

# The longitudinal relationship between set-shifting at 4 years of age and eating disorder related features at 9 years of age in the general pediatric population

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## Abstract

**Background:** Individuals with anorexia nervosa (AN) tend to have rigid thoughts and behaviors regarding their body weight, body image, and eating habits. While a diagnosis of AN implies severe levels of impairment, AN traits can vary on a continuum within the population. However, little is known about how early markers of AN relate to rigid thought patterns and to what extent cognitive rigidity is already present in early childhood. We examined the association of set-shifting abilities as a measure of cognitive flexibility in preadolescents with AN-related features.

**Methods:** Participants included 3,987 children participating in the Generation R Study, a Dutch population-based birth cohort. Set-shifting abilities (mother report) were assessed at 4 years of age, body mass index (BMI) was determined at 4 and 9 years and restrictive eating patterns (mother report) and body image (child report) were assessed at 9 years.

**Results:** Lower set-shifting abilities at 4 years were associated with a lower BMI ( $\beta = -.44$ ,  $p = 2.2 \times 10^{-4}$ ) in girls, and more restrictive eating ( $\beta = 0.15$ ,  $p = 2.7 \times 10^{-6}$ ) in both boys and girls at 9 years of age. Moreover, set-shifting at age 4 was not associated with body image at age 9.

**Conclusion:** These findings contribute to the idea that the association between set-shifting problems and AN-related features are present early in childhood, prior to the typical range of the onset of eating disorders (EDs). Longitudinal studies that capture the peak age for the development of EDs will be important to assess whether early cognitive inflexibility is an early marker of AN.

## KEYWORDS

anorexia nervosa, cognitive flexibility, eating disorders, executive functioning, neuropsychology, set-shifting

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## 1 | INTRODUCTION

Individuals with anorexia nervosa (AN) show rigidity in behaviors and thoughts. This is reflected in patients with AN having difficulties making changes in eating habits, adjusting body image to reflect reality, and lowering the often excessive frequency and intensity of their physical activities. This so-called cognitive inflexibility is one of the most prominent risk and maintenance factor for AN (Tchanturia et al., 2012) and dramatically interferes with treatment (Sato et al., 2013). Yet, the exact role of cognitive inflexibility in the etiology of AN is still unclear, mainly because longitudinal research is lacking.

One approach to measuring cognitive flexibility is by administering neuropsychological tests of set-shifting. Set-shifting is defined by Monsell as “the ability to move back and forth between tasks, operations or mental sets” (Monsell, 1996). Roberts, Tchanturia, and Treasure (2010) have shown that weak set-shifting skills are associated with a poor prognosis of AN, as indicated by a prolonged illness duration and more self-imposed rules and regulations regarding eating behavior. Furthermore, they showed that poor set-shifting skills are associated with lower self-esteem, anxiety, and depression. Generally, poor set-shifting skills are most profound in patients with the restrictive AN subtype, especially those who are in the acute phase of their illness (Wu et al., 2014). Some evidence suggests that set-shifting problems persist after weight recovery (Aloi et al., 2015; Lang, Stahl, Espie, Treasure, & Tchanturia, 2014; Tenconi et al., 2010), although results are mixed (Bentz et al., 2017; Bühren et al., 2012; Nakazato et al., 2010).

Interestingly, evidence from research investigating set-shifting skills in adolescents with AN shows that these skills are impaired when measured with questionnaires, but do not seem to differ from healthy controls when measured with neurocognitive tasks (Miles, Gnatt, Phillipou, & Nedeljkovic, 2020). This indicates that set-shifting difficulties in adolescent AN seem to be evident on a behavioral or perceived level, but not on a more generalized cognitive level. Also we hypothesize that earlier set-shifting problems could predispose one to different eating patterns, whereas later, there are no differences either due to catch up in development, or compensation due to increased cognitive strategies.

Since the studies to date focus on individuals already diagnosed with AN, it is unclear whether set-shifting problems are present prior to the onset of the disease or whether these problems occur together with the onset of AN. For instance, Shott et al. (2012) suggested that abnormal set-shifting abilities at a young age may be a predisposing factor for the emergence of AN in adulthood. The finding that set-shifting is a heritable trait, as indicated by research among AN patients, their offspring and other unaffected relatives (Lang, Treasure, & Tchanturia, 2016; Tenconi et al., 2010), supports this hypothesis. However, evidence is needed to ascertain whether set-shifting difficulties are indeed present before the onset of AN.

To elucidate the temporal sequence and to obtain more knowledge on the predictive and possibly causal role, studies with a longitudinal design starting much earlier than the age-of-onset of AN are needed. Given the low prevalence of AN, such studies also need a

very large sample size to ensure the incidence of sufficient eating disorder (ED) cases. As this is a costly and time-consuming endeavor, studies investigating nonclinical features of EDs should be considered as they may aid to increase our insight in the temporal sequence of emerging AN and those with subclinical AN traits. To date, no population-based approach has been applied to help elucidating whether associations between set-shifting difficulties and ED features are present before AN has emerged and to what extent premorbid set-shifting problems contribute to the onset of AN (Kothari, Rosinska, Treasure, & Micali, 2014).

This prospective study examines the association of set-shifting skills, as measured with parent reports, at preschool age with body mass index (BMI), restrictive eating, body dissatisfaction and a distorted body image at the age of 9 years in a large Dutch birth cohort. These features may be possible early markers of AN, and are also associated with other somatic and psychological disorders, such as obesity, depression (Geliebter & Aversa, 2003; Van Strien, 2018) and autism (Brede et al., 2020; Brown & Stokes, 2020). We hypothesize that lower set-shifting skills in early childhood are associated with a lower BMI, more restrictive eating, greater body dissatisfaction and a distorted body image 5 years later. Such findings will provide support that set-shifting plays a role in the etiology of ED-related features and may contribute to early diagnosis and treatment of young people by identifying a high-risk group early in life.

## 2 | METHOD

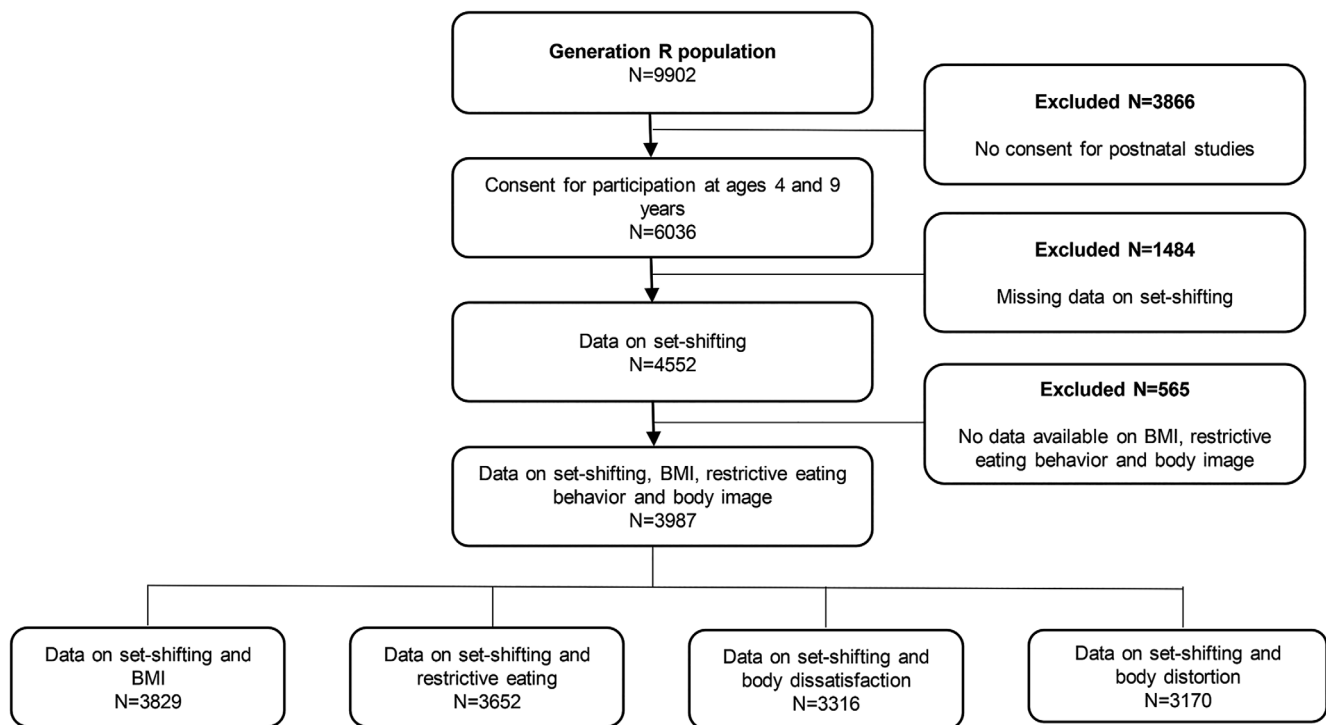
### 2.1 | Design

This study is embedded in Generation R, a prospective population-based cohort in Rotterdam, the Netherlands, examining health and development from fetal life onwards (Kooijman et al., 2016). Since inclusion (2002–2006), regular measures were performed with the latest data collection wave finished at age 13 years (Jaddoe et al., 2012). The Medical Ethical Committee of the Erasmus MC University Medical Center Rotterdam approved the study. Legal representatives of the children provided written informed consent.

### 2.2 | Participants

Of the initial population of 9,902 live-born children, (Figure 1) informed consent for postnatal studies was obtained from 6,036 participants. Information on set-shifting skills was collected at child age 4 years. At age 9, information was collected on children's BMI, eating behaviors, and body image. Participants without set-shifting data were excluded ( $N = 1,484$ ), as were participants who had missing data on all four outcome measurements ( $N = 565$ ), leading to a sample size of 3,987 children. Due to missing data in separate outcome measures, the number of participants varied per analysis.

We performed a nonresponse analysis to assess the generalizability of the findings. Excluded children ( $n = 2049$ ) more often had a



**FIGURE 1** Flowchart of participants

non-Dutch ethnicity ( $\chi^2 = 333.98$ ,  $df = 2$ ,  $p = 2.2 \times 10^{-16}$ ), had a higher BMI-SDS at age 9 (MD = 0.29,  $t = 7.23$ ,  $df = 1,347$ ,  $p = 8.3 \times 10^{-13}$ ), and exhibited more restrained eating behavior (MD = 1.16,  $t = 4.65$ ,  $df = 770$ ,  $p = 4.0 \times 10^{-6}$ ) and more body dissatisfaction ( $\chi^2 = 24.26$ ,  $df = 2$ ,  $p = 5.4 \times 10^{-6}$ ) than included children ( $n = 3,987$ ). Mothers of excluded children had a relatively lower educational background ( $\chi^2 = 357.61$ ,  $df = 2$ ,  $p = 2.2 \times 10^{-16}$ ).

### 2.3 | Measures

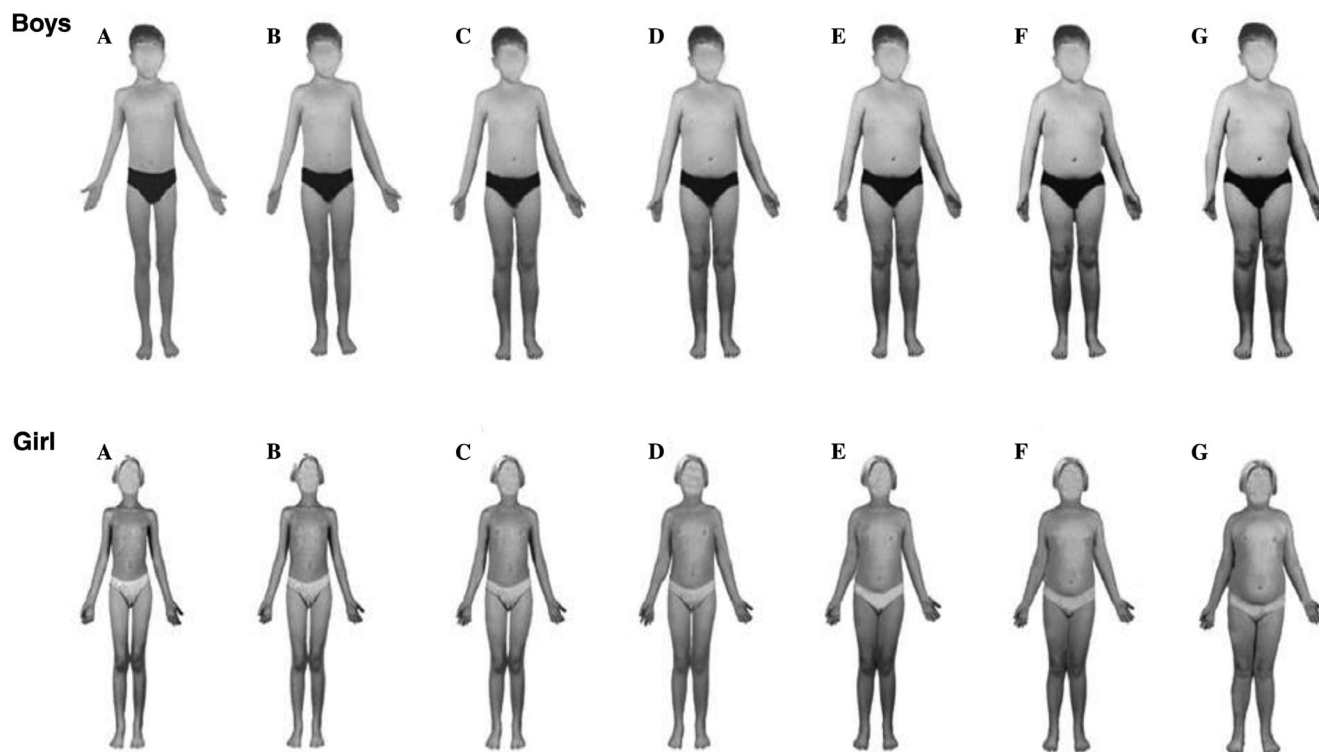
**Behavior Rating Inventory of Executive Function—Preschool Version (BRIEF-P):** The BRIEF-P includes 63-items assessing five dimensions of executive function: inhibition (16 items, Cronbach's alpha [ $\alpha$ ] = .88), shifting (10 items,  $\alpha = .80$ ), emotional control (10 items,  $\alpha = .83$ ), working memory (17 items,  $\alpha = .89$ ) and planning/organizing (10 items,  $\alpha = .77$ ) (Gioia, Andrew, & Isquith, 2003; Sherman & Brooks, 2010). At child age 4, parents (mostly mothers, 88%) reported whether assessed behaviors occurred within the last month (answering options: never, sometimes, often). Raw scores were summed and converted into  $t$ -scores, based on age and sex equivalent norms. Higher BRIEF-P scores correspond with more executive functioning problems (Gioia et al., 2003). The BRIEF-P has a good test–retest reliability and content validity (Sherman & Brooks, 2010). This study focuses on the shift subscale which assesses the capability to shift between activities.

**BMI-Standard Deviation Score (BMI-SDS):** Trained employees at the child health centers measured height and weight of the participants at 4 years of age as part of routine visits. At 9 years, these

characteristics were obtained by trained staff at our research center (Kooijman et al., 2016). A SECA mechanical personal scale was used to measure weight, while the children wore light-weight clothes. A Holtain Limited stadiometer was used to assess height while children were standing. BMI was calculated ( $\text{kg}/\text{m}^2$ ). BMI-SDS were adjusted for age and sex based on Dutch reference growth curves (Fredriks et al., 2000).

**Dutch Eating Behavior Questionnaire (DEBQ)—parent version:** To collect data on restrictive eating behavior, the caregivers filled in the DEBQ at age nine of the child (Braet & Van Strien, 1997). In Generation R, a slightly adapted version of the DEBQ was used, in which the item assessing eating in the evening was excluded from the list, since 9-year-old children do not eat regularly after dinner in the Netherlands. For this particular study we only used the Restrained Eating scale of the DEBQ, which has a good internal consistency ( $\alpha = .89$ ). The parents filled in the items on a 5-point Likert scale from 1 = never to 5 = always. The raw scores were summed into sum scores. Higher DEBQ scores point to more restrictive eating behavior in children.

**Children's Body Image scale (CBIS):** At 9 years, the children filled in the CBIS to assess their body perception and their body satisfaction. The perception of the body was measured with the question “Which body is most like yours?”, which was used to determine body distortion. Seven sex-specific figures of increasing adiposity were presented (Figure 2) (Truby & Paxton, 2002) that corresponded to seven BMI categories ranging from a very low to a very high BMI. *Body distortion* is defined by the difference between actual and perceived BMI (Truby & Paxton, 2002), in which the actual BMI was subtracted from



**FIGURE 2** Item body perception CBIS. CBIS, Children's Body Image Scale

the perceived BMI, based on the figure that was chosen. The scores ranged from  $-5$  to  $5$ , in which negative scores indicate that the BMI is lower than the perceived body shape and positive scores indicate that the BMI is higher than the perceived body shape.

*Body satisfaction* was based on the same figures of the CBIS, now asking for body ideal: “Which body would you like to have?”. We calculated a body shape satisfaction score by subtracting the score on the question regarding “ideal body shape” from the score on the question measuring “self-perception” (range  $-6$  to  $6$ ). A negative score indicated that the child has a desire to be heavier, a score of zero that the child is happy with his/her body shape and a score above zero means that the child has a desire to be thinner (Leppers et al., 2017).

## 2.4 | Covariates

Sex, age, child ethnicity, and IQ, as well as mother's educational level and eating pathology were included as possible confounders, since other studies demonstrated associations with children's executive functioning, BMI, eating behaviors and body image (Anderson & Bulik, 2004; Drewnowski, Kurth, & Krahn, 1994; Hoek, 2006; Kanakam, Raoult, Collier, & Treasure, 2013; Lewinsohn, Seeley, Moerk, & Striegel-Moore, 2002; Nevenon & Norring, 2004; O'Dea & Caputi, 2001). Mothers reported in prenatal questionnaires about their educational level, current and lifetime ED diagnoses, and their own and their partner's country of birth, from which child ethnic background was determined.

Child IQ was assessed at age 6 years with two subtests of a validated, Dutch, nonverbal intelligence test (i.e., SON-R 2½-7 [Tellegen, Winkel, Wijnberg-Williams, & Laros, 2005]). In the models with restrictive eating and body image as outcomes, we also adjusted for BMI-SDS at 9 years as a potential confounder. In the model with BMI-SDS at 9 years as outcome, we adjusted for BMI-SDS at 4 years of age in a sensitivity analysis to reveal whether set-shifting was prospectively associated with BMI-SDS.

## 2.5 | Statistical analyses

R version 3.3.2 was used.

Two separate sets of linear regression analyses were performed with set-shifting as determinant and BMI-SDS and restrained eating at 9 years of age as separate outcomes. In addition, two separate multinomial logistic regression analyses were performed with set-shifting as determinant and body image as outcome, in particular the desire to be thinner or heavier (reference group: satisfied with the body) in the first analysis and perceiving oneself as heavier or thinner than oneself actually is (reference group: accurate body shape perception) in the second analysis. The regression analyses were unadjusted in Model 1 and adjusted for covariates in Model 2.

In a sensitivity analysis, the analysis with BMI-SDS at 9 years as outcome was additionally adjusted for BMI-SDS at 4 years to determine whether set-shifting was prospectively associated with BMI-SDS. In addition, we tested for nonlinear relationships, sex interactions and

**TABLE 1** Characteristics of 3,987 generation R participants included in this study

Characteristics	Statistic	N	Percentage, median (IQR) or mean (SD) <sup>a</sup>
<b>Child</b>			
Age at predictor assessment (years)	Median, IQR	3,987	4.0 (4.0, 4.1)
Age at outcome assessment (years)	Mean, SD	3,884	9.8 (0.31)
BMI-SDS at 4 years	Mean, SD	2,600	0.1 (0.9)
Underweight (BMI-SDS $\leq -1.3$ )	Percentage	152	5.8
Normal weight (BMI-SDS $-1.3$ to $1.3$ )	Percentage	2,381	91.6
Overweight (BMI-SDS $\geq 1.3$ )	Percentage	219	8.4
BMI-SDS at 9 years	Mean, SD	3,829	0.2 (1)
Underweight (BMI-SDS $\leq -1.3$ )	Percentage	227	5.9
Normal weight (BMI-SDS $-1.3$ to $1.3$ )	Percentage	3,065	80
Overweight (BMI-SDS $\geq 1.3$ )	Percentage	537	14
<b>Sex %</b>			
Boys	Percentage	1,964	49.3
Girls	Percentage	2,023	50.7
IQ score	Mean, SD	3,452	103.8 (14.6)
<b>Ethnicity</b>			
Dutch	Percentage	2,737	68.9
Other Western	Percentage	375	9.4
Non-Western	Percentage	857	21.6
<b>BRIEF-P score</b>			
Set-shifting	Mean, SD	3,987	3.9 (0.2)
Planning	Mean, SD	3,976	3.8 (0.2)
Working memory	Mean, SD	3,936	3.8 (0.2)
Emotional control	Mean, SD	3,981	3.9 (0.2)
Inhibition	Mean, SD	3,931	3.8 (0.2)
Restrained eating score (DEBQ)	Mean, SD	3,652	12.4 (4.8)
<b>Body dissatisfaction (CBIS), %</b>			
Satisfied	Percentage	2,113	63.7
Desire to be heavier	Percentage	225	6.8
Desire to be thinner	Percentage	978	29.5
<b>Body distortion (CBIS), %</b>			
Accurate body image	Percentage	878	27.7
Think of self as too thin	Percentage	1,956	61.7
Think of self as too heavy	Percentage	336	10.6
<b>Mother</b>			
<b>Education level, %<sup>b</sup></b>			
High	Percentage	2,309	60.2
Medium	Percentage	1,372	35.8
Low	Percentage	153	4.0
History of an eating disorder, % yes	Percentage	233	8.2

Abbreviations: BMI-SDS, Body Mass Index-Standard Deviation Score; BRIEF-P, Behavior Rating Inventory of Executive Function—Preschool Version; CBIS, Children's Body Image Scale; DEBQ, Dutch Eating Behavior Questionnaire for children.

<sup>a</sup>Values are percentages for categorical variables, medians (interquartile range [IQR]) for continuous nonnormally distributed variables and means (standard deviation [SD]) for continuous normally distributed variables, derived from the imputed dataset.

<sup>b</sup>High: higher vocational education and higher academic education. Medium: lower vocational training. Low: ranging from no education to high school level.

**TABLE 2** The association between set-shifting at age 4 years and covariates with body mass index and restrained eating at 9 years

Outcome	Model	Predictor	$\beta$	95% CI for $\beta$		p Value	R <sup>2</sup>	95% CI for R <sup>2</sup>		R <sup>2</sup> change	
				Lower	Upper			Lower	Upper		
BMI-SDS	Model 1—Girls <sup>a</sup>	Set-shifting	-.56	-0.82	-0.29	$4 \times 10^{-5}$	.01	0.00	0.02	-	
	Model 2—Girls <sup>a</sup>	Set-shifting	-.44 <sup>b</sup>	-0.68	-0.21	$2.2 \times 10^{-4}$	.26	0.23	0.30	0.25	
			Low education level	.27	0.05	0.49	.02				
			Middle education level	.22	0.14	0.30	$2.7 \times 10^{-7}$				
			Non-Western ethnicity	.33	0.23	0.44	$9.2 \times 10^{-10}$				
			Western ethnicity	.15	0.03	0.28	.02				
			Mother's history of an eating disorder	.04	-0.11	0.20	.59				
			Child IQ	-.00	-0.01	-0.00	.02				
			BMI-SDS at 4 years	.51	0.46	0.55	$2.2 \times 10^{-16}$				
		Model 1—Boys <sup>a</sup>	Set-shifting	-.06	-0.34	0.22	.69	.00	0.00	0.00	-
		Model 2—Boys <sup>a</sup>	Set-shifting	-.13	-0.38	0.13	.32	.23	0.20	0.26	0.23
			Low education level	.31	0.09	0.53	.01				
			Middle education level	.23	0.14	0.32	$6.6 \times 10^{-7}$				
	Restrictive eating	Model 1	Set-shifting	.10	0.03	0.16	.00	.00	0.00	0.00	-
Model 2		Set-shifting	.15 <sup>b</sup>	0.09	0.21	$2.7 \times 10^{-6}$	.00	0.00	0.00	0.00	
			Sex	.06	0.03	0.07	$7.2 \times 10^{-10}$				
			Low education level	.10	0.03	0.17	$7.7 \times 10^{-3}$				
			Middle education level	-.03	-0.02	-0.00	.02				
			Non-Western ethnicity	.08	0.05	0.11	$6.1 \times 10^{-8}$				
			Western ethnicity	.00	-0.03	0.04	.88				
			Mother's history of an eating disorder	-.00	-0.04	0.03	.69				
			Child IQ	-.00	-0.00	0.00	.25				
			BMI-SDS at 9 years	.12	0.11	0.13	$2.2 \times 10^{-16}$				

Note: Model 1 is unadjusted; Model 2 is adjusted for the listed variables. Standardized beta's and R<sup>2</sup> of the full models are presented.

Abbreviations: BMI-SDS, Body Mass Index-Standard Deviation Score; CI, confidence interval.

<sup>a</sup>Significant interaction between set-shifting and sex ( $\beta = -.46, p = .02$ ).

<sup>b</sup>Analyses remained significant after statistical control for multiple testing.

interactions with BMI-SDS at 9 years of age. Significant sex interactions were stratified by sex. Significant BMI-SDS interactions were stratified by contrasting the participants within the lowest 25% range of BMI-SDS versus those within the 25% highest BMI-SDS range. Also, associations between the other BRIEF subscales (planning, working memory, emotional control, and inhibition) and the outcome variables were examined to test the specificity of the shift subscale.

Log transformations were performed on skewed variables (i.e., Restrained Eating (DEBQ), and all five BRIEF scales). One hundred imputed datasets were created using multiple imputation with chained equations (Van Buuren & Groothuis-Oudshoorn, 2011) to estimate missing values in the covariates. Control for multiple testing was performed using the Benjamini-Hochberg approach (Benjamini & Hochberg, 1995) adjusting for eight analyses (i.e., one determinant,

four outcomes [two continuous; two categorical variables, each with three categories]).

### 3 | RESULTS

#### 3.1 | Population characteristics

In total, 3,987 participants (50.7% female) were included (see Table 1). Compared to the girls, boys had a higher BMI-SDS ( $t = 3.62$ ; degrees of freedom [ $df$ ] = 3,811;  $p = 3 \times 10^{-5}$ ; Cohen's  $d$  [ $d$ ] = 0.12) at 9 years, had more set-shifting problems (MD = 0.05,  $t = 9.03$ ,  $df = 3,958, p = 2.2 \times 10^{-16}, d = 0.29$ ), less restrictive eating patterns (MD = -0.58,  $t = -3.60, df = 3,649, p = 7.5 \times 10^{-7}, d = -0.12$ ),

**TABLE 3** The association between set-shifting at 4 years and covariates with body image at 9 years

Outcome	Model	Predictor	OR	95% CI for OR		p Value
				Lower	Upper	
Body dissatisfaction—Desire to be heavier vs. satisfied with body image	Model 1	Set-shifting	1.98	0.87	4.52	.10
	Model 2	Set-shifting	1.45	0.60	3.53	.41
		Sex	0.95	0.72	1.27	.75
		Low education level	2.43	1.09	5.44	.03
		Middle education level	1.44	1.06	1.95	.02
		Non-Western ethnicity	2.24	1.57	3.20	.00
		Western ethnicity	1.32	0.79	2.20	.29
		Mother's history of an eating disorder	0.92	0.53	1.61	.77
		Child IQ	0.99	0.98	1.00	.19
		BMI-SDS at 9 years	0.42	0.35	0.50	.00
Body dissatisfaction—Desire to be thinner vs. satisfied with body image		Model 1—Girls <sup>a</sup>	Set-shifting	0.77	0.41	1.47
	Model 2—Girls <sup>a</sup>	Set-shifting	1.41	0.62	3.22	.42
		Low education level	2.29	1.11	4.72	.03
		Middle education level	0.95	0.73	1.24	.70
		Non-Western ethnicity	0.88	0.62	1.23	.45
		Western ethnicity	1.05	0.71	1.55	.81
		Mother's history of an eating disorder	0.87	0.57	1.33	.53
		Child IQ	1.00	0.99	1.01	.89
		BMI-SDS at 9 years	3.66	3.00	4.47	.00
		Model 1—boys <sup>a</sup>	Set-shifting	2.32	1.15	4.70
Model 2—boys <sup>a</sup>		Set-shifting	2.53	1.10	5.83	.03
		Low education level	1.67	0.87	3.21	.12
		Middle education level	1.09	0.83	1.43	.54
		Non-Western ethnicity	1.47	1.06	2.04	.02
		Western ethnicity	1.22	0.79	1.91	.37
		Mother's history of an eating disorder	1.23	0.79	1.91	.36
		Child IQ	0.99	0.98	1.00	.08
		BMI-SDS at 9 years	2.77	2.22	3.48	.00
Body distortion—Think of self as thinner than actual shape vs. accurate body image		Model 1	Set-shifting	0.97	0.60	1.56
	Model 2	Set-shifting	0.86	0.51	1.47	.59
		Sex	0.51	0.42	0.62	.00
		Low education level	1.05	0.61	1.80	.87
		Middle education level	0.96	0.79	1.17	.72
		Non-Western ethnicity	1.01	0.80	1.29	.91
		Western ethnicity	0.94	0.69	1.26	.66
		Mother's history of an eating disorder	1.05	0.77	1.43	.77
		Child IQ	1.00	0.99	1.01	.96
		BMI-SDS at 9 years	2.08	1.72	2.52	.00
Body distortion—Think of self as heavier than actual shape vs. accurate body image		Model 1	Set-shifting	0.98	0.45	2.14
	Model 2	Set-shifting	0.77	0.34	1.72	.52
		Sex	0.92	0.71	1.19	.51
		Low education level	1.13	0.48	2.67	.78
		Middle education level	0.96	0.72	1.28	.78
		Non-Western ethnicity	1.25	0.89	1.76	.20
		Western ethnicity	0.91	0.59	1.43	.70
		Mother's history of an eating disorder	0.98	0.60	1.61	.93
		Child IQ	1.00	0.99	1.01	.37
		BMI-SDS at 9 years	0.57	0.45	0.74	.00

Note: Model 1 is unadjusted; Model 2 is adjusted for the listed variables.

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup>Analyses were stratified by sex because of a significant interaction between set-shifting and sex (OR = 0.52,  $p = .02$ ).

and were more satisfied with their body ( $\chi^2 = 25.06$ ,  $df = 2$ ,  $p = 3.6 \times 10^{-6}$ , (Cohen's  $W [w] = 0.09$ ).

Since participants with the Dutch ethnicity were overrepresented in our sample, we also show population characteristics by ethnic background in Table S1.

### 3.2 | Set-shifting and BMI-SDS

Table 2 shows the association between set-shifting at 4 years and BMI-SDS at 9 years. BMI-SDS at 4 and 9 years of age was normally distributed (Figures S1 and S2). Considering the significant set-shifting–sex interaction, analyses were stratified by sex. Significant associations between set-shifting and BMI-SDS were found in girls but not in boys. In the unadjusted model, a higher set-shifting score, indicating more set-shifting problems, was associated with a lower BMI-SDS ( $\beta = -.56$ ,  $p = 4 \times 10^{-5}$ ,  $R^2$  full model = .01) in girls. The association remained essentially unchanged after adjustment for the aforementioned covariates and BMI-SDS at 4 years of age ( $\beta = -.44$ ,  $p = 2.2 \times 10^{-4}$ ,  $R^2$  full model = .26). In boys, the results remained nonsignificant.

### 3.3 | Set-shifting and restrictive eating behavior

The association between set-shifting at 4 years and restricted eating behavior at 9 years was tested with multiple linear regression analyses (Table 3). In the unadjusted model, a higher set-shifting score was associated with a higher score on the dietary restrained scale of the DEBQ ( $\beta = .10$ ,  $p = .004$ ,  $R^2$  full model = .00). The association remained essentially unchanged ( $\beta = .15$ ,  $p = 2.7 \times 10^{-6}$ ,  $R^2$  full model = .00) when we adjusted for additional covariates in Model 2. The interaction with sex and BMI-SDS at 9 years was not statistically significant.

### 3.4 | Set-shifting and body image

Regarding body dissatisfaction, set-shifting was not associated with desire to be heavier (Table 3). For the desire to be thinner as outcome, a significant sex interaction was found. Stratified analyses indicated that the association between set-shifting and the desire to be thinner was significant in boys (odds ratio [OR] = 2.53,  $p = .03$ ) but not in girls (OR = 1.41,  $p = .42$ ). However, the significant association in boys did not survive correction for multiple testing. None of the associations between set-shifting and body distortion were significant. We did not find significant interactions with BMI-SDS at 9 years for the outcomes body dissatisfaction (desire to be heavier/thinner) and body distortion (think of self as heavier/thinner than actual body shape).

### 3.5 | Sensitivity analyses

We tested the specificity of our findings for the set-shifting subscale, given the interrelatedness of different executive functions (Miyake

et al., 2000). We repeated the above linear and multinomial regression analyses with the other BRIEF subscales (planning, inhibition, emotional control, and working memory) as predictors instead of the Shift subscale (see Table S2). Interestingly, the other BRIEF scales were not significantly associated with BMI-SDS. However, all BRIEF subscales were significantly associated with restrained eating in the direction that greater executive functioning problems were associated with more restrained eating.

Regarding body dissatisfaction, the association between working memory and a desire to be thinner was significant in boys (OR = 2.94,  $p = .00$ ), but not in girls (OR = 1.05,  $p = .89$ ). The association between planning and a desire to be thinner was significant, irrespective of sex. We found a significant sex interaction with inhibition, but the association between inhibition and a desire to be thinner was neither significant in girls, nor in boys. Emotional control was not significantly associated with body satisfaction.

The associations between the BRIEF subscales and body distortion were not statistically significant. We have found a significant interaction between inhibition and BMI-SDS in our analyses with the thought of self as too heavy as outcome, but when we stratified BMI-SDS by participants with the 25% lowest and 25% highest BMI-SDS, the associations were not significant in either subgroup.

## 4 | DISCUSSION

Our study aimed to examine whether early childhood performance in set-shifting, as measured by parental reports, was associated with distinct characteristics of AN in middle childhood in a population-based cohort. As far as is known, this is the first study that examined these relationships prospectively. Support was found for the hypothesis that lower set-shifting abilities at age four are prospectively associated with a lower BMI-SDS at age nine. This result was only significant in girls, was independent of BMI-SDS in early childhood, and specific for set-shifting skills, as other executive function problems were not related with BMI-SDS. Results of this study also showed that lower set-shifting skills in early childhood are prospectively associated with more restrictive eating behavior in middle childhood. However, this pattern was not specific to set-shifting, as a broader range of executive functioning skills were also associated with restrictive eating.

### 4.1 | Executive functioning and BMI-SDS

Our initial finding reveals that set-shifting difficulties, but not any other executive function skills, at age four are associated with a lower BMI-SDS at age 9 in girls. When including BMI-SDS at 4 years of age as a covariate in the model, the explained variance increased to a medium effect size, reflecting the continuity in body mass across childhood.

Our findings parallel findings in adolescents with AN, who also show set-shifting difficulties, when measured with questionnaires (Miles et al., 2020). By following our sample in time, we were able to



investigate whether early difficulties with set-shifting predated the onset of adolescent restrictive eating patterns, or whether it evolved synonymous with the eating patterns. While we do not yet know which adolescents in our sample will develop AN, those adolescents with a low BMI and who have poor set-shifting skills on a behavioral level are likely at increased risk. However, the number of participants with AN will be small, given the low prevalence of AN (Campbell & Peebles, 2014).

Since the explained variance of our measures of interest is small, the association between set-shifting and BMI is likely influenced by multiple factors, including genetics. A recent GWAS in individuals with AN suggested that genetic factors may contribute to a complex bidirectional relationship between BMI and AN, in which alleles that increase the risk of developing AN may also increase the risk for a low BMI and vice versa (Watson et al., 2019).

Our finding that the association between set-shifting skills and BMI was only significant in girls and not in boys is interesting, especially considering that AN is much more common in girls (Hoek, 2006). To the best of our knowledge, no studies in the general population have been carried out that evaluate sex differences in the relationship between set-shifting skills (or general executive functioning) and BMI. Also clinical studies in ED samples in which these issues are investigated are lacking, mainly because many studies evaluate only girls with AN (Timko, DeFilipp, & Dakanalis, 2019). Since our primary outcomes were related to BMI and restrictive eating patterns, it is unclear if boys with early set-shifting difficulties are at-risk for other types of psychopathology.

## 4.2 | Executive functioning and restrictive eating behavior

Our second finding suggests that lower set-shifting abilities at 4 years of age are associated with increased restrictive eating behavior at 9 years of age. We also found associations of inhibition, emotional control, working memory and planning with restrictive eating. This indicates that in general, poorer executive functions are associated with later restrictive eating behavior patterns, rather than set-shifting in specific. However, since we lacked measurements of restrictive eating and body image at age four, we are unable to assess continuity in these constructs. It is possible that early and consistent restrictive eating patterns or body image concerns are driving the BMI findings, and thus these results should be considered a source for future exploratory research evaluating the temporal, and preferably causal relationships.

Our results do align with research demonstrating a link between executive functioning and restrictive eating behavior, both in clinical and general populations (Dohle, Diel, & Hofmann, 2018). One possible explanation for these findings draws from a biological perspective. The brain needs nutrients to function both physically and mentally. Inadequate nutrition could have an adverse global impact on multiple brain functions (Pollitt, Lewis, Garza, & Shulman, 1982), including cognitive functions and set-shifting speed in specific (Datta et al., 2020). As we first examined set-shifting skills in children and assessed

restrictive eating behavior 5 years later, and also did not assess these concepts repeatedly, we cannot infer on the causal direction of the association. However, since we found earlier executive function problems associated with later restrictive eating patterns independent of BMI-SDS in this study, this would not lend support that it is inadequate nutrition that is driving both findings, but rather executive function performance predates the ED symptoms.

Generally, the small effect sizes in our models suggest a role for other factors that may underlie the associations between executive functioning and restrictive eating behaviors, including parental feeding practices (Jansen et al., 2012; Yee, Lwin, & Ho, 2017), peer influences (Keel, Forney, Brown, & Heatherton, 2013), depressive symptoms and low self-esteem (Haynos, Watts, Loth, Pearson, & Neumark-Stzainer, 2016).

## 4.3 | Executive functioning and body image

We found that lower set-shifting skills were associated with a desire to be thinner in boys, but this association became insignificant after correction for multiple testing. We also found an association between working memory problems and the desire to be thinner in boys and an association between planning and the desire to be thinner, irrespective of sex. Although significant, the effect sizes of these associations were small and warrant replication before we can make firm conclusions. Moreover, we did not find an association of set-shifting, or other executive functions, with body distortion.

The finding that planning skills and set-shifting skills are significantly associated with a desire to be thinner, but not with children's longing to be heavier is partly in line with research among individuals with AN. Individuals with AN show poor set-shifting skills (Wu et al., 2014) and are dissatisfied with their body in which they have a desire to lose weight and they therefore start dieting (Stice & Shaw, 2002). Planning skills are not necessarily associated with AN. As mentioned earlier, this result might be explained by more general psychopathology, which is known to be associated with a broad range of executive functioning problems (Dohle et al., 2018).

We found a nonsignificant association between executive functioning and body distortion. A hypothesis for this finding is that the association only emerges at an older age, when people reach adolescence, a period in which body image is of increasing importance as compared to childhood (Ata, Ludden, & Lally, 2007). Thus, we are curious to monitor the development of our participants longitudinally in order to determine whether this hypothesis is true. It is unclear why the association between set-shifting and body distortion was only significant in boys, however, this relationship may change over the course of pubertal development. It should be further investigated in follow-up studies.

## 4.4 | Strengths and limitations

Strengths of our study include its longitudinal, population-based design, adjustment for multiple covariates and its large sample size.

The prospective design encompassing data collection within different age periods made it possible to interpret the long-term relationships between set-shifting and AN-related features. Yet, we were not able to truly prospectively assess the association of set-shifting skills with ED diagnoses, since we lacked repeated measures for all variables included in this study.

Some limitations to our study should also be considered. First, information on children's executive function and eating behavior was obtained from maternal reports, which may result in shared method bias variance. Second, our nonresponse analysis showed greater loss to follow-up among participants of less affluent backgrounds, limiting the generalizability of findings. Finally, there is no consensus between researchers which test best assesses executive functioning. We used a parent report of children's daily life behaviors related to executive functions, while other researchers have used neuropsychological test batteries (Allen et al., 2013; Kjaersdam Telleus et al., 2015; Phillipou, Gurvich, Castle, Abel, & Rossell, 2015). These tests and questionnaires rarely measure one conceptual dimension (Long, 1996). As a result, it is difficult to compare results.

#### 4.5 | Conclusions and future directions

We found that lower set-shifting performance at 4 years of age predicts BMI-SDS in girls and with restrictive eating behavior in both boys and girls at age 9. BMI-SDS and restrictive eating are the core characteristics of AN (American Psychiatric Association, 2013). Our findings provide preliminary evidence that set-shifting problems may exist prior to, and be related with the onset of AN, but can also be related to EDs in general, given the existence of set-shifting and broader executive functioning problems in those populations as measured with cognitive tasks (Smith, Mason, Johnson, Lavender, & Wonderlich, 2018; Wu et al., 2014) and questionnaires (Dahlgren, Hage, Wonderlich, & Stedal, 2019; Roberts, Barthel, Lopez, Tchanturia, & Treasure, 2011). To address this question, it is crucial to follow these children through puberty, as the early onset of AN and other EDs often begins to emerge around the age of 14, although only a small proportion of children with AN-like features will eventually develop an ED. The incidence of EDs, including AN, is quite low, emphasizing the need for very large-scale, longitudinal studies in healthy populations that follow individuals from childhood into adulthood. Evidence from such studies could provide further insight in the associations between set-shifting and AN, which eventually may allow to shift the focus from detecting, to both detecting and preventing AN, rather than treating EDs only after they have reached a clinical level. Those prevention strategies should be first implemented in high-risk populations, where the impact will be greatest, particularly with respect to body image interventions. We also recommend that future studies examine the broader range of executive functions, both in the context of inhibited and disinhibited ED pathology and associated psychiatric disorders including autism spectrum disorders, obsessive-compulsive disorders and depression, given the relatively high heritability rates and often overlapping symptomatology of these

psychiatric disorders (Huke, Turk, Saeidi, Kent, & Morgan, 2013; Jagielska & Kacperska, 2017; Steinhausen, 2002). Research is needed to gain more insight to what extent poor set-shifting skills present a vulnerability for psychiatric features in general, or if there are subtle differences between psychiatric disorders. Such knowledge is needed to determine whether a general treatment component focused at improving set-shifting skills would be beneficial for multiple disorders.

Clinicians, such as general practitioners and pediatricians, should be aware of the link between set-shifting difficulties and ED-related features. When they are treating girls with a low BMI, who have restrictive eating patterns and rigid thinking styles, they should keep in mind that these girls are possibly vulnerable to develop a restrictive ED. Therefore, it is recommended to carefully monitor the course of these behaviors and intervene in a timely manner.

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#### CONFLICT OF INTERESTS

The authors have no conflict to declare.

#### DATA AVAILABILITY STATEMENT

People who are interested in accessing the data can send a request to [datamanagementgenr@erasmusmc.nl](mailto:datamanagementgenr@erasmusmc.nl). The Management Team of the Generation R Study decides upon these requests.

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