

1 **Dysfunction of Response Inhibition in Eating Disorders**

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2

## 1 **Abstract**

2

3 **Introduction:** Response inhibition in eating disorders (ED) has been studied using  
4 methods such as Go/No-go tasks and cognitive conflict tasks, but the results have been  
5 inconsistent in regard to the presence or absence of impaired response inhibition in ED.  
6 This may be due to variation across the studies in the characteristics of the tasks and in  
7 the degree of underweight of ED participants. **Method:** We investigated the presence or  
8 absence of impaired response inhibition in an ED patient group, including many severe  
9 cases (body mass index < 15 kg/m<sup>2</sup>), by comparing the interference effect of ED patients  
10 and healthy participants with an arrow-space interference task as the cognitive conflict  
11 task.

12 **Results:** There was a significant interference effect on response time in healthy  
13 participants and ED patients, with no significant intergroup difference in response times.  
14 However, the interference effect on error rate was significantly greater in ED patients  
15 than healthy participants. There was no significant difference in this trend across different  
16 ED subtypes (restricting type anorexia nervosa, binge-eating/purging type anorexia  
17 nervosa, and eating disorder not otherwise specified).

18 **Conclusions:** Attentional control such as focused attention and sustained attention are  
19 preserved in ED patients, but there appears to be dysfunction of response inhibition. This  
20 might be the basis of poor impulse control in the eating behavior of ED patients.

21 **Keywords:** anorexia nervosa, response inhibition, Stroop interference, binge-  
22 eating/purging, eating disorders

23

## 1 **Introduction**

2 The Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision  
3 (DSM-IV-TR; American Psychiatric Association (APA), 2000) lists “Disturbance in the  
4 way in which one’s body weight or shape is experienced, undue influence of body weight  
5 or shape on self-evaluation, or denial of the seriousness of the current low body weight”  
6 among the diagnostic criteria for the eating disorder (ED) anorexia nervosa (AN). These  
7 diagnostic criteria suggest that AN is a cognitive disorder, and recent studies on cognitive  
8 dysfunction have focused on executive functions such as decision-making (Cavedini et  
9 al., 2004, 2006; Tchanturia, Liao, Uher, Lawrence, & Treasure, 2007), working memory  
10 (Kemps, Tiggemann, Wade, Ben-Tovim, & Breyer, 2006), set-shifting (for a review see  
11 Roberts, Tchanturia, Stahl, Southgate, & Treasure, 2007) and response inhibition (Butler  
12 & Montgomery, 2005; Fagundo et al., 2012; Rosval et al., 2006; Seed, Dixon, McCluskey,  
13 & Young, 2000). Much of the study on response inhibition has focused on AN, bulimia  
14 nervosa (BN), which is another type of ED, and obesity, but the results have been  
15 inconsistent (Galimberti, Martonib, Cavallinic, Erzegovesic, & Bellodic, 2012). As  
16 discussed below, this inconsistency may be due to variation across the studies in the  
17 characteristics of the tasks and in the degree of underweight of ED participants. For the  
18 present study, we investigated dysfunction of response inhibition using a task selected for  
19 its ability to differentiate between impairments of attention and inhibition, and for its  
20 suitability to the disease group, in an ED patient group that included many patients with  
21 a severe ED (body mass index (BMI) < 15 kg/m<sup>2</sup>) based on the DSM-5 (APA, 2013)  
22 severity criteria.

23 A variety of tasks have been used in response inhibition studies, but a commonly used  
24 task in ED study is the Go/No-go task. The participant is required to respond (e.g. by  
25 pressing a button) to a particular stimulus (Go stimulus), and to inhibit responses to all

1 other stimuli (No-go stimuli). Some researchers who used these tasks to compare AN  
2 patients and healthy controls have reported large numbers of commission errors in  
3 response to No-go stimuli and omission errors in response to Go stimuli (Seed et al.,  
4 2000), while others have reported AN patients having the same amount of omission errors  
5 as healthy controls but a larger number of commission errors and shorter reaction latency  
6 (Butler & Montgomery, 2005). AN is subclassified into restricting type (AN-R) and  
7 binge-eating/purging type (AN-BP), based on the presence or absence of bulimic  
8 symptoms. A study comparing AN subtypes and BN showed that AN-BP and BN patients  
9 both have more commission errors than healthy controls, but that AN-R patients and  
10 healthy controls do not differ (Rosval et al., 2006).

11 Some AN studies have used interference tasks such as Stroop tasks to evaluate response  
12 inhibition. In the original Stroop task (Stroop, 1935), a color name (e.g. the word “red”)  
13 is presented in a color that either matches (e.g. red) or does not match (e.g. blue) the color  
14 denoted by the name, and the participant must name the color of the text. When there is  
15 a mismatch between the color name and the printed color, more naming errors are made  
16 and reading speed is slower compared to when the two colors match, a phenomenon  
17 referred to as the Stroop interference effect. In order to make the correct response (naming  
18 the printed color), the task requires the inhibition of the more automatic response (reading  
19 the word); the interference effect is thus greater when response inhibition is lower. In a  
20 study of the Stroop interference effect in AN, healthy controls and obese patients using a  
21 color-word Stroop task, Fagundo et al. (2012) found that obese patients performed more  
22 poorly than healthy and AN participants, with no difference between the latter two groups.  
23 Modified Stroop tasks have also been used in a number of studies, with the goal of  
24 investigating attentional bias to specific stimuli, for example by comparing other stimuli  
25 to stimuli related to food and the body (for a review see Dobson & Dozois, 2004; Faunce,

1 2002; Lee & Shafran, 2004); however, the effect of these tasks differed in character from  
2 the original Stroop interference effect. Our objective in this study was to investigate  
3 whether response inhibition was decreased in AN patients by comparing the interference  
4 effect in AN and healthy participants. For this purpose we used a task that was similar to  
5 the original Stroop task in that the response triggered by the stimuli irrelevant to the task  
6 had to be deliberately inhibited in order to execute the desired response. Such tasks  
7 generate cognitive conflict.

8 Various cognitive conflict tasks have been devised and applied to a range of clinical  
9 groups, including those with psychiatric disorders, since the original Stroop task, but all  
10 have been found to produce a similar interference effect (for a review see Dobson &  
11 Dozois, 2004; MacLeod, 1991). In a study using a color-word Stroop task, Fagundo et al.  
12 (2012) found no significant difference in the Stroop interference effect between AN and  
13 healthy participants. However, the BMI of AN patients in that study was  $17.2 \pm 1.4$  (mean  
14  $\pm$  standard deviation)  $\text{kg/m}^2$ , which is defined as mild, and the possibility remains that  
15 dysfunction of response inhibition underlies the abnormal eating behavior seen in  
16 extremely underweight AN patients. A study by Seed et al. (2000) of more severely ill  
17 patients with BMI  $15.24 \pm 2.05$  (mean  $\pm$  standard deviation)  $\text{kg/m}^2$  found that response  
18 inhibition was lower in these patients than in healthy controls. We therefore decided to  
19 reinvestigate response inhibition in AN by targeting severely ill patients and using an  
20 interference task better suited to this clinical group. Color-word Stroop tasks are difficult  
21 to apply to patients with a range of functional impairments because these tasks involve  
22 access to the lexico-semantic system and also call on various aspects of visual cognition  
23 unrelated to response inhibition such as color perception. In order to investigate the  
24 presence of decreased response inhibition in AN, we used an arrow-space interference  
25 task and included control tasks with no cognitive conflict before the interference task



1 (Yano, 2011, 2012). This was a modified version of a Simon task used by Castel et al.  
2 (2007) in elderly adults and dementia patients, in which interference exists between the  
3 left/right direction of an arrow and its left-right spatial position. In Fagundo et al.'s (2012)  
4 study, the number of correct responses within a set time (45 seconds) was used as the  
5 indicator of the interference effect, whereas we used response speed and error rate as  
6 indicators, with participants performing a set number of trials on a laptop computer that  
7 presented stimuli and recorded the responses.

8

## 9 **Methods**

### 10 **Participants**

11 The ED group consisted of 36 malnourished women ranging from 17 to 46 years of age  
12 (mean age  $28.81 \pm 8.24$  years; mean years of education  $14.28 \pm 2.04$  years; mean BMI  
13  $13.96 \pm 2.16$  kg/m<sup>2</sup>; BMI range 10.3-19.4 kg/m<sup>2</sup>), who met the DSM-IV-TR criteria for  
14 ED. All women were recruited during their hospitalization for refeeding therapy. We  
15 excluded patients who were male or under 17 years old. Based on the DSM-IV-TR  
16 diagnostic criteria, 26 patients were diagnosed with AN and 10 were diagnosed with  
17 eating disorder not otherwise specified (EDNOS) (BMI range: 11.2-15.1 kg/m<sup>2</sup>). Our  
18 EDNOS group included cases who showed subthreshold psychopathology of AN, and  
19 cases who did not show any AN pathology, such as desire for thinness or fear of gaining  
20 weight. Twenty-six patients (72.22%) were diagnosed as severe cases, having BMI < 15  
21 kg/m<sup>2</sup> (extreme level). Seventeen of the AN patients were classified as AN-BP (BMI  
22 range: 10.3-19.4 kg/m<sup>2</sup>) and nine were classified as AN-R (BMI range: 11.5-18.3 kg/m<sup>2</sup>).  
23 A control group of 39 healthy women, ranging from 19 to 45 years of age, also  
24 participated in the study (mean age  $27.90 \pm 7.48$  years; mean years of education  $15.62 \pm$   
25  $1.68$  years; mean BMI  $21.70 \pm 3.52$  kg/m<sup>2</sup>; BMI range 17.1-33.2 kg/m<sup>2</sup>).

1 Before joining the study, all participants in the ED group were interviewed and  
2 categorized using the Structured Clinical Interview for DSM Disorders (SCID) module  
3 H, and the absence of current or past psychiatric disorders among the control participants  
4 was assessed using the SCID screening module.

5 There was no significant difference in age between the ED group and the healthy control  
6 group ( $t(73) = 0.50$ , 95% confidence interval (CI) = -2.71-4.52,  $p = 0.62$ ,  $d = 0.12$ ). Years  
7 of education ( $t(73) = 3.11$ , 95% CI = -2.19-0.48,  $p = 0.003$ ,  $d = -0.72$ ) and BMI ( $t(63.74)$   
8 = 11.60, 95% CI = -9.08-6.41,  $p < 0.001$ ,  $d = -2.66$ ) were significantly lower in the ED  
9 group than the control group.

10 This study was performed with the approval of the Ethics Committee of Nagoya  
11 University Hospital and after providing written and oral explanations of the study and  
12 obtaining written informed consent from all participants.

13

#### 14 **Arrow-space interference task**

15 This task consisted of three separate tasks performed in a set order. In task 1 (spatial  
16 control task), a fixation point (+) was presented for 50 ms at the center of the PC screen  
17 at the start of each trial, after which a single black circle (●) was presented at either the  
18 left or right of the screen. The participants were required to press the left or right response  
19 button as quickly as possible in accordance with the side where the stimulus was  
20 presented, during stimulus presentation. The stimulus was presented randomly on the left  
21 and right for 20 trials each for a total of 40 trials. When the response button was pressed  
22 or 1500 ms had elapsed, the next trial was initiated after a 50 ms inter-stimulus interval  
23 (ISI; blank screen). Before the main trial, the participants performed 10 practice trials and  
24 were given feedback of either “correct,” “incorrect” or “out of time.”

1 In task 2 (arrow control task), the same fixation point as in the previous task was presented  
2 for 50 ms, after which a single left or right arrow ( $\leftarrow$ ,  $\rightarrow$ ) was presented at the top, middle,  
3 or bottom of the screen. The participants were required to press the left or right response  
4 button as quickly as possible in accordance with the direction of the arrow, regardless of  
5 its position. Left and right arrows were each presented the same number of times at each  
6 position in random order for a total of 120 trials. When the response button was pressed  
7 or 1500 ms had elapsed, the next trial was initiated after a 50 ms ISI. As in the first trial,  
8 the participants performed 10 practice trials with feedback.

9 In task 3 (interference task), a single left or right arrow was presented at the left, center  
10 or right of the screen after presentation of the fixation point for 50 ms, and the participant  
11 was required to press the button corresponding to the arrow direction as quickly as  
12 possible, regardless of its position, as in task 2. Left and right arrows were each presented  
13 in random order the same number of times at each position in a total of 120 trials,  
14 consisting of 40 trials each in the congruent condition (arrow direction matching its  
15 position), the incongruent condition (arrow direction opposing its position) and the  
16 neutral condition (arrow was presented in the center) (Figure 1). When the response  
17 button was pressed or 1500 ms had elapsed, the next trial was initiated after a 50 ms ISI.  
18 Before the main trial, the participants performed 12 practice trials with feedback (four  
19 trials for each trial type).

20 Castel et al. (2007) only used task 3 in their study, but we included two control tasks  
21 before the main interference task in order to enhance the participant's understanding of  
22 the task (i.e. what to ignore and what to respond to), and to allow us to distinguish between  
23 errors due to response inhibition and errors due to lower order attention impairments.  
24 Participants with a correct response rate below 80% in the control tasks (1, 2) were  
25 excluded from the analysis of task 3.

1

## 2 **Statistical analysis**

3 A significance level of 5% was set for the *t*-test, analysis of variance (ANOVA) and  
4 Pearson's product-moment correlation coefficient.

5

## 6 **Results**

### 7 **Correct response rate in control tasks**

8 All participants had a correct response rate above 80% in the control tasks (1, 2), and the  
9 *t*-test detected no difference between the ED group and the control group (spatial control  
10  $t(73) = 0.13$ , 95% CI = -0.01-0.01,  $p = 0.90$ , Cohen's  $d = 0.03$ ; arrow control  $t(73) = 0.11$ ,  
11 95% CI = -0.01-0.01,  $p = 0.91$ , Cohen's  $d = 0.03$ ) (Table 1). Performance on the  
12 interference task was analyzed using the data from all participants, as described below.

13

### 14 **Interference task error rate**

15 The correct response rate in the interference task was generally high, but the ED group  
16 made slightly more errors than in the control tasks (Table 1). Table 2 shows the error rates  
17 (sum of errors by incorrect response excluding timeout errors) for each group in each trial  
18 condition. An ANOVA of error rates with the two factors of groups (ED, healthy control)  
19 and trial types (neutral, congruent, incongruent) found that the main effect of groups was  
20 not significant ( $F(1,73) = 1.84$ ,  $p = 0.18$ ,  $\eta_p^2 = 0.01$ ,  $\eta^2 = 0.01$ ), but that the main effect of  
21 trial types ( $F(2,146) = 22.89$ ,  $p < 0.001$ ,  $\eta_p^2 = 0.24$ ,  $\eta^2 = 0.16$ ) and the interaction effect  
22 ( $F(2,146) = 3.10$ ,  $p = 0.047$ ,  $\eta_p^2 = 0.04$ ,  $\eta^2 = 0.02$ ) were significant. Multiple comparisons  
23 of the trial types using Ryan's method revealed that the error rate in incongruent trials  
24 was significantly higher than in the congruent and neutral trials ( $t = 5.69$ ,  $p < 0.001$ ,  $r =$   
25  $0.43$ ;  $t = 6.03$ ,  $p < 0.001$ ,  $r = 0.45$ ), indicating a significant interference effect. A post-hoc

1 test of the interaction effects revealed that the effect of groups was only significant in the  
 2 incongruent condition ( $F(1,219) = 8.80, p = 0.003$ ), and the effect of trial types was  
 3 significant in both the ED group ( $F(2,146) = 20.94, p < 0.001$ ), with the error rate in the  
 4 incongruent trials being significantly higher than in the congruent and neutral trials ( $t =$   
 5  $5.62, p < 0.001, r = 0.42; t = 5.36, p < 0.001, r = 0.41$ ), and the control group ( $F(2,146)$   
 6  $= 5.06, p = 0.01$ ), with the error rate in the incongruent trials being significantly higher  
 7 than in the congruent and neutral trials ( $t = 3.11, p = 0.002, r = 0.25; t = 2.35, p = 0.02, r$   
 8  $= 0.19$ ).

9

#### 10 **Analysis of response time (RT)**

11 The mean correct response RT (ms) in each group for each task and trial condition is  
 12 shown in Table 3. A  $t$ -test of RTs for correct responses in both control tasks detected no  
 13 significant intergroup differences at the 5% significance level (spatial control  $t(73) = 1.18,$   
 14  $95\% \text{ CI} = -14.24-55.88, p = 0.24, d = 0.27$ ; arrow control  $t(73) = 0.57, 95\% \text{ CI} = -25.51-$   
 15  $46.10, p = 0.57, d = 0.13$ ). An ANOVA of correct response RT in the interference task  
 16 with the two factors of groups (ED, healthy control) and trial types (neutral, congruent,  
 17 incongruent) found that only the main effect of trial types was significant ( $F(2,146) =$   
 18  $142.21, p < 0.001, \eta_p^2 = 0.66, \eta^2 = 0.07$ ), and the main effect of groups ( $F(1,73) = 2.12, p$   
 19  $= 0.15, \eta_p^2 = 0.41, \eta^2 = 0.03$ ) and the interaction effect ( $F(2,146) = 0.11, p = 0.90, \eta_p^2 =$   
 20  $0.001, \eta^2 < 0.001$ ) were not significant. Multiple comparisons using Ryan's method  
 21 revealed that the RTs for correct responses in incongruent trials were significantly longer  
 22 than in the congruent and neutral trials ( $t = 14.23, p < 0.001, r = 0.46; t = 14.98, p < 0.001,$   
 23  $r = 0.78$ ), indicating a significant interference effect.

24

#### 25 **Comparison of ED subtypes**

1 Although there were subgroups with a small amount of data, the ED group was divided  
2 into AN-BP, AN-R, and EDNOS groups and the interference effect on error rates and RT  
3 was compared again as a preliminary analysis (Tables 4, 5). An ANOVA of error rates  
4 with the two factors of groups (AN-BP, AN-R, EDNOS) and trial types (neutral,  
5 congruent, incongruent) found that only the main effect of trial types was significant  
6 ( $F(2,66) = 7.68, p = 0.001, \eta_p^2 = 0.19, \eta^2 = 0.12$ ), and the main effect of groups ( $F(2,33)$   
7  $= 1.49, p = 0.24, \eta_p^2 = 0.05, \eta^2 = 0.03$ ) and the interaction effect ( $F(4,66) = 1.21, p = 0.32,$   
8  $\eta_p^2 = 0.07, \eta^2 = 0.04$ ) were not significant. A multiple comparison of the main effect of  
9 trial types using Ryan's method revealed that, as in the analysis including the control  
10 group, there was no difference between congruent and neutral trials, and the error rate in  
11 incongruent trials was significantly higher than in the congruent and neutral trials ( $t =$   
12  $3.60, p < 0.001, r = 0.41; t = 3.45, p < 0.001, r = 0.39$ ).

13 An ANOVA of RTs for correct responses with the two factors of groups (AN-BP, AN-R,  
14 EDNOS) and trial types (neutral, congruent, incongruent) similarly found that only the  
15 main effect of trial types was significant ( $F(2,66) = 52.07, p < 0.001, \eta_p^2 = 0.61, \eta^2 = 0.05$ ),  
16 and that the main effect of groups ( $F(2,33) = 0.77, p = 0.47, \eta_p^2 = 0.55, \eta^2 = 0.04$ ) and the  
17 interaction effect ( $F(4,66) = 1.47, p = 0.22, \eta_p^2 = 0.08, \eta^2 = 0.002$ ) were not significant. A  
18 multiple comparison of the main effect of trial types using Ryan's method also revealed  
19 that there was no difference between congruent and neutral trials, and the response time  
20 in incongruent trials was significantly higher than in the congruent and neutral trials ( $t =$   
21  $8.66, p < 0.001, r = 0.73; t = 9.63, p < 0.001, r = 0.77$ ).

22

### 23 **Correlation with BMI**

24 An investigation of the correlation of BMI with indicators of interference task error rates  
25 and RT in the ED group found no significant correlations.

1

## 2 **Discussion**

3 Our study targeted an ED group containing a large proportion of severe cases with current  
4 BMI < 15 kg/m<sup>2</sup>, and we used an interference task that generated cognitive conflict  
5 between an arrow's left/right direction and its left/right spatial position, in order to  
6 investigate the presence of dysfunction of response inhibition in ED. Our results found  
7 no significant difference in performance between the ED group and healthy control group  
8 in the control tasks, and also confirmed that focused attention (attention focused on a  
9 particular task or object) and sustained attention (attention sustained throughout  
10 performance of the main task) were preserved in the ED group, at least in this study.  
11 However, when looking at the error rate in the interference task, the interference effect  
12 was significantly greater in the ED group than in healthy participants, suggesting that  
13 response inhibition was lower in the ED group. Participants in interference tasks make  
14 incorrect responses due to the difficulty in deliberately inhibiting automatic responses to  
15 stimuli irrelevant to the task (i.e. the left/right spatial position in this study). Our  
16 participants showed no intergroup differences in RT, but the ED group had a higher error  
17 rate, indicating that they had difficulty inhibiting impulsive responses. In interference  
18 tasks, participants can reduce the error rate by adopting the strategy of lowering their  
19 response speed. However, the lack of difference in RT between the ED group and control  
20 group in our study indicates that either the ED group lacked the metacognitive  
21 understanding that the error rate in the interference task would increase compared to the  
22 control task unless they lowered their response speed, or that despite this metacognitive  
23 understanding, their ability to regulate their response speed and therefore to inhibit  
24 impulsive slip was reduced. Furthermore, interference tasks are characterized by the  
25 interference effect, whereby participants tend to make more errors in incongruent trials

1 than congruent trials even if they lower their response speed to a certain extent. In  
2 incongruent trials the participant must inhibit the conflict information that impedes task  
3 execution, and errors are more likely if this inhibiting ability is impaired, even if the  
4 overall response speed is lowered. The response inhibition required to execute these  
5 interference tasks is the basis for inhibiting inappropriate or undesirable behavior in  
6 everyday life, and it is possible that dysfunction of this response inhibition is the trigger  
7 for the abnormal eating behavior that leads to the extremely low body weight seen in ED  
8 patients such as those in our study. It is also possible, however, that ED onset or a fall in  
9 BMI causes a decline in cognitive function. The question of whether cognitive  
10 dysfunction underlies the onset of ED is discussed below with reference to previous  
11 research.

12 Studies comparing cognitive function before and after treatment are instructive in  
13 determining the causal relationship between ED onset and cognitive dysfunction. For  
14 example, in a comparison of neuropsychological testing of healthy controls and AN  
15 participants with low body weight, Szmukler et al. (1992) reported no difference in  
16 learning tasks such as word memorization, but found that AN patients performed more  
17 poorly in tasks involving visual attention, visuospatial construction and problem-solving  
18 ability. Refeeding resulted in improvement in these declining cognitive functions;  
19 however, since it did not exceed the result in which healthy participants tested on two  
20 occasions were compared, these improvements were probably due to the practice effect.  
21 Moreover, five of 21 participants showed no improvement. Moser et al. (2003) assessed  
22 cognitive function in AN patients before and after inpatient treatment with cognitive  
23 behavioral therapy and nutritional rehabilitation using the Repeatable Battery for the  
24 Assessment of Neuropsychological Status (Randolph, 1998) to minimize the practice  
25 effect. Before treatment, scores were normal for language, but slightly below normal for



1 attention, visuospatial cognition, immediate memory and delayed memory. After  
2 treatment, the only domain showing significant improvement was immediate memory.  
3 Although these studies found evidence of decline in cognitive function due to AN onset  
4 (undernutrition), there was no post-treatment recovery of many cognitive functions, and  
5 it is possible that cognitive dysfunction in these domains was present before disease onset.  
6 In a review of a large number of neuropsychological studies of ED (AN and BN), Lena  
7 et al. (2004) showed that cognitive dysfunction remains even after recovery of nutritional  
8 status to normal levels, and that the severity of cognitive impairment does not correlate  
9 with BMI. They propose that cognitive dysfunctions may pre-exist ED symptoms and  
10 may underlie their onset if present in childhood and adolescence. The lack of correlation  
11 between BMI and indicators of response inhibition in our ED group also supports the idea  
12 that the severity of cognitive dysfunction might not be dependent solely on the degree of  
13 undernutrition. There appear to be a number of factors involved in ED onset, such as  
14 biological factors, social factors, and family pathology, but there is also evidence that  
15 cognitive dysfunction is an important factor.

16 When we compared ED subtypes, which were slightly imbalanced in the numbers of cases  
17 in our study (AN-BP, 17 participants; AN-R, 9 participants; EDNOS, 10 participants),  
18 we found that AN-BP patients had a higher error rate than AN-R and EDNOS patients in  
19 the interference task, but the difference was not statistically significant. In contrast, a  
20 previous study using a Go/No-go task found that AN-BP and BN patients made more  
21 commission errors than healthy participants, but there was no difference between AN-R  
22 and healthy participants (Rosval et al., 2006). The question of whether decreased response  
23 inhibition is involved in the mechanisms underlying bulimic behavior is a topic for future  
24 study.

1 In summary, it is possible that AN develops through a process in which sociocultural  
2 factors and other factors such as family pathology are added to dysfunctions of response  
3 inhibition and other cognitive functions present from childhood or adolescence as  
4 potential factors for AN onset, giving rise to excessive concern over food and body shape.  
5 In some cases the state of undernutrition resulting from AN may cause further cognitive  
6 impairment. Both in terms of prevention and treatment, there is a need for further  
7 elucidation of the relationship between AN onset and cognitive dysfunction through  
8 research on younger patients and long-term longitudinal studies that include recovered  
9 patients. In particular, it is hoped that brain imaging studies will identify the neural basis  
10 of cognitive dysfunction in AN, leading to advances in understanding of the disease and  
11 in treatments.

12

### 13 **Limitations**

14 Although this study clearly demonstrated the existence of decreased response inhibition  
15 in ED, it did not detect any clear differences between ED subtypes, unlike some previous  
16 studies. The small sample size was one limiting factor, but the following study limitations  
17 may also have come into play. There was variation in the period of undernutrition of ED  
18 patients in this study. Also, it was not possible to control for physical conditions in ED  
19 patients such as accidental low blood sugar on the test days. Similarly, there was no  
20 control for the use of psychotropic medication. The comorbidities of ED patients were  
21 also not considered. No quantitative measurement of intelligence was done except years  
22 of education. The psychopathology of participants was not surveyed enough, using  
23 adequate questionnaires. It is possible that clinical diversity interfered with the detection  
24 of intergroup differences. When speculating on the relationship between ED onset and  
25 cognitive dysfunction based on the results of this study, the causal relationship between

1 ED onset or undernutrition and decline in cognitive function remains a matter of  
2 speculation because we did not compare our participants with recovered patients. There  
3 is a need for long-term longitudinal study to investigate whether ED develops as a result  
4 of the addition of sociocultural factors and other factors such as family pathology to  
5 underlying impairments in cognitive development, or whether ED develops first and  
6 decline in cognitive function arises as a result of undernutrition.

7

## 8 **Conclusion**

9 We investigated response inhibition in female ED patients using an arrow-space  
10 interference task as a cognitive conflict task and compared the results with those of  
11 healthy women. We found no difference in error rates in control tasks without cognitive  
12 conflict, and confirmed that the interference effect in the arrow-space interference task  
13 was significantly greater in the ED patients than in healthy controls. This study  
14 demonstrated that ED patients retain attentional functions such as focused attention and  
15 sustained attention, but display dysfunction of response inhibition. We discussed the  
16 possibility that these cognitive characteristics might underlie the poor impulse control  
17 seen in the eating behavior of ED patients.

## 1 **References**

- 2 American Psychiatric Association. (2000). *Diagnostic and Statistical Manual of Mental*  
3 *Disorders* (4th ed. Text Revision). Washington, DC: American Psychiatric Association.
- 4 American Psychiatric Association. (2013). *Diagnostic and Statistical Manual of Mental*  
5 *Disorders* (5th ed.). Arlington, VA: American Psychiatric Association.
- 6 Butler, G. K. L., & Montgomery, A. M. J. (2005). Subjective self-control and behavioral  
7 impulsivity coexist in anorexia nervosa. *Eating Behaviors*, 6, 221-227.
- 8 Castel, A. D., Balota, D. A., Hutchison, K. A., Logan, J. M., & Yap, M. J. (2007). Spatial  
9 attention and response control in healthy younger and older adults and individuals with  
10 Alzheimer's disease: Evidence for disproportionate selection impairments in the Simon  
11 task. *Neuropsychology*, 21, 170-182.
- 12 Cavedini, P., Bassi, T., Ubbiali, A., Casolari, A., Giordani, S., Zorzi, C., & Bellodi, L.  
13 (2004). Neuropsychological investigation of decision-making in anorexia nervosa.  
14 *Psychiatry Research*, 127(3), 259-266.
- 15 Cavedini, P., Zorzi, C., Bassi, T., Gorini, A., Baraldi, C., Ubbiali, A., & Bellodi, L. (2006).  
16 Decision-making functioning as a predictor of treatment outcome in anorexia nervosa.  
17 *Psychiatry Research*, 145(2-3), 179-187.
- 18 Dobson, K. S., & Dozois, D. J. A. (2004). Attentional biases in eating disorders: a meta-  
19 analytic review of Stroop performance. *Clinical Psychology Review*, 23(8), 1001-1022.
- 20 Fagundo, A. B., de la Torre, R., Jiménez-Murcia, S., Agüera, Z., Granero, R., Tárrega, S.,  
21 ...Fernández-Aranda, F. (2012). Executive Functions Profile in Extreme Eating/Weight  
22 Conditions: From Anorexia Nervosa to Obesity. *PLoS ONE*, 7(8), e43382.  
23 doi:10.1371/journal.pone.0043382
- 24 Faunce, G. J. (2002). Eating disorders and attentional bias: A review. *Eating Disorders*,  
25 10, 125-139.

- 1 Galimberti, E., Martonib, R. M., Cavallinic, M. C., Erzegovesic, S., & Bellodic, L. (2012).  
2 Motor inhibition and cognitive flexibility in eating disorder subtypes. *Progress in Neuro-*  
3 *Psychopharmacology & Biological Psychiatry*, 36, 307-312.
- 4 Kemps, E., Tiggemann, M., Wade, T., Ben-Tovim, D., & Breyer, R. (2006). Selective  
5 working memory deficits in anorexia nervosa. *European Eating Disorders Review*, 14,  
6 97-103.
- 7 Lee, M., & Shafran, R. (2004). Information processing biases in eating disorders. *Clinical*  
8 *Psychology Review*, 24, 215-238.
- 9 Lena, S. M., Ficco, A. J., & Leyenaar, J. K. (2004). The role of cognitive deficits in the  
10 development of eating disorders. *Neuropsychology Review*, 14, 99-113.
- 11 MacLeod, C. (1991). Half a century of research on the Stroop effect: An integrative  
12 review. *Psychological Bulletin*, 109, 163-203.
- 13 Moser, D., Benjamin, M. L., Bayless, J. D., McDowell, B. D., Paulsen, J. S., Bowers, W.  
14 A., ...Andersen, A. E. (2003). Neuropsychological functioning pretreatment and  
15 posttreatment in an inpatient eating disorder program. *International Journal of Eating*  
16 *Disorders*, 33, 64-70.
- 17 Randolph, C. (1998). Repeatability Battery for the Assessment of Neuropsychological  
18 Status. San Antonio, TX: The Psychological Corporation.
- 19 Roberts, M. E., Tchanturia, K., Stahl, D., Southgate, L., & Treasure, J. (2007). A  
20 systematic review and meta-analysis of set-shifting ability in eating disorders.  
21 *Psychological Medicine*, 37(8), 1075-1084.
- 22 Rosval, L., Steiger, H., Bruce, K., Israël, M., Richardson, J., & Aubut, M. (2006).  
23 Impulsivity in women with eating disorders: Problem of response inhibition, planning, or  
24 attention? *International Journal of Eating Disorders*, 39, 590-593.

- 1 Seed, J. A., Dixon, R. A., McCluskey, S. E., & Young, A. H. (2000). Basal activity of the  
2 hypothalamic-pituitary-adrenal axis and cognitive function in anorexia nervosa.  
3 *European Archives of Psychiatry and Clinical Neuroscience*, 250, 11-15.
- 4 Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of*  
5 *Experimental Psychology*, 18, 643-662.
- 6 Szmukler, G. I., Andrewes, D., Kingston, K., Chen, L., Stargatt, R., & Stanley, R. (1992).  
7 Neuropsychological impairment in anorexia nervosa: Before and after refeeding. *Journal*  
8 *of Clinical and Experimental Neuropsychology*, 14, 347-352.
- 9 Tchanturia, K., Liao, P. C., Uher, R., Lawrence, N., & Treasure, J. (2007). An  
10 investigation of decision making in anorexia nervosa using the Iowa Gambling Task and  
11 skin conductance measurements. *Journal of the International Neuropsychological*  
12 *Society*, 13, 635-641.
- 13 Yano, M. (2011). Aging effects in response inhibition: General slowing without decline  
14 in inhibitory functioning. *Journal of Human Ergology*, 40, 129-139.
- 15 Yano, M. (2012). Response inhibition can distinguish pathological change from normal  
16 aging: Cognitive rehabilitation and experimental research for enhancing insight into  
17 disease. *Behavioral Science*, 50, 131-142.
- 18
- 19

1 Table 1. Correct response rate in each task.

2

3 *Note.*

4 ED, eating disorders; SD, standard deviation; CI, confidence interval.

5

6 Table 2. Error rate in the interference task.

7 *Note.*

8 ED, eating disorders; SD, standard deviation.

9 An ANOVA of error rates with the two factors of groups (ED, healthy control) and trial  
10 types (neutral, congruent, incongruent) found that the main effect of groups was not  
11 significant ( $p = 0.18$ ), but that the main effect of trial types ( $p < 0.001$ ) and the interaction  
12 effect ( $p = 0.047$ ) were significant. A post-hoc test of the interaction effects revealed that  
13 the effect of groups was only significant in the incongruent condition ( $p = 0.003$ ), and the  
14 effect of trial types was significant in both the ED group ( $p < 0.001$ ), with the error rate  
15 in the incongruent trials being significantly higher than in the congruent and neutral trials  
16 ( $p < 0.001$ ,  $p < 0.001$ ), and the control group ( $p = 0.01$ ), with the error rate in the  
17 incongruent trials being significantly higher than in the congruent and neutral trials ( $p =$   
18  $0.002$ ,  $p = 0.02$ ).

19

20 Table 3. Correct response time (ms) in each task.

21 *Note.*

22 ED, eating disorders; SD, standard deviation; CI, confidence interval.

23

24 Table 4. Error rate in the interference task in each ED subgroup.

1 *Note.*

2 AN-BP, binge-eating/purging type anorexia nervosa; AN-R, restricting type anorexia  
3 nervosa; EDNOS, eating disorder not otherwise specified; SD, standard deviation.

4 An ANOVA of error rates with the two factors of groups (AN-BP, AN-R, EDNOS) and  
5 trial types (neutral, congruent, incongruent) found that only the main effect of trial types  
6 was significant ( $p = 0.001$ ), and the main effect of groups ( $p = 0.24$ ) and the interaction  
7 effect ( $p = 0.32$ ) were not significant. A multiple comparison of the main effect of trial  
8 types using Ryan's method revealed that, as in the analysis including the control group,  
9 there was no difference between congruent and neutral trials, and the error rate in  
10 incongruent trials was significantly higher than in the congruent and neutral trials ( $p <$   
11  $0.001$ ,  $p < 0.001$ ).

12

13 Table 5. Correct response time (ms) in each task in each ED subgroup.

14 *Note.*

15 AN-BP, binge-eating/purging type anorexia nervosa; AN-R, restricting type anorexia  
16 nervosa; EDNOS, eating disorder not otherwise specified; SD, standard deviation.

17 An ANOVA of RTs for correct responses with the two factors of groups (AN-BP, AN-R,  
18 EDNOS) and trial types (neutral, congruent, incongruent) found that only the main effect  
19 of trial types was significant ( $p < 0.001$ ), and that the main effect of groups ( $p = 0.47$ ) and  
20 the interaction effect ( $p = 0.22$ ) were not significant. A multiple comparison of the main  
21 effect of trial types using Ryan's method also revealed that there was no difference  
22 between congruent and neutral trials, and the response time in incongruent trials was  
23 significantly higher than in the congruent and neutral trials ( $p < 0.001$ ,  $p < 0.001$ ).

24



1 Figure 1. Examples of the Simon task.

Table 1. Correct response rate in each task.

	ED group	Control group	<u>t test (one-tailed test)</u>	
	(n = 36)	(n = 39)	<u>t value (95% CI)</u>	<u>p value</u>
	<i>(Mean ± SD) %</i>	<i>(Mean ± SD) %</i>		
Task 1 Spatial control task	99.6 ± 1.1	99.6 ± 1.0	0.13 (-0.01 - 0.01)	0.90 (n.s.)
Task 2 Arrow control task	98.4 ± 2.4	98.4 ± 1.4	0.11 (-0.01 - 0.01)	0.91 (n.s.)
Task 3 Interference task	97.4 ± 3.7	98.3 ± 1.3		

*Footnote*

ED, eating disorders; SD, standard deviation; CI, confidence interval.

Table 2. Error rate in the interference task.

	ED group		Control group	
	(n = 36)		(n = 39)	
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>
Task 3 Interference task				
Neutral condition	0.007	0.013	0.003	0.008
Congruent condition	0.004	0.011	0.011	0.018
Incongruent condition	0.063	0.105	0.035	0.032

*Footnote*

ED, eating disorders; SD, standard deviation.

An ANOVA of error rates with the two factors of groups (ED, healthy control) and trial types (neutral, congruent, incongruent) found that the main effect of groups was not significant but that the main effect of trial types ( $p < 0.001$ ) and the interaction effect ( $p = 0.047$ ) were significant. A post-hoc test of the interaction effects revealed that the effect of groups was only significant in the incongruent condition ( $p = 0.003$ ). The effect of trial types was significant in both groups. In the ED group, the error rate was significantly higher in the incongruent trials than the congruent and neutral trials (both  $p < 0.001$ ). Also in the control group, the error rate was significantly higher in the incongruent trials than the congruent and neutral trials ( $p = 0.002$  and  $p = 0.02$ , respectively).

Table 3. Correct response time (ms) in each task.

	ED group (n = 36)		Control group (n = 39)		<i>t</i> test (one-tailed test)	
	Mean	SD	Mean	SD	<i>t</i> value (95% CI)	<i>p</i> value
Task 1 Spatial control task	523	86.25	502	65.39	1.18 (-14.24 - 55.88)	0.24 (n.s.)
Task 2 Arrow control task	609	90.50	599	63.74	0.57 (-25.51 - 46.10)	0.57 (n.s.)
Task 3 Interference task	641	88.85	615	70.76		

*Footnote*

ED, eating disorders; SD, standard deviation; CI, confidence interval.

Table 4. Correct response time (ms) in the interference task.

	ED group		Control group	
	(n = 36)		(n = 39)	
	<i>Mean</i>	<i>SD</i>	<i>Mean</i>	<i>SD</i>
Task 3 Interference task				
Neutral condition	625	91.00	598	73.57
Congruent condition	628	91.07	600	68.89
Incongruent condition	673	88.33	648	74.53

*Footnote*

ED, eating disorders; SD, standard deviation.

An ANOVA of correct response RT in the interference task with the two factors of groups (ED, healthy control) and trial types (neutral, congruent, incongruent) found that only the main effect of trial types was significant ( $p < 0.001$ ), and the main effect of groups and the interaction effect were not significant.

Table 5. Error rate in the interference task in each ED subgroup.

	ALL (n = 36)		AN-BP (n = 17)		AN-R (n = 9)		EDNOS (n = 10)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Task 3 Interference task								
Neutral condition	0.007	0.013	0.010	0.015	0.006	0.011	0.003	0.008
Congruent condition	0.004	0.011	0.006	0.011	0.003	0.008	0.005	0.016
Incongruent condition	0.063	0.105	0.096	0.144	0.031	0.030	0.038	0.040

*Footnote*

AN-BP, binge-eating/purging type anorexia nervosa; AN-R, restricting type anorexia nervosa; EDNOS, eating disorder not otherwise specified; SD, standard deviation.

An ANOVA of error rates with the two factors of groups (AN-BP, AN-R, EDNOS) and trial types (neutral, congruent, incongruent) found that only the main effect of trial types was significant ( $p = 0.001$ ), and the main effect of groups and the interaction effect were not significant. A multiple comparison of the main effect of trial types using Ryan's method revealed that, as in the analysis including the control group, there was no difference between congruent and neutral trials, and the error rate was significantly higher in the incongruent trials than the congruent and neutral trials (both  $p < 0.001$ ).

Table 6. Correct response time (ms) in each task in each ED subgroup.

	ALL ( <i>n</i> = 36)		AN-BP ( <i>n</i> = 17)		AN-R ( <i>n</i> = 9)		EDNOS ( <i>n</i> = 10)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Task 3 Interference task								
Neutral condition	625	91.00	642	89.67	595	56.75	625	116.69
Congruent condition	628	91.07	634	84.95	604	59.94	638	124.31
Incongruent condition	673	88.33	686	83.97	635	70.08	685	107.21

*Footnote*

AN-BP, binge-eating/purging type anorexia nervosa; AN-R, restricting type anorexia nervosa; EDNOS, eating disorder not otherwise specified; SD, standard deviation.

An ANOVA of RTs for correct responses with the two factors of groups (AN-BP, AN-R, EDNOS) and trial types (neutral, congruent, incongruent) similarly found that only the main effect of trial types was significant ( $p < 0.001$ ), and that the main effect of groups and the interaction effect were not significant. A multiple comparison of the main effect of trial types using Ryan's method also revealed that there was no difference between congruent and neutral trials, and **the response time was significantly higher in the incongruent trials than the congruent and neutral trials** (both  $p < 0.001$ ).

Figure 1. Examples of Simon Task.

