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Abstract

Although much progress has been made in determining the cognitive profile of strengths and weaknesses that characterise individuals with autism spectrum disorders (ASDs), there remain a number of outstanding questions. These include how universal strengths and deficits are; whether cognitive subgroups exist; and how cognition is associated with core autistic behaviours, as well as associated psychopathology. Several methodological factors have contributed to these limitations in our knowledge, including: small sample sizes, a focus on single domains of cognition, and an absence of comprehensive behavioural phenotypic information. To attempt to overcome some of these limitations, we assessed a wide range of cognitive domains in a large sample (N=100) of 14 to 16 year old adolescents with ASDs who had been rigorously behaviourally characterised. In this review, we will use examples of some initial findings in the domains of perceptual processing, emotion processing and memory, both to outline different approaches we have taken to data analysis and to highlight the considerable challenges to better defining the cognitive phenotype(s) of ASDs. Enhanced knowledge of the cognitive phenotype may contribute to our understanding of the complex links between genes, brain and behaviour, as well as inform approaches to remediation.

Keywords: phenotype, cognition, behaviour, autism, subgroups
Autism spectrum disorders (ASDs) are more common than was previously recognised, affecting approximately 1 in 100 children and adolescents (Baird et al., 2006; CDC, 2009). It is well established that ASDs are highly heritable. However, the genetic mechanisms are complex and include rare chromosomal anomalies, several individual genes of major effect, and numerous common variants of small effect (Abrahams & Geschwind, 2010). The term ASDs is now commonly used to describe a range of neurodevelopmental conditions that demonstrate considerable phenotypic heterogeneity, both in terms of presentation at any one age and across development (‘the autisms’; Geschwind & Levitt, 2007), and which are likely to differ in underlying aetiology. However, they all share a primary impairment in social relatedness and reciprocity, alongside impairments in the use of language for communication and an ‘insistence on sameness’, which is in keeping with Kanner’s (1943) description of classically ‘autistic’ children. The presence of social and communication abnormalities, in combination with limited imagination and generativity, was characterised as the ‘triad of impairments’ by Wing and Gould (1979). The current classification systems include three domains of difficulties: reciprocal social interaction, abnormalities in communication, and patterns of non-functional restricted, repetitive and stereotyped behaviours (DSM-IV-TR; APA, 2000; ICD-10; WHO, 1993). However, the proposed revision for DSM-V combines the social and communication impairments into one domain, with the restricted, repetitive patterns of behaviour, interests, and activities forming the second domain (www.dsm5.org). These difficulties were once considered a particular characteristic of rare individuals, but are now more understood as a broad dimension of individual difference that is widely distributed in the general population (Constantino & Todd, 2003).

In addition to recognition of the heterogeneous aetiology and behavioural phenotype in ASDs, another challenge to perceiving autism as a unitary disorder has come from
‘fractionation’ of the autistic ‘triad’ of symptom domains, namely social impairments, communication impairments and rigid and repetitive behaviours (Happé, Ronald & Plonim, 2006). Ronald and colleagues’ work on a large UK general population twin sample found that correlations between continuous measures of social, communication and repetitive behaviour were lower than expected. Further, whilst each aspect of the triad was highly heritable, the genetic influences on each of these domains of behaviour were largely non-overlapping (Ronald et al., 2005, 2006a,b). Happé and Ronald (2008) went on to review the evidence for ‘fractionation’ at the behavioural and cognitive level in diagnosed cases and found broadly supportive evidence.

*Positioning the cognitive phenotype amongst genes, brains and behaviour*

There is increasing evidence that multiple aetiologies may converge to disrupt the development and function of several brain systems that are implicated in the social and non-social behaviours that define ASDs (Happé & Ronald, 2008; Schroeder et al., 2010), including the frontal and temporal neocortex, the caudate, and the cerebellum (Abrahams & Geschwind, 2010). In addition, there is converging evidence from genetic studies and from brain imaging studies that decreases in functional connectivity between the frontal lobes and other brain systems may be characteristic of ASDs, leading to the suggestion that ASDs are ‘developmental disconnection syndromes’ (Frith. 2004; Geschwind & Levitt, 2007; Minshew & Williams, 2007). There is also intriguing evidence that there might be an abnormal brain growth trajectory in the first year of life in individuals with ASDs, which might account for the abnormal connectivity seen later (Carper & Courchesne, 2005). These perturbations precede the behavioural regression or setback that is seen in between one quarter and one third of cases. However, the processes underlying regression are unknown and no association has been found between head circumference trajectory and a history of regression (Webb et al., 2007).
Understanding the cognitive phenotype of ASDs may play a critical role in establishing the links between genes, brain development and behaviour, which will have far-reaching implications for science and practice. Increasing amounts are known from clinical and non-clinical populations about the brain systems that subserve particular cognitive functions. This means that when a cognitive profile is identified – with some cognitive abilities being impaired, others being spared/intact and still others being enhanced – this can act as a signpost pointing ‘back’ to the structure and function of the particular brain systems and circuits that are involved in these processes, and back further still to the genetic and epigenetic influences on these neural systems. In a different way the cognitive phenotype signposts ‘forward’ to behaviour on the assumption that cognition is one of the ‘drivers’ of behaviour. Sometimes cognition might be characterised not merely by intact/impaired/enhanced processing but by the recruitment of alternative or compensatory mechanisms to solve problems, which will become more pronounced as development proceeds.

Investigating the cognitive phenotype of ASDs may also provide insights into the ‘autistic experience’. There has been a growing interest amongst cognitive psychologists in directly investigating how people with autism process (and therefore experience) the world around them. This interest has been enhanced by new technologies, such as eye tracking, which gave an insight in the ‘world view’ of individuals with autism outside of a set task or experiment (see the Yale ‘Virginia Woolf Study’ for one of the first, and perhaps most striking, examples; Klin et al., 2002). Another influence has been the experiential accounts of higher functioning individuals with ASDs, who have described their own unusual (and often aversive) sensory experiences and their self-developed strategies to minimise or manage these (Grandin, 2009; Williams, 1992). These experiences have not been easily accounted for by the dominant cognitive models that emerged in the 1980s. Put crudely, the ‘theory of mind account’ (Baron-Cohen et al., 1985) of ASDs was primarily motivated by consideration of
which cognitive difficulties could explain social communication impairments, and the
‘executive dysfunction account’ (Ozonoff et al., 1991) was primarily motivated to explain
lack of generativity, and repetitive and stereotyped behaviours. Partly in response to such
personal accounts, and with the growing realisation that neither theory of mind nor executive
dysfunction would provide a ‘unitary account’ of the autism behavioural phenotype,
alternative cognitive theories emerged. These included Frith and Happé’s weak central
coherence account (Frith, 1989; Happé & Frith, 2006), Mottron’s ‘enhanced perceptual
functioning’ account (Mottron et al., 2006), Plaisted’s (2001) theory of reduced
generalisation and enhanced discrimination ability, and Baron-Cohen’s notion of ‘hyper-
systemising’ (Baron-Cohen et al., 2005). The weak central coherence account has specifically
limited its explanatory scope to non-social assets and deficits seen in ASDs (Happé & Frith,
2006). Mottron’s and Plaisted’s accounts have been less clear in stating their explanatory
scope, and the in/dependence of systemizing and empathizing is still somewhat uncertain (see
Happé & Ronald, 2008), but in keeping with growing awareness of the heterogeneity of
ASD, the zeitgeist has moved on from unitary accounts that attempt to account for all of the
behavioural phenotype of ASDs to focus on explaining particular behavioural phenomena.

Searching for subtypes on the autism spectrum

The realisation that the clinical syndrome of autism is heterogeneous in aetiology and
presentation presents significant challenges to a number of scientific enterprises. The search
for genes or brain abnormalities might be more efficient if ‘true’ subgroups within ASD
could be identified for study, rather than the heterogeneous whole. One approach to
subgrouping is to study biological syndromes of known aetiology that are frequently
associated with ASD, such as fragile-X syndrome (Belmonte & Bourgeron, 2006) or tuberous
sclerosis (de Vries, 2010). However, it might not be the case that biological subtypes will be
associated with ‘neat’ cognitive or behavioural phenotypes; even in biologically based
syndromes where ASDs show raised prevalence there exists considerable behavioural and cognitive (e.g., IQ) heterogeneity (Chonchaiya, Schneider & Hagerman, 2009; Pratha & de Vries, 2004).

Conversely, there is some (though as yet, fairly weak) evidence that constraining the *behavioural* phenotype to a narrower subgroup within ASD might help identify the genetic underpinnings. Some studies have found increased linkage when studying samples characterised or subgrouped on the basis of social responsiveness (Duvall et al., 2007), language delay (Alarcon et al., 2002) or ‘insistence on sameness’ (Shao et al., 2003). There is currently a considerable industry dedicated to determining behavioural subtypes that might provide insights or even breakthroughs into understanding the aetiology of ASDs (e.g. Ingram et al., 2008; Munson et al., 2008). To date, however, few distinct behavioural subtypes have been identified and none is yet well-replicated.

The existence of *cognitive* subgroups might have considerable practical implications for intervention. Identifying subgroups of individuals with ASD who have atypicalities in a particular cognitive domain would give scope for carefully targeted interventions, focused on improving areas of weakness through practice or providing alternative/augmentative pathways to task performance and learning. Further, if cognitive strengths exist in an identifiable subgroup of individuals with ASDs, then not only could positive outcomes be gained by developing and nurturing areas of ability but it might be possible to utilise these ‘talents’ to overcome areas of weakness. For example, Scheuffgen, Happé, Anderson and Frith (2000) showed that inspection time (a marker of processing speed and efficiency) was far better in ASD than would be expected from measured IQ (e.g. on Wechsler scales), and suggested that non-social routes to learning might maximise this potential. Conversely, in our study of a large population-based sample of young people with ASD, we found high rates of specific underachievement in numeracy and/or literacy, given general intellectual ability
(Jones et al., 2009a). Each of these studies illustrate the value of cognitive research for guiding education and intervention, and suggest that interventions targeted at specific areas of difficulty would be an efficient way of bringing about positive change for individuals with ASD.

Another informative psychological approach is to link cognition to behaviour. Although this does not demonstrate that the cognition is driving the behaviour, it is consistent with the view that cognition and behaviour might be associated with (and, during the course of development, influence) each other. However, another possibility is that other aetiological factors are shared in common that affect the development both of behaviour and of cognition. Demonstrating specific cognition-behaviour associations might inform approaches to intervention, and intervention studies, in turn, can help move beyond association to establish likely causality. For example, the identification of cognitive impairments that are most closely associated with behaviours that parents and carers find very problematic (e.g. sensory abnormalities, anxiety) could open the route for the development of novel cognitive training approaches to treatment, which to date have largely been overlooked. Cognition-behaviour associations have already been identified in ASDs. Joseph and Tager-Flusberg (2004) found that both theory of mind and executive function abilities were associated with communication (but not social or repetitive) symptoms, even once language abilities had been accounted for. We found that self-reported auditory sensory experiences were associated with auditory discrimination abilities in a computerised task where participants had to successfully discriminate the frequency, intensity and duration differences in pairs of sounds (Jones et al., 2009b). However, these associations have not been as easy to demonstrate as was once hoped (for negative examples see Pellicano et al., 2006; Ozonoff et al., 2004). In one of the largest studies of its kind, Ozonoff et al. (2004) examined the extent to which planning and set shifting (as measured by the Cambridge Neuropsychological Test Automated Battery;
CANTAB) was associated with behaviour in a sample of 79 individuals with autism. They found no associations between performance on the executive tasks and autism symptoms as measured by the ADI-R and ADOS-G, but did find that performance on the planning task was (negatively) associated with adaptive behaviour. Whether this difficulty in making cognition-behaviour links reflects methodological limitations of the studies conducted to date, or indicates that straightforward associations across explanatory levels may not be found, remains to be determined.

**General cognitive abilities in ASDs**

The long-established view of intellectual abilities in ASDs was that up to 75% of individuals had an intellectual disability (previously referred to as ‘mental retardation’), defined by an IQ<70, alongside accompanying impairment in everyday functioning. Since the original description by Lockyer and Rutter (1970), it has been a widespread clinical view that Performance IQ (PIQ) is typically higher than Verbal IQ (VIQ). In addition there is evidence at a subtest level (e.g., on Wechsler intelligence tests) of a characteristic profile of strengths (or ‘peaks’) on subtests such as Block Design and weaknesses (or ‘troughs’) on subtests such as Comprehension (Happé, 1995; Mayes & Calhoun, 2003). However, many of these widely held views about the intelligence of children with ASDs were first formed several decades ago when conceptualisation of autism was very different from today. It may be the case that historical data do not apply to children who currently receive an ASD diagnosis (Charman et al., 2009; Fombonne, 2009). Particularly, the evolving diagnostic criteria for ASDs have widened to include a more heterogeneous population of individuals, especially those at the more able end of the intellectual spectrum.

Reflecting this, recent epidemiological studies, including our own on the sample reported in this paper, have found that only approximately half of children with an ASD have
intellectual disability (Bertrand et al., 2001; Chakrabarti & Fombonne, 2005; Charman et al., in press). Further, we found only weak support for a distinctive PIQ-VIQ profile: at a group mean level PIQ was higher than VIQ (but only by a few points) and when examined at the level of clinically meaningful PIQ-VIQ discrepancies the most common profile was for PIQ to be similar to VIQ (Charman et al., in press). There was some support for a distinctive profile at the WISC subtest level but it was only partly consistent with the previous literature. In line with other studies, we found that performance on the Vocabulary and Comprehension subtests was poor compared to other abilities. However, neither Block Design nor Object Assembly was a significant strength as has been reported previously (Happé, 1995; Lincoln et al., 1995; Mayes & Calhoun, 2003; Caron et al., 2006). Instead, Picture Completion and Picture Arrangement, which both heavily rely on visual materials, were areas of strength (‘peaks’) in the total ASD sample and in the subgroup with IQ>70. In addition, we found no support for the idea that individuals with a non-verbal advantage have higher levels of social impairment, casting doubt on this as a putative meaningful subgroup (Tager-Flusberg & Joseph, 2003). In sum, ASDs can be found in individuals with both a low and high IQ, is associated with an uneven profile of cognitive abilities, and can also be associated with delayed language development. Any explanatory account of the ‘cognitive phenotype’ needs to be minded of these varying characteristics.

**Limitations of the extant literature and rationale for the SNAP cognitive phenotype study**

Although some aspects of the cognitive phenotype of ASD have been well characterised, the approach taken to identifying the profile of strengths and impairments has been somewhat piecemeal. Few studies have included children across the breadth of the autism spectrum (in terms both of IQ and symptom severity) and most have employed small samples, which limits the ability to identify subtypes. Studies have tended to measure abilities in one
cognitive domain (or at most two domains; see Pellicano, 2010, in press, for a rare exception) only and few have comprehensively behaviourally characterised their participants.

In response to this we have conducted a study that examined a wide range of cognitive processes in a large and well characterised sample of adolescents with ASDs. One motivation was to provide a profile of cognitive strengths and weaknesses across a wide variety of cognitive domains; another was to examine the pattern of associations between cognition and behaviour (both autistic behaviours and common comorbidities). We also wanted to use the dataset to examine whether any true cognitive subtypes existed. The present paper will summarise published findings from initial analysis of this complex dataset and will illustrate the challenges to characterising the cognitive phenotype of ASDs outlined above.

We took advantage of a large, well-characterised cohort of children with ASDs who had been assessed as part of a prevalence study of autism in the UK: The Special Needs and Autism Project (SNAP; Baird et al., 2006). As part of the SNAP study over 150 10-to-14-year-olds met consensus (GB, ES, TC) clinical ICD-10 diagnoses for childhood autism or ‘other ASDs’ using information from the Autism Diagnostic Interview – Revised (ADI-R; Lord, Rutter & Le Couteur, 1994) and Autism Diagnostic Observation Schedule (ADOS-G; Lord, Risi, Lambrecht, et al., 2000) as well as IQ, language, psychopathology and adaptive behaviour measures (see Baird et al., 2006; for details). Parents had also completed a pack of questionnaires measuring other common comorbidities: repetitive behaviour, sensory behaviour, pragmatics and executive dysfunction.

For the SNAP cognitive phenotype study, 100 of the adolescents with an ASD (54 childhood autism; 46 other ASD) were seen several years later to complete a broad battery of cognitive tasks and additional parent- and self-report (N~60) behavioural questionnaires. The
cognitive tasks included both standardised and experimental measures (described below). Controls comprised some of the non-ASD children (N=26) who were seen as part of the SNAP study and typically developing children from mainstream schools (N=31). Both groups were seen at a mean age of 15 years 6 months (SD=6 months, range 14;2 to 16;11). IQ was assessed using the Wechsler Abbreviated Scale of Intelligence (WASIUK; Wechsler, 1999). The mean Full Scale IQ of both groups fell within the average-to-low average range (ASD = 84.2 (19.0); non-ASD = 88.0 (22.2)) although a wide range of IQ was included (50 to 133). There was no significant difference in intellectual ability between the two groups.

Measures

Across two testing sessions lasting approximately 3 to 3-and-a-half hours each (excluding breaks), the participants completed a total 58 tasks (see Figure 1). They completed one of two fixed orders of tasks with verbal, pen-and-paper and computerised tasks being intermingled to maintain concentration and attention. Whilst most participants completed the majority of the task battery some data were missing on some tasks due to task difficulty, non-cooperation, equipment failure or time limitations. This review will principally refer to three sets of analysis that form part of the initial output from the study. The first investigated auditory perceptual processing (Jones et al., 2009b), the second took a structural equation modelling approach to emotion recognition ability (Jones et al., in press a) and the final was an investigation of ‘everyday memory’ abilities (Jones et al., in press b).

Challenges to establishing the cognitive phenotype(s) of ASDs

We will outline some of the challenges to establishing the cognitive phenotype and report our experiences of attempting to address these issues from the SNAP cognitive phenotype study.

a. Heterogeneity
Heterogeneity seems to exist at all levels in ASDs: biological, cognitive and behavioural. One strategy that follows from the suggestion that the triad of behavioural impairments is ‘fractionable’ (Happe & Ronald, 2008) would be to examine how specific cognitive abilities map onto specific behavioural features of ASDs, rather than simply discriminating between ASD cases and controls (see Joseph & Tager-Flusberg, 2004). In the same way that the distinct constellation of social, communication and rigid/repetitive behaviours are immediately apparent when they present in a clinical setting (i.e. a behavioural phenotype that ‘hangs together’), there may be cognitive characteristics that are found in all or most children with an ASD, even those with different aetiologies or presentations.

Most of the experimental work on cognition in autism adopts the between-group experimental paradigm, where task performance is compared between a group of individuals with an ASD and a control or comparison group. However, the reporting of these findings (in terms of the group with ASDs being ‘impaired’ or ‘advanced’, depending on the direction of group differences) de-emphasises variability within the group with ASDs, and the overlap in scores between the groups. Furthermore, there is often greater heterogeneity in the ASD group than in the comparison group (SDs tend to be larger). To give one example from our own dataset, on the Ekman facial emotional recognition task, where the total possible score is between zero and 60 (chance performance would be 10), 8-out-of-10 of the lowest scoring (<28) and 8-out-of-10 of the highest scoring (>53) adolescents were from the ASD group (see Jones et al., in press a; data not published). In the past few years, investigators have been tackling this issue head on and identifying subgroups with impaired/intact performance and demonstrating the spread of scores of the ASD and the control group, paying attention to overlap and to outliers, as well as to mean group differences (see Milne et al., 2006; Pellicano, in press; White et al., 2009; for some of the best examples of this approach). The
fact that there is nearly always overlap in performance between the ASD group and the 
comparison group serves as a reminder that we are investigating the degree to which 
cognitive systems are differently ‘set’ or ‘tuned’ compared to typically developing 
individuals and not the absolute presence or absence of an all-or-none cognitive 
function/ability. Alternatively, tasks might be tapping into an end point of development, with 
compensation and other factors causing variation in outcome on tests even when an initial 
impairment has been shared by all members of the group.

b. Sample size and subtypes

Another significant challenge has been an acceptance in the field of small sample sizes. This 
was traditionally the only practical route to study autism, given the rarity of the diagnosis in 
the 70’s or 80’s. In addition, most researchers are interested in findings of large effect size, 
given the dramatic nature of the difference between ASD and TD in so many domains. 
However, multiple studies reporting on small samples increase the chance of spurious 
findings entering the literature. It can be hard to be confident that a hypothesis of group 
difference in cognitive domain X has been disproved. Fortunately, this has begun to change 
in the past few years and, increasingly, researchers are recruiting larger samples. This is 
particularly the case if one positively wants to study both lower and higher IQ individuals. 
Finally, if one of the primary aims of a study is to test whether subgroups or subtypes of 
ASDs exist (that might or might not be associated with particular behavioural or biological 
subtype) then large sample sizes are required.

This is demonstrated by our experience of studying auditory discrimination in our 
adolescent sample (see Jones et al., 2009b). Whilst at a group level auditory discrimination 
abilities (frequency, intensity, duration) were not different in individuals with ASD compared 
to controls, enhanced frequency discrimination was present in around 1 in 5 individuals with 
ASD in the frequency domain. Because 16 adolescents with an ASD failed to pass a hearing
screen they were excluded from the study (or at least their data was not analysed) leaving a sample size in the ASD of only 72. From this the enhanced frequency subgroup was ~20% or 14 children. In this study we used the threshold of >1.65 SD above the control group to define ‘enhanced’ performance but the pattern was invariant when a more stringent threshold of >2 SD was used, suggesting that a systematic association existed between enhanced frequency detection and membership of the ASD, as opposed to the control, group. This is a large enough putative subgroup that we have some confidence that the developmental profile we identified of average or above average IQ but a history of delayed language milestones might be reliable and have some meaning (see Table 4, Jones et al., 2009b). There was also an a priori motivation to examine this developmental profile as it has been suggested that that an over-focus on perceptual cues, particularly pitch, during speech negatively impacts upon linguistic processing (Järvinen-Pasley et al., 2008b). It remains to be determined whether the frequency sensitivity of our subgroup interfered with their language development or whether this was due to other factors. Our finding has since been replicated using a similar paradigm by Bonnel and colleagues (Bonnel et al., 2010), providing independent evidence of a putative cognitive and behavioural subtype.

A typically sized study of 25 participants would have resulted in just 5 such individuals being identified and the likely confidence in any associated behavioural profile would have been considerably reduced. The traditional model of science in the cognitive field has been an investigator-led lab devising novel experimental tasks or adaptations to existing experimental tasks and publishing modest size studies independently. In future, there will be the need for significant collaborative effort (and funders will have to acknowledge this and support such collaborations) in the cognitive field in the same way that there has been in the behavioural and genetic fields, as exemplified by the AGRE (www.agre.org) and Simons
Simplex (www.sfari.org) collaborations, to achieve the samples required to identify putative cognitive subtypes of the ASDs.

c. Modelling approaches to analysis

Accumulating thousands of variables from the (close to) 58 tasks completed by the 100 adolescents with an ASD made us aware of the need for a parsimonious approach to data analysis. One example where there was good synergy between statistical parsimony and theoretical rigour was on a set of 3 tasks that the participants completed looking at basic-level emotion recognition abilities. Evidence suggests that emotion recognition in different domains is underpinned by a multimodal emotion processing ability (e.g. Scott et al., 1997). However, current research into emotion recognition ability in ASD investigates visual or vocal emotion recognition ability discretely. We tested both visual (facial) and auditory (verbal and non-verbal vocalisations) basic emotion recognition in adolescents with ASD compared to age and IQ matched controls, including both high and low IQ participants (see Jones et al., in press a). A structural equation modelling (SEM) approach allowed us to model ‘emotion recognition ability’ for each emotion as a composite ‘latent’ trait, measured by the three tasks. This approach enables us to encapsulate emotion recognition ability as a multimodal construct, which we argue better illustrates competence in recognising emotion than focusing on one modality. Using this approach we found no evidence of a fundamental impairment in emotion recognition ability in adolescents with ASD, although emotion recognition ability was strongly associated with IQ across both ASD and non-ASD groups (Jones et al., in press a).

The sample completing these tasks in our study (N=99 ASD participants), although large by the standards of traditional psychological analyses, was at the lower limits of feasibility and power for modelling. In the behavioural field, complex modelling approaches are used with ASD sample sizes in the hundreds (Munson et al., 2008) and thousands (Frazier
et al., 2010; Ingram et al., 2008). Any single experimental paradigm measures one aspect of cognitive processing only and multiple experimental measures will measure different elements of an underlying ‘latent’ cognitive construct. This makes the adoption of SEM and other modelling approaches, such as latent class analysis (LCA), a parsimonious and attractive approach to analysis of cognitive data. Pooling of datasets will be required to undertake such analyses. With the increasing computerisation of many experimental paradigms, which can help (but not entirely eliminate) concerns about uniform administration, such collaborations should be possible.

d. Development

Given that ASDs are emergent developmental disorders, one clear limitation of our study is that we studied a sample at one age only. The rationale for this, in part, was that by this age adolescents with ASDs would be able to withstand a lengthy testing battery; though in truth it seemed expedient to study a sample on whom we had already acquired in-depth behavioural phenotyping (SNAP study). Studying individuals who may have reached developmental maturity in a cognitive domain can make interpretation of results difficult when performance on a task is unimpaired. For example, the Jones et al. (in press a) emotion recognition study failed to find group differences but we cannot discount that differences might have been apparent had we tested participants at an earlier age. On the Ekman facial emotion recognition task, both the ASD and the non-ASD high IQ subgroups (IQ>=80) performed at approximately the same level as typically developing 15-17 years olds (Campbell et al., 2006), so even if they had previously had difficulties with such stimuli they had achieved the normative level of competence by adolescence.

Clearly, developmental approaches to establishing the cognitive phenotype of ASDs are required given that ASDs are developmental disorders, notwithstanding the practical (and funding) difficulties of conducting such studies. The few longitudinal cognitive studies that
have been conducted have provided important information about the associations, and possible developmental relations, between different domains of cognition over time. For example, Pellicano (2010) found that executive function and central coherence skills were longitudinally predictive of change in children's theory of mind test performance, independent of age, language, nonverbal intelligence, and early mentalising skills, but that predictive relations in the opposite direction were not significant (see also Munson et al., 2008). One emerging methodology that promises much in this regard is the prospective study of genetically at-risk younger siblings of a brother or sister with an ASD diagnosis. Several groups are using experimental behavioural and neuroimaging measures of cognitive processes in such studies, which by their nature are longitudinal in design (see Yirmiya & Charman, 2010; for a review).

e. IQ

In our study we included adolescents across a very wide range of IQ from 50 to 130, excluding only the lowest functioning adolescents who would have found the experiments and the testing session inaccessible. There has been a vogue amongst many cognitive psychologists for studying only ‘higher functioning’ individuals, by which people mean individuals with average or above average IQ. This is presented as avoiding the ‘contamination’ of lowered intellectual ability, allowing a more informative study of the autism itself and not comorbidities, which are more common in individuals (both ASD and non-ASD) with lower IQ. Certainly, in our study IQ was strongly related to performance on most of the cognitive endophenotype measures (we have yet to find one to which it does not relate but it will be of potential interest when we do).

However, it is also the case that not all important associations are carried by IQ. In our study of everyday memory, IQ was equally strongly associated with performance on the everyday memory task and the verbal (list) recall task ($r=.53$ and $r=.48$, respectively) but only
prospective remembering in a proxy ‘everyday memory’ context (but not verbal recall) was associated with autism symptom severity as measured by the ADOS (independently of IQ), with poorer social and communicative abilities relating to diminished capacity for prospective remembering (Jones et al, in press b). We interpreted this as evidence of the impact of poor social and communication skills in ASD on everyday memory competence; although it cannot be discounted that developmental difficulties with everyday memory may impact upon the development of social and communication abilities. The fact that adolescents with ASD were poorer than controls on the everyday memory task and that these abilities were associated with social and communication impairments, should motivate further investigation of such memory abilities, which have largely been overlooked due to a focus on formal standard memory measures.

More generally, the view that it is preferable for cognitive psychologists to only study individuals of at least average intelligence contains several assumptions that need to be challenged (or at the very least tested). First, in ASDs comorbidity is the norm and not the exception. Approximately 50% of individuals with an ASD also have an intellectual disability (IQ<70; Charman et al., in press) and approximately 70% meet criteria for a child psychiatric disorder (Simonoff et al., 2008). Second, determining whether the profile of cognitive abilities differs in low vs. higher IQ individuals with an ASD is potentially highly informative and is something we plan to test in our dataset. To our knowledge there is no evidence, as yet, for a specific or different cognitive phenotype in high vs. low IQ individuals with ASDs and this remains a testable empirical question.

f. Hypothesis-testing experimental designs vs. broad characterisation of cognitive profiles

It is pertinent to remind ourselves of how much we have learnt from the last 5 decades of hypothesis-driven experimental study of individuals with ASD, initiated by the seminal work of Hermelin and O’Connor in the 1960s (O’Connor & Hermelin, 1967). The potential
downside to our approach of covering a wider range of cognitive domains in the same sample is the risk of less informative and potentially spurious differences emerging. When such a wide range of cognitive processes are studied it is not possible to include every possible control condition or manipulation, which is the strength of more focused experimental studies. These can be helpful in determining precisely which aspects of a particular experiment paradigm participants had difficulties with. Another limitation is the time that data collection on large samples on a wide range of measures takes, limiting the ability to reflexively respond to emerging findings.

Meyer-Lindenberg (2010) gives a useful reminder that ‘not all intermediate phenotypes are created equal’ – some will be more strongly associated with the genotype than others but at the outset one does not know which these are. One has more confidence to invest time and effort in studying phenotypes for which there are strong associations and plausible mechanisms. Therefore, just as in the genetic field where there needs to be a mixed economy of atheoretical designs such as large genome wide association studies (GWAS) and empirically-driven approaches such as candidate gene studies, efforts to establish the cognitive phenotype(s) of ASDs requires both focused, hypothesis-driven approaches and large, exploratory studies.

Concluding comments
The findings presented here from some initial analyses of this large and complex dataset, generated by 100 adolescents with an ASD completing all or most of 58 standard and experimental cognitive tasks, are clearly only preliminary. Currently we are using a number of statistical approaches, including exploratory and confirmatory factor analytic techniques, latent class analysis and structural equation modelling to adopt parsimonious approaches to reducing the data, identifying subgroups and examining the associations between cognition and behaviour.
Why is establishing the cognitive phenotype of ASDs important? The contributions discussed above of, (i) targeting remediation and (ii) providing a window into the ‘autistic experience’, stand for themselves. However, given the limitations of the heterogeneous behavioural phenotype, both to establishing a diagnosis and to the design and conduct of scientific studies in fields such as neuroimaging and genetics, should we consider using cognitive phenotypes to aid clinical practice and science? We are clearly some way from establishing what a diagnostically useful cognitive phenotype (or profile) looks like. However, diagnostic evaluation currently relies on behavioural and developmental information and, in future, could be usefully enhanced by information on cognition (beyond general ability, which is already utilised). Indeed, there are particular benefits to using cognitive assessments, which are likely to be less influenced by situational factors (i.e. how the child feels on the day and how they perform in a particular social scenario) and can be far more easily and objectively scored than behavioural assessments. If it is possible to establish ‘true’ cognitive subtypes of ASDs then they might well advance the pace of discovery in neuroimaging and genetic fields. Another important task that has only just begun to be addressed is to distinguish the ASD cognitive phenotype from that of other disorders; including those that are common comorbidities such as anxiety and ADHD (Simonoff et al., 2008; see Yerys et al., 2009).

Only large studies will possess sufficient power and size to reliably identify subtypes. Further, there needs to be a step-up in methods and analysis, for example by the use of test and replication samples that are common in the genetics field. With exciting progress being made in the fields of genetics and developmental neurobiology, which are changing our view of ‘the autisms’, cognitive psychology has to ‘step up to the plate’ and be ambitious in order to play its part in illuminating the relations between genes, the brain and behaviour; as well as in developing empirically-based approaches to cognitive remediation.
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References


Figure 1 Battery of cognitive measures by domain

<table>
<thead>
<tr>
<th>Theory of Mind</th>
<th>Face/Emotion processing</th>
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| 1. 1st and 2nd order false belief tasks  
   a. Combined 1st + 2nd order story  
   b. 1st order story  
   c. 2nd order story  
2. ToM failers: Desires story  
3. ToM failers: Unexpected contents  
4. ToM failers: Picture sequencing  
5. ToM passers: Frith-Happé animations  
6. ToM passers: Strange stories  
7. Reading the mind in the eyes task  
8. Penny hiding  |
| 1. Whole/Part face processing (1 & 2)  
   a. Un-prompted  
   b. Prompted  
2. Benton facial recognition test  
3. Ekman-Friesen test of affect recognition  
4. Vocal expressions of emotion  
   a. Verbal  
   b. Non-verbal  
5. Egocentric eye gaze task  
6. Sorting task  
7. Kaufman face recognition test for children  
8. Emotion production  |

<table>
<thead>
<tr>
<th>Central coherence</th>
<th>Executive function</th>
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</table>
| 1. Navon  
   a. Divided attention  
   b. Selective attention  
2. Sentence completion  
3. Embedded figures  
4. Homographs  
5. Memory for stories (CMS)  
6. Segmented block design  |
| 1. Luria hand game  
2. Trail making test  
3. Planning/drawing  
4. Zoo map test (BADS-C)/Mazes (WISC)  
5. Card sort  
6. Verbal fluency  
7. Design fluency  
8. Opposite worlds (TEA-Ch)  |

<table>
<thead>
<tr>
<th>Perceptual processing</th>
<th>Memory and attention</th>
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</table>
| 1. Auditory frequency discrimination  
2. Auditory intensity discrimination  
3. Auditory duration discrimination  
4. Auditory risetime discrimination  
5. Motion coherence  
6. Form from motion  
7. Biological motion  |
| 1. 1. Children’s Auditory Verbal Learning Test-2 (CAVLT)-2Digit span (CMS)  
2. Picture locations (CMS)  
3. 1st and 2nd name (RBMT)  
4. Belonging (RBMT)  
5. Appointment (RBMT)  
6. Route (RBMT)  
7. Score! (TEA-Ch)  
8. Map mission (TEA-Ch)  |

a See Appendix 1 for references for all tests
Appendix 1: References for tasks used in the SNAP cognitive phenotype study

Theory of Mind

9. 1st and 2nd order false belief tasks
   a. Combined 1st + 2nd order story
   b. 1st order story
      a. 2nd order story

10. ToM failers: Desires story

11. ToM failers: Unexpected contents

12. ToM failers: Picture sequencing

13. ToM passers: Strange stories

14. ToM passers: Frith-Happé animations

15. Reading the mind in the eyes – children’s version

16. Penny hiding
**Face/Emotion processing**

9. Whole/Part face processing
   a. Un-prompted
   b. Prompted


10. Benton facial recognition test


11. Ekman-Friesen test of affect recognition


12. Vocal expressions of emotion
   a. Verbal
   b. Non-verbal


13. Egocentric eye gaze task


14. Sorting task


15. Kaufman face recognition test for children


16. Emotion production


**Central coherence**

7. Navon
   a. Divided attention
   b. Selective attention


8. Sentence completion

9. Embedded figures


10. Homographs

11. Memory for stories (CMS)

12. Segmented block design

Executive function

9. Luria hand game


10. Trail making test

11. Planning/drawing

12. Zoo map test (BADS-C)/Mazes (WISC)

13. Card sort

14. Verbal fluency


15. Design fluency

16. Opposite worlds (TEA-Ch)

Perceptual processing

8. Auditory frequency discrimination
9. Auditory intensity discrimination
10. Auditory duration discrimination
11. Auditory risetime discrimination

12. Motion coherence
13. Form-from-motion
14. Biological Motion

Memory and attention


10. Digit span (CMS)
11. Picture locations (CMS)

12. **1st and 2nd name (RBMT)**
13. Belonging (RBMT)
14. Appointment (RBMT)
15. Route and Message (RBMT)


16. **Score! (TEA-Ch)**
17. **Map mission (TEA-Ch)**


Key: ToM = Theory of Mind; CMS = Children’s Memory Scale; BADS-C = Behavioural Assessment of the Dysexecutive Syndrome in Children; WISC = The Wechsler Intelligence Scale for Children; RBMT = Rivermead Behavioural Memory Test; TEA-Ch = Test of Everyday Attention for Children;