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Impaired executive functioning in young adults born very preterm

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Abstract

Individuals born very preterm (VPT) are at increased risk of perinatal brain injury and long-term cognitive and behavioral problems. Executive functioning, in particular, has been shown to be impaired in VPT children and adolescents. This study prospectively assessed executive function in young adults who were born VPT (<33 weeks of gestation) [$n = 61$; mean age, 22.25 ($\pm$1.07) years; range, 20.62–24.78 years] and controls [$n = 64$; mean age, 23.20 ($\pm$1.48) years; range, 19.97–25.46 years]. Tests used comprised the Wechsler Abbreviated Scale of Intelligence (WASI), the Hayling Sentence Completion Test (HSCT), the Controlled Oral Word Association Test (COWAT), the Animal and Object test, the Trail-Making Test (TMT), and the Test of Attentional Performance (TAP). VPT participants showed specific executive function impairments in tasks involving response inhibition and mental flexibility, even when adjusting for IQ, gender, and age. No significant associations were observed between executive function test scores and perinatal variables or neonatal ultrasound classification. The results suggest that, although free from major physical disability, VPT young adults perform worse than controls on tasks involving selective aspects of executive processing, such as mental flexibility and response inhibition.
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Keywords: Premature birth, Gestational age, Neuropsychology, Wechsler Scales, Inhibition (Psychology), Cognition

INTRODUCTION

The mortality rate among very preterm (VPT) (e.g., <33 completed weeks of gestation) and very low birth weight (VLBW) (e.g., <1500 grams) infants has greatly decreased in recent decades, especially among the least mature individuals (Hack & Fanaroff, 1999). VLBW infants are either born prematurely or are small for gestational age (United Nations Children's Fund and World Health Organization, 2004). Therefore, VPT and VLBW individuals share several characteristics.

Follow-up studies of VPT or VLBW individuals have identified long-term cognitive and behavioral sequelae in childhood (Aylward, 2002; Bayless & Stevenson, 2006; Breslau et al., 1996; Curtis et al., 2002; Foulder-Hughes & Cooke, 2003; Hack & Taylor, 2000; Olsen et al., 1998; Roth et al., 1993), adolescence, and young adulthood (Allin et al., 2006a, b; Hack et al., 2002; Nosarti et al., 2004, 2005; Rushe et al., 2001; Taylor et al., 2004b;). Several studies have suggested that VPT and VLBW preschoolers and school-age children exhibit impaired executive function (Anderson & Doyle, 2004; Luciana et al., 1999; Waber & McCormick, 1995; Woodward et al., 2005). Specific deficits have been reported in object working memory, planning abilities, motor sequencing and inhibition, verbal conceptual reasoning and working memory, spatial conceptualization and organization, visual reasoning, and spatial working memory (Anderson & Doyle, 2004; Harvey et al., 1999; Luciana et al., 1999; Woodward et al., 2005). A gradient relationship between spatial organization and cognitive flexibility and birth weight has been reported (Taylor et al., 1998; Waber & McCormick, 1995).

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Longitudinal studies investigating neurodevelopmental outcome have shown that some impairments in neuropsychological function in VPT and VLBW samples persist into adolescence and early adulthood. These impairments have been found in attention, perceptual–motor and organizational abilities (Taylor et al., 2004a), visual–motor skills and memory (Taylor et al., 2004b), spatial working memory (Curtis et al., 2002), academic achievement (Cooke, 2004; Hack et al., 2002; Pharoah et al., 2003), general intellectual ability (i.e., IQ), and several neurosensory domains (Allin et al., 2006b; Hack et al., 2002), as well as psychological functioning (Gale & Martyn, 2004). Neurodevelopmental outcome has been associated with perinatal variables and risk for brain damage (Taylor et al., 2004a). Other studies reported that the differences between VPT individuals and controls in terms of educational performance (Tideman, 2000) and IQ scores (Peng et al., 2005) disappeared by adulthood/late adolescence, suggesting a developmental delay with subsequent "catch-up" in performance. Perinatal variables may mediate longitudinal changes in cognitive performance, as Taylor et al. (2004b) reported that, between the ages of 7 and 14 years, children of $<$750 g birth weight showed increased impairments over time compared with controls, whereas those of $>$750 g birth weight showed few deficits and no specific impairments. A point worth considering when interpreting cognitive differences between preterm samples and controls is the extent to which impaired processing speed may contribute to cognitive performance. Slowed processing speed is associated with VPT birth (Faust et al., 1999, Rose et al., 2002), with measures of processing speed accounting for as much as 60% of IQ differences between VPT individuals and controls in one study (Rose & Feldman, 1996).

Neuropsychological and neurological outcomes may be closely associated. A large body of literature suggests that even mild neurological impairment may affect cognitive processes (Allin et al., 2006b). Learning disabilities (Olsen et al., 1998) and verbal comprehension skills (Yliherva et al., 2001) are associated with minor neurological abnormalities in VPT children and mild motor delay with lower academic achievement scores (Sullivan & Margaret, 2003). Several investigations have reported associations between neurological outcome and IQ in VPT/VLBW samples of different ages (Allin et al., 2006b; Breslau et al., 2000; Hertzig, 1981).

Findings from previous follow-up studies of the VPT cohort followed by our research group at 8 years reported that, although the mean full-scale IQ of the VPT individuals was within the normal range, half the participants showed differences in neuropsychological scores (Roth et al., 1993). At 14–15 years of age, the cognitive performance of the VPT subjects was unrelated to the presence of gross brain abnormality, except that reading age was lower in VPT individuals with abnormal scans, as qualitatively rated (Stewart et al., 1999). At adolescent assessment, the VPT individuals of the current cohort were significantly impaired relative to controls only on verbal fluency tasks (Rushe et al., 2001). Neuropsychological function and perinatal variables were not significantly associated, contrary to the findings of other studies (Breslau et al., 1996; Cooke, 2005; Taylor et al., 1998). When investigating quantitative magnetic resonance imaging (MRI) results and cognitive function in adolescence, although global neurodevelopmental scores (i.e., individual composite scores derived by neurological and cognitive outcome data, see Nosarti et al., 2002, for further details) were not associated with MRI results and perinatal variables (Nosarti et al., 2002), cerebellar volume was associated with childhood IQ and adolescent reading ability (Allin et al., 2001) and verbal IQ and verbal fluency scores were associated with callosal size (Nosarti et al., 2004).

The current study describes the latest follow-up of these VPT individuals who have now reached adulthood, with an assessment of global cognitive function, and executive function in particular. The rationale for undertaking this study was twofold: first, to assess executive function more widely than we had previously done and, second, to determine whether the cognitive deficits detected in childhood and adolescence would continue to manifest into adulthood. To our knowledge, no studies have yet comprehensively investigated adult executive function outcomes in VPT populations. Additionally, we were interested in exploring whether perinatal variables such as birth weight, gestational age, Apgar scores, and neonatal ultrasound results would be associated with adult neuropsychological outcomes, as inconsistent findings are reported in the literature (e.g., Rushe et al., 2001; Taylor et al., 2004b, Vollmer et al., 2003). The identification of the selective cognitive weaknesses associated with VPT birth that persist into adulthood may have important implications for vocational as well as postgraduate training, by highlighting areas that could possibly improve by means of explicit teaching of organizational strategies and other methods to enhance learning (Taylor et al., 2004b).

Based on adolescent data from the same cohort and others (Rushe et al., 2001; Taylor et al., 2004b), it was hypothesized that young adults born VPT would have lower verbal fluency scores than full-term born controls, as well as lower scores on other tests of executive function. It was further hypothesized that preterm young adults would have lower global cognitive outcome scores compared with controls (Hack et al., 2002). A secondary goal was to determine whether deficits in adults born VPT on measures of executive function would be found even when controlling for IQ.

METHODS

Participants

The sample was recruited from a larger cohort of VPT individuals as part of a follow-up study on the long-term consequences of prematurity, which drew on 224 infants born before 33 completed weeks of gestation admitted to the Neonatal Unit of University College Hospital (UCH) in 1979–1982 within 5 days of birth and later discharged. Of

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this cohort, 24 individuals died within 24 months; the remaining 200 entered long-term follow-up. Prospective assessments of neurological and cognitive status were done at 1, 4, and 8 years (Roth et al., 1994). At 14–15 years, 148 individuals were administered neuropsychological and behavioral assessments and structural MRIs performed (Nosarti et al., 2002, 2004, 2005; Rushe et al., 2001; Stewart et al., 1999). The present study was conducted between 2001 and 2004 and involved contacts with 101 individuals from this cohort who could be traced to UK addresses. Thirty-six individuals declined assessment, whereas 65 individuals (64.4% of those invited to participate) took part in the study. Four individuals completed only part of the assessment due to severe motor (cerebral palsy) ($n = 1$) or hearing impairment (sensory neural hearing loss) ($n = 3$) and were excluded from the analyses. The individual with cerebral palsy had a classification of periventricular hemorrhage (PVH) and ventricular dialation (DIL) on neonatal ultrasound, whereas one of the three VPT individuals with sensory neural hearing loss had uncomplicated PVH, the remaining two being classified as normal.

Sixty-four controls matched by year of birth were recruited from advertisements in the local and national press, after being screened on the telephone. Inclusion criteria were full-term birth (37–42 weeks of gestation) and English as a first language; exclusion criteria included birth complications (e.g., low birth weight defined as <2500 g, preterm birth defined as less than 37 completed weeks of gestation, endotracheal mechanical ventilation), prolonged gestation (>42 weeks), history of psychiatric illness, severe hearing and motor impairment, and mental retardation indicated by an IQ < 70. All participants received travel expenses, refreshments, and a nominal remuneration for participation in the study.

Individuals with VPT birth who were not available for investigation did not differ from those studied on most sociodemographic and neurological variables collected at 8 years of age, including neurodevelopmental, neurological, and socioeconomic status and neonatal ultrasound findings. However, nonparticipants (NP) had lower estimated IQ scores than participants (P), as measured by the Wechsler Intelligence Scale for Children-Revised (WISC-R) (Wechsler, 1974) conducted at 8 years of age (Verbal IQ: mean P = 109, $SD = 17$; mean NP = 102, $SD = 20$; $F = 8.38$; $df = 195$; $p = .004$; Performance IQ: mean P = 103, $SD = 14$; mean NP = 95, $SD = 17$; $F = 5.88$; $df = 195$; $p = .02$; Full-Scale IQ: mean P = 106, $SD = 15$; mean NP = 98, $SD = 20$; $F = 8.81$; $df = 195$; $p = .003$).

Ethics

Ethical approval for the study was obtained from the Institute of Psychiatry/South London and the Maudsley National Health Service Trust Ethical Committee. Written informed consent for the assessment was obtained from all participants.

Procedures

Sociodemographic data were collected for all participants. Perinatal data were available for only the VPT group. Because 13 VPT individuals (21.3%) and 12 controls (17.2%) were still in full-time education, socioeconomic status was defined based on paternal occupation using Her Majesty's Stationary Office Standard Occupational Classification criteria (HMSO, 1991). If details on paternal occupation were not available, maternal occupation was used. Socioeconomic groups were collapsed into two categories, the first comprising individuals in professional and managerial roles, the second individuals in all other types of occupation. However, socioeconomic status for the subsample of participants in full-time employment was also detailed (controls, $n = 43$; VPT individuals, $n = 35$). Information on participants' educational attainment (successful completion of postsecondary education) and living arrangements (living with parents) was collected. For the VPT group, Apgar scores at 1 and 5 min, which are indicative of neonatal hypoxia, were categorized into two groups: 0–5 and 6–10. Low scores signify increased severity of hypoxia. The 1-min score refers to the birthing process, whereas the 5-min score refers to the adaptation to the environment. Neonatal ultrasound results were summarized as (a) normal (NM), (b) uncomplicated PVH, or (c) PVH and DIL (Nosarti et al., 2002; Stewart et al., 1983). The Wechsler Abbreviated Scale of Intelligence (WASI) (Wechsler, 1999), which comprises four subtests: Vocabulary, Block Design, Similarities, and Matrix Reasoning, was administered to obtain estimates of Full-Scale, Verbal, and Performance IQ. Measures of executive functioning were also given and are described below.

The Hayling Sentence Completion Test (HSCT) (Burgess & Shallice, 1997) assesses the ability to initiate responses, to inhibit unwanted responses and to form strategies to improve performance. The test consists of two sets of 15 incomplete sentences. In Part A (straightforward completion), the examiner reads each sentence aloud and participants are requested to simply complete the sentences with an appropriate word (e.g., the old house will be torn . . . down). Part A obtains a measure of response initiation speed. In Part B (anomalous completion condition) participants are asked to complete the sentences with a word that does not makes any sense in the context of that sentence (e.g., The captain wanted to stay with the sinking . . . interest), yielding measures of response suppression and thinking time for strategy generation. Response latencies are recorded for both sections of the task. Omissions or words unrelated to the meaning of the sentence are regarded as errors in Part A. In Part B, semantically related responses and omissions are regarded as errors. As an indication of the difference made by the experimental manipulation in Part B, a score is obtained by subtracting response time in Part A from response time in Part B (e.g., the time needed to suppress unwanted responses), which Burgess and Shallice (1996) regard as representing the additional time required to produce a semantically unrelated word relative to the appropriate word. Scores used in the analysis included Part A: Response Time (seconds), Part B: Response Time (seconds), Part B: Response Time minus Part A: Response Time (seconds) (Part B–Part A), Total Number of Errors, and a Total Score, obtained by adding Part A, Part B, and Errors scaled scores and transforming the value into a Total or Overall Scaled Score, ranging from 1 = *impaired* to 10 = *very superior*.

Two tests were used to assess verbal fluency. To measure phonemic or letter fluency, we administered the Controlled Oral Word Association Test (COWAT) (Benton & Hamsher, 1976). In this task, participants are requested to overtly produce words beginning with a given letter: F, A, and S, in 60 seconds. To assess category fluency, we administered the Animal Naming and Object Naming tests. In these tests, participants are required to say as many names of animals and objects as they can in 60 seconds for each category (Goodglass & Kaplan, 1972). Verbal fluency assesses the executive system that enables initiation of response, mental flexibility, and the ability to use different strategies, such as clustering, where words are produced in subcategories, either phonemic or semantic (Spreen & Strauss, 1991). Verbal fluency tasks place demands on short-term memory of phonological information and simple word retrieval processes as well as on executive function (Abrahams et al., 2000). Scores used in the analysis included the total number of words produced during the F, A, and S trials for the COWAT. Category Fluency was defined as the number of words produced on the Animal Naming and Object Naming tests combined.

The Trail-Making Test (Trails A and Trails B) (TMT) (Reitan & Wolfson, 1985) consists of two parts: Trails A provides a measure of visuomotor speed, and Trails B assesses conceptual tracking and cognitive flexibility. In Trails A, participants are asked to draw a line connecting consecutively numbered circles. Trails B consists of connecting numbers and letters by alternating between the two sequences. The time to complete each of the two tasks was used in analysis. The differences in times (Trials B minus Trials A) were also examined as a measure of cognitive flexibility that controlled for motor sequencing.

Three subtests of the Test of Attentional Performance (TAP, Zimmerman & Fimm, 1995) were administered to assess attention. In the Divided Attention (TAP/DA) subtest, participants were presented with a simultaneous visual (detection of a square among crosses) and auditory (detection of irregularities in a sequence of tones) discrimination task. The test measures the ability to perform two tasks simultaneously (scores are given for mean time needed to respond to the stimuli on each different task, number of omissions, and number of lapses). In the Go/No-go (TAP/GNG) subtest, participants were presented with five stimuli, of which two were defined as the critical stimuli. The test was designed to assess the ability of subjects to suppress undesired responses (scores are given for mean response time, number of omissions, and number of lapses). In the Incompatibility (TAP/I) subtest, participants were asked to indicate if the arrow presented to them pointed to the left or the right, regardless of whether the arrows were presented in the left or right visual field. The test measures response inhibition (scores are given for mean response time and number of lapses). Lapses represent the number of delayed responses performed during the tasks (i.e., longer than the individual mean plus 2.35 times the standard deviation) and are a measure of lapses of attention.

All assessments were conducted by a trained psychologist (E.G.) and a trained psychiatrist (N.M.). Inter-rater reliability was satisfactory (Cohen's $\kappa > .7$) on all noncomputerized tests.

Statistical Analysis

Data were analyzed with SPSS 11.0 (SPSS, Chicago, IL). Sociodemographic variables were analyzed with χ^2 tests; anthropometric characteristics and estimated IQ scores were analyzed with univariate analyses of variance (ANOVAs). Estimated IQ scores were also analyzed controlling for parental socioeconomic status (SES) with univariate analyses of covariance (ANCOVAs). Parental as opposed to participant's SES was used on the analyses, as this information was available for the majority of individuals assessed, while own SES was still undefined for a large proportion of participants who were in full-time education or looking for employment at the time of assessment (also see the Results section). Differences in executive test scores between VPT individuals and controls were assessed with ANOVA and ANCOVA, defined by a between-subject group factor (preterm and full-term subjects), adjusting for estimated full-scale IQ, age at assessment, and gender. Within the VPT group, only IQ and executive scores were analyzed, with univariate ANOVA defined by the following between-subject group factors: Apgar score at 1 and 5 min ($\leq$5 or $>$5) and neonatal ultrasound classification (NM, PVH, and PVH+DIL). The association between birth weight and gestational age, and estimated IQ and executive scores was analyzed with linear regression models again in preterm individuals only (for whom data were available). Some of the variables were non-normally distributed and were made to approximate normality using logarithmic transformation before analysis (Bland, 1995). Whereas summary statistics referring to raw values are given in results, statistical analyses were carried out on log transformations. Statistical significance was defined as a p value of $<.05$. For both parametric and nonparametric variables mean values, standard deviations, pooled standard deviations (strength of effect estimates), and 95% confidence intervals for the studied groups are presented, although it is acknowledged that for nonparametric variables the median may be more appropriate. We did not control for multiple comparisons, as is generally advisable in hypothesis-driven studies involving multiple comparisons, because there is a paucity of prior information on executive function in adult survivors; hence, this study is regarded as largely exploratory.

RESULTS

Sociodemographic Data

Table 1 presents data on group characteristics. Analysis failed to reveal group differences in parental or participants' sociodemographic status or in the number of participants who lived with their parents. In terms of gender, there were more females in the control group compared with the preterm group ($\chi^2 = 4.17$; $df = 1$; $p < .05$). The mean age at assessment of the two groups also differed ($F = 16.78$, $df = 124$; $p < .001$), although both VPT participants and controls were born between 1979 and 1982. Between-group differences are due to the fact that controls were recruited by year of birth to match the age of the VPT group; however, controls were tested an average of 1 year after the VPT participants. There were significant between-group differences in educational attainment, that is, completion of postsecondary education (46.9% of controls and 14.8% of VPT participants; $\chi^2 = 15.03$; $df = 2$; $p = .001$), and these differences persisted after taking participants' age differences into account and comparing the number of individuals who were still in postsecondary education together with those who had already obtained a degree (62.5% of controls and 41.0% of VPT participants; $\chi^2 = 5.79$; $df = 1$; $p < .02$). The mean estimated WASI Verbal IQ and Full-Scale IQ scores were significantly lower in the VPT participants compared with controls ($F = 13.67$, $df = 121$, $p = .003$; and $F = 10.48$, $df = 121$, $p = .002$; respectively). These differences persisted after adjusting for parental SES (Verbal IQ: $F = 9.79$, $df = 112$, $p = .003$; Full Scale IQ: $F = 6.02$, $df = 112$, $p = .015$). The two groups did not differ in Performance IQ ($F = 1.87$; $df = 121$; $p = .18$). No significant gender differences were observed in any of the perinatal variables (see Table 2).

Performance on Measures of Executive Function

On the HSCT, the performance of VPT participants on the Total score was significantly poorer compared with that of the controls (see Table 3). VPT participants required more time to perform both Part A and Part B of the HSCT than the controls. Group differences were also found in the Part B minus Part A score and the number of errors in both parts of the test. VPT volunteers performed significantly worse than controls on measures of verbal fluency (COWAT, Category Fluency) and the VPT group was also significantly slower than controls on Trails A and Trails B of the TMT, although there were no significant between-group differences in the Trails B minus A score. Group differences were likewise found on the TAP/DA and TAP/I "lapses." When the executive function data were analyzed adjusting for estimated Full-Scale IQ, gender, and age, between-group differences persisted in several HSCT scores (Total score, Part A, Part B,

Table 1. Characteristics of very preterm (VPT) and control groups

	Preterm ($n = 61$)	Controls ($n = 64$)
Parental socioeconomic status, no. (%)[a]		
I, II	22 (36.1%)	33 (51.6%)
III, IV, V	33 (54.1%)	26 (40.6%)
Missing	6 (9.8%)	5 (7.8%)
Participant's socioeconomic status, no. (%)		
I, II	12 (19.7)	15 (23.4)
III, IV, V	24 (39.3)	28 (43.8)
In full-time education	13 (21.3)	12 (18.7)
Looking for work	7 (11.5)	9 (14.1)
Missing	5 (8.2)	0
Living with parent, no. (%)	29 (47.5)	26 (40.6)
Males, no. (%)*	33 (54.1%)	23 (35.9%)
Age (in years) at assessment, mean (*SD*), range***	22.25 (±1.07) 20.62–24.78	23.20 (±1.48) 19.97–25.46
Degree level education, no. (%)[b]*	25 (41.0)	40 (62.5)
Height (in cm), mean (*SD*), range	169.41 (±11.07) 148–190	168.72 (±9.39) 155–198
Weight (in kilograms), mean (*SD*), range	67.73 (±16.10) 39–109	66.77 (±12.26) 50–93
Verbal IQ, mean (*SD*), range**	99.86 (±12.54) 72–131	108.50 (±13.18) 73–145
Performance IQ, mean (*SD*), range	109.91 (±12.73) 75–129	112.75 (±10.16) 83–131
Full Scale IQ, mean (*SD*), range**	105.14 (±11.99) 81–134	111.75 (±10.56) 82–141

[a]Paternal occupation was defined using Her Majesty's Stationary Office Standard Occupational Classification criteria (HMSO, 1991). When paternal details were unavailable, maternal occupation if available was classified. Missing data was regarded as the lack of availability of both paternal and maternal occupation details.
[b]Individuals who had completed postsecondary education as well as those who were still in full-time postsecondary education.
*$p < .05$.
**$p < .01$.
***$p < .001$.

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Table 2. Perinatal characteristics of preterm individuals

	Males (n = 33)	Females (n = 28)	All (n = 61)
Birth weight (in grams), mean (*SD*), range	1321.79 (±263.67) 1040–1970	1265.64 (±332.00) 720–1947	1296.02 (±295.77) 720–1970
Birth weight ≤ 750 g, no. (%)	0	1 (3.6%)	1 (1.6%)
Gestation (in weeks), mean (*SD*), range	29.36 (±1.76) 28–32	29.57 (±1.87) 25–32	29.46 (±1.80) 25–32
Gestation ≤ 26 weeks, no. (%)	2 (6.1%)	2 (7.1%)	4 (6.6%)
Apgar scores at 1 min, no. (%)			
0–5	18 (54.5%)	13 (46.4%)	31 (50.8%)
6–10	15 (45.5%)	15 (53.6%)	30 (49.2%)
Apgar scores at 5 min, no. (%)			
0–5	4 (12.1%)	5 (17.9%)	9 (14.8%)
6–10	29 (87.9%)	23 (82.1%)	52 (85.2%)
Neonatal ultrasound diagnosis, no. (%)			
Normal	18 (54.5%)	14 (50%)	32 (52.5%)
Uncomplicated PVH	12 (36.7%)	10 (35.7%)	22 (36.1%)
PVH and DIL	3 (8.8%)	4 (14.3%)	7 (11.4%)

Note. PVH = periventricular hemorrhage; DIL = ventricular dilatation. All differences are nonsignificant.

Table 3. Executive function scores of preterm and full-term participants (ANOVA and ANCOVA)

	Raw mean scores (*SD*)				Mean scores adjusted[a] (95% CI)			VPT ≤ 1 *SD*[b]
	Preterm	Controls	Pooled *SD*	F	Preterm	Controls	F	
HSCT								
Total	5.7 (±1.4)	6.4 (±0.9)	3.55	^12.28***	5.7 (5.4–6.1)	6.4 (6.1–6.7)	^6.06*	14 (23.0%)
Part A: RT	7.5 (±6.4)	3.8 (±4.5)	18.69	^16.74***	7.0 (5.3–8.6)	4.2 (2.8–5.6)	^7.96**	0
Part B: RT	29.9 (±20.6)	18.8 (±16.9)	55.12	^13.16***	28.8 (22.9–34.6)	19.3 (14.2–24.3)	^10.21**	1 (1.6%)
Part B–Part A	22.5 (±17.9)	15.0 (±16.2)	38.67	^5.28*	22.1 (16.7–27.4)	15.2 (10.6–19.7)	^1.79	4 (6.6%)
Errors	3.4 (±3.5)	1.8 (±2.1)	8.64	^6.71*	3.3 (2.5–4.2)	1.9 (1.1–2.6)	^3.82*	0
Verbal Fluency								
Letter fluency	39.3 (±13.0)	50.8 (±13.5)	63.63	^^23.03***	41.5 (38.0–45.0)	49.3 (45.9–52.6)	^^9.91**	27 (44.3%)
Category fluency	43.7 (±13.2)	50.5 (±12.6)	37.55	^^8.48**	45.5 (42.3–48.6)	48.7 (45.7–51.7)	^^3.07	15 (24.6%)
TMT								
Trail A: RT	34.4 (±15.6)	27.8 (±11.9)	35.71	^8.30**	34.9 (31.1–38.9)	27.1 (23.5–30.6)	^7.85**	2 (3.3%)
Trail B: RT	66.4 (±24.5)	56.6 (±19.0)	53.28	^5.91*	64.2 (58.3–70.2)	57.7 (52.4–63.1)	^1.79	7 (11.5%)
Trails B–A	33.1 (±19.4)	30.1 (±18.6)	16.06	^0.03	30.5 (25.6–35.5)	32.0 (27.5–36.5)	^0.85	9 (14.8%)
TAP/DA								
Mean score	730.6 (±77.1)	736.2 (±82.8)	30.57	^0.51	730.3 (707.0–753.6)	736.8 (715.5–757.9)	^^0.83	9 (14.8%)
Omissions	1.8 (±2.4)	2.1 (±2.2)	1.71	^0.01	1.7 (1.1–2.4)	2.2 (1.6–2.8)	^0.11	0
Lapses	0.9 (±0.7)	0.8 (±0.6)	0.9	^5.24*	0.9 (0.8–1.1)	0.8 (0.6–0.9)	^5.09*	14 (23.0%)
TAP/GNG								
Mean score	646.4 (±92.5)	668.8 (±104.9)	121.71	^1.45	642.2 (616.0–668.5)	670.5 (645.9–695.1)	^2.51	7 (11.5%)
Omissions	0.9 (±2.9)	1.4 (±2.4)	2.59	^3.07	0.4 (−0.1–1.0)	1.5 (1.0–2.0)	^4.05	0
Lapses	0.5 (±0.5)	0.2 (±0.4)	1.65	^0.42	0.5 (0.4–0.6)	0.2 (0.04–0.3)	^0.07	0
TAP/I								
Mean score	499.9 (±123.2)	485.3 (±95.4)	77.81	^0.36	501.5 (469.3–533.7)	484.1 (455.7–512.5)	^0.68	4 (6.6%)
Lapses	1.1 (±0.8)	0.7 (±0.6)	1.66	^6.87**	1.1 (0.9–1.3)	0.7 (0.5–0.9)	^4.99*	11 (18.0%)

Note. ANOVA = analysis of variance; ANCOVA = analysis of covariance; CI = confidence interval; VPT = very preterm; HSCT = Hayling Sentence Completion Test (Total score, Part A, Part B, Part B minus Part A, total number of errors); RT = response time in seconds; Letter fluency = Controlled Oral Word Association Test; Category fluency = combined scores of the Animal Naming test and the Object Naming test; TMT = Trail-Making Test (Trail A and Trail B); TAP/DA = Test of Attentional Performance Divided Attention subtest; TAP/GNG = Test of Attentional Performance Go/No-go subtest; TAP/I = Test of Attentional Performance Incompatibility subtest; F = *F* value (ANOVA).
[a]Scores adjusted for IQ, sex, and age; ^= statistics calculated on log transformed values; ^^= statistics calculated on raw values as normally distributed; [b]Number and percentage of VPT individuals scoring ≤ 1 *SD* below the control group's mean.
*$p < .05$.
**$p < .01$.
***$p < .001$.

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Errors), COWAT, Trails A, TAP/DA, and TAP/I "lapses," although the group differences were no longer significant for HSCT Part B minus Part A score, Category Fluency subtest, and TMT/Trails B. For the findings below, nonsignificant results reflect $p > .05$.

Relationship Between Perinatal Variables and Scores on Tests of Executive Functioning Scores in VTP Adults

Scores on measures of executive function did not differ according to neonatal ultrasound categorization (NM, PVH, and PVH+DIL). Furthermore, results from regression analysis failed to reveal associations of any of the measures of executive function with gestational age, birth weight, or Apgar score at 1 and 5 min (used as a continuous variable). In addition to neonatal variables, participants' age at assessment, gender, and parental socioeconomic status were used as independent variables.

DISCUSSION

To our knowledge, the present study is the first to provide a broad assessment of executive function in VPT young adults. The results suggest that selective aspects of executive function are impaired in VPT individuals compared with controls, even after adjusting for estimated IQ, gender, and age at time of assessment. The neuropsychological battery used in the study included tests of response initiation and response inhibition (HSCT, TAP), divided attention (TAP), conceptual tracking (TMT), cognitive flexibility (COWAT, Category fluency, TMT, TAP), shifting of attention (TMT), and employment of strategies (COWAT, Category fluency). Preterm young adults exhibited impairment in several dimensions, namely letter fluency (COWAT), visuomotor speed (TMT Part A), and response initiation and inhibition (HSCT), suggesting specific executive function impairments in tasks involving response inhibition and mental flexibility. Significant group differences in other tests of response inhibition (TAP/I) and divided attention (TAP/DA) were only observed in reference to "lapses," which refer to delayed responses and are in line with other studies reporting processing speed differences between VPT individuals and controls (Faust et al., 1999; Rose et al., 2002; Rose and Feldman, 1996). The areas tested where no statistically significant group differences were detected involved conceptual tracking (TMT/Trail B). Other executive-type abilities such as planning and organizational ability were not assessed, and it would be important for future studies to investigate these skills in VPT/VLBW adults. The findings of selective impairment in various aspects of executive function are supported by the fact that between group differences persisted even after adjusting for estimated IQ and age, in line with previous studies investigating VLBW children (Taylor et al., 2004a). Furthermore, it should be considered that the VPT individuals assessed were healthy individuals without any major neurological deficit and very likely represented "high functioning" preterm young adults, as indicated by their higher estimated IQ scores in childhood compared with those VPT individuals who were not followed-up. This finding means that our results are conservative and that the nonparticipants may have shown greater impairment in their executive abilities compared with controls.

Our results are in line with studies that have shown that preterm birth has long-term effects on cognitive development (Hack & Taylor, 2000; Saigal, 2000; Taylor et al., 2004a). Until now, executive function in VPT and VLBW individuals has only been studied in children and adolescents and has been generally found to be impaired compared with controls. Executive domains investigated have included planning, sequencing, response inhibition, impulse control, verbal and spatial working memory, and set-shifting (Anderson & Doyle, 2004; Aylward, 2002; Bohm et al., 2004; Espy et al., 2002; Luciana et al., 1999; Taylor et al., 2004a). The importance of delineating predictors of longer-term outcome has been also highlighted (Peterson et al., 2003).

In addition to impaired executive function, we found that the mean estimated Full-Scale IQ scores of VPT adults were lower compared with controls, although it is worth noting that the VPT group means were within the average range and very close to or above the normative mean. The observation of lower IQ scores in VPT individuals compared with controls is, however, in line with other studies (Aylward, 2002; Foulder-Hughes & Cooke, 2003; Rickards et al., 2001) and does not replicate evidence of "catch-up" to control IQ scores by adolescence reported in some VPT cohorts (Peng et al., 2005). Furthermore, we noted that preterm children had similar Performance IQ scores to controls, but lower Verbal IQ scores. The reduced letter fluency scores in VPT individuals we report in this study may in fact be a reflection of their less well developed verbal (language) skills. Gabrielson et al. (2002) reported lower Verbal IQ scores in school-age VPT children, although their findings implicated that Performance IQ was affected for at least some of the participants, as children with postnatal morbidity had lower Performance IQ scores. In the light of differences in processing speed observed between VPT individuals and controls in the current study and others (Faust et al., 1999; Rose et al., 2002; Rose & Feldman, 1996), another interpretation could be that the present estimates of Performance IQ (derived from an abbreviated WASI) may represent overestimates of the participants' true Performance IQ scores, as the WASI subtests (i.e., Block Design and Matrix Reasoning) place relatively less demands on processing speed than some of the subtests (e.g., Digit-Symbol Coding and Symbol Search) that would have been included in the full Wechsler Adult Intelligence Scale. Selective language impairments in VPT and VLBW samples have been previously documented, including receptive language delays in the preschool years (Vohr et al., 1989) and expressive language and sentence repetition at school age (Wolke & Meyer, 1999), although other studies have found no differences in receptive language skills (Klein et al., 1985; Rickards et al., 1987). In adolescence, the only significant differences observed between VPT individuals (some of whom we studied) and controls were in verbal fluency scores (Rushe et al., 2001), which were associated with the size of the corpus callosum (Nosarti et al., 2004). However, some debate remains as to the specificity of cognitive impairments. Contrary to the current findings, Taylor et al. (2004b) reported that, in VLBW adolescents, visuomotor skills, memory, and executive function scores were more impaired than language scores.

The current study provides evidence for selective impairments on tests of executive function, tapping response initiation and response inhibition, cognitive flexibility, and visuomotor speed. Selective executive dysfunction in VPT individuals might be explained in different ways. Preterm birth is associated with a high risk of perinatal brain injury (Inder et al., 2003; Volpe, 1995). At an earlier follow-up, which included part of the present cohort, VPT adolescents were found to have reduced whole brain, cortical gray matter, and hippocampal volumes, accompanied by an increased size of the lateral ventricles compared with controls (Nosarti et al., 2002), as well as reduced size of the corpus callosum (Nosarti et al., 2004). Preterm children at age 8 have been reported to have smaller volumes of the amygdala, the hippocampus, and the basal ganglia (Peterson et al., 2000). These structural abnormalities, associated with early perinatal brain insult, underline the selective vulnerability of some brain areas to early damage and are considered at least partly responsible for the neuropsychological impairments found in VPT populations (Abernethy et al., 2004; Nosarti et al., 2004; Peterson et al., 2000; Stewart et al., 1999). As there is evidence that executive functions may be underpinned by neuronal activity in frontal–striatal circuits (Rubia et al., 2006; Woodward et al., 2005), damage to these areas could aid the understanding of the selective executive impairments observed in the current study in the absence of general cognitive abnormalities (estimated IQ). However, the relationship between neuropsychological performance and perinatal brain insult is not always clear (Nosarti et al., 2002). This finding may be because the presence of an early brain injury has altered brain development, such that functions have become aberrantly mapped in the brain (Stiles et al., 2005). Thus perhaps, the normal adult structure–function relationship no longer holds in VPT samples. Furthermore, brain plasticity may enable the young brain to overcome injury, to reorganize its structure, and spare its essential functions (Allin et al., 2004). The current study was, however, unable to draw firm conclusions regarding the nature of specific impairments in executive function, as potential but unmeasured deficits in processing speed may contribute to some of the observed group differences (Faust et al., 1999, Rose et al., 2002). Furthermore, controls were more likely than VPT participants to have received postsecondary education (completed or in progress), and there is evidence that executive functions and academic achievement may be strictly interrelated (St. Clair-Thompson & Gathercole, 2006).

The lack of a significant correlation between the test results and birth weight, gestational age, and other perinatal variables replicates the results of some studies of preterm adolescents (Rushe et al., 2001; Tideman, 2000). However, there are inconsistencies in the literature, as other studies with VLBW school age children and adolescents have reported a significant association between cognitive performance and birth weight and gestational age (Breslau et al., 1996; Cooke, 2005; Taylor et al., 1998, 2004b). The current results could be explained by a decrease in cognitive problems with age, or the fact that, in VPT individuals, the cognitive and behavioral differences observed in childhood may be partly overturned by the influence of environmental variables (Jefferis et al., 2002; Taylor et al., 2004a). However, is it also possible that birth weight and gestational age did not correlate with executive function scores due to a limited range of values and to the fact that few individuals in our sample fell into the extreme categories associated with the most adverse neurodevelopmental outcomes (e.g., birth weight < 750 g and gestational age < 26 weeks) (Hack & Fanaroff, 1999; Taylor et al., 2004b).

We did not observe differences in executive function scores within the VPT group according to neonatal ultrasound diagnosis, even in the group who sustained the greatest degree of injury, i.e., PVH+DIL, in line with other studies with VLBW adolescent samples (Taylor et al., 2004b). However, other investigations have reported significant relationships between adverse developmental consequences, including neurological and neuropsychological outcome, intraventricular hemorrhage, and periventricular leucomalacia (Fawer et al., 1995; Patra et al., 2006; Sherlock et al., 2005), and the extent and the effects of persistence of the arterial duct through PVH+DIL in preterm children (Cooke, 2005). Our results are thus encouraging as they suggest that processes of neuronal and possibly functional plasticity may be able to compensate for the effect of severe perinatal lesions. They also draw attention to the limits of plasticity (Taylor et al., 2004b), as preterm young adults without major physical disability still perform worse than controls on a variety of tasks involving executive processing. Other interpretations could be that the subset of individuals with PVH+DIL on neonatal ultrasound was too small to detect an effect ($n = 7$), or that critical factors to long-term outcome, such as white matter injury (Volpe, 2003; Woodward et al., 2006), to which ultrasound techniques are insensitive, were not analyzed.

The main methodological limitation of the present study was the relatively low follow-up rate, partly because some individuals could not be traced, but also because a considerable part of the cohort did not wish to participate in the study. Losses to follow-up are a methodological issue of long-term follow-up studies that needs to be addressed. Other longitudinal studies of preterm and VLBW individuals to adulthood have reported successful tracing of 63% of the original cohort (Feingold et al., 2002), as well as 50% loss of participants (Cooke, 2004). It should be noted that both studies used questionnaires that where sent to the participants through the post office. On the other hand, the present investigation involved a face-to-face comprehensive assessment, which lasted a few hours. In the current study, we tried to diminish the bias due to dropout by investigating the characteristics of the nonparticipants. Participants had higher estimated IQ scores in childhood compared with nonparticipants. It was thus speculated that our results refer to those VPT young adults with the most favorable cognitive outcome, and had we been able to assess a larger proportion of the original cohort, group differences in executive functioning would have been even more pronounced. Another limitation of the current study was the control group consisting of volunteers responding to media advertisements, who may not be representative of the general population.

To summarize, our current results suggest that VPT birth has long-term effects on cognitive development, and impairments on tests of executive function, particularly involving mental flexibility and response inhibition, are increased in VPT young adults compared with controls. These differences were at least partially independent of estimated IQ, gender, and age at time of assessment. Considering that the VPT individuals assessed were healthy individuals without any major neurological deficit and had higher estimated IQ scores in childhood compared with those VPT individuals lost to follow-up, our results, although conservative, suggest a specificity of cognitive impairments. These deficits may reflect dysfunction in frontal–striatal circuits, which are particularly vulnerable to neurodevelopmental damage following preterm birth (Nosarti et al., 2006; Peterson et al., 2000).

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