PAPER

Deficient saccadic inhibition in Asperger's disorder and the social-emotional processing disorder

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Background: Both Asperger's disorder and the social-emotional processing disorder (SEPD), a form of non-verbal learning disability, are associated with executive function deficits. SEPD has been shown to be associated with deficient saccadic inhibition.
Objective: To study two executive functions in Asperger's disorder and SEPD, inhibition and task switching, using a single saccadic paradigm.
Methods: 22 control subjects and 27 subjects with developmental social processing disorders—SEPD, Asperger's disorder, or both syndromes—performed random sequences of prosaccades and antisaccades. This design resulted in four trial types, prosaccades and antisaccades, that were either repeated or switched. The design allowed the performance costs of inhibition and task switching to be isolated.
Results: Subjects with both Asperger's disorder and SEPD showed deficient inhibition, as indicated by increased antisaccade errors and a disproportionate increase in latency for antisaccades relative to prosaccades. In contrast, task switching error and latency costs were normal and unrelated to the costs of inhibition.
Conclusions: This study replicates the finding of deficient saccadic inhibition in SEPD, extends it to Asperger's disorder, and implicates prefrontal cortex dysfunction in these syndromes. The finding of intact task switching shows that executive function deficits in Asperger's disorder and SEPD are selective and suggests that inhibition and task switching are mediated by distinct neural networks.

Executive functions play a critical role in adaptive human behaviour. They include planning, inhibition, working memory, set maintenance, and flexibility of thought and action. On a purely descriptive level, many cardinal features of developmental disorders that affect social processing, such as Asperger's disorder, can be seen to reflect deficient executive function. Asperger's disorder is characterised by inflexible behaviour, rigid adherence to routines, narrow interests, stereotyped behaviours, and difficulty in inhibiting responses.[1 2] Individuals with Asperger's disorder perseverate, have difficulty in establishing a cognitive set, demonstrate poor planning, and have spatial working memory deficits.[1–5] Deficient executive function may also contribute to deficient theory of mind.[2] Theory of mind involves internally representing and acting upon the mental states of others, using inhibitory processes to guide responses.[1] These observations suggest that executive function deficits contribute to the defining social and behavioural features of Asperger's disorder.

In the present study we investigated two different executive functions—inhibition and task switching—in Asperger's disorder and the social-emotional processing disorder (SEPD), a form of non-verbal learning disability. Inhibition is the ability to suppress prepotent responses. Task switching refers to moving flexibly from one behaviour to another in response to changing environmental contingencies. We designed a paradigm that measured task switching and inhibition during identical saccadic tasks. Subjects undertook prosaccade and antisaccade trials. Prosaccade trials required subjects to look towards a suddenly appearing target; antisaccade trials required them to look in the opposite direction. While prosaccades are a relatively automatic response, antisaccades require the inhibition of the prosaccade and the generation of the novel behaviour of looking *away* from a target.[6] We presented prosaccade and antisaccade trials in a randomly mixed sequence. This random sequence of trials required subjects to either switch between tasks or to repeat the previous task. As both executive functions were measured during a single paradigm, the stimuli and required motor responses were identical and the demands of other functions, such as sustained attention and working memory, were equal.

Saccadic eye movements during these tasks provide objective measures of inhibition and task switching. They use a control system with relatively well delineated neuroanatomy and thereby allow us to examine the integrity of specific neural systems in individuals with Asperger's disorder and SEPD. We previously reported deficient saccadic inhibition in SEPD.[7] Based on earlier findings in autism and high functioning autism,[8 9] we hypothesised that individuals with Asperger's disorder would also show deficient saccadic inhibition. In addition, we wanted to determine whether these groups have task switching deficits, given their perseverative behaviour. Finally, we examined the relations between inhibition and task switching measures. Correlated deficiencies would be consistent with a single dysfunctional control system mediating both executive functions. In contrast, selectively impaired and uncorrelated performance would suggest separate executive control systems.

The variety of labels applied to developmental conditions that affect social processing reflects a lack of consensus regarding their diagnosis and the different approaches applied to describe them. SEPD is described in the neurological literature and is thought to arise from congenital or early acquired damage to the right hemisphere.[10–13] It has also been referred to as right hemisphere learning disability[11] and is quite similar to non-verbal learning disability, which is defined by largely overlapping criteria.[14–16] These disorders do

Abbreviations: SEPD, social-emotional processing disorder; SPD, social processing disorder

not appear in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM). Asperger's disorder, in contrast, is described primarily in the psychiatric literature and first appeared in the DSM in 1994 (DSM-IV).[17]

The DSM-IV criteria for Asperger's disorder overlap with the criteria for SEPD. The defining feature of both disorders is a developmental history of deficient interpersonal relations. Both diagnoses also require normal language acquisition and development. The primary distinctions between Asperger's disorder and SEPD are the Asperger's disorder criterion of restricted, repetitive, and stereotyped patterns of behaviour, interests, and activities, and the SEPD criterion of a neuropsychological profile implicating the right hemisphere. SEPD has been associated with right hemisphere dysfunction on the basis of clinical neurodiagnostic studies (for example, electroencephalography and magnetic resonance imaging).[13 18] Published reports are inconclusive as to whether Asperger's disorder is also characterised by a right hemisphere implicating neuropsychological profile.[19–22]

The considerable phenomenological overlap between Asperger's disorder and SEPD has led to a debate about whether or not these syndromes represent distinct entities.[19 21–23] More valid diagnosis will be facilitated by understanding their neural bases and determining whether current diagnostic distinctions have external validity. In other words, do the diagnostic distinctions predict outcome on measures that are independent of diagnosis? Executive function deficits are independent of the diagnosis of Asperger's disorder and SEPD, but are key associated features[1 3 5 7] which may contribute to defining social and behavioural symptoms.[3] A secondary goal of this study was to compare executive function in the Asperger's disorder and SEPD samples. We expected to replicate our finding of deficient saccadic inhibition in SEPD[7] and to extend it to Asperger's disorder.

METHODS

Diagnosis of subjects with developmental social processing disorders

The subjects of the present investigation met criteria for Asperger's disorder, SEPD, or both disorders. We will refer to these groups in aggregate as the social processing disorder (SPD) group. SPD subjects, aged 16 and over, were recruited from adult outpatient clinics offering neuropsychological assessment in the Boston area. We limited our sample to age 16 and over, because saccadic inhibition does not develop fully until late adolescence.[24 25] The initial SPD diagnosis was made by the referring neuropsychologist. A second licensed neuropsychologist (DSM), blind to study outcome, made a research diagnosis based on a thorough review of medical records, interviews with the subject and—whenever possible—a parental or immediate family informant, and behavioural observations. We obtained detailed histories with attention to birth related events, developmental milestones, emotional adjustment, and social and family history. Behavioural observations of paralinguistic communication ability—including the use of eye contact, facial expression, and gesture—were recorded.

Diagnostic criteria are enumerated in table 1. The diagnosis of Asperger's disorder was based on DSM-IV criteria. All subjects had at least average verbal intellect (verbal IQ $\geqslant$90) and histories of normal language acquisition defined as the use of single words by the age of two years and communicative phrases by the age of three. SEPD subjects were required to have right hemisphere implicating neuropsychological profiles, operationally defined as verbal IQ greater than performance IQ by 10 points or more (a 10 point discrepancy is significant at the 0.05% level[26]). Subjects were excluded if they had histories of acquired brain disease or significant brain injury after the age of five. Healthy control subjects, without a history of psychiatric or neurological illness, were recruited from the community by poster advertisements.

Table 1 Diagnostic criteria for developmental social processing disorder subgroups

Criterion	Asperger's disorder (n = 4)	SEPD (n = 11)	Both (n = 12)
Social impairment	+	+	+
Repetitive behaviour	+	−	+
Significant impairment in function	+	+	+
Normal language acquisition	+	+	+
No clinically significant general delay in cognitive development	+	+	+
No autism, PDD, or schizophrenia	+	+	+
Right hemisphere dysfunction	−	+	+

PDD, pervasive development disorder; SEPD, social-emotional processing disorder.

All subjects were screened to exclude substance abuse or dependence within the past six months and any independent conditions that might affect brain function. Two SPD and four control subjects did not complete the protocol. The final sample size was 27 SPD subjects and 22 controls (table 2). Of the 27 SPD subjects, four met criteria for Asperger's disorder alone, 11 met criteria for SEPD alone, and 12 met criteria for both Asperger's disorder and SEPD (BOTH).

Nineteen SPD subjects were on drug treatment, primarily for mood disorders (for example, depression, dysthymia) or attention deficits. Twenty SPD and 16 control subjects were strongly right handed, as determined by a laterality score of 70 or above on the modified Edinburgh handedness inventory.[27] The control and SPD groups did not differ in age, sex, handedness, estimated verbal IQ based on a test of single word reading,[28] or parental socioeconomic status.[29] Control subjects showed a trend to more years of education.

The study was approved by the committee on clinical investigations at Beth Israel Deaconess Medical Center. All subjects gave written informed consent after the experimental procedures had been fully explained, according to the Declaration of Helsinki.

Supplemental neuropsychological assessment of SPD subjects

All SPD subjects had undergone neuropsychological evaluations for clinical purposes, and supplemental measures were administered as necessary to characterise and compare SPD subgroups (table 3). As IQ scores contributed to SPD subgroup diagnosis, it is not surprising that subjects with Asperger's disorder had lower verbal and higher performance IQs on the Wechsler adult intelligence scale–revised or third edition.[26 30] The subgroups did not differ significantly in performance of the logical memory or visual reproduction subtests of the Wechsler memory scale (revised or third edition[31 32]). Although not statistically significant, the SEPD and BOTH subgroups recalled stories better than visual figures. All subgroups recognised words better than faces on the recognition memory test.[33] The subgroups did not differ in academic achievement (wide range achievement test–revised or third edition[34 35]) and performed better on tests of single word reading and spelling than arithmetic. The subgroups were not impaired and did not differ in the visual discrimination of faces (facial recognition test[36]) or in judgement of line orientation.[37] On the grooved pegboard,[38] SEPD subjects showed a tendency to perform more slowly

Table 2 Demographic data and rating scale scores

Subject characteristics	Healthy subjects (n = 22)	SPD subjects (n = 27)	*t* Value	p Value
Age	34.6 (11.2)	34.4 (11.2)	0.03	0.98
Sex	11M/11F	17M/10F	$\phi = 0.13$†	0.40
Laterality score (handedness)	70.2 (50.4)	68.2 (51.2)	0.14	0.89
Education (years)	17.4 (4.1)	15.3 (3.4)	1.88	0.07*
Estimated verbal IQ	108.5 (13.2)	111.1 (7.9)	0.86	0.39
Parental SES‡	1.7 (1.1)	1.9 (1.1)	$z = 0.61$†	0.54

Values are mean (SD).
*$p \leqslant 10$.
†The ϕ value is the result of a Fisher's exact test. The *z* value is the result of a non-parametric Mann-Whitney U test comparison.
‡A lower score denotes higher status.
SPD, social processing disorder; SES, socioeconomic status.

than Asperger's disorder subjects with the left hand. Mean scores on the Beck depression inventory–II[39] were in the minimal range.

Eye movement apparatus and protocol

We recorded eye movements with a magnetic search coil technique, using a scleral contact lens and a three foot field coil (Crist Instruments, Bethesda, Maryland, USA). The subject's head was secured in a chin rest, with the cornea 81 cm away from a tangent screen. Displays were generated by a Power Macintosh 9600/233, using programs written in C++ on the Vision Shell programming platform (www.kagi.com/visionshell), and back projected with an Eiki LC-7000U LCD projector. The lens was placed in the left eye. The system was calibrated by having the subject sequentially fixate nine targets in a square grid spanning 50°. Twelve data points were collected at each of the target locations, and a regression method was used to find the best linear fit. Eye position was digitised at 500 samples/s. A five point central difference algorithm[40] was used to derive velocity from eye position. The saccadic tasks are described in fig 1.

Before testing, subjects were informed that they would receive a monetary bonus for each correct response. Subjects practiced with each of three different block types: prosaccade only, antisaccade only, and mixed task blocks. The single task blocks had 26 trials. The mixed task blocks consisted of 52 trials of prosaccades and antisaccades presented in random order. Each block type was repeated four times in a counterbalanced order to mitigate the effects of learning and fatigue. All subjects began with a single task block (half began with prosaccades, half with antisaccades), followed by the other type of single task block, followed by a mixed task block. The order of the three block types was then reversed. The entire sequence of six blocks was repeated for a total of 12 blocks. This generated about 104 trials of each of six trial types: blocked (from single task blocks) and repeated and switched trials (for example, preceded by the same trial type or not) of both prosaccades and antisaccades.

We were primarily interested in the mixed task blocks as they provide measurements of both inhibition and task switching. However, because most studies present prosaccade and antisaccade trials in single task blocks, we first compared

Table 3 Comparisons of the social processing disorder subgroups on neuropsychological test scores

Test		Asperger's disorder (n = 4)	SEPD (n = 11)	Both syndromes (n = 12)	p Value
WAIS	Verbal IQ	106.8 (16.4)**	122.1 (8.8)	117.8 (15.0)	IQ by subgroup: 0.0002*
	Performance IQ	111.5 (14.5)*	95.2 (8.9)	92.7 (13.5)	
WMS centile	LM I	40.0 (47.8)	65.4 (28.6)	52.1 (25.1)	Subgroup: 0.80
	LM II	61.0 (35.0)	68.9 (25.8)	56.6 (30.2)	Subtest (LM *v* VR): 0.41
	VR I	58.7 (50.1)	52.6 (40.2)	25.3 (25.6)	Subgroup by subtest: 0.60
	VR II	58.3 (37.0)	48.1 (37.6)	48.8 (25.6)	
RMT (max = 50)	Words	49.5 (1.0)	47.7 (2.9)	48.8 (2.2)	Subgroup: 0.33
	Words (centile)	>75	68	>75	
	Faces	43.5 (3.9)	40.4 (6.1)	42.1 (5.0)	Subtest (word *v* face): <0.0001*
	Faces (centile)	54	21	39	Subgroup by subtest: 0.91
WRAT centile	Reading	58.2 (22.9)	70.4 (18.7)	76.5 (11.9)	Subgroup: 0.11
	Spelling	61.8 (26.7)	71.1 (17.4)	83.8 (7.8)	Subtests: 0.0002*
	Arithmetic	39.5 (8.2)	60.4 (12.7)	48.7 (33.3)	Subgroup by subtest: 0.25
Benton faces		46.7 (2.9) (high average)	44.0 (7.5) (average)	45.3 (3.5) (average)	Subgroup: 0.75
Line orientation		27.0 (2.6) (high average)	23.6 (7.3) (average)	22.4 (3.5) (low average)	Subgroup: 0.44
Grooved peg† (s)	Left	68.0 (8.8)**	96.0 (35.4)	89.3 (20.0)	Subgroup: 0.22
	Right	71.3 (15.3)	82.0 (21.6)	81.8 (18.2)	Subgroup: 0.60
Beck depression inventory–II		12.0 (12.5)	12.5 (9.8)	8.9 (8.6)	Subgroup: 0.66

Values are mean (SD).
*$p \leqslant 0.05$; **$p \leqslant 0.10$ (the p values are for the appropriate F statistic).
†A lower score denotes faster performance.
IQ, intelligence quotient; LM, logical memory; max, maximum; RMT, recognition memory test; VR, visual reproduction; WAIS, Wechsler adult intelligence scale; WMS, Wechsler memory scale; WRAT, wide range achievement test; I, immediate recall; II, delayed recall.

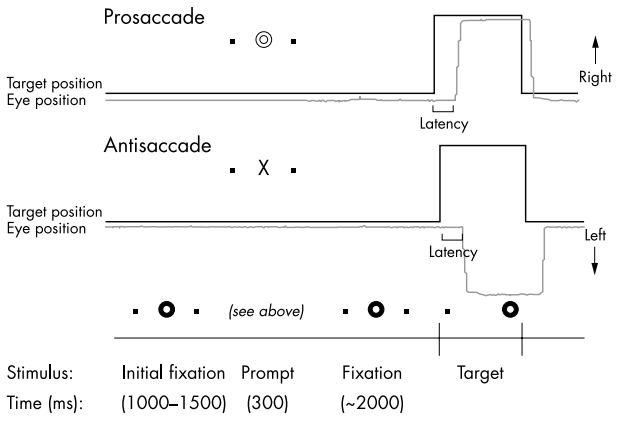

Figure 1 Saccadic tasks. Illustration of target position and eye position during correct performance of the prosaccade and antisaccade tasks. The initial stimulus presentation display consisted of a dark background with a white fixation ring at the centre, of 1.0˚ diameter and luminance of 20 cd/m^2. The fixation ring was flanked by two dots of 0.7˚ diameter and equal luminance placed 20˚ right and left of centre. These two peripheral dots were visible in each trial until obscured by a target. The subject was required to look at the central fixation point, and each trial began when a subject's eye fell within 3˚ of the fixation point. After a period randomly varying between 1.0 and 1.5 s, the fixation point was replaced by one of two symbols: a yellow ''O'' with a surrounding ring of 4.5˚ diameter was the prompt for a prosaccade, and a blue ''X'' spanning 4.5˚ was the prompt for an antisaccade. Prompts lasted 300 ms and were then replaced by the white fixation ring. After a mean interval of 2 s, the fixation ring disappeared and a similar ring appeared around one of the two peripheral dots, the side determined randomly. This was the cue for the subject to make their saccade as quickly and accurately as possible. The white ring remained in the peripheral location until either the subject's eye had fallen within 3˚ of the desired end position or 10 seconds had elapsed, at which time it returned to the central fixation point for the next trial.

trials from the single task blocks with repeated trials from the mixed task blocks to determine whether the randomised presentation of prosaccade and antisaccade trials resulted in increased errors and latencies. The presentation of trials in mixed task blocks slowed performance marginally but did not affect the number of errors and, more importantly, did not affect the groups differentially. Because the inhibition findings from the single task blocks are replicated in the mixed task blocks, only the analyses or the mixed task blocks are presented.

Scoring of eye movement protocols

We identified saccades as eye movements with velocities exceeding 46.9˚/s. The onset of a saccade was defined as the point at which the velocity of the eye first exceeded 31.3˚/s, and the end of a saccade was the point where the eye's velocity fell below this baseline. For each saccade, we recorded directional accuracy with respect to the required response and latency from target onset for the directionally correct responses only. The first trial of each block was eliminated from analysis as neither repeated nor switched. We also eliminated trials with saccadic latencies under 100 ms or over 2500 ms (less than 1% of total responses).

Data analysis

Accuracy and latency

We analysed per cent errors with repeated measures analysis of variance (ANOVA) with a *group* factor (control, SPD), and *task* (prosaccade, antisaccade) and *condition* (repeated, switched) as repeated measures. Latencies for correct trials were analysed using randomised block ANOVA with subjects nested within group as the random factor, and group, task, and condition as factors. Pairwise comparisons were evaluated with contrasts. We isolated executive function costs by subtracting the baseline performance from other trial types. Repeated prosaccades were used as the baseline because they require neither an antisaccade nor a task switch. The formulas for these costs are given in table 4. Pearson correlation coefficients were used to describe the relations between performance costs.

Table 4 Formulas used to isolate antisaccade and task switching error and latency costs

	Task	
Condition	**PS**	**AS**
Repeated	PS_R	AS_R
Switched	PS_S	AS_S

Repeated prosaccades (PS_R) are the baseline because they require neither an antisaccade nor a task switch. To isolate the antisaccade cost, the baseline was subtracted from repeated antisaccades. To isolate task switching costs, the baseline was subtracted from switched prosaccades. To isolate the task switching cost specifically for antisaccades, repeated antisaccades were subtracted from switched antisaccades.
Antisaccade cost: $AS_R - PS_R$
Task switch cost for PS: $PS_S - PS_R$
Task switch cost for AS: $AS_S - AS_R$
AS_S, switched antisaccade; AS_R, repeated antisaccade; PS_R, repeated prosaccade; PS_S, switched prosaccade.

RESULTS

Inhibition

Errors

These results are given in fig 2A. Subjects made more antisaccade than prosaccade errors (task: $F(1,47) = 50.60$, $p<0.0001$). As predicted, there was a significant group×task interaction ($F(1,47) = 6.79$, $p = 0.01$). SPD subjects did not differ from control subjects in prosaccade errors ($t(47) = 1.31$, $p = 0.19$) but made more antisaccade errors ($t(47) = 4.22$, $p<0.0001$). The mean (SD) antisaccade error rate for SPD subjects (22 (13)%) was almost twice that of control subjects (12 (9)%). This finding of impaired inhibition was not restricted to a particular SPD subgroup. The similarity of the antisaccade error rates in the SPD subgroups suggested that the failure to find a difference between the subgroups did not reflect decreased power because of small sample sizes (Asperger's disorder: 24 (19)%; SEPD: 21 (11)%; BOTH: 22 (12)%). In addition, each subgroup made significantly more errors than control subjects (Asperger's disorder: $t(24) = 2.40$, $p = 0.02$; SEPD: $t(31) = 2.83$, $p = 0.008$; both conditions: $t(32) = 3.07$, $p = 0.004$). The SPD subgroups did not differ from one another or from control subjects on prosaccade errors. Drug treated and untreated SPD subgroups showed comparable antisaccade error rates (drug treated: 22 (13)%; no drug treatment: 20 (14)%; $t(25) = 0.44$, $p = 0.66$), and both made significantly more errors than control subjects (drug treated: $t(39) = 3.44$, $p = 0.001$; no drug treatment: $t(28) = 2.26$, $p = 0.03$).

Latency

These results are given in fig 2B. Antisaccade latencies were longer than prosaccade latencies (task: $F(1,47) = 454.15$, $p<0.0001$). There was a group×task interaction ($F(1,47) = 15.47$, $p<0.0001$). Although the latencies for SPD subjects did not differ significantly from those of control subjects on either task (prosaccade $t(47) = 0.34$, $p = 0.74$; antisaccade $t(47) = 0.72$, $p = 0.47$), SPD subjects showed a disproportionate relative increase in latency for antisaccades compared with prosaccades (control: 15 (10)% increase; $t(21) = 12.00$, $p = 6e{-}33$; SPD: 22 (11)% increase;

t(26) = 18.29, p = 2e−73). For the analysis of SPD subgroups *v* controls, the group×task interaction remained significant (F(3,45) = 7.23, p<0.0001). In addition, each SPD subgroup showed a disproportionate increase in latency for antisaccade *v* prosaccade trials relative to controls (Asperger's disorder: 29 (9)% increase; SEPD: 20 (11)%; BOTH: 21 (11)%). Drug treated and untreated SPD subjects did not differ in latency (F(1,25) = 0.98, p = 0.33) for either prosaccades (t(25) = 0.45, p = 0.66) or antisaccades (t(25) = 1.50, p = 0.13), suggesting that drugs were not an important factor in our findings.

Task switching

Errors

These data are shown in fig 3A. There were significantly more errors on switched compared with repeated trials (condition: F(1,47) = 46.61, p<0.0001), but the groups did not differ in task switching errors (group×condition: F(1,47) = 0.01, p = 0.92) or in task switch costs for either prosaccades or antisaccades (prosaccades: t(47) = 1.08, p = 0.29; antisaccades: t(47) = 0.91, p = 0.37) (fig 3C). Dividing the SPD sample into subgroups did not affect the findings. In summary, control and SPD subjects showed significant task switching error costs for both prosaccades and antisaccades and did not differ in the magnitude of these costs.

Latency

These results are given in fig 3B. The main effect of condition (repeated *v* switched) was not significant (F(1,47) = 0.48, p = 0.49). This is because task switching affected the latency of prosaccades and antisaccades differently (condition×task interaction: F(1,47) = 35.99, p<0.0001). For prosaccades, switched trials were significantly slower than repeated trials (t(47) = 4.87, p<0.0001). The opposite was true for antisaccades (t(47) = 3.64, p = 0.0003). Group did not interact with condition (F(1,47) = 1.52, p = 0.22) or with condition × task (F(1,47) = 0.001, p = 0.98). In summary, there were no significant group differences in task switching latency costs (fig 3C). This finding was also true for SPD subgroups.

Relation of inhibition and task switching costs

The error and latency costs of saccadic inhibition and task switching were not related in either group (errors: control: $r = -0.06$, p = 0.79; SPD: $r = -0.22$, p = 0.27; latency: control: $r = 0.29$, p = 0.19; SPD: $r = 0.23$ p = 0.26). In the control group, the error costs of antisaccades (7 (6)%) and task switching (7 (8)%) were approximately equal. In the SPD group, error costs were significantly greater for inhibition (17 (15)%) than for task switching (9 (6)%; t(26) = 2.61, p = 0.02). Latency costs were significantly greater for antisaccades than for task switching in both groups (control: t(21) = 4.29, p = 0.0003; SPD: t(26) = 6.21, p<0.0001).

DISCUSSION

Subjects with Asperger's disorder, SEPD, and those who met criteria for both disorders showed deficient inhibition on the antisaccade task. They made more errors than control subjects and showed a disproportionate increase in latency for antisaccades relative to prosaccades. Deficient saccadic inhibition has previously been reported in autism,[8] high

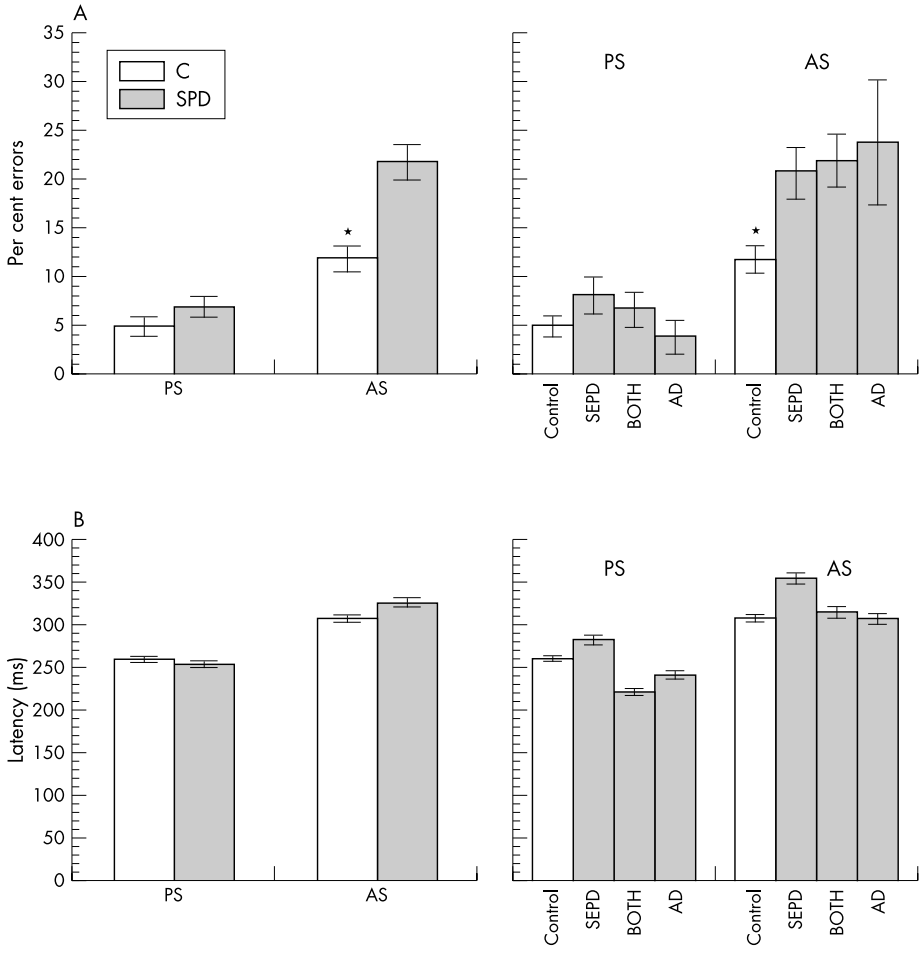

Figure 2 Inhibition: bar graphs with standard error bars for (A) per cent errors and (B) latency for prosaccades and antisaccades. The graphs are collapsed across *condition* (repeated *v* switched). On the right, the developmental social processing disorder (SPD) subgroups are graphed separately. An asterisk indicates that the comparison between adjacent bars is significant at p ⩽ 0.05. AD, Asperger's disorder; AS, antisaccade; BOTH, subjects meeting criteria for both syndromes; C, control; PS, prosaccade; SEPD, social-emotional processing disorder.

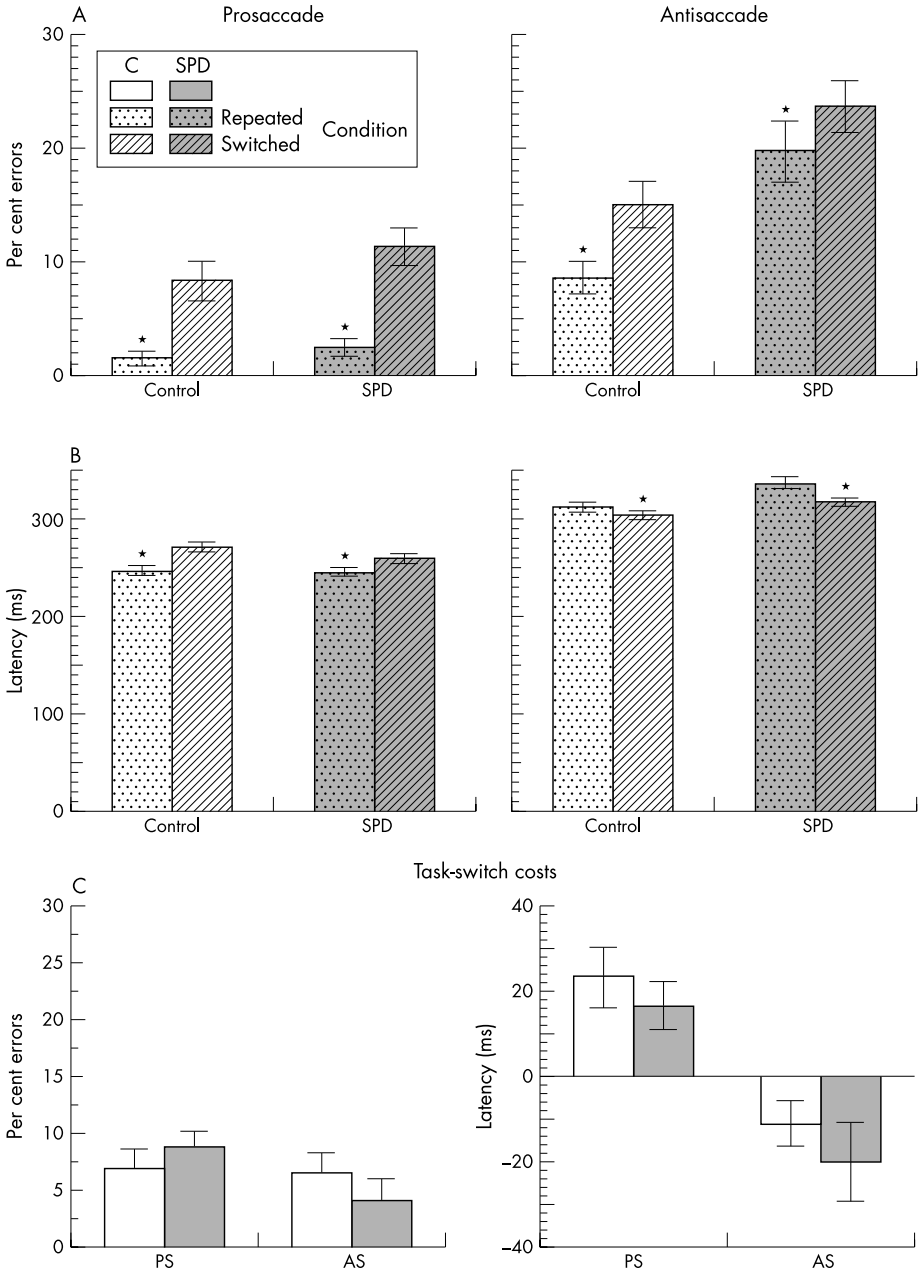

Figure 3 Task switching: bar graphs with standard error bars for (A) per cent errors and (B) latency separated by task (prosaccades: left; antisaccades: right) and by condition (repeated *v* switched). Isolated task switch costs for prosaccades and antisaccades are graphed in (C) (see formulas in table 4). An asterisk indicates that the comparison between adjacent bars is significant at $p \leqslant 0.05$. AS, antisaccade; C, Control; PS, prosaccade; SPD, social processing disorder.

functioning autism,[9] and SEPD.[7] This study replicates the finding of deficient saccadic inhibition in SEPD and extends it to Asperger's disorder. In contrast, task switching was intact in Asperger's disorder and SEPD, and the performance costs of inhibition and task switching were not related. This behavioural dissociation shows that executive function deficits in Asperger's disorder and SEPD are selective.

The finding of a selective impairment of inhibition is unlikely to reflect reduced sensitivity of the task switching measurements. In the control group, error costs were equivalent for antisaccades and task switching, and performance was not at ceiling levels. In addition, although latency costs were significantly smaller for task switching than antisaccades, both groups showed similar significant task switching costs, indicating that the measurements were sensitive. Our finding of a selective impairment suggests that inhibition and task switching are mediated by distinct anatomical networks, only one of which is dysfunctional in Asperger's disorder and SEPD. Because saccadic eye movements use a control system with a relatively well delineated neuroanatomy and physiology, these findings can guide the generation of testable hypotheses regarding dysfunctional neural circuitry in these disorders.

In both Asperger's disorder and SEPD, prosaccade performance was intact but antisaccade performance was deficient. Neuroimaging studies reveal increased activation in many cortical and subcortical areas for antisaccades compared with prosaccades, including the dorsolateral prefrontal cortex in many[41–44] but not all studies.[45] Patients with large frontal lobe excisions[46 47] and with more circumscribed lesions of the dorsolateral prefrontal cortex, but not of the frontal eye field or supplementary motor area, have saccadic inhibition deficits.[48–50] A recent EEG study showed that while the same basic neural circuitry supports prosaccade and antisaccade performance, antisaccades are characterised by additional dorsolateral prefrontal cortical activity occurring 160–60 ms

before saccade generation.[51] These findings suggest that antisaccade performance relies on activation in a distributed neural network that includes the dorsolateral prefrontal cortex. The finding of deficient saccadic inhibition in Asperger's disorder and SEPD is consistent with other evidence that implicates the prefrontal cortex in these syndromes. This includes findings of increased concentrations of N-acetylaspartate (NAA) in the prefrontal cortex[52] and reduced grey matter in frontostriatal pathways.[53]

While both Asperger's disorder and SEPD have an early onset, saccadic inhibition does not develop fully until late adolescence, presumably reflecting delayed maturation of the prefrontal cortex.[24 25] While the saccadic inhibition deficit may be secondary to having a developmental social processing disorder, we hypothesise that it represents instead a late manifestation of neurodevelopmental dysfunction of the prefrontal cortex. We propose that deficits in executive function, and specifically inhibition, are present early in life and contribute to the development of social and behavioural problems in these syndromes. Studies using age appropriate measures are needed to establish the time course of these deficits and their relation to social and behavioural symptoms.

Deficits of saccadic inhibition are not specific to Asperger's disorder or SEPD. They are also found in several psychiatric disorders including schizophrenia.[54] However, the saccadic inhibition deficit in Asperger's disorder may be qualitatively and quantitatively distinct. In contrast to schizophrenia, subjects with Asperger's disorder had normal latencies, amplitudes, and peak velocities for both prosaccades and antisaccades,[55] and made one third fewer antisaccade errors.[54] This suggests that Asperger's disorder is characterised by a more circumscribed and less severe saccadic inhibition deficit. Neuroimaging studies are necessary to characterise the distinct neural signatures of antisaccade deficits in these neurodevelopmental disorders.

The finding of intact task switching seems to contrast with clinical observations of perseverative behaviour in Asperger's disorder. It is important to note that task switching comprises several components and that the timing parameters for the current paradigm specifically tapped ''residual'' task switch costs. Studies of switching have suggested an early process of initiating a new task set that is triggered by an instructional cue and completed in 600–800 ms.[56 57] Even with long cue lead times, some switching effects on latency and accuracy remain. These are termed residual switch costs, and may reflect residual influences of stimulus–response configurations from the previous trial.[58] In addition, our paradigm measures task switching in relative isolation—it involves a fairly pure stimulus–response remapping. When studied in this manner, task switching is intact in Asperger's disorder and SEPD. The deficiency in Asperger's disorder responsible for perseverative behaviour may involve a closely related process, rather than the simple requirement to switch.

There are ongoing diagnostic controversies concerning the overlap and distinctiveness of Asperger's disorder and other developmental social processing disorders such as high functioning autism and SEPD.[19 21 22 59] We examined neurocognitive functions that are independent of diagnosis and found that the performance of individuals who met criteria for Asperger's disorder and SEPD could not be distinguished. Although the sample sizes were small, this inability to distinguish subgroups did not reflect a lack of power. The means for saccadic inhibition were quite similar, and each subgroup was significantly different from the control group. Perhaps this is not surprising given the considerable overlap in the criteria for these two disorders. The SEPD criteria used were consistent with our previous studies[7 11 13 60] and similar to those employed by other groups.[12 14–16] It is also noteworthy that many subjects met criteria for both Asperger's disorder and SEPD. The findings of indistinguishable saccadic performance and considerable overlap in diagnosis add to the debate about whether Asperger's disorder and SEPD are different disorders or the same disorder defined according to different nosological traditions. Determining whether there are valid distinctions between these diagnoses clearly requires further study with larger samples. Because all the subjects in the present study had been referred for neuropsychological evaluation, the sample may have been biased to greater neurocognitive impairment.

The study of Asperger's disorder and SEPD in late adolescence and in adults presents several challenges. Reports of early history and symptoms are necessarily retrospective, and parental informants are not consistently available. Moreover, the definition of Asperger's disorder is largely based on case studies of children, and most standard diagnostic instruments were developed for use with children and their parents. There is clearly a need for further development of standardised methods of assessment and diagnosis in older individuals with developmentally based social processing disorders. Adults with Asperger's disorder represent an underidentified and understudied group. Saccadic inhibition may be just one example of a deficit which, because of its late maturation, may only be apparent later in life. Longitudinal studies will be necessary to determine how the other cognitive deficits and symptoms that characterise Asperger's disorder evolve over the course of development.

Conclusions

Identifying intact and impaired neurocognitive function in developmental social processing disorders can guide investigations of neuropathology, clarify diagnosis, and reveal basic cognitive deficits that may contribute to symptom presentation. In this study we showed that both Asperger's disorder and SEPD are characterised by saccadic inhibition deficits and this is consistent with other evidence that implicates the prefrontal cortex.

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