become experts, all participants completed a 2-week training program with novel objects, known as Greebles. Level of expertise was assessed throughout training by measuring the ability to identify Greebles on an individual level. The perceptual strategies acquired as a result of expertise were measured through an inversion effect task completed before and after training, in which performance with upright Greebles and faces was compared to performance with inverted Greebles and faces.



After expertise training, it was found that individuals in both the ASC and the typical group successfully achieved expertise and showed an enhanced Greeble inversion effect as a result of training. The development of an inversion effect with Greebles suggests that individuals with ASC may employ the same processing strategies as the typical group. Although exploratory, these findings have implications for understanding the nature of the face processing deficit in ASC as well as offering potential insights into face processing interventions for individuals with ASC.

PMID: 21710603

Funding: funding from the MRC; in association with the NIHR CLAHRC for Cambridgeshire and Peterborough NHS Foundation Trust.

8. Brief Report: Female-To-Male Transsexual People and Autistic Traits

Jones, R. M., Wheelwright, S., Farrell, K., Martin, E., Green, R., Di Ceglie, D. and Baron-Cohen, S. (2011) *Journal of Autism Development Disorders*

The 'extreme male brain' theory suggests females with Autism Spectrum Conditions are hyper-masculinized in certain aspects of behavior. We predicted that females with Gender Identity Disorder (who are masculinized) would have elevated Autism Spectrum Quotient (AQ) scores. AQ scores from five groups were compared: (1) n = 61 transmen (female-to-male transsexual people); (2) n = 198 transwomen (male-to-female transsexual people); (3) n = 76 typical males; (4) n = 98 typical females; and (5) n = 125 individuals with Asperger Syndrome (AS). Transmen had a higher mean AQ than typical females, typical males and transwomen, but lower than individuals with AS. Transmen have more autistic traits and may have had difficulty socializing with female peers and thus found it easier to identify with male peer groups.

PMID: 21448752

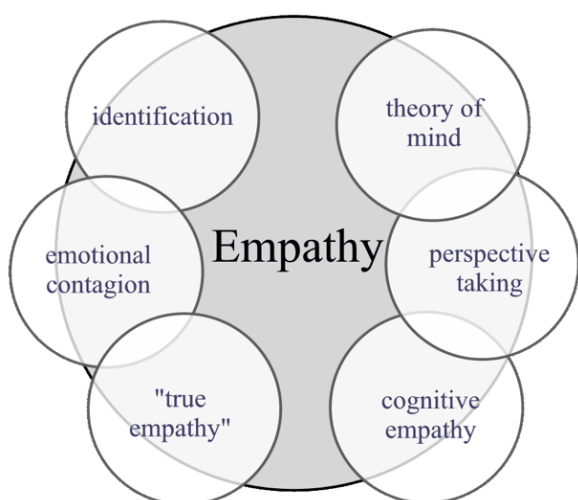
Funding: MRC; Nancy Lurie Marks Family Foundation; The Gates Cambridge Trust.

9. A Behavioral Comparison of Male and Female Adults with High Functioning Autism Spectrum Conditions

Lai, M-C., Lombardo, M. V., Pasco, G., Ruigrok, A. N. V., Wheelwright, S. J., Sadek, S. A., Chakrabarti, B., MRC AIMS Consortium, and Baron-Cohen, S. (2011) *PloS One, Volume 6, Issue 6*

Autism spectrum conditions (ASC) affect more males than females in the general population. However, within ASC it is unclear if there are phenotypic sex differences. Testing for similarities and differences between the sexes is important not only for clinical assessment but also has implications for theories of typical sex differences and of autism. Using cognitive and behavioral measures, we investigated similarities and differences between the sexes in age- and IQ-matched adults with ASC (high-functioning autism or Asperger syndrome). Of the 83 (45 males and 38 females) participants, 62 (33 males and 29 females) met Autism Diagnostic Interview-Revised (ADI-R) cut-off criteria for autism in childhood and were included in all subsequent analyses. The severity of childhood core

autism symptoms did not differ between the sexes. Males and females also did not differ in self-reported empathy, systemizing, anxiety, depression, and obsessive-compulsive traits/symptoms or mentalizing performance. However, adult females with ASC showed more lifetime sensory symptoms ($p = 0.036$), fewer current socio-communication difficulties ($p = 0.001$), and more self-reported autistic traits ($p = 0.012$) than males. In addition, females with ASC who also had developmental language delay had lower current performance IQ than those without developmental language delay



($p < 0.001$), a pattern not seen in males. The absence of typical sex differences in empathizing-systemizing profiles within the autism spectrum confirms a prediction from the extreme male brain theory. Behavioral sex differences within ASC may also reflect different developmental mechanisms between males and females with ASC. We discuss the importance of the superficially better socio-communication ability in adult females with ASC in terms of why females with ASC may more often go under-recognized, and receive their diagnosis later, than males.

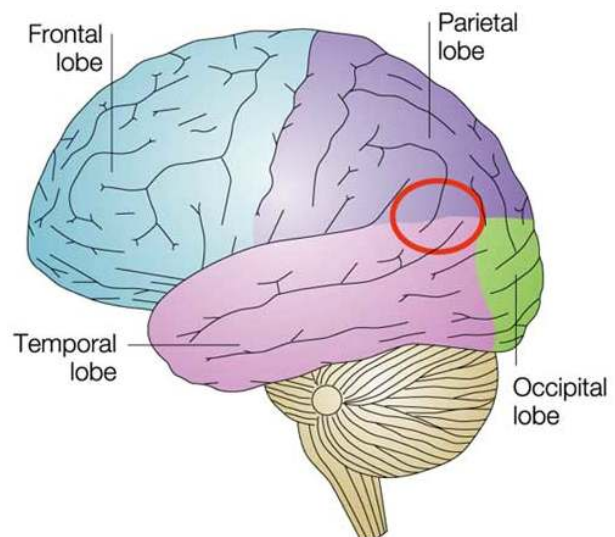
PMID: 21695147

Funding: MRC; Taiwan Government.

10. Specialization of right temporo-parietal junction for mentalizing and its relation to social impairments in autism

Lombardo, M. V., Chakrabarti, B., Bullmore, E. T., MRC AIMS Consortium, and Baron-Cohen, S. (2011) *NeuroImage*, 56, 1832–1838

Over the last 25 years, “mindblindness” (deficits in representing mental states) has been one of the primary explanations behind the hallmark social-communication difficulties in autism spectrum conditions (ASC). However, highlighting neural systems responsible for mindblindness and their relation to variation in social impairments has remained elusive. In this study we show that one of the neural systems responsible for mindblindness in ASC and its relation to social impairments is the right temporo-parietal junction (RTPJ). Twenty nine adult males with ASC and 33 age and IQ-matched Controls were scanned with fMRI while making reflective mentalizing or physical judgments about themselves or another person. Regions of interest within mentalizing circuitry were examined for between-group differences in activation during mentalizing about self and other and correlations with social symptom severity. RTPJ was the only mentalizing region that responded atypically in ASC. In Controls, RTPJ was selectively more responsive to mentalizing than physical judgments. This selectivity for mentalizing was not apparent in ASC and generalized across both self and other. Selectivity of RTPJ for mentalizing was also associated with the degree of reciprocal social impairment in ASC. These results lend support to the idea that RTPJ is one important neural system behind mindblindness in ASC. Understanding the contribution of RTPJ in conjunction with other neural systems responsible for other component processes involved in social cognition will be illuminating in fully explaining the hallmark social-communication difficulties of autism.



PMID: 21356316

Funding: MRC; AIMS Consortium; The Shirley Foundation; The Cambridge Overseas Trust; in association with the NIHR CLAHRC.

11. The role of the self in mindblindness in autism

Lombardo, M. V. and Baron-Cohen, S. (2011) *Consciousness and Cognition*, 20, 130–140

Since its inception the ‘mindblindness’ theory of autism has greatly furthered our understanding of the core social-communication impairments in autism spectrum conditions (ASC). However, one of the more subtle issues within the theory that needs to be elaborated is the role of the ‘self’. In this article, we expand on mindblindness in ASC by addressing topics related to the self and its central role in the social world and then review recent research in ASC that has yielded important insights by contrasting processes relating to both self and other. We suggest that new discoveries lie ahead in understanding how self and other are interrelated and/or distinct, and how understanding atypical self referential and social-cognitive mechanisms may lead to novel ideas as to how to facilitate social-communicative abilities in ASC.

PMID: 20932779

Funding: Shirley Foundation; MRC.

12. Are Autism Spectrum Conditions More Prevalent in an Information-Technology Region? A School-Based Study of Three Regions in the Netherlands

Roelfsema, M. T., Hoekstra, R. A., Allison, C., Wheelwright, S., Brayne, C., Matthews, F. E. and Baron-Cohen, S. (2011) *Journal of Autism & Developmental Disorders*

We tested for differences in the prevalence of autism spectrum conditions (ASC) in school-aged children in three geographical regions in the Netherlands. Schools were asked to



Picture from: Google Images

provide the number of children enrolled, the number having a clinical diagnosis of ASC and/or two control neurodevelopmental conditions. Prevalence was evaluated by negative binomial regression and adjustments were made for non-response and size of the schools. The prevalence estimate of ASC in Eindhoven was 229 per 10,000, significantly higher than in Haarlem (84 per 10,000) and Utrecht (57 per 10,000), whilst the prevalence for the control conditions was similar in all regions. Phase two is planned to validate school-reported cases using standardized diagnostic methods and to explore the possible causes for these differences.

PMID: 21681590

Funding: NIHR CLAHRC; MRC; Target Autism Genome; The Nancy Lurie Marks Family Foundation; The Erasmus fund; The Bekker la Bastide fund; The University of Amsterdam; The Netherlands Organisation for Scientific Research (NWO Rubicon).

13. The Autism-Spectrum Quotient - Italian Version: A Cross-Cultural Confirmation of the Broader Autism Phenotype

Ruta, L., Mazzone, D., Mazzone, L., Wheelwright, S. and Baron-Cohen, S. (2011) *Journal of Autism and Developmental Disorders*

The Autism Spectrum Quotient (AQ) has been used to define the 'broader' (BAP), 'medium' (MAP) and 'narrow' autism phenotypes (NAP). We used a new Italian version of the AQ to test if difference on AQ scores and the distribution of BAP, MAP and NAP in autism parents (n = 245) versus control parents (n = 300) were replicated in a Sicilian sample. Parents of children with autism spectrum conditions scored higher than the control parents on total AQ, social skills and communication subscales, and exhibited higher rates of BAP, MAP and NAP. We conclude that the Italian AQ is a cross-culturally reliable measure of these different phenotypes, and can be used to identify a phenotypic gradient of severity of autistic traits in families. To understand the molecular basis of these phenotypes will require its use in genetic association studies.

PMID: 21626054

Funding: MRC; The Nancy Lurie Marks Family Foundation; NIHR CLAHRC.

14. Increased serum androstenedione in adults with autism spectrum conditions

Ruta, L., Ingudomnukul, E., Taylor, K., Chakrabarti, B. and Baron-Cohen, S. (2011) *Psychoneuroendocrinology*, 36, 1154–1163

Molecular and behavioural evidence points to an association between sex-steroid hormones and autism spectrum conditions (ASC) and/or autistic traits. Prenatal androgen levels are associated with autistic traits, and several genes involved in steroidogenesis are associated with autism, Asperger Syndrome and/or autistic traits. Furthermore, higher rates of androgen related conditions (such as Polycystic Ovary Syndrome, hirsutism, acne and hormone-related cancers) are reported in women with autism spectrum conditions. A key question therefore is if serum levels of gonadal and adrenal sex-steroids (particularly testosterone, estradiol, dehydroepiandrosterone sulfate and androstenedione) are elevated in individuals with ASC. This was tested in a total sample of n = 166 participants. The final eligible sample for hormone analysis comprised n = 128 participants, n = 58 of whom had a diagnosis of Asperger Syndrome or high functioning autism (33 males and 25 females) and n = 70 of whom were age- and IQ-matched typical controls (39 males and 31 females). ASC diagnosis (without any interaction with sex) strongly predicted androstenedione levels (p < 0.01), and serum androstenedione levels were significantly elevated in the ASC group (Mann–Whitney W = 2677, p = 0.002), a result confirmed by permutation testing in females (permutation-corrected p = 0.02). This result is discussed in terms of androstenedione being the immediate precursor of, and being converted into, testosterone, dihydrotestosterone, or estrogens in hormone-sensitive tissues and organs.

PMID: 21398041

Funding: MRC; The Nancy Lurie Marks Family Foundation; NIHR CLAHRC.

15. A novel functional brain imaging endophenotype of autism: the neural response to facial expression of emotion

Spencer, M. D., Holt, R. J., Chura, L. R., Suckling, J., Calder, A. J., Bullmore, ET, Baron-Cohen, S. (2011) *Translational Psychiatry*, 1.

Siblings of individuals with autism have over 20 times the population risk of autism. Evidence of comparable, but less marked, cognitive and social communication deficits in siblings suggests a role for these traits in the search for biomarkers of familial risk. However, no neuroimaging biomarkers of familial risk have been identified to date. Here we show, for the first time, that the neural response to facial expression of emotion differs between unaffected siblings and healthy controls with no family history of autism. Strikingly, the functional magnetic resonance imaging (fMRI) response to happy versus neutral faces was significantly reduced in unaffected siblings compared with controls within a number of brain areas implicated in empathy and face processing. The response in unaffected siblings did not differ significantly from the response in autism. Furthermore, investigation of the response to faces versus fixation crosses suggested that, within the context of this study, an atypical response specifically to happy faces, rather than to faces in general, accounts for the observed sibling versus controls difference and is a clear biomarker of familial risk. Our findings suggest that an atypical implicit response to facial expression of emotion may form the basis of impaired emotional reactivity in autism and in the broader autism phenotype in relatives. These results demonstrate that the fMRI response to facial expression of emotion is a candidate neuroimaging endophenotype for autism, and may offer far-reaching insights into the etiology of autism.

PubMedID: unavailable

Funding: MRC; The Gates Cambridge Scholarship Trust.

16. Olfactory Detection Thresholds and Adaptation in Adults with Autism Spectrum Condition

Tavassoli, T. and Baron-Cohen, S. (2011) *Journal of Autism and Developmental Disorders*

Sensory issues have been widely reported in Autism Spectrum Conditions (ASC). Since olfaction is one of the least investigated senses in ASC, the current studies explore olfactory detection thresholds and adaptation to olfactory stimuli in adults with ASC. Eighty participants took part, 38 (18 females, 20 males) with ASC and 42 control participants (20 males, 22 females). A subgroup of participants (N = 19 in each group) also conducted an adaptation task. Standardized "Sniffin' Sticks" were used to measure olfactory detection levels and adaptation. Adults with and without ASC showed similar olfactory detection thresholds, and similar adaptation to an olfactory stimulus. Since diminished adaptation in ASC has been previously suggested, future research needs to examine adaptation in other modalities as well.

PMID: 21732210

Funding: The Pinsent Darwin Trust; Autistica; MRC; NIHR CLAHRC.

17. Psychophysical measures of visual acuity in autism spectrum conditions

Tavassoli, T., Latham, K., Bach, M., Dakin, S. C. and Baron-Cohen, S. (2011) *Vision Research*, 51, 1778–1780

Previously reported superior visual acuity (VA) in autism spectrum conditions (ASC) may have resulted from methodological settings used (Ashwin, Ashwin, Rhydderch, Howells, & Baron-Cohen, 2009). The current study re-tested whether participants with (N = 20) and without (N = 20) ASC differ on psychophysical measures of VA. Participants' vision was corrected before acuity measurement, minimising refractive blur. VA was assessed with an ETDRS chart as well as the Freiburg Visual Acuity and Contrast Test (FrACT). FrACT testing was undertaken at 4 m (avoiding limitations of pixel-size), using 36 trials (avoiding fatigue). Best corrected VA was significantly better than the initial habitual acuity in both groups, but adults with and without ASC did not differ on ETDRS or FrACT binocular VA. Future research should examine at which level of visual processing sensory differences emerge.

PMID: 21704058 [PubMed - indexed for MEDLINE]

Funding: the Pinsent Darwin Trust; Autistica; MRC; The Wellcome Trust; NIHR CLAHRC.

18. Taste Identification in Adults with Autism Spectrum Conditions

Tavassoli, T. and Baron-Cohen, S. (2011) *Journal of Autism and Developmental Disorders*

Sensory issues are widely reported in Autism Spectrum Conditions (ASC). Since taste perception is one of the least studied senses in ASC we explored taste identification in adults with ASC (12 males, 11 females) compared to control participants (14 males, 12 females). 'Taste strips' were used to measure taste identification overall, as well as bitter, sour, sweet and salty tastes. Results revealed lower taste scores overall in the ASC group, as well as for bitter, sour and sweet tastes. Salty taste scores did not differ between the groups. Examining error types showed that adults with ASC more often misidentified a taste as salty or as no taste. Future studies should investigate underlying mechanisms of taste identification difficulties in ASC.

PMID: 22006402

Funding: The Pinsent Darwin Trust; Autistica; MRC UK; NIHR CLAHRC.

Peer-Reviewed Collaborative Research with the ARC

The ARC has links with many research groups. In 2011, these collaborations resulted in the publication of the following papers:

19. No major effect of twinning on autistic traits

Curran, S., Dworzynski, K., Happé, F., Ronald, A., Allison, C., Baron-Cohen, S., Brayne, C. and Bolton, P. F. (2011) *Autism Research* Oct; 4(5): 377-82



It has been questioned whether the process of twinning might be a risk factor for autism spectrum conditions (ASC) and autistic traits. Aim: We sought to determine whether autistic traits and probable disorder, as measured by the Childhood Autism Spectrum Test (CAST), were more pronounced in twins compared to singletons. SAMPLES: Data were analyzed from two large population-based samples of UK children, twins (n = 5,142 twin pairs, aged 8 years) and singletons (n = 2,805, aged 5-9 years). RESULTS: Distributions of CAST scores in both groups were negatively skewed and scores for twins were more variable than singletons.

Mean CAST total scores and standard errors (SE) were not significantly different for twins (5.1; SE 0.04) compared to singletons (4.9; SE 0.08). Moreover, contrary to expectations, the likelihood of scoring above the threshold for possible ASC was significantly lower in the twins than the singletons (OR = 0.69; P = 0.002). Subsidiary analyses of CAST scores according to sex, twin type, and subscale scores representing the subdomains of autism found a few significant differences (P < 0.01), but the effect sizes for these differences were small and none exceeded $\eta(2) = 0.005$. The explanation for these small differences remains obscure, but the very small effect sizes mean they are of little importance. CONCLUSIONS: Our results do not provide evidence to support twinning as a risk factor in the development of autistic traits.

PMID: 21766464

Funding: MRC; UK NIHR Biomedical Research Centre for Mental Health at the Institute of Psychiatry, Kings College London; The South London and Maudsley NHS Foundation Trust.

20. Differential habituation to repeated sounds in infants at high risk for autism

Guirauda, J. A., Kushnerenkob, E., Tomalskib, P., Daviesa, K., Ribeiroa, H., Johnsona, M. H., and The BASIS Team (2011) *NeuroReport* 22: 845–849

It has been suggested that poor habituation to stimuli might explain atypical sensory behaviours in autism. We investigated habituation to repeated sounds using an oddball paradigm in 9-month-old infants with an older sibling with autism and hence at high risk for

developing autism. Auditory-evoked responses to repeated sounds in control infants (at low risk of developing autism) decreased over time, demonstrating habituation, and their responses to deviant sounds were larger than responses to standard sounds, indicating discrimination. In contrast, neural responses in infants at high risk showed less habituation and a reduced sensitivity to changes in frequency. Reduced sensory habituation may be present at a younger age than the emergence of autistic behaviour in some individuals, and we propose that this could play a role in the over responsiveness to some stimuli and undersensitivity to others observed in autism.

PMID: 21934535

Funding: Autistica; MRC.

21. Fronto-striatal circuitry and inhibitory control in autism: Findings from diffusion tensor imaging tractography

Langen, M., Leemans, A., Johnston, P., Ecker, C., Daly, E., Murphy, C. M., Dell'acqua, F., Durston, S.; The AIMS Consortium, and Murphy, D. G. (2011) *Cortex* May 30.

INTRODUCTION: Repetitive behaviour and inhibitory control deficits are core features of autism; and it has been suggested that they result from differences in the anatomy of striatum; and/or the 'connectivity' of subcortical regions to frontal cortex. There are few studies, however, that have measured the micro-structural organisation of white matter tracts connecting striatum and frontal cortex. **AIMS:** To investigate differences in bulk volume of striatum and micro-structural organisation of fronto-striatal white matter in people with autism; and their association with repetitive behaviour and inhibitory control. **METHODS:** We compared the bulk volume of striatum (caudate nucleus, putamen and nucleus accumbens) and white matter organisation of fronto-striatal tracts using (respectively) structural magnetic resonance imaging (sMRI) and tract specific diffusion tensor imaging (DTI) measures in 21 adults with autism and 22 controls. We also assessed performance on a cognitive inhibition (go/nogo) task. **RESULTS:** Bulk volume of striatal structures did not differ between groups. However, adults with autism had a significantly smaller total brain white matter volume, lower fractional anisotropy of white matter tracts connecting putamen to frontal cortical areas, higher mean diffusivity of white matter tracts connecting accumbens to frontal cortex and worse performance on the go/nogo task. Also, performance on the go/nogo task was significantly related to anatomical variation when both groups were combined; but not within the autism group alone. **CONCLUSIONS:** These data suggest that autism may be associated with differences in the anatomy of fronto-striatal white matter tracts.

PMID: 21718979

Funding: The South London and Maudsley NHS Trust (National Division); MRC; AIMS network; the Ter Meulen Fund; the UMC Utrecht International Office.

22. The Empathy Quotient: a cross-cultural comparison of the Italian version

Preti, A., Vellante, M., Baron-Cohen, S., Zucca, G., Petretto, D. R. and Masala, C. (2011) *Cognitive Neuropsychiatry*, Jan; 16(1): 50-70

INTRODUCTION: The Empathy Quotient (EQ) is a self-report questionnaire that was developed to measure the cognitive, affective, and behavioural aspects of empathy. We evaluated its cross-cultural validity in an Italian sample. **METHODS:** A sample of 18- to 30-

year-old undergraduate students of both sexes (N=256, males=118) were invited to fill in the Italian version of the EQ, as well as other measures of emotional competence and psychological distress. RESULTS: The EQ had an excellent reliability (Cronbach's alpha=.79; test-retest at 1 month: Pearson's $r=.85$), and was normally distributed. Females scored higher than males, and more males ($n=14$, 11.9%) than females ($n=4$, 2.9%) scored lower than 30, the cut-off score that best differentiates autism spectrum conditions from controls. EQ was negatively related to the Toronto Alexithymia Scale (TAS) and positively related to the Marlowe-Crowne Social Desirability Scale (SDS). Principal component analysis retrieved the three-factor structure of the EQ. Lower emotional reactivity correlated with higher scores in measures of risk in both the schizophrenia-like (Peters *et al.* Delusions Inventory) and the bipolar (Hypomanic Personality Scale) spectra. CONCLUSIONS: The Italian version of the EQ has good validity, with an acceptable replication of the original three-factor solution, yielding three subscales with high internal and test-retest reliability.

PMID: 20737328

Funding: MRC.

23. Identification of a biological signature for schizophrenia in serum

Schwarz, E., Guest, P. C., Rahmoune, H., Harris, L. W., Wang, L., Leweke, F. M., Rothermundt, M., Bogerts, B., Koethe, D., Kranaster, L., Ohrmann, P., Suslow, T., McAllister, G., Spain, M., Barnes, A., van Beveren, N. J. M., Baron-Cohen, S., Steiner, J., Torrey, F. E., Yolken, R. H., and Bahn, S. (2011) *Molecular Psychiatry*, 1–9.

Biomarkers are now used in many areas of medicine but are still lacking for psychiatric conditions such as schizophrenia (SCZ). We have used a multiplex molecular profiling approach to measure serum concentrations of 181 proteins and small molecules in 250 first and recent onset SCZ, 35 major depressive disorder (MDD), 32 euthymic bipolar disorder (BPD), 45 Asperger syndrome and 280 control subjects. Preliminary analysis resulted in identification of a signature comprised of 34 analytes in a cohort of closely matched SCZ ($n=71$) and control ($n=59$) subjects. Partial least squares discriminant analysis using this signature gave a separation of 60–75% of SCZ subjects from controls across five independent cohorts. The same analysis also gave a separation of 50% of MDD patients and 10–20% of BPD and Asperger syndrome subjects from controls. These results demonstrate for the first time that a biological signature for SCZ can be identified in blood serum. This study lays the groundwork for development of a diagnostic test that can be used as an aid for distinguishing SCZ subjects from healthy controls and from those affected by related psychiatric illnesses with overlapping symptoms.

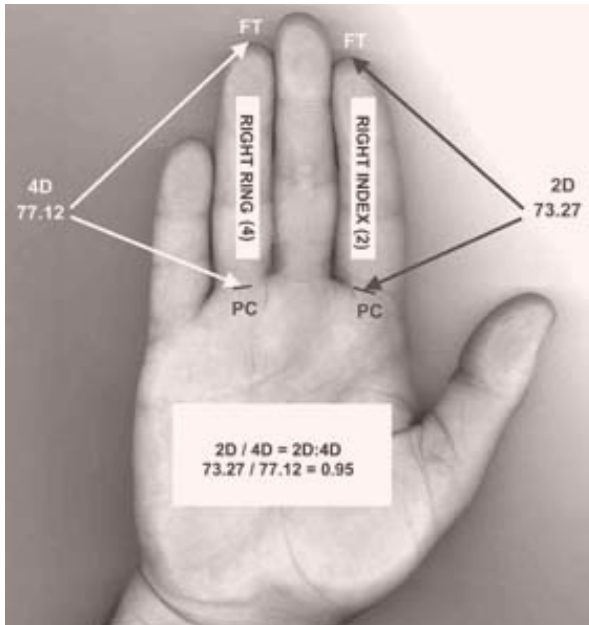
PMID: 21483431

Funding: The Stanley Medical Research Institute (SMRI); Psynova Neurotech; The European Union FP7 SchizDX research programme.

24. Testosterone administration impairs cognitive empathy in women depending on second-to-fourth digit ratio

van Honk, J., Schuttera, D. J., Bosa, P. A., Kruijtc, A.-W., Lentjesd, E. G. and Baron-Cohen, S. (2011) *Proceedings of the National Academy of Sciences*: 2011; Feb 22; 108(8): 3448-52

During social interactions we automatically infer motives, intentions, and feelings from bodily cues of others, especially from the eye region of their faces. This cognitive empathic ability is one of the most important components of social intelligence, and is essential for



effective social interaction. Females on average outperform males in this cognitive empathy, and the male sex hormone testosterone is thought to be involved. Testosterone may not only down-regulate social intelligence organizationally, by affecting fetal brain development, but also activationally, by its current effects on the brain. Here, we show that administration of testosterone in 16 young women led to a significant impairment in their cognitive empathy, and that this effect is powerfully predicted by a proxy of fetal testosterone: the right-hand second digit-to-fourth digit ratio. Our data thus not only demonstrate down-regulatory effects of current testosterone on cognitive empathy, but also

suggest these are pre-programmed by the very same hormone prenatally. These findings have importance for our understanding of the psychobiology of human social intelligence.

PMID: 21300863

Funding: Utrecht University; Hope for Depression Research Foundation; Netherlands Society of Scientific Research; Netherlands Society of Scientific Research Brain and Cognition; MRC; The Nancy Lurie Marks Family Foundation.

SOME OF THE FIGURES ABOVE ARE REPRODUCED FROM GOOGLE IMAGES

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The Pinsent-Darwin Fund Scholarship
The Royal Society
The Shirley Foundation
The Three Guineas Trust
The Wellcome Trust
The Waterloo Foundation

The ARC Club 2011

The ARC hosts the ARClub, a fortnightly seminar in term-time, to bring together autism researchers from across Cambridge University and to hear about latest research from across the world. Below is a list of some of those who have given talks this year:

Charlton Cheung, Hong Kong University
Lauren Hollier, University of Western Australia
Dr. Chris Ashwin, University of Bath
Dr. Olivier Joubert, Aldebaran Robotics, Paris
Dr. Joe McCleery, University of Birmingham
Dr. Elisabeth von den Hagen, MRC Cognition and Brain Science Unit, Cambridge
Rachel Grove, Macquarie University, Australia
Raliza Stoyanova, Cognition and Brain Science Unit, Cambridge
Friedemann Pulvermuller and Rachel Moseley, MRC Cognition and Brain Sciences Unit, Cambridge
Professor Clayton, Department of Experimental Psychology, University of Cambridge
Dr Owen Churches, Department of Psychiatry, University of Cambridge

To view upcoming talks taking place at the ARC, see:

<http://talks.cam.ac.uk/show/index/9692>

Want to Volunteer as a Research Participant in our Research Projects?

If you are an adult with a diagnosis on the autistic spectrum, **OR** if you are a parent with a child who has a clinical diagnosis such as autism or Asperger Syndrome, please consider registering as a research volunteer to help our research projects at the ARC. You can register online by clicking on the “Volunteer Now” icon and filling out the requested details, on our website: <http://www.autismresearchcentre.com>

ARC Volunteers: Update your information

We are currently in the process of updating our database of volunteer families. We would be grateful if you would update the information that you have previously provided (especially if you have moved or had another child). Do register **ALL** of your children, as we are interested in research involving the whole family. There also may be some new questionnaires and tests on our website waiting for you to complete.

To update your details, please go to:

<http://www.autismresearchcentre.com/volunteers/default.asp>

Donations

You can help support the work of the ARC through the Autism Research Trust (www.autismresearchtrust.org). You can donate online at <http://www.justgiving.com/> or send a donation by post to:

c/o Sylvie Nunn
Wrigleys Solicitors LLP
19-21 Cookridge Street
Leeds LS2 3AG



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We remain indebted to our volunteers without whom progress would not be possible

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