"MENTALISING ON THE BROADER AUTISM PHENOTYPE: A GLOBAL OR MODULAR IMPAIRMENT?" & CLINICAL RESEARCH PORTFOLIO VOLUME I

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DEDICATION

To my dad, who taught me that sometimes the most vulnerable people are also the strongest and most resilient, even in their darkest hours. From watching you I learned that when people are vulnerable they need compassion, not judgement. You dedicated yourself and your life to helping those people, inspiring me to choose a career path geared towards making a difference. You taught me to believe in myself, and to never give up; and to have the courage and the determination to challenge everything, and to see things through whatever barriers there may be. You touched the lives of so many people, and your influence lives on long after your loss. Although you will always be loved and missed; rest in peace. These were the values I learned from you:

"IF you can keep your head when all about you

Are losing theirs and blaming it on you,

If you can trust yourself when all men doubt you,

But make allowance for their doubting too;

If you can wait and not be tired by waiting,

Or being lied about, don't deal in lies,

Or being hated, don't give way to hating,

And yet don't look too good, nor talk too wise:

If you can dream - and not make dreams your master;

If you can think - and not make thoughts your aim;

If you can meet with Triumph and Disaster

And treat those two impostors just the same;

If you can bear to hear the truth you've spoken

Twisted by knaves to make a trap for fools,

Or watch the things you gave your life to, broken,

And stoop and build 'em up with worn-out tools:

If you can make one heap of all your winnings

And risk it on one turn of pitch-and-toss,

And lose, and start again at your beginnings

And never breathe a word about your loss;

If you can force your heart and nerve and sinew

To serve your turn long after they are gone,

And so hold on when there is nothing in you

Except the Will which says to them: 'Hold on!'

If you can talk with crowds and keep your virtue,

' Or walk with Kings - nor lose the common touch,

if neither foes nor loving friends can hurt you,

If all men count with you, but none too much;

If you can fill the unforgiving minute

With sixty seconds' worth of distance run,

Yours is the Earth and everything that's in it,

And - which is more - you'll be a Man, my son!”

Rudyard Kipling

1895

30th April 2012

A SYSTEMATIC REVIEW OF COGNITIVE AND BEHAVIOURAL PHENOTYPIC MARKERS IN FIRST-DEGREE RELATIVES OF PEOPLE WITH HIGH FUNCTIONING AUTISM OR ASPERGER'S SYNDROME.

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ABSTRACT

Background

We review the evolving literature relevant to cognitive phenotypic markers in first-degree relatives of people with Asperger's Syndrome/High Functioning Autism (AS/HFA).

Methods

Fourteen papers pertaining to thirteen studies were identified by applying specific exclusion and inclusion criteria to a database search. Corresponding authors were contacted to determine whether their studies met criteria. A modified STROBE checklist was then used by two reviewers to evaluate methodological quality. Meta-analysis was not performed due to the fact it is less appropriate for studies which are heterogeneous in samples, outcome measures or results; on all counts of which the identified BAP studies varied considerably. Further, meta-analysis would be less accurate when utilising small sample sizes, which were prevalent (Eggar, 1997). As such, methodological quality ratings were important when weighing the evidence.

Results

Eleven papers assessed the Broader Autism Phenotype (BAP) in parents while five pertained to siblings. No evidence was found of an Executive Function (EF) deficit in siblings, whereas difficulties with Social Cognition (SC) were identified in two studies. Some evidence was found of Weak Central Coherence (WCC) in fathers, manifesting as superior performance on the Embedded Figures Task (EFT). Evidence of SC difficulties in fathers was also found. Three studies describe specific altered patterns of brain activity in first-degree relatives during EF and SC tasks which may underpin the BAP.

Conclusions

Despite significant methodological limitations, there is evidence that a social-cognitive phenotype exists in a proportion of first-degree relatives. There is some evidence of a stronger phenotype in parents than in siblings, particularly fathers. As the molecular basis of autism becomes better understood, behavioural phenotyping methods are increasingly important.

What this study adds:

- A review of the SC and EF BAP literature pertaining specifically to families where the proband has a diagnosis of AS/HFA.
- Methodological limitations in the current literature are discussed.
- No evidence was found of an Executive Function (EF) deficit in siblings, whereas difficulties with Social Cognition (SC) were identified in two studies.
- There is some suggestion of a stronger phenotype link in fathers.
- The role of gender on the BAP requires further exploration.

Key words: Asperger's Syndrome, High Functioning Autism, Broad Autism Phenotype, Siblings, Parents, Cognitive, Behavioural

INTRODUCTION

People with Asperger's Syndrome/High Functioning Autism (AS/HFA) display a triad of impairments comprising social interaction, communication and imagination in the absence of learning disability (DSM-IV[1]). Estimates of the prevalence of Autism Spectrum Conditions (ASCs) range from 1.2-2.6%[2–4]. In recent years, there has been considerable interest in whether first-degree relatives of people with ASCs may be affected by a milder cognitive or behavioural phenotype, categorised by some as the "Broader Autism Phenotype" (BAP) [5].

The absence of a consistent definition of genotype and phenotype in the literature cause difficulties in conducting a literature review[6]. Mahner et al[6(P62)] define phenotype as follows: ´Set of all types of traits of an organism or of one of its subsystems´. Studying a subset of phenotypic characteristics of interest is more likely to offer consistency and allow replication across studies. Studying cognitive phenotypes may therefore be a useful step in bridging the gap between genome and syndrome[7]. Furthermore, identifying cognitive phenotypes in first-degree relatives may provide a way to correlate specific neuropsychological markers with genetic markers involved in ASC.

Discussion of the genetic basis of ASC dates back to Leo Kanner (1943)[8], who noted that the parents of children with autism appeared to share some of their children's characteristics. Later, Hans Asperger (1944)[9] was more explicit in hypothesising that the parent-child similarities in ASCs reflected genetic factors, and focussed on the potential transmission link between father and son. More recent studies have indicated that relatives are likely to share autistic traits to varying extents[10–11].

It has been argued that the sex ratio in autism (four boys: one girl), and in HFA/AS (nine boys: one girl) suggests a neurodevelopmental difference between the sexes, and points to a genetic origin[12–13]. Recent theories suggesting that high intra-uterine testosterone levels could be associated with ASC may have a bearing on the predominance of males with the condition[14]. However,

testosterone has not been linked to visuo-spatial ability, in which people with autism are often proficient, and it has been argued that questionnaires measuring autistic traits do not differentiate between typical male behaviour and autism[15].

Ozonoff et al[16] utilised a large sample of 664 infant siblings and a prospective longitudinal design to examine recurrence risk where an older sibling was known to have an ASD. A total of 18.7% of the infants developed ASD; a substantially higher recurrence risk than previously estimated, when drawn from smaller samples with methodological limitations. Male gender in the infant sibling and the presence of more than one older affected sibling increased the likelihood of later ASD diagnosis in the infant sibling. Other studies indicate that siblings of people with ASC are over twenty times more likely to have an ASC than the general population[17].

Studies have shown that siblings of those with ASC also have difficulties with Theory of Mind (ToM) tasks, such as "Reading the Mind in the Eyes (RME-R)"[18]. It may be that the degree of autistic traits a sibling has may determine performance on ToM measures, rather than proband diagnosis *per se*. This suggestion was evidenced by another study, [19] which found that the more autistic traits their adult participants displayed, the lower their scores on the RME-R and the Reading the Mind in the Voice test – Revised (RMV-R).

Genetic studies offer evidence that ASC is highly heritable. Muhle et al[20] cite evidence from twin studies of greater than 60% concordance rates for autism between monozygotic twins with no concordance rate between dizygotic twins. Lintas et al[21] discuss the implications of recent advances in genetic testing, including high resolution genomic analysis. The authors suggest that the clinical heterogeneity of autism likely reflects complex genetic underpinnings. These include multiple contributing loci, epistasis and gene-environment interactions. Environmental factors such as

teratogens, toxic exposures, perinatal insults, and prenatal infections account for few cases in epidemiological studies[20].

Fernandez[22] states that about 10% of cases may be associated with a Mendelian syndrome (e.g., fragile X syndrome and tuberous sclerosis complex). Of note, up to 76% of cases of tuberous sclerosis and learning disability may be on the autism spectrum, compared with 24% of those without learning disability[23]. Turner Syndrome in girls is also associated with a risk of autism 200 times higher than for females with intelligence in the normal range[23]. Muhle et al[20] distinguish Rett Syndrome from other conditions linked to the BAP in that it can be attributed to mutations of a specific protein (the methyl-CpG-binding protein). High comorbidity also exists between ASC and epilepsy, with up to a third of individuals with ASC affected by epilepsy by adulthood[20]. Fernandez[22] cite a further 5-7% of cases of ASD as associated with a cytogenetically visible chromosome abnormality, the most frequently observed being a maternally derived duplication of *15q11-13.*

More recently, De Novo Copy Number Variations (CNVs) have been observed in 7-10% of sporadic ASD patients and in 2-3% of affected individuals from multiplex families. Establishing causality within a spectrum of heterogeneous behaviourally defined conditions is complex, and subtyping based on establishing genetic linkage may allow more specific phenotypes to be identified within the autistic spectrum[24]. Freitag et al[24] indicate that CNVs may also underpin some cases of HFA/AS; however, Muhle et al[20] make the point that single gene links are more likely in cases of 'Kanner's' autism. Genetic screening conducted by several research groups has found neurologin mutations to be rare in patients with autism (0.8%), while SHANK3 mutations, deletions or duplications are also rare, affecting 1.1%[21].

Several recent studies have examined PTEN germline mutations on chromosome 10 and the link between these and 'Kanner's' autism. Butler et al[25] examined children aged 3-18 years and found a

link between extreme macrocephaly (+4.5-8 SDs above normal head circumference for the 3 affected) and 'Kanner's' autism. Caglayan[23] highlights that macrocephaly appears present in 15-35% of individuals with autism. Butler et al[25] undertook PTEN gene mutation analysis on genomic DNA in eighteen children (thirteen male, five female) and in their parents where possible; one of the three affected by a mutation was adopted. Three male children (17% of the sample) were found to have PTEN germline mutations on chromosome 10; two of their fathers also had macrocephaly. The authors concluded that PTEN genetic mutation analysis should be considered for children with autism and macrocephaly. However, the study had a small sample size, and due to inclusion of adopted children it was not possible in all cases to trace genetic heritage. Orrico et al[26] screened the nine exons of the PTEN gene in forty patients with neurodevelopmental disorders. Orrico et al[26] found that three participants had de novo PTEN germline mutations; two boys had autism, while a girl with the mutation had a neurodevelopmental disorder. Some fathers were macrocephalic, along with the mother of the 5 year old boy. The authors concluded that the phenotype associated with PTEN germline mutations is broader than the autism spectrum. Further, they recommended that children with macrocephaly should be screened for PTEN mutations due to a potential elevated risk of cancer and that additional studies should be done to delineate the phenotype associated with PTEN germline mutations.

The majority of 'unexplained' ASD cases are presumed to have multifactorial forms of ASD; linkage scans have mapped candidate risk loci. Data from whole genome screens in multiplex families indicate that ten or more genes interact to cause autism[20]. Multiple susceptibility genes on different chromosomes may be required to make an individual vulnerable to autism. Muhle et al[20] argue that pre- and peri-natal factors may then modify the phenotypic expression of this disorder. For example, elevated mean levels of some neuropeptides, of which the concentration is under genetic control, were found in the cord blood of children later diagnosed with autism, but were normal in non-autistic children with cerebral palsy. Thus, brain development and the complex behavioural

sequelae are multi-determined across a series of stages. The findings of cytogenetic abnormalities and single gene disorders associated with ASC also indicate genetic heterogeneity and different modes of inheritance in individual families. Consequently variability in phenotype is to be expected.

Despite scientific interest, the search for strong evidence of a genetic link continues, and is encumbered with analytical and methodological challenges. Limited power by way of relatively small sample sizes in genome-wide scans, varying designs, genotyping and analyses and imprecise phenotypic definitions are some of the limitations[27]. Phenotypic heterogeneity has challenged molecular searches for genes and made genome wide scans challenging[13]. Genome-wide association studies represent a more powerful, less biased approach than candidate gene studies[15]. Since 2008, this approach has begun to be applied, having previously been considered unviable in terms of cost and technical considerations.

Two reviews pertaining to the BAP were conducted around 12 and 6 years ago respectively[28–29]. A general review of the BAP was also published recently[30], but did not focus specifically on AS/HFA. Chutapisith et al[31] found presence of a cognitive phenotype in siblings of children with ASD and LD; where the proband had higher IQ, the sibling did also. Clearly defined proband groups are therefore desirable, as IQ has been linked in turn to cognitive aspects of ToM. Due to the high comorbidity with Learning Disability (LD), there is also a difficulty in distinguishing the cause of the phenotypic markers where pre- and peri-natal factors such as encephalopathy may have had an influence. Yirmiya et al[29] found that studies often used mixed-ability probands and varied in the selection of TD vs. LD control group, leading to inconsistent results across studies, and concluded there was a need to look at different functioning levels and comparison groups separately in systematic review. Whilst we acknowledge likely overlap in phenotype with other conditions, including tuberous sclerosis, studies pertaining to these related disorders will not be addressed within the current review.

Therefore, we focus on behavioural and cognitive phenotypic markers of HFA/AS examined in first-degree relatives.

Research Questions

Is there evidence of a) Social-Cognitive (SC) or b) Executive Function (EF) phenotypic markers characteristic of first-degree relatives of people with AS/HFA?

Is evidence of such markers stronger in parents versus siblings?

METHOD

Search Strategy

The following databases were searched using OvidSP: medlineR 1950- December week 1 2010, embase 1980-2010 week 49, Health and Psychosocial Instruments 1985 – December 2010, AMED (Allied and Complementary Medicine), 1985 – December 2010, ERIC, 1965 – December 2010, journals@ovidfulltext 1.12.10, books@ovid 1.12.10, your journals@ovid and PsychInfo.

The above databases were searched using the following terms: Asperger* Syndrome, AS, High Functioning Autis*, HFA, Sibling*, Brother*, Sister*, parent*, mum*, mother*, dad*, father*, maternal, paternal, phenotyp*, broad autism phenotype, endophenotype, genotyp*, gen*, cogniti*, behavio*. As an Initial step, the search terms were entered individually. Next, words indicating HFA/AS were combined using "OR". Words indicating sibling were similarly combined using "OR", as were words indicating phenotype. Then a search was conducted combining these searches with "AND".

Next, the reference lists of all identified meta-analyses, systematic reviews and guidelines were consulted, and articles which met inclusion criteria were located. Additionally a manual search of key journals (Autism, Journal of Autism and Developmental Disorders, journal of Child Psychology and

Psychiatry, Developmental Medicine and Child Neurology) spanning the past decade was performed to identify any additional relevant studies.

The following inclusion criteria were applied: 1. studies with a primary aim of examining BAP phenomena in full biological siblings and parents whose off-spring had a confirmed diagnosis of HFA/AS. 2. First-degree relatives referenced in methodology of abstract. 3. Cognitive or behavioural phenotypic markers included in aims/ research questions. The following exclusion criteria were applied: 1. Studies examining only probands with HFA/AS 2. Studies examining relatives of children with "Kanner's" autism (for reasons outlined above). 3. Studies examining second-degree relatives. 4. Studies including step-siblings, half-siblings or adoptive-siblings.

This process left a total of one hundred and thirty three articles which appeared to meet criteria. See figure 1 for an illustration of the further selection process.

Insert figure 1 about here

Methodological appraisal of included studies

A methodological quality checklist was adapted from the STROBE guideline with additional items included relevant to current good practice standards for research in HFA/AS (see Appendix 1.1). Each paper could attain a maximum score of 69, which was then converted into a percentage. Studies scoring over 75% were considered high quality, 50-75% medium quality and less than 50% low quality. The reliability of the checklist was verified by having a second reviewer rate methodological quality. Overall agreement was substantial, producing kappa = .73, $p < .001$. Any disagreements were resolved by discussion with a third reviewer.

Analysis of data

Following quality appraisal, studies were categorised into those examining possible deficits in social (e.g. personality, theory of mind) vs. non-social information processing styles (e.g. WCC, EF).

RESULTS

Below, tables 1 and 2 show results of methodological appraisal of studies examining the BAP in siblings and parents respectively.

Insert table 1 here

Insert table 2 here

In addition to these tables, more detailed information is provided below.

Siblings

One cognitive theory of autism, known as the "weak central coherence" (WCC) theory, suggests that people with autism may have a different information processing style from others whereby they may focus on detail to the exclusion of "gist" or overall meaning. Happe et al[32–33] considered potential advantages of this processing style, and suggested that fathers of boys with HFA/AS may be more likely to be skilled at visual tasks.

Dorris et al[18] found that siblings performed more poorly on the RME than TD controls. Spencer et al[17] carried out fMRI scanning of participants' neurological functioning while they viewed happy versus neutral facial expressions. They found that siblings' brains showed reduced activation in 7/11 areas

studied, which did not differ from that in the brains of children with autism. Contrastingly, TD children's brains showed significantly more activation in these areas. Strengths of this study included a relatively large sample size, and the inclusion of probands for comparison. A weakness lay in not matching the sibling and control groups for gender, with more female siblings than female controls. Analysis of covariance was utilised however, and gender was not found to have a significant impact on the results. The authors suggest that activation in these brain areas may trigger empathy in TD children, and that an atypical fMRI profile in those affected by the BAP may suggest they do not experience this implicit empathic reaction. Yoder et al[34] utilised a novel methodology of assessing infant siblings. They aimed to detect early traits of BAP and hence predict diagnosis. However, this design offers limited scope to measure IQ and therefore to differentiate AS/HFA from 'Kanner's' autism. A further limitation concerned the strategy of group matching for mental age but not for gender[34]. The authors acknowledge variability in their sample, a bias which could have been controlled for with a matched-pairs design.

Parents

Happe et al[32–33] found evidence of WCC in fathers of boys with HFA/AS. In a second experiment with the same sample, both mothers and fathers of boys with HFA/AS showed social and non-social preferences fitting with WCC. De Jonge et al[35] utilised the Embedded Figures Task (EFT), a measure of WCC in the visuo-spatial domain. Attention to detail whilst ignoring context information is required for successful performance. The task requires participants to quickly locate a simple shape within a complex design on a card. De Jonge et al[35] reported strengths in fathers of boys with AS/HFA in that they made fewer incorrect attempts before finding the correct shape. Including proband participants in the study adds validity when linking task performance to BAP. The authors noted a lack of power (albeit with a large effect size), and deviation from the test manual for scoring procedures, which casts some doubt on the generalisability of their results. Koczat et al[36] examined spatial accuracy in parents. Parents showed poorer spatial accuracy than controls. However, there

were considerable methodological limitations, such as the use of a small sample spanning a wide age range. The sample included mainly mothers (2:1 ratio), which may have a significant bearing on the findings given evidence suggesting that females generally perform more poorly than males on these measures[12]. Generalisability may therefore be limited, and this aspect of BAP requires further investigation.

Scheeren et al[37] found that fathers whose child had HFA/AS were slower to respond to social cues than controls. This effect was not due to higher AQ scores in the fathers group, as the AQ scores were similar in the control group. Losh et al[5] found significant SC deficits on the RME-R, but only in a sub-group of parents characterised as 'aloof'. The authors report deliberately including this sub-group who were known to be high in BAP, which carries a risk of a false positive effect that would not generalise to relatives as a whole group. Low RME-R scores in this group were associated with low-quality friendships and problems with pragmatic language use, suggesting the measure has ecological validity. However, a mixed control group of parents of TD and parents of children with Downs Syndrome was selected. The former were included due to difficulties recruiting the latter, and groups were not IQ or gender-matched. In view of this, an alternative approach may have involved Analysis of Covariance to remove the confounding effect of these variables. The authors acknowledge the need for replication due to these limitations.

Lennox et al[38] conducted one of the first studies to examine the idea of shared parent-child traits of a BAP. Lennox et al[38] controlled for social class but not IQ, and did not find presence of BAP. Whitehouse et al[39] examined language skills in parents. Parents of children with ASC as a group had elevated scores on the AQ domains of communication and attention-switching. Coupled with the finding that they performed better than parents of children with specific language impairment on measures of language, this suggests it is the SC aspect of the BAP that may cause social language difficulties rather than more general language impairment. Although Whitehouse et al[39] described matching groups for age, IQ, gender and socio-economic status (SES), the reported demographic

data include more female controls than mothers and fewer male controls than fathers. This may have biased results towards a false positive BAP finding due to between-group gender differences.

Studies looking at both parent and siblings

Baron-Cohen et al[12] carried out a pilot study examining both SC and EF in parents, and found some evidence parents were less accurate on the RME-R and quicker on the EFT. The authors clearly report the limits of their design, particularly in terms of a lack of matched-controls, and highlight a need for more research to clarify theories of BAP and brain-behaviour links. Baron-Cohen et al[40] later used f-MRI technology to image the neurological responses of parents whilst they completed these tasks. Parents showed more activity in the left inferior frontal gyrus than their matched-controls during the RME-R; and less activity in the extra-striate cortex during the EFT[40]. This study therefore indicates that the BAP observed in parents of children with AS/HFA may reflect observable neurological differences during information processing, thus providing construct validity for the RME-R and the EFT. As this was a pilot study, a larger scale study would add weight to these interesting findings.

Methodological quality ratings were considered when weighing the balance of evidence. There is evidence from high quality studies to support that siblings have subtle SC difficulties, but no evidence that they have any EF differences from TD peers. For parents, high quality studies show that they have EF differences from adults without a child on the autism spectrum. Several medium quality studies indicate that parents also have subtle SC difficulties.

DISCUSSION

Siblings – Main Outcomes

The studies by Happe et al[32–33] included both parents and siblings in their analyses, and found no evidence that siblings were affected by an EF BAP. There is no other evidence to suggest that siblings

are at any increased risk of EF deficits. Yoder et al[34] and Dorris et al[18] found evidence suggesting siblings are affected by the social-cognitive BAP. This may be an area where siblings require support. Additionally, Spencer et al[17] found evidence using fMRI to suggest that there may be a neurological underpinning to these findings.

Parents – Main Outcomes

There is evidence from several studies that parents are affected by the social-cognitive BAP. Clinicians may need to consider this when working with families, to offer parents appropriate support. Studies using the EFT have consistently found the presence of a BAP around WCC in parents of children with HFA/AS. This has positive as well as negative implications.

Strengths and limitations of literature

It is encouraging that some studies focussed on cognitive advantages conferred by the presence of a BAP. This fits with clinical knowledge that fathers of boys with autism frequently achieve career success as engineers, mathematicians and IT professionals[41].

Consistent use of the RME-R and EFT tasks across studies has allowed some replication of results and perhaps confidence in the presence of an SC BAP. The literature has begun to establish brain-behaviour links with performance on standard measures of EF and SC. As endophenotype methodologies advances, there is the potential to correlate SC and EF performance with neurological and genetic markers.

Certain weaknesses permeated most studies however. Only one study justified sample size, utilising a power equation[18]. Most studies used small sample sizes, and without the use of a power equation it is not clear whether a null finding was due to a lack of power. Some studies reference recruitment challenges. It may be that those relatives willing to participate in research on the BAP are different in some way from those who choose not to; for example, they may be motivated to do so due to

feeling that they may have difficulties themselves. One recruitment solution would be increased multi-centre collaborations. Additionally, this would allow for more rigorous methodological designs, e.g. matched-pairs designs with stricter matching criteria covering age, IQ, gender and SES.

Studies have varied in their choice of TD versus LD control groups. Different control groups may lead to inconsistent results across studies in terms of BAP. Use of multiple comparison groups and reporting data on each separately would allow comparisons across studies.

Matching procedures also varied. Parents were at times matched with non-parents, which may have confounded results[36, 40], as being a parent may have an impact on SC and EF. Groups were not always IQ and gender-matched, despite evidence that these variables affect ToM performance[42]. Group-matching designs were generally adopted, and while pragmatic, may introduce more bias from confounding variables than matched-pairs designs. Studies generally did not match for SES, although there is some evidence this may affect SC[43]. Such variability makes it difficult to draw general conclusions from the literature and may explain why findings are not consistently replicated.

There is also variability among studies in the method used to ascertain diagnosis of AS/HFA. DSM-IV criteria have been used[5], although often with limited detail regarding application. Other studies have used structured tools (e.g. the ADOS or ADI-R) as part of a multidisciplinary assessment. Where protocols for establishing diagnosis are less robust, there is less certainty in valid diagnosis. Blurring of proband groups could mean weaker or less robust findings regarding the BAP[13].

Future research

While it is well replicated that some first-degree relatives of people with HFA/AS show impaired performance on the RME-R, it would be of use for more studies to examine whether this generalises to other measures of SC, including real-life measures[42], and across other sensory modalities[18].

Dorris et al[18] suggested that female siblings affected by the social BAP might be particularly impaired relative to TD peers. There were relatively few female participants however, and other studies have similarly had a higher proportion of males. Further research may specifically examine the bearing of gender on the BAP. Given 3-4 times as many boys as girls are diagnosed with autism, and comparatively less is known about how females are affected, the BAP literature around siblings (rather than mothers) mirrors this pattern and suggests we need to know more about how girls may be affected by the BAP.

In light of social learning theories, research may also examine the impact of sibling position within a family on BAP presence, and whether the gender of the proband with HFA/AS has an impact. Longitudinal research tracking siblings' developmental progression could address the question of whether BAP phenomena are stable across time, as with people with AS/HFA. Similarly, further research could examine whether supportive intervention can enhance SC for those affected by the BAP. There is evidence that children with HFA/AS have difficulty generalising social rules, and in applying these to every-day life. Understanding whether or not this is also the case with those affected by the BAP could inform family based intervention.

Further research incorporating observational methods could also examine interaction patterns within families affected by BAP. It could be that SC and EF patterns are transmitted by modelling, mimicry and reinforcement. Theories of learning on the autistic spectrum may help explain how this process occurs for individuals and within families affected by BAP[44]. The assortative-mating theory[40] argues that autism may be the result of parents initially being attracted to each other due to their similar hyper-systematising processing styles. They may then model this manner of understanding the world for their children. Evidence for this theory includes both mothers and fathers of children with HFA/AS showing superior performance on the systematising quotient, a test of the ability to analyse rule-governed systems. Alternatively, stress may play a role[45], or families with a child with HFA/AS may have difficulty accessing opportunities in which adaptive social skills can be observed,

modelled and practiced[46]. Understanding which of these variables is most relevant could inform service planning and provision.

Losh et al[5] examine parents showing the BAP separately from parents who do not, whereas other studies have simply examined relatives as a group. The sub-group strategy may appropriately reflect the argument that if genes influence the phenotype, relatives may or may not be affected. Therefore it is to be expected that there may be a BAP + and BAP – group as Losh et al[5] found, and it may be of interest to examine the genotype further within the BAP + group alongside probands. Perhaps BAP families may comprise both BAP + and BAP – members, and function whereby complementary roles may develop, and the BAP- members may develop to nurture the BAP + members[47].

Presence of additional difficulties such as ADHD and dyslexia for probands are not always reported[48]. It would be of interest to examine whether presence of comorbid difficulties represents a more severe phenotype as manifested on SC or EF tests, and if relatives of these people are then more likely to also be affected in these areas.

Practical Applications

Significant impairment in social cognition is a defining clinical feature of HFA/AS and the current literature indicates that a milder version of these difficulties extends to a proportion of both siblings and parents of those with HFA/AS[30]. As such, screening of relatives who report difficulties with SC utilising a questionnaire measure may be useful[13]. Where there is an evidence base for carrying out genetic testing (perhaps with children with autism and macrocephaly due to the link with PTEN germline mutations), such methodology can offer some answers for parents about the cause of their child's difficulties, potentially leading to the alleviation of negative emotions such as 'felt guilt' and anxiety. For some parents in this situation, willingness to participate in treatment programmes may also increase[21].

Scientific Implications

The evidence of a social-cognitive BAP when combined with recent advances in genetic research methods has scientific implications; further research may fruitfully be conducted to delineate phenotypes associated with particular CNVs and cytogenetic abnormalities associated with the BAP. Not all those affected by PTEN germline mutations experience a BAP[26], and the possibility of possessing a predisposing gene but not displaying the social-cognitive phenotype requires further investigation. It is unknown how prevalent this situation is in families affected by the BAP, and little is known regarding whether environmental factors can mediate or moderate the emergence of a BAP where an individual possesses a combination of pre-disposing genes[20]. This knowledge may enable early psychosocial intervention to be implemented more effectively.

There is now potential for studies to examine social-cognition using reliable and valid psychological tests which have well replicated ability to detect subtle social-cognitive deficits in a BAP population. Further, the ecological validity and clinical significance of poorer scores on these tests in terms of real world impairment may be measured using interview or observational methods. In a multi-disciplinary collaboration, genetic analyses and fMRI readings could be taken of the same participants who took the psychological tests. This might enable us to understand more fully the mechanisms underpinning normal versus abnormal social-cognition. It may be that those with a deficit differ qualitatively rather than just quantitatively in their social-cognitive processes, perhaps using intellectual rather than affective means to formulate a response[17]. Combined methods could address whether such qualitative differences have a genetic basis. These methods also have the potential to assist in delineation of broader phenotypes associated with other clinical conditions with a known or theorised genetic component (e.g. Fragile X[22]). The measures currently available to quantify personality traits associated with social cognition (e.g. the Autistic Spectrum Quotient) [49] may assist in identifying factors associated with poorer social-cognition and ToM within the general population. As social cognition and ToM deficits have been linked to mental health difficulties, and

there may be co-morbidity between a BAP and mental health difficulties such as depression[50], it is perhaps helpful to examine any neuropsychological or genetic basis for this combined vulnerability. Recent studies have also highlighted the importance of understanding social-cognitive phenotypes associated with psychopathy and violent behaviour[51]. Research methods which can illuminate social-cognitive phenotypes both within and beyond the BAP therefore have a key role in furthering scientific knowledge and understanding, which in turn may help inform assessment and intervention approaches for a range of presenting problems facing clinicians.

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MENTALISING ON THE BROADER AUTISM PHENOTYPE: A GLOBAL OR A MODULAR IMPAIRMENT?

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ABSTRACT

BACKGROUND

Previous research has shown that children with a diagnosis of Asperger's Syndrome or High Functioning Autism (AS/HFA) have difficulty with mentalising tasks. There is also limited evidence that siblings may also have subtle deficits in 'theory of mind' consistent with a broader autistic phenotype model. This study aims to investigate whether deficits in mentalising about others is specific to sensory modality (modular) or mediated by a global impairment in mentalising.

METHODS

Thirteen children who had a sibling with AS/HFA were compared to thirteen children who did not, matched on age, gender and verbal IQ. Children completed a range of self and other mentalising tasks.

RESULTS

No significant differences in mentalising were detected between the groups. Descriptive statistics indicated a trend for male siblings to have higher AAQ scores and longer mean response times on the RME than female siblings and controls.

CONCLUSIONS

Larger samples and replication would be required to ascertain whether any significant impairment in mentalising about others across modalities is present in siblings, and to clarify the impact of gender and social learning theory. Formal modification of the auditory test (RMV) for younger children would be helpful in order to robustly compare differences in performance across modalities both within and between groups.

KEYWORDS:

High Functioning Autism/ Asperger Syndrome, Siblings, Mentalising, Theory of Mind

ABBREVIATIONS:

HFA/ AS = High Functioning Autism/ Asperger Syndrome, TD = Typically Developing, ToM = Theory of Mind, BPVS = British Picture Vocabulary Scale, AAQ = Adolescent Autistic Spectrum Questionnaire, RME = Reading the Mind in the Eyes Test, RMV = Reading the Mind in the Voice Test.

BACKGROUND

People with Asperger Syndrome/ High Functioning Autism (AS/HFA) have difficulty across a triad of impairment comprising social interaction, communication and imagination (American Psychiatric Association, 2000). Estimates of the prevalence of Autism Spectrum Conditions (ASCs) range from 1.2-2.6% (Baird et al., 2006, Baron-Cohen et al., 2009, Kim et al., 2011). A number of cognitive theories of autism have been influential, one hypothesis being that social communication difficulties stem from impaired theory of mind (ToM) (Kaland, Smith, & Mortensen, 2007). Previous studies have established that children with AS/HFA have particular difficulty with understanding both others' minds (Baron-Cohen, Wheelwright, Spong, Scahill & Lawson 2001) and their own (Dritschel, Wisely, Goddard, Robinson, & Howlin, 2010).

Efforts have been made to aid diagnosis, understanding and treatment for families affected by autism through research into the aetiology of the condition (Sucksmith, Roth & Hoekstra, 2011). There is mounting evidence for a genetic basis of AS/HFA, with the implication that relatives are likely to share these autistic traits to a greater or lesser extent (Chakrabarti et al., 2009); (Losh, Childress, Lam, & Piven, 2008). In identical twin pairs, one member of whom has autism, the concordance rate for autism is 60% and the concordance rate for a disorder on the autism spectrum is over 90% (Cassel et al., 2007). Another study found that about half of all boys diagnosed with AS/HFA have a paternal family history, and 71/100 individuals with AS/HFA had one or more first or second-degree relatives who had raised concerns about behavioural traits consistent with the disorder (Gillberg & Cederlund, 2005). However, the search for unequivocal evidence of autism susceptibility genes continues, due to analytical and methodological challenges. Small sample sizes with varying inclusion criteria predominate in the literature, perhaps reflecting recruitment challenges (see **Systematic Review**). As a result, limited power and differences between samples may have contributed to inconsistent findings. Varying designs and imprecise phenotypic definitions are other limitations (Losh et al, 2008). A Broader Autistic Phenotype (BAP) has been shown to

characterize some relatives of people with AS/HFA (Losh, et al., 2008). BAP mild impairments identified in relatives include those in the domains of language, social functioning, restricted interests and behaviour and neurocognitive functioning (Sucksmith et al, 2011).

Some studies have shown that siblings have difficulties with ToM tasks, such as "Reading the Mind in the Eyes (RME)" (Dorris, Espie, Knott, & Salt, 2004). However, perhaps due to methodological differences and weaknesses other studies have not detected significant differences between siblings and normal children (Shaked, 2006), posing questions as to the sensitivity of tests in detecting the more subtle impairment likely in those affected by the BAP. Studies have not generally recorded response time for siblings, which may indicate level of effort or 'cognitive fluency' in completing the task. One study found that while children with AS/HFA were globally slower to respond on a range of cognitive tasks than controls, they were particularly slow on a mental state inference task (Kaland, et al., 2007). Spencer et al (2011) found that when viewing other's facial expressions, siblings showed a pattern of brain activation more similar to those with HFA/AS than to normally-developing children. Reduced activation was seen in those with HFA/AS and their siblings, and Spencer et al (2011) posited that these brain regions were activated when empathy was experienced; and that this was more so in the normally-developing children. If so, siblings may decipher other's emotions intellectually and still be correct, but it might take them longer and involve different brain systems. In naturalistic social situations, this could lead to subtle impairment.

It may also be that the degree of autistic traits determines performance on ToM measures, rather than simply whether or not one has a sibling with AS/HFA. This hypothesis was investigated in another study (Golan, Baron-Cohen, Hill, & Rutherford, 2006), which found that the more autistic traits their adult participants had, the lower their scores on the RME-R and the Reading the Mind in the Voice test – Revised (RMV-R).

Another question arises as to whether ToM deficits are specific to a particular sensory modality or are multi-modal. The RMV-R (Adult) has been positively correlated with the RME-R (Adult) in normal adults and those with AS/HFA, suggesting a common basis for emotion and mental state recognition abilities across perceptual domains (Golan et al 2006), however as limited evidence has been provided more research is needed to clarify this.

While ToM difficulties among AS/HFA populations are well established, recent research has examined self-mentalising ability. Difficulties in accessing, representing and expressing thoughts and feelings may impact social competence and hold strong associations with communicative barriers evident in autism (Losh & Piven, 2007). TD children attribute more knowledge about their own internal states to significant others until around the age of 10 (Burton & Mitchell, 2003). In a study by Dritschel et al (2010), a measure of self-concept was administered to a group of young adolescents with AS/HFA and a group of age, gender and verbal IQ-matched TD control children. The measure included two control questions to check the participants understood the task and six targeted self-knowledge questions. These questions required the young person to reflect on whether they or an identified other knew more about their own internal states. Those with AS/HFA thought others knew more than them about their own internal states, whereas TD matched controls stated clearly that they had superior knowledge about their own internal processes, suggesting a diversion from typical adolescent development in self-mentalising in AS/HFA.

It has been suggested that while self- and other-mentalising may both be difficult in AS/HFA; the impairment may differ in magnitude. Siblings, in addition to experiencing subtle deficits in ToM, may also show less understanding of their own minds. If so, this would add to our understanding of the mechanisms underpinning ToM processes within the BAP.

The AAQ (Baron-Cohen, Hoekstra, Knickmeyer, & Wheelwright, 2006) is a measure of severity of autistic traits and can allow exploration of variance in performance on tasks known to be impaired in

HFA/AS which is explained by scores on a general measure of BAP. This then enables the question of whether there is a global deficit on the BAP in mentalising about both self and others, which can be detected by scores on a general measure. Alternatively, a pattern of modular strengths and weaknesses may prevail which could not be predicted solely by AAQ score. An argument has been presented to support this (Losh et al., 2007), hypothesizing that distinct impairments may segregate independently as discrete endophenotypes on the BAP. Behavioural features of the BAP were examined in relation to performance on the RME-R with parents of children with autism. Parents were not found to be impaired in general, but those classified as aloof during a personality interview displayed significant social cognitive deficits on the RME-R. Poorer performance was in turn associated with poorer quality friendships and problems with pragmatic language use. Identifying such endophenotypes may provide a way to isolate specific neuropsychological mechanisms of biological and genetic significance to autism. This goal is of interest conceptually, in terms of the breadth of impairment on the BAP and the proposed theoretical link between the ability to mentalise about self and about others (Carruthers, 2009).

The reader is directed to the **MRP Proposal (see appendix 2.2)** and **Systematic Review** for a fuller discussion of the background literature, its strengths and limitations.

Aims

The principal aim of this study is to explore whether deficits in mentalising are global or modular on the BAP. Further, we aim to explore whether performance on auditory and visual modalities correlate in support of a shared underlying ToM module.

Research Questions

1. Do siblings have more autistic traits than TD peers?

2. Is there a relationship between overall AQ score and performance on the target measures?

3. Is it more effortful for siblings to solve mentalising tasks than for TD children?

4. Are siblings impaired in ToM tasks across sensory modalities?

5. Do siblings have a general impairment in self-mentalising?

METHODS

Experimental Design

The following hypotheses underpinned the study:

1. It is predicted that there will be a significant difference between the groups on ToM tasks in terms of both test performance and response latency; and these differences may be apparent across sensory modalities. Siblings may additionally perform differently on self-concept tasks.
2. AAQ score will predict variance in scores on the RME and the RMV, and the self-concept task.

In order to test these predictions a matched-control between group design was utilised. A power equation, calculated using PASS 2008 software and following the procedure indicated by Mueller (23,24), was utilized to establish the number of participants required for Multivariate Analysis of Variance (MANOVA). Using data from previous studies which used the target measures (3, 4, 12); a means matrix and covariance matrix were produced. Due to large effect sizes produced in studies using the target measures, the power calculation indicated that if a Wilks Lambda approximate F test was used a sample of 25 participants per group would be adequate to test the hypothesis with .8 power at $p < .05$.

Participants

Two groups of participants were recruited. Siblings of children with HFA/AS were recruited from the Scottish Centre for Autism, the Community Autism Teams across the four Community Health Partnership areas in Greater Glasgow, and the Lanarkshire Autistic Spectrum Disorder Service. Additional participants were sought from support groups affiliated with the National Autistic Society across Scotland. When potential participants were identified, the researcher contacted the parent by telephone to ascertain that the sibling met inclusion criteria and to verify the diagnosis of the index child. This information was later obtained along with further demographic information on a Family Information Questionnaire (see appendix 2.3). Recruiting 25 siblings concordant with inclusion criteria proved more challenging than anticipated. For inclusion, siblings required to be aged at least 10, to have a full sibling with a diagnosis of HFA/AS, and not to have known special educational needs or diagnoses of developmental disorders or mental health problems. Several families did not meet criteria for the following reasons; the sibling was too young (8 children); the potential participant was only a half sibling (2 children); the sibling had a diagnosis of ADHD (1 child); the sibling had a diagnosis of dyslexia (1 child); the index child had a diagnosis of Kanner's Autism (1 child). In two cases, parents showed interest in the study, but later reported that the young person was not willing. In these instances parents were assured that their child was under no pressure to take part in line with ethical guidelines. We therefore recruited 13 siblings from 11 families (6 boys, 7 girls, mean age = 13 years; SD = 2.45; range = 10 years 0 months – 16 years 11 months) (mean BPVS = 109.38; SD = 12.494; range = 90-130). The majority of index children were diagnosed either at the Scottish Centre for Autism or at the Lanarkshire Autistic Spectrum Disorder Service. Both are specialist centres for the assessment and diagnosis of ASD and utilise a multidisciplinary assessment emphasising information gathering from local health and education sources, a comprehensive parental interview and a structured assessment of children's social and communication abilities.

Data regarding IQ were not routinely collected by either service, and as such index child IQ is not available. Parents were asked whether any other family members had a diagnosis of ASD.

TD children were recruited from two local schools following ethical approval from Education Services of Glasgow City Council and agreement from the Head Teachers of the schools contacted. In total, 13 control children were selected from a larger sample of normally-developing children on the basis of matching siblings for gender and as closely as possible for age and BPVS score (6 boys, 7 girls, mean age = 12.85; SD = 2.38; range = 10-16 years), (mean BPVS = 110; SD = 17.31; range = 86-141) prior to any further data analyses. T-tests showed that there were no significant differences between the groups on the basis of BPVS score or age. Children were not matched on socio-economic status for pragmatic reasons, but additional sibling participants (n=3) were recruited from participating schools.

Research Procedures

Ethical and Research and Development approval was obtained from the West of Scotland NHS Research Ethics Committee, and from Greater Glasgow Council in February 2011. For further details of the ethical approval process, see **MRP proposal (appendix 2.2)**. Subsequently, NHS Multi-Centre Ethical Approval was obtained and subsequent Research & Development approval for NHS Lanarkshire was granted in August 2011. Data collection took place from March 2011-January 2012. Informed consent was obtained from all families.

Participants were all seen individually in a quiet room, normally at their own school, or at a clinic. A laptop with the computer-based tasks installed was utilised to run the protocol. Firstly children completed the BPVS, then the RME, the RMV and finally the Self Concept Questionnaire. Response latency data for the RME was recorded using a stopwatch: as soon as the test question was asked, the stopwatch started. When the participant answered, the stopwatch stopped and the exact

answer was recorded. Effort was made to time discreetly so as not to cause undue anxiety. Testing time was approximately 1 hour.

Parents of both groups of children were asked to complete the AAQ. Where parents attended a clinic with their child, they completed the AAQ and Family Information Questionnaire in a separate room whilst their child was in the session. Otherwise, the AAQ was posted out to the parent and returned in a stamped addressed envelope. The response rate was 92%, 2 forms were not returned by parents of children seen at school. Appropriate preparations were also made in the event that any young people or their parents had concern regarding their social communication following participation in the study (see ethics). One sibling scored highly on the AAQ (score =44), but no control participants did so. While some parents of TD children seen in school contacted the researcher to clarify how to complete the AAQ and comment on their children's social development over time, none expressed concern that their child may have an undiagnosed ASC, or indicated that they wished to discuss any concerns with the second author, a Consultant Paediatric Neuropsychologist, who would have been available in that eventuality.

Some siblings took the opportunity to briefly discuss their views and feelings about having a sibling with an ASC with the researcher, but none stated that they or their parents were worried in any way about their own social development.

Measures

Adolescent Autism Spectrum Quotient (AAQ) (Baron-Cohen et al., 2006)

This is a parent-report questionnaire, adapted from the Adult AQ. The AAQ measures the degree to which any child aged 9-15 possesses traits related to the autism spectrum, but it is not a diagnostic measure. Scores range from 0 – 50, with higher scores reflecting more traits. Using a cut-off score of 30, Baron-Cohen et al (2006) found that no controls scored above this level but all AS/HFA girls and

86.7% of the AS/HFA boys did. It also showed good test-re-test reliability and high internal consistency.

The British Picture Vocabulary Scale (BPVS, Dunn, Dunn, Whetton & Burley. 1997).

The BPVS is a frequently used brief picture-based measure of receptive vocabulary, standardized for children aged 3 to 18.

Self-concept Questionnaire (Mitchell & O'Keefe, 2008) see appendix 2.4

This measure requires participants to first identify a comparison individual. Each participant then participates in a verbally administered self-concept interview in which they are asked to rate first their own expertise and then the comparison individual's expertise on two control questions and six focal self-knowledge topics including knowing when you feel ill, tired, sad, happy, are daydreaming and about what kind of person you are.

Child Reading the Mind in the Eyes test (RME) (Baron-Cohen, 2001)

This task is a modified version of the original adult version of the RME-R task. The main adaptation is reduced complexity in vocabulary. It is a computer-based task, supported by verbal explanation from the experimenter. It has 28 items, in which participants are presented with a photograph of the eye area of the face and are asked to choose from four adjectives to describe the person's mental state. These items include subtle emotions, and a practice item precedes the first trial. Lesion and fMRI studies have implicated specific neural circuitry involved with performance on the RME, suggesting that this measure may be particularly well suited to investigating biological pathways for studies of the brain and the genetic basis of autism (Baron-Cohen et al., 2006).

Reading the Mind in the Voice test (RMV) (Golan, et al., 2006)

This measure has demonstrated good reliability and discriminative validity. Again, this is a computer-based task, with the child required in this instance to decide from a choice of four adjectives which best represents the mental state of the speaker of a voice clip. Unfortunately this measure has not been modified as yet for younger children. Golan et al (2006) had adult participants run the task for themselves using DMDX software and headphones and found that verbal IQ was a significant covariate. Due to the age of the participants and the complexity of vocabulary, the procedure was modified somewhat. The experimenter firstly provided children with definitions of words on a hand-out, which children familiarized themselves with prior to participating in the task, reducing any issues regarding impact of vocabulary. Where necessary the experimenter supplemented this with further explanation of word meanings. The experimenter then went through each item with the child, playing the voice clip and reading through the response options.

RESULTS

Scoring

Results for the RMV and RME total score were calculated by adding the total number of correct responses per participant. RME response time was calculated by summing the total response time taken for each of the 28 items, and then dividing by 28 to obtain a mean response time. The AAQ was scored according to the accompanying scoring key (see Baron-Cohen et al., 2006). The BPVS was scored according to the manual. Self-concept responses were entered into the database as given for each participant. For the 6 focal mental state questions, a total self-knowledge score was calculated for each participant, and a mean self-knowledge score was obtained by dividing this number by 6. The same process was followed to calculate a mean score allocated to other.

Descriptive statistics were then used to examine sample characteristics (see table 1).

Insert table 1 about here

Analysis of skewness and kurtosis showed that not all variables were normally distributed. RMV Total Score data appeared mesokurtic with minimal skewness (kurtosis = -.99, skewness = .077), as did RME Total Score data (kurtosis = .416, skewness = -.326). However, the distribution of RME response time data appeared leptokurtic (kurtosis = 21.158) and positively skewed. The Kolmogorov-Smirnoff and Shapiro–Wilks tests of normality were significant for both groups. Outliers were detected but not excluded due to the small sample size, as they were taken to represent individual differences likely to be found among the general population. As such non-parametric tests were considered for response time data. Similarly, a leptokurtic distribution (kurtosis = 4.029) presented for AAQ data with a slight positive skew (skewness = 1.71). The Kolmogorov-Smirnoff and Shapiro-Wilks tests of normality were statistically significant for both sibling and control groups. Again outliers were detected in both groups, but retained for analysis with non-parametric tests considered for AAQ data.

Do siblings have more autistic traits than TD peers?

Male siblings had a higher median number of autistic traits than any other subgroup (msib-fsib, *d* = .853; msib-mtd, *d* = .66; msib-ftd, *d* = .75), while female siblings had a slightly higher median number of traits than controls (see figure 1). The Mann Whitney U test detected no significant differences in the distribution of AAQ scores between groups. The Kruskall-Wallis test would have been used to test for sub-group differences had the sample sizes been larger.

Insert graph 1 here

Is it more effortful for siblings to solve ToM tasks than for TD children?

Descriptive statistics indicated a trend for male siblings to have longer response times on the RME than any other group (msib-fsib, *d* = .57, msib-mtd, *d* = .643, msib-ftd, *d* =.74), with female siblings taking longer than female controls, who responded similarly to male controls (see graph 2). A Mann Whitney U test detected no significant differences in response time between groups. The Kruskall-Wallis test would have been used to test for sub-group differences had the sample sizes been larger.

Insert graph 2 here

Are siblings impaired in ToM tasks across sensory modalities?

MANOVA was anticipated to lack power to detect differences due to a small sample size. An independent-samples t-test was therefore selected which showed no significant differences between the groups on RME (*d* = .29) or RMV (*d* = .13) total score. Using Spearman's rho RME mean response time correlated with RMV (r = .424, n = 26, p = .031, r^2 = .16 indicating a large effect), but a Pearson correlation detected no significant relationship between the RME and RMV total scores.

Is there a relationship between AAQ score and performance on the target measures?

Spearman's rho correlations did not reveal any linear relationship between AAQ score and performance on the RME or RMV.

In addition to previously documented impairment in mindreading (others) are siblings also impaired in self-mentalising?

For siblings, age correlated with the mean rating assigned to 'self' on the self-concept questionnaire (r = .813, n = 13, p = .001, r^2 = .65 indicating a large effect). This pattern was not present in the control sample (see graph 3).

Insert graph 3 about here

The planned analysis using repeated-measures ANOVA could not be reliably computed due to the risk of skewness in data from small samples, and the unequal covariance matrix which would violate the assumptions of normality underpinning ANOVA.

Descriptive statistics suggested that siblings had generally said their subject knowledge of their favoured TV programme was better than their mother's (mean for self on question 1 = 6.962, mean for other on question 1 = 2.769), whereas they generally thought their mother knew more about her favoured programme (mean for self on question 2 = 5.154, mean for other = 7.038). This suggests siblings had understood the nature of the task.

For control participants descriptive statistics suggested they had generally said their subject knowledge of their own favoured programme was better than their mother's (mean for self on question 1 = 8.231, mean for other on question 1 = 5.269), whereas they generally thought their mother knew more about the mother's favoured programme than they did (mean for self on question 2 = 4.615, mean for other on question 2 = 6.808), suggesting they too understood the task.

On the 6 focal mental state questions, means for question and rating showed that siblings said that they knew slightly better than their parent for questions 3, 4, 5, 7 and 8. However, the means suggested that siblings tended to say their parent knew better than they did regarding question 6: what sort of person they were (mean for self = 7.57, mean for other = 8.362). A paired samples t-test revealed that there was no significant difference in siblings' mean ratings for self vs. other (self mean = 8.27, other mean = 7.81, $t(12) = 1.942$, $p = .076$).

For the control group, means for question and rating showed that control children typically said they knew better than their parent, and means indicated that on questions 4 (self mean = 8 other mean = 8.077) and 6 (self mean = 8.346, other mean = 8.731) they rated their parent's ability very similarly to their own. A paired samples t-test revealed that there was no significant difference in control

participant's mean ratings for self vs. other (self mean = 8.2, other mean = 7.97, t (12) = 1.079, p = .302).

DISCUSSION

Main findings

Contrary to stated hypotheses, no significant impairments were detected in the sibling group's ToM abilities in either the visual or verbal modality. Although RME and RMV total scores were not correlated, a correlation between the RME response time and RMV score emerged, partially supporting the idea of a shared module for ToM across sensory modalities. Although there was a trend for male siblings in particular to show a higher mean number of autistic traits on the AAQ and to have a longer mean response time on the RME, there was no statistically significant group difference. On the self-concept questionnaire, age was correlated with confidence in self-knowledge for siblings, with younger siblings lacking confidence in their own self-knowledge. Neither group showed a statistically significant tendency to state that they had superior knowledge of their own mental states in comparison to a parent.

Effect size calculations were performed based on the means and standard deviations of the results pertaining to hypothesis 1. The effect sizes regarding differences between the groups on the RME and RMV total scores were small, suggesting the groups were similar in accuracy. On the response latency measure for the RME however, there were medium-large effect sizes for group differences and sub-group differences. This suggests that there is a real difference between the groups in response time. No statistically significant difference between the groups was detected on this variable, but the medium-large effect size suggests this may be due to a lack of power, and that further data collection may reveal a significant group difference. Additionally, further data collection would allow statistical analysis of sub-group differences which may then reach statistical significance. Further, effect sizes were calculated based on means and standard deviations of group

and sub-group AAQ scores. A large effect size pertained to the difference between male and female sibling' AAQ scores, while a medium effect size pertained to the difference between male siblings and male controls; there was a negligible effect size however between female siblings and female controls. This suggests that further data collection may reveal significant sub-group differences in AAQ score, and indicate a potential real difference whereby male siblings have markedly higher AAQ scores than other sub-groups.

Discussion of findings in the context of the literature

Null findings in terms of any difference between the groups on the RMV and RME may be due to a lack of power, which could be addressed by further data collection and replication with larger samples. This may particularly be the case where non-parametric tests were used, which lack power to detect subtle differences with small samples. The following discussion offers speculation and reflection on the findings. Further questions are raised which further research could address.

Considering the hypothesis that genetics may lead to presentation of subtle ToM deficits in some family members, we would not expect that all siblings would be affected by a BAP (Dorris et al., 2004). As such, it could be expected that a proportion of siblings would not show impairment (BAP-) whereas some may (BAP+) (Losh et al., 2009). In a small sample, few BAP + participants may present. Losh et al (2009) found that only those relatives who showed personality characteristics of the social BAP showed poorer performance on the RME relative to controls. There were no significant differences between BAP- parents and their controls. In other studies, a proportion of siblings have scored highly on ToM measures in comparison to their matched controls (Dorris et al., 2004). It would also be expected that traits of autism and ToM abilities may vary on a continuum among the general population, and as such some controls would be expected to have higher AAQ scores and to score more poorly on ToM measures, in line with the findings (Baron Cohen et al., 2009).

Previous studies have indicated that siblings of children with HFA/AS may have had difficulties with understanding other's mental states as synthesised from visual cues. In particular, studies have used the RME and found a significant difference between siblings and matched-controls (Dorris et al., 2004). However, in the Dorris et al (2004) study, there were few female siblings, whereas in this study female siblings constitute 54% of the sample. It is known that HFA/AS is more common in males, and the same may be the case with autistic traits (Mullard, 2009). In the current study, there was a trend for male siblings to have a higher mean number of autistic traits than female siblings on the AAQ. As such, it may be that in a sample involving more female family members, both less autistic traits and less impairment in ToM is detected at a whole group level. A review by Sucksmith et al (2011) indicated that in domains where BAP was found, such as reciprocal social interaction and cognition, brothers and fathers appeared to be particularly affected. Relatively little at present is documented in the research literature about the impact of gender on mentalising abilities on the BAP (See **Systematic Review**). In parallel, Golan et al (2006) also note a gap in the literature regarding the role of gender in mentalising about complex mental states on the autism spectrum. As such, further research involving a larger sample would be required to better understand the role of gender in complex ToM tasks on the BAP.

Golan et al (2006) found the AQ to be correlated with ToM ability across modalities in normal adults and among those with AS/HFA. Using Spearman's rho, no linear relationship was detected between the AAQ and RMV or RME performance in this study. This suggests that while possession of autistic traits may be one variable affecting ToM for siblings, there may be other factors affecting the development of mentalising abilities. Studies of social learning accounts of ToM development in normally developing children suggest that position in the family may have a bearing (e.g. Ruffman, Perner, Naito, Parkin & Clements, 1998). In this study, over half (n=7) of siblings were oldest children. Those with a younger sibling with HFA/AS will not have relied upon their sibling to model or support their own social skill development, and the impact of BAP accrued through social learning

may therefore be less than for a child whose older sibling has HFA/AS. Other studies have collected this information (e.g. Dorris et al., 2004) but comparison across samples or in a large scale study would be necessary to allow investigation of the impact of social learning models on siblings' ToM.

Dritschel et al (2010) found that children with HFA/AS were impaired relative to controls in self mentalising, in that children with HFA/AS were more likely to say that their parent knew best about their own mental state, whereas controls were more likely to say that they themselves knew best. In our sample, older siblings were more confident in their own self-knowledge than younger siblings. Neither group showed a significant difference however in stating that they consistently knew better about their own mental state than their parent, in contrast to previous research (Dritschel et al., 2010). It may be that this is due to the larger impact of individual differences in small samples.

Limitations

Unfortunately there were significant difficulties in recruiting an adequate sample of adolescent siblings. This may be due to several factors. Parents may make more use of support groups and diagnostic services when their children are younger (under 10). Support group organisers commented on this, and several parents with younger children offered to take part. Parents of adolescents may have transitioned through these services already and therefore be less accessible via these routes. Adolescents themselves have competing priorities that may reduce their motivation to take part in research; for example, academic work and wishing to spend time with friends.

This project may be considered as a pilot study, as larger samples would be required for adequate power to robustly test the hypotheses using more sophisticated statistical methods. Two variables were non-parametric (AAQ score and RME mean response time). Non-parametric tests lack power to detect significant results with small samples; on the other hand parametric tests may not be robust, and as such non-parametric tests were chosen for these variables to avoid false positive results.

Due to the need to maximise inclusion of suitable participants in the study, two siblings from the same family were included where available (n=2 families). This may mean that sibling dyads not affected by BAP could have contributed to null findings, and that the data could not be considered as independent. With a bigger sample, cluster analysis could be used to investigate the significance of the effect; alternatively, only one child per family could be entered into the analysis.

Another issue concerns the lack of formal modification of the RMV for younger children. The RMV contains a more sophisticated vocabulary than the RME. Golan et al (2006) found that verbal IQ positively correlated with performance, and acknowledged the unavoidable additional verbal demands of complex mental states recognition tasks in the auditory domain as a limitation of the measure. Particularly for younger children, they were frequently unfamiliar with some of the words given, although explanation was given as to the word's meaning, and children were encouraged to ask when unsure. This likely added a significant cognitive demand and as such could have reduced task performance in comparison to the RME, which uses a simpler vocabulary. Younger participants frequently commented they found the RME easier due to the language demands. The participants in the current study generally had good receptive vocabulary scores on the BPVS; without modification to simplify vocabulary however, the RMV may not be an optimal reflection of verbal ToM ability in younger or less able participants.

Suggestions for further work

The RMV was produced with voice clip samples featuring local accents (Cambridgeshire). In some cases there was an impact of accent and cadence on the accessibility for Scottish participants of emotional valence. Several participants commented on it being hard to decipher the words used in the voice clips. There therefore may be some merit in developing a Scottish version of the RMV, with simpler wording to aid accessibility by younger participants, and norms for children. Such

modifications may improve the RMV's accuracy in measuring ToM in younger or less able participants.

CONCLUSIONS

Larger samples are required to verify whether null results were due to a lack of power, or to the other factors discussed above. Gender effects and the impact of social learning in ToM on the BAP across sensory modalities could perhaps be explored in further research with larger samples using measures sensitive enough to detect subtle differences, such as response time. Modification of the RMV for children would also be desirable in furthering the findings.

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COURSE 12 REFLECTIVE ACCOUNT ABSTRACT: EMOTIONAL LABOUR IN CLINICAL PRACTICE

It is required of us as psychologists to regulate our emotional expression in order to meet our employer's expectations in terms of good quality patient care. The emotional labour literature offers a framework for therapists to manage their own emotional regulation for the benefit of patients during clinical practice. The literature also postulates that it may benefit therapists to consciously undertake emotional labour in terms of longer term wellbeing at work and sustaining work performance over time. My account is written using Gibbs' reflective cycle (1988) repeatedly in order to illustrate the process of my reflection on utilising this model in practice in terms of my development needs, learning, putting new knowledge into practice and then repeating the cycle again.

COURSE 13 REFLECTIVE ACCOUNT ABSTRACT; MAINTAINING PERSONAL AND PROFESSIONAL INTEGRITY IN A CLIMATE OF TARGETS; IDEALISM MEETS REALISM

My reflective account discusses the challenges facing me upon qualifying as a Clinical Psychologist in the current socio-political context. As a trainee, I have been in a protected position and am aware this will be changing very soon. At present, service managers are obliged to meet demanding government targets in terms of both saving money and reducing waiting lists. In effect, this means clinicians are under pressure to either work harder, smarter or both without utilising any extra resources. My account uses De Bono's thinking hats to discuss the positive and negative implications of this for both clinicians and service users. I then proceed to suggest some creative ways to meet the challenges involved, professional issues to consider and discuss my plans for managing the likely requirements of a Clinical Psychologist job in the current NHS Scotland context.