Conceptual and Perceptual Set-shifting executive abilities in young adults with Asperger’s syndrome

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ABSTRACT

Neuropsychological models of frontal lobe functioning have led to a greater appreciation of the dissociations among various aspects of executive functions. Theories of executive function have been proposed to account, at least in part, for the unique social and emotional difficulties experienced by individuals with Asperger’s syndrome (AS). Given the paucity of research regarding the neural correlates of executive function in AS, this investigation research involves an examination of a well-established measure of executive, frontal-striatal function in young adults with AS. Findings provide preliminary evidence to support a specific type of executive dysfunction and in particular, extradimensional or conceptual set-shifting difficulties in individuals with AS that implicates prefrontal cortex and frontal-striatal function.

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1. Introduction

1.1. Executive functions in Asperger’s syndrome

Impairments in executive functions (EF) have been implicated in the autism spectrum disorder (ASD) literature since empirical investigation of EF began over two decades ago (Ozonoff, South, & ProvencaL, 2005), however, the neural substrates of EF in Asperger’s syndrome (AS) are still not well understood. One of the most prominent brain regions implicated in EF is the frontal cortex and its connections to striatal brain regions (Schroeter, Zysset, Wahl, & von Cramon, 2004). Anatomical and metabolic abnormalities in frontostriatal pathways have been reported in adults with ASD (Abell et al., 1999; Carper & Courchesne, 2005; McAlonan et al., 2002). Moreover, frontal lobe pathology has been hypothesized by some to represent the underlying cause of the clinical symptoms of ASD, such as perseveration, rule-bound behaviours, and obsessuality (Russell, 1997). Further, deficits in cognitive flexibility and empathy often observed in individuals with ASD are also evident in the behaviour of individuals with frontal lobe damage (Grattan, Bloomer, Archambault, & Eslinger, 1990).

1.2. Frontal-striatal pathways and set-shifting abilities

One method of investigating the integrity of the frontal-striatal cortex in AS is to examine set-shifting performance and in particular, to compare extradimensional (ED) and intradimensional (ID) set-shifts. Successful set-shifting performance on
the Intra-Extradimensional (IED) Set Shift task of the Cambridge Neuropsychological Test Automated Battery (CANTAB; Cambridge Cognition, 2007) requires the ability to make both extradimensional and intradimensional set-shifts (Watson, Azizian, & Squires, 2006). ED set-shifts occur when an individual shifts from a previously reinforced categorization rule to a new rule (e.g., from sorting stimuli by colour to sorting by shape). ID set-shifts occur when an individual maintains a previously reinforced categorization rule when presented with perceptually novel exemplars (e.g., continuing to sort by shape but shifting from sorting triangles to sorting circles). Furthermore, the processes that underlie ID and ED set-shifts have been reported as cognitively and neurophysiologically distinct (Watson et al., 2006; see Rogers, Andrews, Grasby, Brooks, & Robbins, 2000 for a review). Ozonoff et al. (2004) argue that only the ED shift requires conceptual flexibility (i.e., shifting from one concept or cognitive set to another). In contrast, the ID set-shift is believed to only require perceptual flexibility (i.e., shifting from one exemplar to another within the same cognitive set).

Neuropsychological dissociations between ED and ID set-shifts have been demonstrated using the IED Set Shift task of the CANTAB (Downes et al., 1989; Robbins et al., 1994, 1998). While this task is similar to popular measures of executive function such as the Wisconsin Card Sorting Test (WCST; Berg, 1948), it was developed to examine specific components of cognition, particularly those related to frontal-striatal regions of the brain (Kaufmann et al., 2012; Ozonoff et al., 2004; Robbins et al., 1994), and it is designed to offer experimental control in parsing the cognitive and neuropsychological correlates of ID and ED set-shift performance (Watson et al., 2006). Data from studies employing this task suggest that ED shifts, but not ID shifts, depend on the integrity of the frontostriatal system (Watson et al., 2006). Individuals with insult to the prefrontal cortex (PFC; Owen, Roberts, Polkey, Sahakian, & Robbins, 1991), Parkinson’s disease (Downes et al., 1989), Huntington’s disease (Lawrence et al., 1996), and schizophrenia (e.g., Elliott, Mcken, Robbins, & Sahakian, 1995) demonstrate ED set-shift impairments despite intact ID set-shifting abilities. Similarly, lesion studies of non-human primates in a similar paradigm are commensurate with these findings (e.g., Dias, Robbins, & Roberts, 1996; Dias, Robbins, & Roberts, 1997). Rogers et al. (2000) also reported similar findings in a PET study of typically developing adults; ED set-shifts (and not ID set-shifts) were correlated with activation of bilateral prefrontal regions, further supporting the hypothesis that ED set-shifts (but not ID set-shifts) are dependent upon prefrontal and frontal-striatal activity. These findings are also consistent with other imaging work that reports PFC circuitry in ED set-shifting (Konishi et al., 1998, 1999, 2002; Smith, Taylor, Brammer, & Rubia, 2004; Watson et al., 2006). Furthermore, the IED Set Shift task has been used in functional imaging, animal, and human lesion studies (Baker et al., 1996; Dias et al., 1996; Owen, Doyon, Petrides, & Evans, 1996; Roberts, Robbins, & Everitt, 1988), which permit cross-species comparisons and inferences about the underlying neural circuitry involved in task performance (Ozonoff et al., 2004).

To date, four known investigations have used the IED set shift task with individuals with ASD (Hughes, Russell, & Robbins, 1994; Ozonoff, South, & Miller, 2000; Ozonoff et al., 2004; Turner, 1997), and results from these studies are mixed. Hughes and colleagues documented intact ID shifting but impaired ED shifting in participants with autistic disorder (AD) and a comorbid diagnosis of mental retardation. Further, Turner (1997) replicated these findings in individuals with AD and mental retardation; however, no deficits were found in a group of higher functioning individuals with AD and without mental retardation. Similarly, Ozonoff et al. (2000) found no ED shifting difficulties in individuals with high-functioning (intellectual abilities within the average range) autism relative to IQ-matched, typically developing controls. Most recently, Ozonoff et al. (2004) found ED (and not ID) shifting difficulties in participants with AD, relative to age-, sex-, and IQ-matched controls. The authors argue that the findings provide evidence to support specific types of executive dysfunction and specifically, attention shifting, in individuals with AD that implicate PFC function. At the cognitive level, shifting within a category or rule does not appear problematic (ID shifts); however, shifting between categories, sets, or rules (ED shifts) is particularly challenging for individuals with AD. Further, the results are purported to contribute to the accumulating evidence of frontal lobe involvement in AD. Although the neural circuitry that causes autistic symptomatology is likely widely distributed throughout the brain, the results indicate that the PFC is involved in these circuits at some level and consequently, the PFC should remain an active area of future investigation (Ozonoff et al., 2004). Hughes et al. (1994) also argue that the lack of association between performance on ID and ED shifting suggests separable elements of executive control and different types of executive dysfunction consistent with neuroanatomical studies. Further, this fractionation of function is proposed to create opportunities for explaining the heterogeneity of symptoms observed in ASD.

2. Study rationale and research questions

This study examined the integrity of the prefrontal and frontal-striatal cortices by investigating particular components of cognition associated with these brain regions. No known studies have examined the neural substrates of set-shifting in young adults with AS using the IED task, which is supported by lesioned animal and human neuroimaging evidence to preferentially involve the prefrontal and frontal-striatal system. This investigation was therefore interested in better understanding the neural substrates of executive, set-shifting abilities in young adults with AS. To this end, the following research questions were posed:

1. What can performance on measures of ID and ED shifting (as measured by the CANTAB Intra-Extradimensional Set Shift Task) tell us about the neural substrates of hypothesized executive dysfunction in young adults with AS? Given findings from previous research that suggests that ED shifts implicate prefrontal and broader frontal-striatal systems, young
adults with AS were hypothesized to have difficulties with ED shifts. In accordance with previous study on ID shifts in AD, young adults with AS were hypothesized to have no difficulties with ID shifts.

(2) How does performance on measures that preferentially engage prefrontal and frontal-striatal systems (as measured by ID and ED shifts on the CANTAB) of individuals with AS compare to (age- and sex-matched) typically developing peers? Given ED shift sensitivity to prefrontal and frontal-striatal function (suspected to be impaired in autism spectrum disorders), individuals with AS were hypothesized to experience more difficulties with ED shifts than their typically developing peers.

3. Method

This research was part of a larger tri-university collaboration conducted through the universities of Calgary, Saskatchewan, and Manitoba. The overarching goal of this research initiative was to investigate the unique emotional and executive abilities of young adults with ASD and to subsequently utilize that information to support individuals with AS as they transition into adulthood (Montgomery et al., 2008). The clinical sample included 34 young adults diagnosed with AS (M = 18.86 years, range 16.3–21.5 years, 76.5% male) and 34 age- and sex-matched typically developing young adults (M = 18.90 years, range 16.0–21.5 years).

3.1. Procedures

3.1.1. Inclusionary criteria

(1) Clinical diagnosis: Clinical participants must have received a diagnosis of Asperger’s disorder from a licensed medical doctor, psychologist, or psychiatrist. These participants were required to provide documentation specifying the professional who provided their diagnosis, as well as information pertaining to their developmental history. This information was subsequently reviewed by the researcher to ensure that adherence to DSM-IV-TR criteria for AS prior to inclusion into the study.

(2) Validation of diagnosis: Further validation of the Asperger’s disorder diagnosis was also elicited. Participants were required to display a classification within the high to very high ranges of likelihood of having AS on the Krug Asperger Disorder Index (KADI; Krug & Arick, 2003), a measure designed to distinguish individuals with AS from other forms of high-functioning autism, as well as from typically developing individuals.

(3) Intellectual ability: All participants were required to demonstrate verbal IQ (VIQ), nonverbal or performance IQ (PIQ), and full scale intelligence (FSIQ) in the average or higher ranges (i.e., standard scores of 85 or greater) on the Wechsler Abbreviated Scales of Intelligence (WASI; Wechsler, 1999). These inclusionary criteria were necessary to ensure both the integrity of the clinical diagnosis for the individuals with AS, as well as to ensure that potential poor performance on the EF tasks was not attributable to lower cognitive ability. The control participants were not matched according to VIQ, PIQ, or FSIQ, as research has shown that individuals with AS often demonstrate an uneven and uncommon profile of intellectual abilities that results in challenges in IQ matching (Mottron, 2004). Moreover, the purpose of the control group was to provide a comparison of individuals typical of the normative population (whom do not share this uneven profile of intellectual abilities). Importantly however, both groups exhibited relatively similar FSIQ (as illustrated in Table 1). The VIQ, PIQ, and FSIQ performance for the sample are presented in Table 1. The current participant groups (i.e., those with AS, and age- and sex-matched typically developing peers) did not differ with respect to age (t (66) = −0.106, p = 0.916); VIQ (t (66) = 1.777, p = 0.080); PIQ (t (66) = −0.401, p = 0.689), or FSIQ (t (66) = 0.982, p = 0.330).

(4) Typical early language development: Participants must not have experienced a language delay in early childhood (i.e., single words by two years of age and communicative two to three word phrases by 3 years of age). The age- and sex-matched typically developing cohort was also required to exhibit normal language development.

(5) Neurological integrity: Finally, all participants were required to have no history of head injury or diagnosis of neurologically based medical conditions.

3.1.2. Measures

The Krug Asperger’s Disorder Index (KADI; Krug & Arick, 2003) is designed to discriminate between AS and other forms of high-functioning autism. It is a norm-referenced, 32-item report completed by a clinician with ratings provided by

<table>
<thead>
<tr>
<th>Wechsler Abbreviated Scale of Intelligence</th>
<th>Asperger’s syndrome (n = 34) M (SD)</th>
<th>Typically developing peers (n = 34) M (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-Scale Intelligence Quotient</td>
<td>112.76 (10.73)</td>
<td>110.44 (8.68)</td>
</tr>
<tr>
<td>Verbal Intellectual Quotient (VIQ)</td>
<td>114.29 (12.02)</td>
<td>109.32 (11.02)</td>
</tr>
<tr>
<td>Performance Intellectual Quotient (PIQ)</td>
<td>108.03 (11.06)</td>
<td>109.03 (9.42)</td>
</tr>
</tbody>
</table>

Note: All scores are presented in standardized form, with a mean of 100 and a standard deviation of 15.
close friends, parents or relatives of the individual. It is important to note that rather than reflecting numbers of individuals in the general population who manifest the characteristics, this scale reflects the number of participants with AS who achieved a score in the various ranges. For example, if an individual receives a score of 100 or higher, this would indicate that 50% of individuals with AS scored the same as or higher than that individual. For this study, individuals with a score of 80 or higher (i.e., standard score in the 80–115 range) corresponding to the ‘somewhat likely’, ‘likely’ and ‘very likely’ KADI qualitative classification ranges were included. While many screens for AS do not have acceptable psychometric properties, the KADI meets standards for psychometric adequacy, and it appears to currently be one of the most reliable and valid screens for identifying individuals with AS (Campbell, 2005; Stoesz, Montgomery, Smart, & Hellsten, 2011).

The Wechsler Abbreviated Scales of Intelligence (WASI; Wechsler, 1999) is an individually administered, standardized and abbreviated test of cognitive intelligence. It contains four subtests (Vocabulary, Similarities, Block Design, and Matrix Reasoning) and is useful for individuals ages 8–89 in providing a measure of verbal- and performance-(non-verbal) intelligence, as well as a full-scale IQ. The WASI was administered following the standardized instructions outlined in its administration manual. Raw scores were converted to norm-referenced standard scores ($M = 100, SD = 15$).

Originally developed by Roberts et al., 1988, the Intra-Extradimensional Set Shift Task is part of the Cambridge Neuropsychological Tests Automated Battery (CANTAB; Cambridge Cognition, 2007), which is a standardized assessment battery that measures cognitive functions, and that has been validated in hospital and neuro-scientific research settings. It is a computerized assessment battery with touch screen technology that consists of 13 subtests that include measures of motor skill, visual attention, memory, and working memory. All task stimuli are nonverbal, consisting of geometric designs or simple shapes, and language proficiency is necessary only to understand the instructions prior to task initiation (Luciana, 2003). Luciana (2003) reports that the validity of the CANTAB for assessing brain–behaviour relations in adults has been supported by numerous studies of patients with brain lesions, degenerative disorders, and psychiatric illness (Fowler, Saling, Conway, Semple, & Louis, 1997; Owen et al., 1991; Owen, Iddon, Hodges, Summers, & Robbins, 1997; Rahman, Robbins, & Sahakian, 1999). More recently, functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have identified the neural substrates underlying adults’ performance on CANTAB tasks (Lee, Owen, Rogers, Sahakian, & Robbins, 2000). The CANTAB is believed to be sensitive to the presence of brain atypicalities and to aid in the discrimination among subtypes of brain disorder (Luciana, 2003).

The IED set-shifting task allows for reversal and attentional set-shift elements to be assessed independently within a visual discrimination paradigm. Two stimuli are displayed, each in one of the available boxes positioned at the top, bottom, left or right of the computer screen. On each trial, the participant has to choose one of the stimuli by clicking on it with the mouse pointer. This choice is followed by positive or negative feedback, both visually (message on screen reading CORRECT or WRONG) and auditorily (high or low tone). Two dimensions are used in this task, colour-filled shapes and white lines. Simple stimuli are made up of just one of these dimensions, whereas compound stimuli are made up of both, namely white lines overlying colour-filled shapes. Participants progress through the task by satisfying a set criterion of learning at each stage (6 consecutive correct responses). If at any stage the participant fails to reach this criterion after 50 trials, the task terminates. The task begins with two colour-filled shapes. The participant must learn which of the stimuli is correct by using the mouse to click on it. Once the criterion is reached, the contingencies are reversed so that now the previously incorrect stimulus is correct. Without the criterion changing, the second dimension is then introduced, initially lying adjacent to, and then overlapping the first dimension. Once criterion has been reached with the overlapping compound stimulus, the contingencies are reversed within the original dimension. It is important to note that the second dimension is entirely redundant to the solution of the problem at this stage.

Once the participant has learned the compound discrimination, new compound stimuli are presented, still varying along the same two dimensions (of shape and of line). Participants are initially required to continue to attend to the previously relevant dimension of shape and learn which of the two new exemplars is correct (the “intradimensional” shift). For the next stage, participants are required to shift attention to the previously irrelevant dimension of lines and learn which of the two new exemplars in this dimension is now correct (the “extradimensional” shift). There are a number of reversal stages within the task, where reward contingencies of the currently relevant dimension are reversed, as well as stages in which the categorical dimension necessary to attend to is reversed. The dependent measure is the number of trials needed to reach criterion after the shift.

More specifically, the IED task measures the ability to attend to specific attributes of compound stimuli, shifting attention from one attribute to another when required (Ozonoff et al., 2004). Participants are presented with a series of multidimensional stimuli consisting of shapes and lines. In stages 1 through 5 of the task, the discrimination and learning stages, participants learn through trial and error to respond selectively to one specific shape, ignoring the other shape and the lines. In stage 6, the intradimensional shift, new shapes and lines are introduced, but shape continues to be the salient response dimension. In stage 7, the intradimensional reversal, the previously nonreinforced shape now becomes the correct response. The shifts at stages 6 and 7 are not thought to be primary measures of flexibility, as participants continue to respond to the same rule or set as in previous trials. At stage 8, during the critical extradimensional shift, however, the correct rule now changes to the other dimension (e.g., the line) that has been irrelevant for the preceding dozens of trials. Finally, in stage 9, the extradimensional reversal, participants must respond to the previously non-reinforced line. Research in primates indicates that only stages 8 and 9 require prefrontal function, with the extradimensional shift using dorsolateral prefrontal cortex and the extradimensional reversal tapping orbitofrontal cortex (Ozonoff et al., 2004). The primary variables of interest
on the IED task are the number of errors committed. If AS involves selective deficits in prefrontal function, a dissociation between performance at stages 6/7 and stages 8/9 would be present.

4. Results

The performance of individuals with AS on the measure of intra- and extradimensional set-shifting abilities was first examined descriptively and subsequently compared to the performance of their typically developing peers, utilizing a single independent t-test. Means and standard deviations for both groups are presented in Table 2.

As predicted, individuals with AS performed similarly to their typically developing peers on the intradimensional set-shift; however, they made more errors than their typically developing peers on the extradimensional set-shift task ($t(66)=2.43, p = .018, d = 0.60$). In addition, examination of the associated standard deviations revealed more variability in the extradimensional set-shift performance in individuals with AS than their peers. This finding highlights the heterogeneous nature of performance in individuals with AS.

Collectively, these findings suggest that individuals with AS do not exhibit difficulties maintaining a previously reinforced categorization rule when presented with perceptually novel exemplars (e.g., continuing to sort by shape, but shifting from sorting triangles to sorting circles); this intradimensional set-shift is believed to only require perceptual flexibility (i.e., shifting from one exemplar to another within the same cognitive set (e.g., shape)). In contrast, individuals with AS, as a group, appear to experience difficulties shifting from a previously reinforced categorization rule to a new rule (e.g., from sorting stimuli by colour to sorting by shape); this extradimensional set-shift requires conceptual flexibility (i.e., shifting from one concept or cognitive set to another).

5. Discussion

The overarching aim of this study was to examine the integrity of the prefrontal and frontal-striatal cortices in AS using the IED task (in which the neural underpinnings may be better understood relative to other executive function measures). Specifically, performance on measures of ID and ED shifting were explored in an effort to understand the neural substrates of hypothesized executive dysfunction in young adults with AS. Given findings from previous research that suggested that ED shifts implicate prefrontal and frontal-striatal systems and associated cognitive flexibility (Watson et al., 2006), young adults with AS were hypothesized to have difficulties with ED shifts. In accordance with previous studies on ID shifts in AD (Hughes et al., 1994; Ozonoff et al., 2000, 2004; Turner, 1997), young adults with AS were hypothesized to have no difficulties with ID shifts. The performance of ID and ED shifts in individuals with AS was subsequently compared to (age- and sex-matched) typically developing peers to determine what utility perceptual and conceptual set-shifting may have in understanding EF in individuals with AS.

As predicted based on previous literature, individuals with AS performed similarly to typically developing peers on measures of intradimensional or perceptual set-shifting; however, they made significantly more errors on extradimensional or conceptual set-shifting measures. These preliminary findings enable us to draw a number of conclusions. First, the results of the IED task may help to clarify the nature of perseverative difficulties in AS. Since each stage of the IED task is conditional upon success on all prior states, cognitive processes involved in the proceeding stages (i.e., discrimination learning, rule reversal, and transfer of learning) can be eliminated from accounts of performance deficits (Hughes et al., 1994) associated with AS. Further, between group comparisons of IED performance suggest that the “stuck-in-set perseveration” (Hughes et al., 1994) may be specific to AS, or perhaps the broader ASD population. Although additional research with other clinical groups (e.g., individuals with ADHD) is necessary to determine how unique the stuck-in-set perseveration is to AS and possibly to the broader autism spectrum, it appears that young adults with AS may have significantly greater difficulty with conceptual set-shifting than their typically developing peers, and this finding has implications for set-shifting in everyday life.

Although interstudy comparison is limited due to the lack of research with young adults with AS, findings from the current investigation are consistent with those found in a number of studies investigating set-shifting in the broader autism

Table 2

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Standard deviation</th>
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<tbody>
<tr>
<td>(1) CANTAB Intrdimensional Set Shift Task, Total Raw Error Scores: Perceptual Flexibility</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Individuals with Asperger’s</td>
<td>0.47</td>
<td>0.62</td>
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<tr>
<td>Typically developing peers</td>
<td>0.32</td>
<td>0.54</td>
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<tr>
<td>(2) CANTAB Extrdimensional Set Shift Task, Total Raw Error Scores: Conceptual Flexibility</td>
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<td></td>
</tr>
<tr>
<td>Individuals with Asperger’s</td>
<td>7.97</td>
<td>9.18</td>
</tr>
<tr>
<td>Typically developing peers</td>
<td>3.97</td>
<td>2.37</td>
</tr>
</tbody>
</table>

* $p < .05$; two-tailed.
spectrum. Hughes et al. (1994) found specific extradimensional or conceptual set-shifting deficits in a group of children and adolescents with both AD and mental retardation relative to comparison groups of individuals with moderate learning disabilities and typically developing peers. Ozonoff et al. (2004) replicated these findings of specific difficulties with conceptual set-shifting in a larger sample of individuals with AD across the lifespan.

6. Conclusions

Converging evidence from human lesion, animal lesion, and human functional neuroimaging studies provides strong support for the role of the prefrontal and frontal-striatal systems in performance on the IED task. Previous work implicates these brain regions in performance at a specific stage of the IED task (i.e., the extradimensional shift engages the prefrontal and frontal-striatal systems, whereas the intradimensional shift does not; Rogers et al., 2000; Watson et al., 2006). The present study’s sample of individuals with AS appeared to experience difficulties, relative to typically developing peers, with extradimensional shifts. In contrast, they performed similarly to their peers during earlier IED task stages requiring discrimination learning and intradimensional shifting. Similar to the findings reported by Ozonoff et al. (2004) in a sample of individuals with AD, not all types of attention shifting appear to be impaired in AS—only those that require prefrontal and frontal-striatal function. Perceptual set-shifting, or shifting within a category or rule, does not appear impaired, whereas conceptual set-shifting, or shifting between categories, sets, or rules, is deficient. This dissociation between intra- and extradimensional performance relative to typically developing peers suggests that AS may involve selective deficits in prefrontal and frontal-striatal function. These findings provide preliminary evidence to support a specific type of executive dysfunction and in particular, conceptual shifting difficulties in individuals with AS that implicate the prefrontal and frontal-striatal cortices.

6.1. Clinical Implications

Findings from this study suggest that conceptual set-shifting may be compromised in individuals with AS. As such, environments and educational approaches that promote mental flexibility may be of benefit. This clinical recommendation, however, is inconsistent with common ASD treatment approaches that are highly focused upon consistency and predictability. Although it is often critically important to focus on consistency and structuring for predictability (to prevent confusion and associated mental distress), it is also important to recognize that these foci may not promote mental flexibility, and associated social and emotional adaptability.

6.2. Limitations

Although the neuropsychological measure used in this study has been validated through converging human lesion, animal lesion, and human functional neuroimaging research, it is important to state that this measure provides only an indirect measure of brain function. Consequently, all neurophysiological conclusions drawn in the present investigations should be considered exploratory and in need of further replication with more direct measures of brain function such as neuroimaging. Furthermore, it is important to highlight the difficulty associated with localization of dysfunction in the brain. As Owen et al. (1991) have outlined, localization of frontal-striatal dysfunction is complicated by complex neuronal networks connecting the frontal cortex to other brain regions such as the basal ganglia. Damage to subcortical structures therefore inevitably effect the expression of cortical functioning via defined cortico-striatal feedback loops. Consequently, this study’s preliminary conclusion of frontal-striatal dysfunction in individuals with AS only demonstrates that suspected deficits in frontal-striatal functioning, although presumed sufficient, may not be necessary to produce a selective deficit in conceptual set-shifting.

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