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Behavioural aspects of cerebellar function in adults with Asperger syndrome

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Abstract
Aside from social deficits, Asperger and autistic individuals also exhibit motor control abnormalities such as impaired gait, balance, manual dexterity and grip. One brain area that has consistently been reported on autopsy and imaging studies to be abnormal in such individuals is the cerebellum. As the cerebellum controls sensorimotor coordination and lesions here typically cause hypotonia, dysmetria and dyscoordination, we performed a series of quantitative tests aimed at investigating cerebellar function in Asperger individuals. Tests examining visually guided movement (rapid pointing), speeded complex movement (finger tapping, rapid hand turning), muscle tone (catching dropped weight), prediction, coordination and timing (balance, grip force and interval timing) were conducted on 12 Asperger subjects and 12 age and IQ matched controls. In comparison to control subjects, Asperger subject's demonstrated: (i) decreased pointing accuracy and rate, (ii) increased postural instability, and (iii) decreased timing accuracy. IQ was found to co-vary with some parameters of each of these tasks and no further impairments were found on the remaining tests. We suggest that these specific deficits reflect impairment in the ability to integrate sensory input with appropriate motor commands and are consistent with cerebellar dysfunction in Asperger syndrome.

Key words: *Cerebellum, Asperger syndrome, balance, timing*

Introduction

Autism is a lifelong developmental disorder, characterized by abnormalities in social interaction, impairments in verbal and non-verbal communication and a restricted repertoire of interests and activities (ICD-10, World Health Organization 1992; DSM-IV, American Psychiatric Association 1994). It includes a wide spectrum of disorders, encompassing individuals at all levels of intelligence and language ability (1). Asperger syndrome refers to individuals with the typical social and communication impairments of autism but who have fluent language and good academic abilities; it differs from high-functioning autism in that no delay in language and cognitive development exists (2). It is unclear whether there are any differences between those individuals without language delay compared to those who acquire fluent speech later in development, but such behavioural criteria is used because no specific biological markers are known at present (1).

Aside from the social deficits, Asperger and autistic individuals also exhibit motor control abnormalities. Previous studies have observed impairments of gait (3,4), motor preparation (5), grip (6), manual dexterity, ball skills, locomotion and balance (4,7–10). One area of importance for motor control is the cerebellum. Evidence suggests that it plays a role in the control of sensory guided actions (for review see ref. 11), the coordination of different motor systems (12–14) in timing (15–16) and motor learning (11,13).

Abnormalities of the cerebellum in autistic individuals have been consistently reported. Postmortem evidence reveals much inter-subject variability with findings including Purkinje cell loss in the vermis and cerebellar hemispheres and cerebellar hyper and hypoplasia (18–21). In addition, hypoplasia and hyperplasia of the cerebellar hemispheres and vermis have been identified using Magnetic Resonance Imaging (MRI) (17,22,23). It should be noted however, that post mortem studies have frequently been conducted on less than 10 subjects and the relationship between cerebellar pathology and function remains unclear, exemplified in cases where cerebellar symptoms do not correspond to the suspected pathological area (24).

There is also accumulating evidence to suggest that the cerebellum plays a role in more cognitive,

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social and emotional functions (25–26) which has led some authors to speculate that the cerebellum could contribute to other socio-emotional manifestations of autism (27,28). Indeed, some of the most frequent signs of cerebellar hypoplasia include poor fine motor skills, hypotonia and autistic features (24). Therefore, the aim of the current work was to establish whether individuals with Asperger syndrome demonstrate motor deficits that could reflect cerebellar dysfunction. We tested Asperger subjects on a range of tasks modified around the traditional test battery designed to clinically assess cerebellar patients (29). The tasks examined performance of visually guided movement, speeded complex movements, muscle tone, coordinated movements, and timing accuracy as cerebellar patients classically demonstrate, dysmetria, dysdiadochokinesis, hypotonia, dyscoordination and inaccurate timing abilities (29). Previous studies (3,7–10) employed qualitative methods such as The Movement Assessment Battery for Children (30) and the Bruininks-Oseretsky test (31). We undertook a fully quantitative assessment of motor performance.

Methods

Subjects

Subjects were 12 Asperger individuals (8 males) and 12 sex, age and IQ matched healthy controls (Table I). Average age $\pm$ standard deviation of the Asperger and control participants was 27.42 ± 11.08 and 28.17 ± 11.7 respectively. Average IQ $\pm$ standard deviation (abbreviated WAIS) was 104 ± 22.08 and 112.42 ± 15.92 for the Asperger and control participants respectively. Age and IQ did not significantly differ between the two groups (*t*-test; $p = > 0.05$). Diagnosis of Asperger syndrome was based on outside clinical assessment (DSM-IV criteria, American Psychiatric Association 1994). Mean autism-spectrum quotient (AQ) scores $\pm$ standard deviation for the Asperger group was 33.27 ± 6.2. It has been suggested that a score of 32+distinguishes individuals who have clinically significant levels of autistic traits (32). Each gave written informed consent to participate and the study was approved by a local ethical committee.

Apparatus

A Polhemus electromagnetic motion tracking system, with an accuracy of 0.8 mm was used to measure the position of the finger, hand or body in x, y and z coordinates. Sampling rate was 60 Hz or 120 Hz depending on whether one or two sensors were used. In the following four tasks, one Polhemus sensor was attached to the back of the index finger and sampled at 120 Hz. Subjects used their preferred hand.

Tasks

Visually-guided movement: Rapid Pointing (dysmetria). Subjects moved their index finger back and forth between proximal and distal black spots (0.5×0.5 cm) that were placed 25 cm apart. They were instructed to point as accurately and as quickly as possible to each target over a period of 10 sec. This was repeated three times and data were averaged over the three trials. Pointing rate (Hz) and mean error (cm) over all three axis was calculated.

Speeded complex movement: Tapping (dysdiadochokinesis). With their hand on a flat surface, subjects tapped their index finger on the surface as many times as possible in 10 sec. This was repeated three times and data were averaged over the three trials. Tapping rate in Hz was calculated.

Speeded complex movement: Rapid Hand turning (dysdiadochokinesis). Subjects pronated and supinated the wrist of one hand, alternately placing the palm or back of the hand against the other palm as many

Table I. Characteristics of Asperger and Control subjects.

Asperger subjects					Control subjects			
Subject no.	Gender	Age	IQ	ASQ	Subject no.	Gender	Age	IQ
1	M	44	109	40	1	M	47	115
2	M	31	134	34	2	M	30	129
3	F	19	132	35	3	F	20	130
4	M	19	135	29	4	M	17	127
5	M	37	80	22	5	M	39	84
6	M	18	76	25	6	M	18	88
7	M	18	91	35	7	M	18	103
8	M	49	91	30	8	M	50	127
9	F	19	94	40	9	F	22	111
10	M	25	102	35	10	M	25	103
11	F	32	123	41	11	F	33	125
12	F	18	81	–	12	F	19	107

times as possible in 10 sec. This was repeated three times and data were averaged over the three trials. The number, amplitude (°) and duration (ms) of hand turns were calculated.

Muscle tone: Catching dropped weight (hypotonia). Subjects positioned their hand a distance of 10 cm above a flat surface, while a 200 g bean bag was dropped from a height of 30 cm directly onto the palm of their hand. Their eyes remained open and they were instructed to catch the bean bag without closing their grasp. This was repeated three times and data were averaged over the three trials. The level of muscle tone was estimated by the distance in cm between the maximum and minimum hand position in the x, y and z axis separately, immediately after contact.

Prediction and coordination: Grip force. Subjects lifted a 200 g device containing a force sensor and accelerometer off a flat surface and moved it smoothly up and down for a period of 10 sec. They were instructed to grip the device between thumb and index and middle fingers. This was repeated three times and data were averaged over the three trials. Calculated parameters included mean modulation of grip and load forces (mean difference between the minimum and maximum force for each up and down movement), mean force, standard deviation of mean force and mean phase difference (time of peak grip force subtracted from time of peak load force, averaged over each 10 sec trial).

Prediction and coordination: Balance. Two Polhemus sensors were positioned on each subject and sampled at 60 Hz: one was attached to a baseball cap and positioned on the forehead; the second sensor was attached to the back of the neck by a collar. Subjects were instructed to place one foot directly in front of the other (heel to toe) and balance for 10 sec. This was repeated three times with and without eyes closed and data were averaged over the three trials. Balance ability was measured by calculating the total distance in cm travelled by the Polhemus sensor in all three x, y and z axes.

Timing: Interval Timing. Subjects performed two auditory timing tasks: synchronization and continuation. In the former, a sequence of four beeps was heard with equal intervals. Subjects were instructed to press the keyboard spacebar in time with the third and fourth beeps. In the continuation task only the first two beeps were audible and subjects were required to press the spacebar in time with when they thought that the third and fourth beep should occur. On different trials, the timing intervals between beeps were pseudo-randomly presented and consisted of 400, 500, 600, 700 and 800 ms. These were each presented 6 times, giving a total of 30 trials in each task.

Four different measurements were calculated:

Absolute error. The absolute difference between the subjects' two responses (inter-response interval) and the third and fourth beep (inter-stimulus interval).

Relative error. The difference between the subjects' two responses (inter-response interval) and the third and fourth beep (inter-stimulus interval). Positive values indicate shorter inter-response intervals and negative values indicate longer inter response intervals.

First stimulus-response asynchrony (SRA1). Onset time of third beep subtracted from subjects' first response. Positive responses indicate early responses and negative values indicate late responses.

Second stimulus-response asynchrony (SRA2). Onset time of fourth beep subtracted from subjects' second response. Positive responses indicate early responses and negative values indicate late responses.

Results

Visually guided movement: Rapid pointing

Table II displays the pointing rate and mean and standard deviation of the proximal and distal errors for Asperger and control subjects. A multivariate ANOVA of group and measurement parameters revealed that control subjects were significantly faster than Asperger subjects, exhibited a significantly higher proximal error standard deviation and displayed a significantly lower mean distal error ($F(1,70) \geq 4.7$, $p \leq 0.03$). When IQ was covaried out, the proximal error standard deviation $F(1,69) = 4.27$, $p = 0.04$) and mean distal error $F(1,69) = 9.56$,

Table II. Calculated performance measures for the pointing task in Asperger and control subjects.

Measurement	Asperger subjects	Control subjects
Rate (Hz)	0.90	1.04
Mean error at proximal target (cm)	1.0	1.02
Standard deviation of proximal target error (cm)	0.7	1.07
Mean error at distal target (cm)	0.86	0.66
Standard deviation of distal target error (cm)	0.37	0.35

Table III. Calculated performance measures for the rapid hand turn task in Asperger and control subjects.

Measurement	Asperger subjects	Control subjects
Rate ± standard error (Hz)	14.60 ± 0.65	15.80 ± 0.61
Duration of turns ± standard deviation (ms)	0.74 ± 0.09	0.64 ± 0.07
Amplitude of hand turns ± standard deviation (°)	143.88 ± 11.68	140.93 ± 6.37

Table IV. Amount of movement in x, y and z planes for the muscle tone task in Asperger and control subjects.

Movement in axis ± standard error (cm)	Asperger subjects	Control subjects
x plane	−0.62 ± 0.31	−0.50 ± 0.17
y plane	0.02 ± 0.34	−0.29 ± 0.23
z plane	8.29 ± 0.48	9.24 ± 0.69

$p=0.03$) remained significantly different between the two groups. Therefore, despite being accurate at the beginning of the movement (proximal point) and moving more slowly, the Asperger group were less accurate than the controls at the end of the movement (distal point).

Speeded complex movement: Tapping

Mean tapping rate ± standard error for the Asperger and control subjects was 5.06 ± 0.11 Hz and 5.27 ± 0.12 Hz respectively. There was no significant difference between the two groups (Students *t*-test, $p=0.21$).

Speeded complex movement: Rapid hand turning

Table III displays the mean rate, amplitude and duration of hand turns for Asperger and control subjects. There were no significance differences between the two groups ($p \geq 0.09$).

Muscle tone: Catching dropped weight

The amount of movement made in each axis for Asperger and control subjects can be seen in Table IV. There were no significance differences between the two groups ($p \geq 0.3$). Average (± SD) values of anticipatory movement (elevation of the hand just prior to the weight being caught) made in the z plane over the three different trials for the Asperger and control groups were 0.78 ± 0.63 cm and 1.15 ± 0.83cm respectively. However, a 2 × 3 (group × trial) mixed-design ANOVA revealed no significant differences in the amount of anticipatory movement between the two subject groups, between the trials or an interaction between the groups and trials ($F(2,36) \leq 3.83$, $p \geq 0.13$).

Prediction and coordination: Grip force

A 2 × 3 (group × trial) multivariate ANOVA revealed no significant differences in the mean modulation of grip force, mean grip force, standard deviation of force or phase between Asperger and control groups ($F(4,17)=0.65$, $p=0.64$; Table V). There was no significant main effect of trial number and no significant interaction between trial number and subject group ($F(8,13) \leq 0.68$, $p \geq 0.70$).

Prediction and coordination: Balance

Figure 1 (a & b) displays the neck and head movement speed for Asperger subjects (grey bars) and control subjects (black bars) during eyes open and closed conditions when performing the heel-to-toe balancing task. A 2 × 2 × 2 (subject group × eyes open/closed × sensor position) mixed design ANOVA revealed that sway was significantly higher in the Asperger group ($F(1,70)=201.29$, $p<0.001$), with eyes closed ($F(1,70)=19.89$, $p<0.001$) and was significantly higher in the eyes closed condition for the Asperger subjects in comparison to the control subjects ($F(1,70)=4.18$, $p=0.045$). There was no main effect of sensor position ($F(1,70)=0.987$, $p=0.324$), and no significant interactions between eye condition and sensor position ($F(1,70)=0.832$, $p=0.365$), or between subject group, eye condition and sensor position ($F(1,70)=1.627$, $p=0.206$). A 2 × 2 × 2 ANCOVA showed that when IQ was covaried out, the main effect of subject group ($F(1,69)=12.94$, $p=0.01$)

Table V. Calculated performance measures for the grip force task in Asperger and control subjects.

Measurement	Asperger subjects	Control subjects
Mean modulation (N)	3.18	2.65
Mean force (N)	9.09	9.85
Standard deviation of mean force (N)	1.90	1.75
Phase difference (ms)	−12.47	3.20

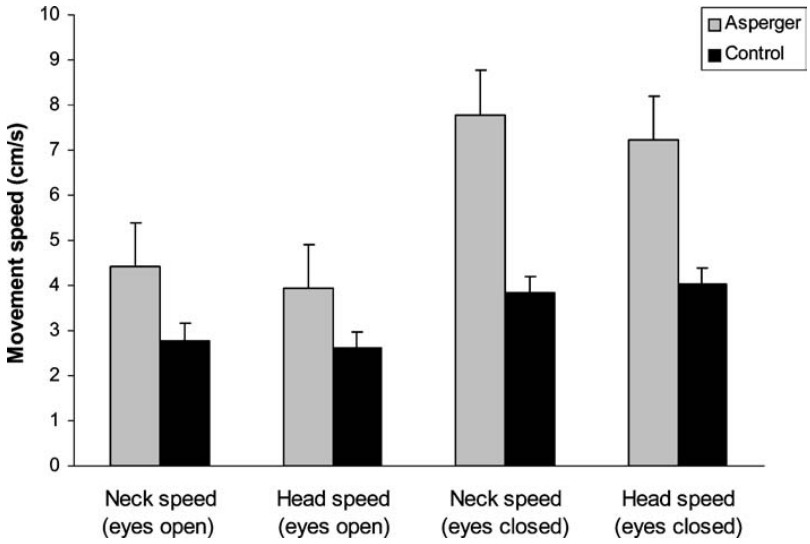

Figure 1. Balance performance: Neck and head movement speed in Asperger (grey bars) and control subjects (black bars) during eyes open and eyes closed balancing conditions. Standard error bars are shown.

remained significant but the main effect of closing the eyes was no longer significant ($F(1,69)=0.977$, $p=0.326$); the interaction between subject group and eye condition was not significant ($F(1,69)=3.7$, $p=0.059$).

A $2\times2\times2$ (group $\times$ eyes open/closed $\times$ sensor position) mixed ANOVA on movement speed standard deviations (within each 10 sec trial) revealed a significant main effect of group ($F(1,70)=15.35$, $p<0.001$) and eye condition ($F(1,70)=19.89$, $p<0.001$) indicating movement variability was greater in the Asperger group and when the eyes were closed. There was no significant differences between head and neck movement ($F(1,70)=0.987$, $p=0.324$). No significant interactions between sensor position (head vs. trunk) and group, sensor position and eye condition or between all three factors were observed ($F(1,70)\leq1.0$, $p\geq0.21$).

We also performed a frequency analysis of the instability of each group of subjects. During eyes open conditions, average modal frequency ($\pm$standard deviation) for the Asperger and control subjects was 0.05 ± 0.3 Hz and 0.06 ± 0.04 Hz respectively, and during eyes closed conditions was 0.06 ± 0.03 Hz and 0.06 ± 0.03 Hz respectively. A 2×2 mixed design ANOVA revealed a significant difference between the two subject groups ($F(1,138)=7.09$, $p=0.01$) but no significant main effect of eyes open/closed and no significant interaction between eyes open/closed and group ($F(1,138)\leq2.62$, $p\geq0.11$).

Timing: Interval timing task

Coefficient of variation (COV). A $5\times2\times2$ (interval $\times$ task $\times$ group) mixed design ANOVA revealed no significant main effects of timing interval ($F(4,88)=2.54$, $p=0.08$), task or group ($F(1,22)\leq0.44$, $p\geq0.51$) indicating that there was no difference in COV over the different intervals or between the different tasks or subject groups. There was also no significant interaction between timing interval and group ($F(4,88)=0.68$, $p=0.61$), but a significant interaction between timing interval and task ($F(4,88)=3.06$, $p=0.02$), indicating that in comparison to the continuation task, the synchronization task exhibited lower COV at shorter intervals and higher COV at longer intervals. However, as there were no significant interactions between interval, task and group ($F(4,88)=0.55$, $p=0.70$), we grouped the timing intervals together in the following analysis.

Synchronization task. During the synchronisation task (Figure 2a) both groups of subjects tended to respond early (positive stimulus-response asynchronies) and with shorter inter-response intervals (positive relative error). A 1-way multivariate ANOVA across all four response parameters did not reveal a significant overall difference between the two groups of subjects ($F(4,19)=2.18$, $p=0.11$). However, Asperger subjects demonstrated significantly greater absolute error ($F(1,22)=10.04$, $p=0.004$) and significantly greater stimulus-response asynchrony (SRA2: $F(1,22)=4.66$, $p=0.04$) indicating that they underestimated the second interval and tended to respond earlier than the control subjects. A 1- way ANCOVA indicated that when IQ was covaried out, absolute error remained significant between the two groups ($F(1,22)=8.57$, $p=0.08$), but SRA2 did not ($F(1,22)=3.48$, $p=0.84$). We also examined standard deviations using a 1-way multivariate ANOVA across all four response parameters and found that Asperger subjects had significantly higher standard deviations for all response parameters

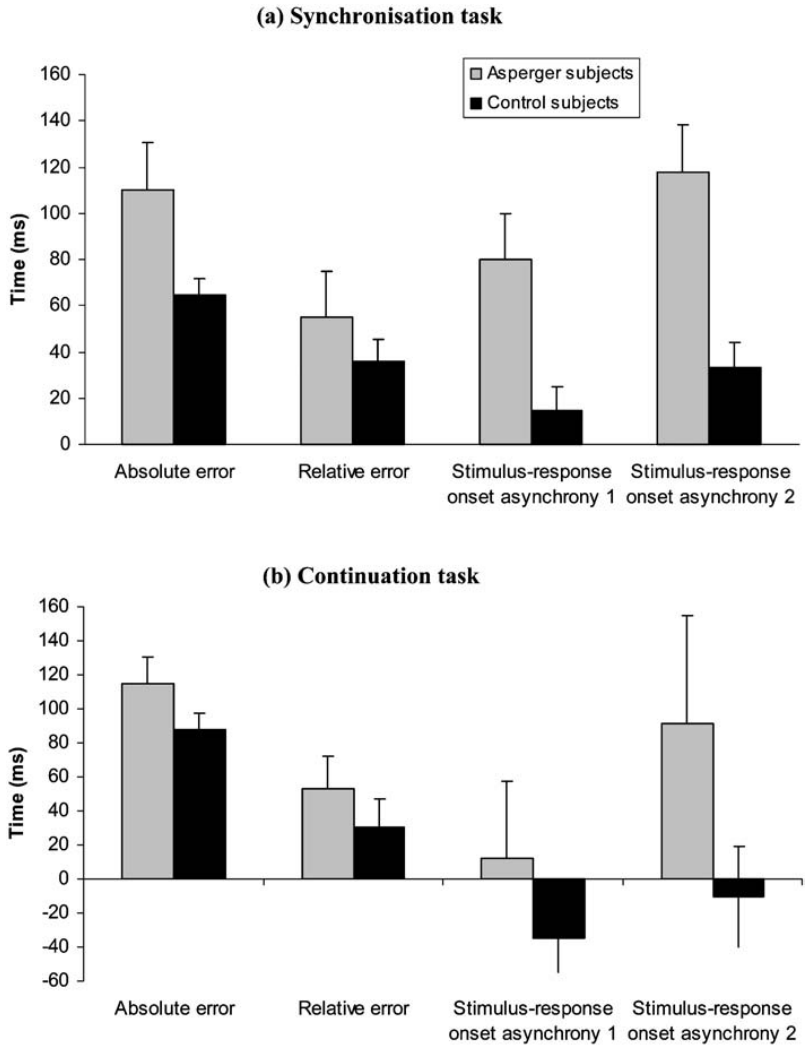

Figure 2. Timing performance: Absolute error, relative error, stimulus-response asynchrony 1 and 2 for the synchronization (a), and continuation (b) timing task. Grey bars indicate Asperger subjects, black bars indicate control subjects. Standard error bars are shown.

($F(1,20) \geq 5.1$, $p \leq 0.04$) which remained significant when IQ was covaried out ($F(1,19) \geq 4.4$, $p \leq 0.05$), except for SRA2 ($F(1,19) = 3.9$, $p = 0.06$).

Continuation task. A one way multivariate ANOVA across all four response parameters did not reveal a significant overall difference between the two groups of subjects ($F(4,19) = 1.0$, $p = 0.43$) or on any of the individual response parameters ($F(1,22) = 2.55$, $p = 0.13$). Even so, during the continuation task, the same patterns as for the synchronisation task were observed: there was a trend for Asperger subjects to underestimate the inter-stimulus interval and to display earlier responses in comparison to the control group (Figure 2b). Standard deviations of the Asperger subjects were higher for all response parameters ($F(1,20) \geq 4.31$, $p \leq 0.05$) except absolute error ($F(1,20) = 3.57$, $p = 0.08$). When IQ was covaried out, SRA2 ($F(1,19) = 4.74$, $p = 0.04$) remained significant.

Comparison between tasks. A 2×2 (group $\times$ task) multivariate ANOVA across the four different response parameters revealed no significant main effect of task ($F(1,22) = 3.45$, $p = 0.08$) for any response parameter. There were no significant interactions between subject group, task and response parameter ($F(1,22) = 1.56$, $p = 0.23$). However, it is worth noting that for the continuation task, the control subjects tended to respond after the supposed beep occurrence as demonstrated by the negative values of the stimulus-response asynchronies (SRA1 and SRA2, Figure 2b). In contrast the Asperger subjects continued to respond earlier. Additionally, control subjects demonstrated greater absolute error on the continuation task, as opposed to the synchronisation task, a pattern that was not present in the Asperger subjects.

Additional analyses

Individual outliers. In order to assess whether there were any consistent outliers in the Asperger population that we studied, we computed z scores for the control and Asperger subjects using the mean

and standard deviation from the control subjects and identified those individuals who were outside ± 1.65 SD. We chose this value as it corresponds to the 5th percentile. This was performed for all tests and on each task measure separately (Figure 3 (a–d); Figure 4 (a–c)). No one subject was consistently above or below ± 1.65 SD on all task measures. The greatest deviation was 16 out of the 30 task measures (Subject 6); the median was for each subject to be an outlier on 8 tests. For the controls, as expected the median dropped to 2. Subject 6 had an AQ score of 25 which is below the suggested 32 threshold (32) but demonstrated the lowest IQ, 76, of the Asperger group. However, it can be seen from Figures 3 and 4 that on the majority of task measures, that this subject is not the only or the most deviant outlier.

Correlation with autism-spectrum quotient (AQ) scores. Finally, we compared the autism-spectrum quotient (AQ) scores (32) for each subject with the results from each task and found no significant correlation between the AQ and any performance measure ($p = > 0.05$).

Discussion

Reports of increased clumsiness in autistic and Asperger individuals are common. In agreement with previous studies that have examined motor control in such subjects (3–10), we also found evidence of impaired motor control in Asperger subjects. However, differences were not found on all motor tests, but appear most pronounced only on those tasks where accuracy depends upon incoming sensory signals such as in pointing, balancing and timing.

Visually-guided movement

In comparison to the control group, the Asperger subjects were slower during the rapid pointing task and less accurate. Even though Asperger subjects

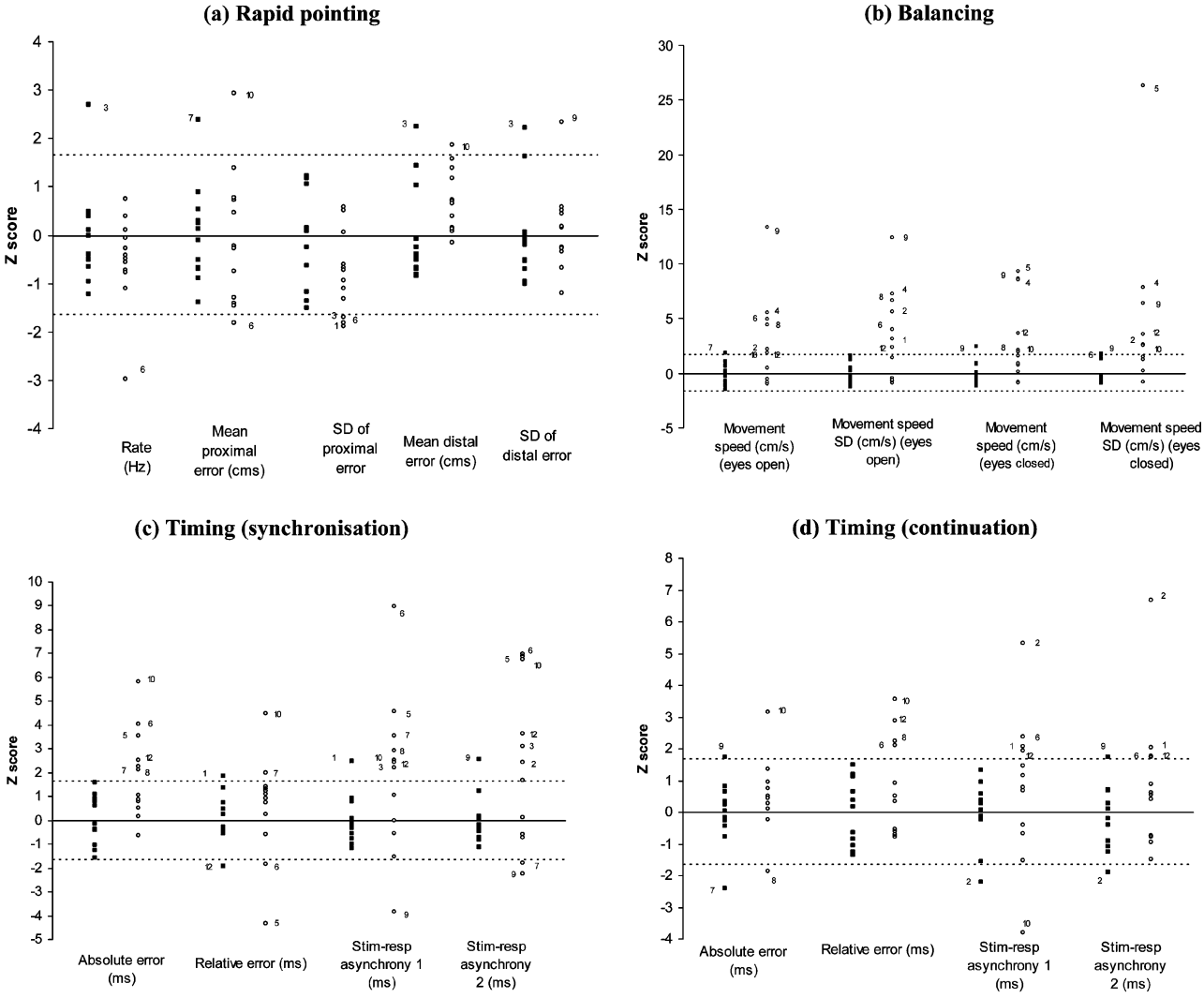

Figure 3. Individual z scores of each task measurement for: (a) rapid pointing, (b) balance, (c) synchronization, and (d) continuation timing task. The solid line indicates the control mean and the dashed lines indicate 1.65 SD above and below the control mean. Deviant individuals are identified.

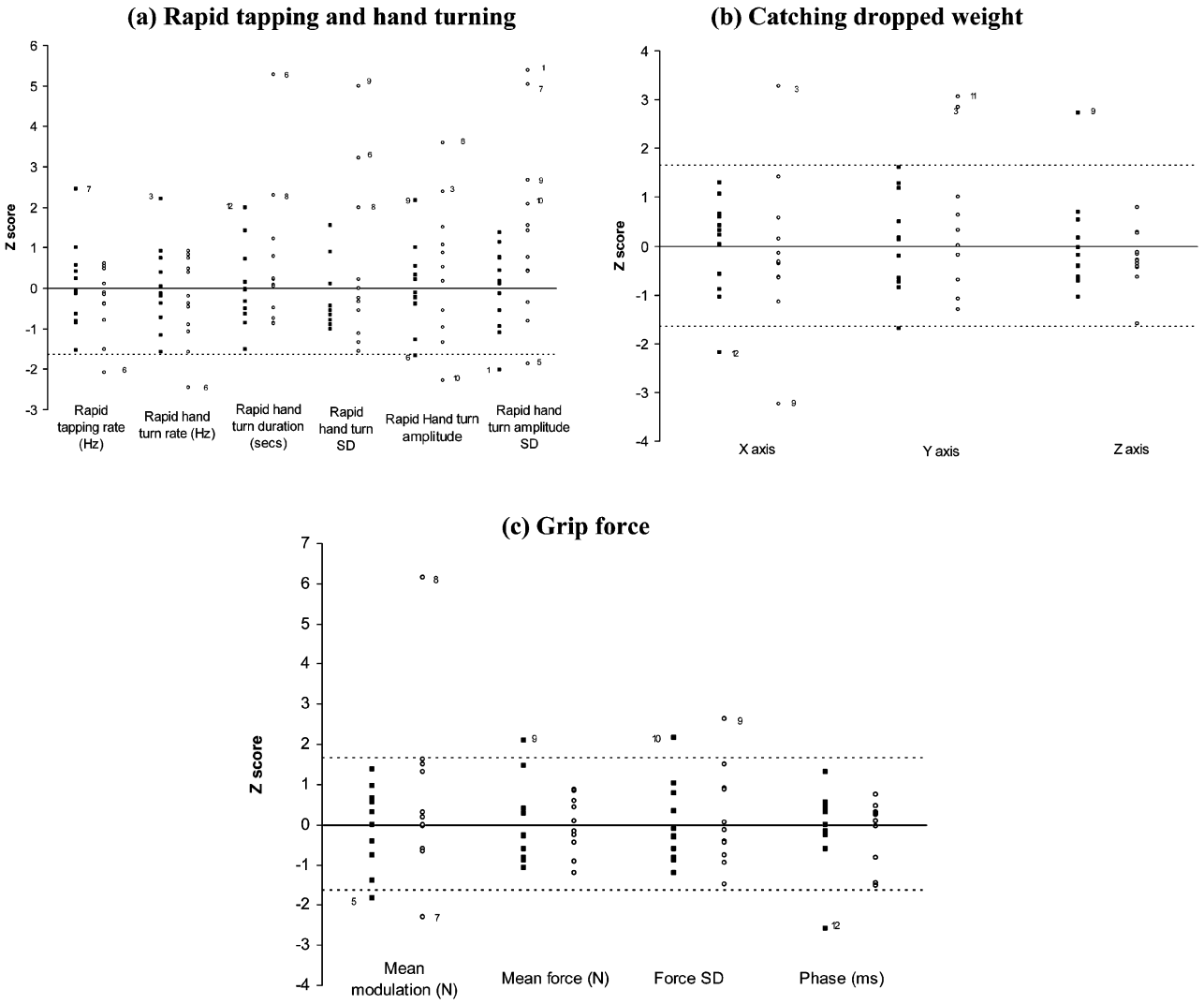

Figure 4. Individual z scores of each task measurement for: (a) rapid tapping and hand turning, (b) catching a dropped weight, and (c) grip force task. The solid line indicates the control mean and the dashed lines indicate 1.65 SD above and below the control mean. Deviant individuals are identified.

reduced their movement speed and were accurate when commencing the movement they were still unable to correct end point errors. The fact that no differences were observed on the rapid tapping and hand turn tasks suggests that Asperger subjects have difficulty performing tasks requiring visual feedback and eye-hand coordination but are able to complete tasks at the same speed as normal subjects when reliance on exteroceptive feedback is less vital. Normal tapping rates in Asperger individuals have been reported before (4) and they appear to exhibit difficulties in motor preparation as opposed to execution (5). Our finding of equivalent muscle tone in the two groups also underlines that impaired movement execution was unlikely to be a contributing factor to the observed pointing differences.

Such observations are reminiscent of poor hand-eye coordination in cerebellar patients who show more impairment during combined eye-hand tracking than during tracking with the eye or hand alone (14). Indeed, activation of the cerebellum during fMRI is directly correlated with eye-hand tracking performance: activation is highest when error between the eye and hand is minimal (12). Furthermore, slower performance on the pegboard test, a task that requires combined hand-eye coordination has been observed in both individuals with autism (6,33) (but see ref. 4 for contrasting results) and during inhibition of the cerebellum using rTMS (34).

Prediction and coordination

The tasks involving grip-force coupling and balance all employed prediction and coordination to different extents. Prediction is a key feature of the grip task, where in order to precisely stabilize and time grip force against self-imposed loads, healthy subjects anticipate load changes so that temporal delays between grip force and load are minimal. This is thought to be performed by internal forward models located in the cerebellum (35). Patients with cerebellar pathology show grip/load force abnormalities

including raised grip force and increased onset latency of lift force after onset of grip force (36). As we did not find a significant difference between the Asperger and control subjects in terms of grip force and latency, this suggests that our Asperger subjects were able to use predictive control on this task.

However, Schmitz et al. (2003) documented reactive rather than predictive postural adjustments in a group of autistic children during a load lifting task, as well as an increase in the duration of voluntary unloading (37). The authors hypothesized that this slowing down allows proprioceptive information to be exploited to control postural stability, a strategy that appears similar to the reduced pointing rate observed in our subjects. The (non-significantly) smaller amount of anticipatory movement we found during the muscle tone task would also support the argument that such individuals are impaired at predicting future actions and the sensory consequences of these movements. Because they could see the weight being released, they could anticipate its impact, and in such circumstances anticipatory elevation of the hand is normally seen (38) but this is impaired in cerebellar subjects (39). Perhaps a more sensitive test of predictive ability would highlight subtle differences between our Asperger subjects and controls.

Despite the normal grip force coordination of our subjects, the Asperger group demonstrated less postural stability than the control subjects during both eyes open and eyes closed conditions. The cerebellar vermis is believed to use information from the vestibular, visual and proprioceptive systems in order to coordinate muscle timing so that the centre of gravity stays within the limits of stable upright standing (40,41). Damage to the cerebellum, in particular the vermis (42) results in more postural sway than in control subjects (43,44). Decreased postural stability would correspond with abnormalities of the vermis observed in autistic subjects (17–23). However, previous work indicates normal tilt suppression of post-rotary nystagmus and normal saccade metrics (both behaviours that involve the cerebellar vermis) in autistic subjects (45,46; but see 47).

Increased sway in Asperger subjects has been reported before (3,4). Weimer et al. (2001) suggested that as balancing ability appeared to be unaffected during the eyes open conditions, the Asperger individuals exhibited proprioceptive deficits (4). Although our subjects did exhibit relatively more sway during eyes closed conditions then control subjects, balance was also impaired when the eyes were open and the effect of eye closure was removed when IQ was covaried out. In addition, their intact performance on tasks that are less reliant on visual feedback (such as finger tapping, rapid hand turning and grip/load coupling) suggests that impaired proprioception cannot fully explain the observed motor impairments. Rather, this may reflect difficulties in coordinating the different sensory inputs with the correct motor output combination.

Timing

For the normal control subjects, our results in the timing task are consistent with previous studies that have reported, first, responses to precede pacing stimuli by approximately 30–50 ms on the synchronization task and, second, an increase in absolute error on the continuation task (48,49). Overall, in comparison to the control subjects, the Asperger subjects tended to judge the inter-stimulus interval as shorter, to respond earlier and were more variable in their responses. Their responses did not vary between the synchronization and continuation tasks unlike for the controls, suggesting a fixed and non-adjustable mechanism of timing control. These findings are reminiscent of the abnormal timing of conditioned eye-blink responses found previously in autistic subjects (50). The earlier acquisition and extinction of conditioned eye-blink responses together with shorter response latencies were hypothesised to be due to an impaired ability to modulate the timing between paired stimuli, related to cerebellar pathology.

The exact contribution of the cerebellum to timing is unclear (51) and many other brain regions have been associated with timing tasks including M1, the dorsal lateral premotor cortex, inferior parietal lobe, supplementary motor area, superior temporal gyrus, caudal putamen, ventrolateral thalamus and inferior frontal gyrus (48,49,52). Abnormalities of some of these areas, such as the inferior frontal gyrus and superior temporal gyrus (22,53) have been reported in autistic subjects rendering it difficult to isolate the cerebellum in this task. However, increased timing variance has been observed in patients with cerebellar disorders (15) and rTMS delivered to the medial cerebellum has been shown to increase variability in a timed tapping task (54). Our Asperger subjects also displayed increased timing variance. Rao et al. (1997) have suggested that activation of the dorsal dentate nucleus in timed tapping tasks is due to the coordination of external (synchronization) and internal (continuation) stimulus events with output from the motor system (49). The responses of the Asperger subjects imply that they could not perform this coordination and perhaps responded earlier as a compensatory measure. A deficit based on impaired sensorimotor integration, rather than on an impaired pure timing system would fit with the motor deficits observed on the pointing and balancing tasks.

A deficit of sensory processing and integration?

What is it that dissociates the pointing, balance and timing tasks from the remaining tests? A

fundamental function of the cerebellum is thought to be interpreting and integration of incoming sensory signals, identifying and correcting errors on line and coordinating these incoming signals with motor output (11–16,34). All three tasks involved coordinating sensory signals (vision, proprioception, sound) with appropriate motor output (pointing to a target, balancing stably, tapping in time). Therefore, we believe that our results reflect deficits in the integration of sensory signals with motor output and provide support for the occurrence of cerebellar dysfunction in Asperger individuals.

It could be argued that the remaining tasks, particularly the grip task, also involve sensori-motor coordination. Why were there no significant differences on these tasks? Firstly, there was less externally imposed constraint on spatial and temporal accuracy and therefore extrinsic sensory demands were reduced. Increasing the demands of these tasks, such as adding visual/proprioceptive constraints or employing different grip loads may yet reveal subtle differences between Asperger and control groups. The observation of consistent motor impairments across tests in previous studies could be attributed to their use of qualitative measures (7–10). Secondly, it should be remembered that behavioural deficits may be hidden by the developmental nature of Asperger syndrome, allowing time for idiosyncratic adaptation to motor deficits to occur (55). We should instead emphasize the importance of finding consistent statistically significant results, albeit in a subset of the tests we used, given that we were examining a developmental condition, in a small population of less severely affected autistic individuals.

Conclusions

In summary, we find that our data support the occurrence of motor deficits in Asperger individuals, and point to an impairment in the ability to integrate sensory input with the appropriate motor commands. As our test battery was weighted towards cerebellar function, and this structure is implicated in processing incoming sensory signals, detecting error and adjusting motor output accordingly, we suggest that the deficits observed are consistent with cerebellar dysfunction. Further in depth studies investigating eye-hand coordination, balance and timing in combination with the use of fMRI to isolate affected brain areas will be necessary to further elucidate the exact nature of this impaired sensori-motor integration in relation to cerebellar function.

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