Inhibitory mechanisms in Down syndrome: Is there a specific or general deficit?

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Abstract

The cognitive profile of individuals with Down syndrome (DS) is known to be characterized by an impaired executive functioning, but inhibition-related processes have not been extensively examined in this setting. The aim of the present study was to investigate whether individuals with DS have any specific or general deficit in inhibitory processes. Tasks measuring prepotent response inhibition (the animal Stroop test), proactive interference (proactive interference task and intrusion errors), and response to distracters (directed forgetting task) were administered together with a working memory test to 19 individuals with DS and 19 typically developing (TD) children matched for mental age. Confirming previous findings, our results showed that the DS group performed less well in a verbal working memory task than the TD children. Analyzing our findings for the three inhibitory tasks yielded a picture of the DS children having a generalized difficulty in suppressing information that is irrelevant, or no longer relevant, to the goals of the task. These results suggest that DS is related not to specific, but rather to generalized inhibitory difficulties.

1. Introduction

Several studies have examined executive functioning, i.e. the higher-order control mechanisms that can regulate human behavior and cognition (e.g. Stuss & Alexander, 2000), in individuals with Down syndrome (DS). They have generally shown an impairment in individuals with DS in tasks assessing set-shifting, sustained attention, planning, inhibition/preservation and working memory (Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010; Rowe, Lavender, & Turk, 2006).

Few studies have concentrated on inhibitory mechanisms in individuals with DS, however, although inhibition is a mechanism (or rather a family of functions) with a central role in contributing to efficient cognitive performance (Garavan, Ross, & Stein, 1999).

Some such studies analyzed the efficacy of intentional motor inhibition in DS using variations of the “go/no-go” task (where participants are required to respond – go – when a particular stimulus is presented, and not to respond – no-go – when another stimulus appears, or when the former is presented in conjunction with another stimulus, such as a tone), and of the “stop-signal” paradigm (where participants are asked to stop an action or thought in response to the appearance of a specific stimulus (Logan, 1985); see Nigg, 2000 for a review).

Using the go/no-go task, Pennington, Moon, Edgin, Stedron, and Nadel (2003) found no differences in terms of accuracy between 11- and 19-year-old individuals with DS and a group of typically developing (TD) children of the same mental age. Rowe et al. (2006) used a motor perseveration task to compare the performance of a group of adults with DS (23–40-years...
old) with a group of individuals with learning disabilities of unknown etiology. The task involved participants tapping the table once if the examiner tapped twice, and twice if the examiner tapped once, so it measured their ability to suppress a prepotent response. Here again, Rowe et al. found no differences between the two groups in their performance of this task.

In contrast, using a stop-signal task, Brunamonti et al. (2011) found longer stop-signal reaction times for adolescents with DS compared with a group of individuals matched for mental age with learning disabilities of unknown etiology; in accordance with the race model described by Logan and Cowan (1984), this result would suggest that DS coincides with general, amodal difficulties in inhibiting ongoing actions or thoughts.

Kittler, Krinsky-McHale, and Devenny (2006) studied cognitive inhibition instead, and particularly the ability to prevent irrelevant information from interfering with recall. They analyzed the performance of a group of adults with DS (mean age 47.2 years, SD = 4.7) in a verbal working memory (WM) task in terms of both correctly recalled words and intrusion errors, i.e. the recall of irrelevant information, which usually increases in association with inhibitory deficits (e.g. Carretti, Borella, Cornoldi, & De Beni, 2009). Their results showed that individuals with DS made a higher proportion of intrusion errors than individuals with an unspecified intellectual disability matched for IQ and receptive vocabulary.

Two other studies analyzed interference control in response to stimulus competition with variations of the classic color-word Stroop task, reporting a difficulty in controlling prepotent responses in groups of adolescents (Lanfranchi et al., 2010) and adults with DS (Hippolyte, Iglesias, & Barisnikov, 2009).

From this review, it therefore emerged that individuals with DS of various ages generally have difficulties in effortful inhibition; it is worth noting, however, that these studies focused mainly on one aspect of inhibitory mechanisms, the control of prepotent responses. It would therefore be interesting to find out whether other functions of cognitive inhibition are impaired in individuals with DS.

To address this issue, the aim of the present study was to examine the performance of a group of individuals with DS in tasks measuring different inhibition-related mechanisms. It has recently been suggested that cognitive inhibition should be seen not as a unitary process, but as a family of functions, a set of attentional control processes that actively suppress irrelevant information, clearing irrelevant actions or thoughts, and reducing interference from competing distracters in order to remain focused on the goal of the task or to ensure coherent and organized behavior (e.g. de Ribaupierre, Borella, & Delaloye, 2003; Friedman & Miyake, 2004; Nigg, 2000). Though different theoretical distinctions have been drawn between inhibition-related functions (see Dempster, 1991; Nigg, 2000), Friedman and Miyake (2004) recently proposed an empirically supported taxonomy distinguishing between three inhibition-related functions, based on Nigg’s (2000) proposal and Dempster’s (1991) inhibitory definitions. The first function proposed was named “prepotent response inhibition”, which enables dominant and prepotent motor or cognitive responses automatically activated by the stimulus presented to be blocked; the second was “response to distracter inhibition”, which enables attention to be focused on relevant items by ignoring simultaneously presented irrelevant items; and the third was termed “resistance to proactive interference” and refers to the ability to dampen the activation of no longer relevant items and thus resist memory intrusions (intrusion errors).

To examine the dimensionality of inhibition-related cognitive function in individuals with DS, and thus see whether they have any general or specific impairment in their inhibitory processes, we used the classical tasks used in the literature to measure the three inhibition-related functions (see Friedman & Miyake, 2004). The children’s version of the Stroop task (animal Stroop; Wright, Waterman, Prescott, & Murdoch-Eaton, 2003) was used to ascertain the presence of a deficit in prepotent response inhibition, since the dominant information has to be prevented from gaining control (see Friedman & Miyake, 2004). In fact, the irrelevant response is highly activated and is incompatible with the correct response: in the animal Stroop test, combinations of animals’ bodies and heads are presented (a pig with a cow’s head, for instance, in the incongruent condition), and participants are asked to name the animal that the body belongs to. A proactive interference task (adapted from Borella, Carretti, & Pelegrina, 2010) was used to examine the ability to delete information that is no longer relevant, i.e. the resistance to proactive interference function. The directed forgetting task (Harnishfeger & Pope, 1996) was used to examine the ability to prevent goal-irrelevant information from occupying WM, i.e. the response to distracter inhibition function (see also de Ribaupierre et al., 2003). In the directed forgetting test, with blocked-cueing procedure, participants are shown a list of items (words) that they are asked to memorize. After the first half of the list has been presented, a signal is given to indicate whether the stimuli should be forgotten (in which case only the subsequently presented items should be remembered for later recall) or remembered. The items to be forgotten have presumably been encoded and stored in memory before participants are told that they can forget them. Efficient forgetting involves suppressing access to previously encoded information that is no longer relevant in order to facilitate the learning of new information.

Finally, a WM task was also used to confirm the impairment, as repeatedly reported in the literature (see for example Lanfranchi, Baddeley, Gathercole, & Vianello, 2012; Lanfranchi, Cornoldi, & Vianello, 2004), in individuals with DS in situations that require both the active storage and the manipulation of information.

2. Methods

2.1. Participants

Our study sample consisted of 19 individuals with DS (7 males and 12 females) with a mean chronological age (CA) of 14 years and 5 months (SD = 30 months; age range 10–19 years) and a mean mental age (MA) of 5 years and 6 months (SD = 2 months).
All these participants were still attending normal schools. They were contacted through associations for people with DS in Northern Italy. The selection criteria were age and the absence of behavioral or hearing problems.

Our control group comprised 19 TD children (8 males and 11 females) with a mean chronological age of 5 years and 2 months (SD = 8 months; age range 3–6 years). These children were contacted in kindergartens and primary schools.

The two groups were matched one to one based on their raw scores at the PPVT-R test (Dunn & Dunn, 1997) (see Table 1). In addition, since individuals with DS may have a discrepancy between their verbal and nonverbal abilities, Raven's colored matrices test (Raven, Court, & Raven, 1998) was administered to both groups to measure their nonverbal abilities.

The two groups’ performance was comparable in both the PPTV-R ($F < 1$) and the Raven test, $F(1, 36) = 2.29$, $p = .14$.

Participants’ characteristics are given in Table 1.

## 2.2. Materials

### 2.2.1. Working memory

#### Verbal dual task (e.g. Lanfranchi et al., 2004, 2012). The child was presented aurally with a list of 2–5 words and asked to remember the first word on the list and to tap on the table when the word *ball* was presented. The word *ball* was presented once in each trial, its position in the list varying across trials. A score of 1 was awarded for each correctly completed trial, when the children remembered the first word in the list and correctly performed the tapping task; otherwise they scored 0. The total number of correctly completed trials was considered as the dependent variable. The minimum score was 0 and the maximum score was 8.

### 2.2.2. Inhibition

#### Prepotent response inhibition. Animal Stroop (adapted from Wright et al., 2003 by Nichelli, Scala, Vago, Riva, & Bulgheroni, 2004). The task, based on the classic Stroop paradigm, consists of a series of animal figures (goose, sheep, cow and pig) in which the congruency between the head and the body is manipulated and participants have to name the animal based on its body. The test includes four experimental conditions, each comprising 24 stimuli: (1) incongruent condition: each animal’s head is replaced by the head of one of the others; (2) congruent condition: the stimuli are the same as the prototypes presented to the child during the training phase; (3) control shape (structural control) condition: the head is replaced with a geometrical figure (a square, circle, or triangle); and (4) control face (semantic control) condition: the head is a caricature of human faces. Participants are asked to name the animal that the body belongs to as quickly as possible. In each experimental condition, the 24 stimuli are presented to the child in a notebook, each page containing 8 stimuli (which are balanced in terms of which way the faces are oriented: 4 facing right and 4 facing left). The different conditions (congruent, control shape, control face, incongruent) are presented to the participants in random order and the time taken to respond to the stimuli on each page is timed using a stopwatch. In Stroop tasks, strong responses to cues have to be restrained in order to produce a less dominant response. The total time, in seconds, taken to respond to all the stimuli within a given condition (three pages) was considered as a dependent variable. The total number of errors per condition was also considered, however, because the erroneous responses were included in the response times (RTs), as in all clinical versions of this task (see Ludwig, Borella, Tettamanti, & de Ribaupierre, 2010).

An interference index, based on the differences between the incongruent and control face condition (see Nichelli et al., 2004), was calculated on the RTs and errors. A higher score in the interference index thus implies a greater difficulty in controlling the prepotent response in the incongruent condition, and a consequently less efficient inhibition.

#### Resistance to proactive interference. The proactive interference (PI) task (adapted from Borella et al., 2010) was used, which consists of 16 lists of words belonging to four categories (fruits, animals, body parts, and professions), divided into four blocks. Each block contained four word lists of four words each, three belonging to the same category (e.g. fruits) and one to a different category (e.g. animals) to enable the release from proactive interference. Each list consisted of words with a similar frequency and imagery value. The lists were presented aurally at a rate of one word every 1 s. Participants were asked to listen to each list. Between the presentation of the list and the recall phase, participants counted forward for 16 s (rehearsal-prevention task). Participants then had to recall as many words as possible, regardless of presentation order.

### Table 1

<table>
<thead>
<tr>
<th></th>
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<th>TD group</th>
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<td>$SD$</td>
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<td>$SD$</td>
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</table>

Nichelli et al., 2004.
For each participant we calculated the number of correctly recalled words, the proportion of intrusion errors (out of the total number of words recalled) and two indices of susceptibility to interference, using the formula: (List 2 – List 1) and (List 3 – List 1). In this task, irrelevant information from prior trials had to be deleted to avoid the build-up of PI across trials.

2.2.2.3. Response to distracter inhibition. Directed forgetting – blocked method (adapted from Borella, 2006; Borella, Ghisletta, & de Ribaupierre, 2011). The task consisted of two lists of 8 unrelated words, each presented in two conditions ‘Remember All’ and ‘Forget All’, which differed only in the cue (remember or forget) that participants received after hearing the first half of the list (the first 4 words). For each of the two conditions, the experimenter read the words at a rate of 3 s per word. The inter-list cue was given after the fourth words. In the ‘Remember All’ condition, participants were told that the previous list (apart from the first 4 words) should be remembered for the next test. In the ‘Forget All’ condition, after the first 4 words had been presented, the experimenter pretended to have made a mistake and given the wrong instruction, so participants had to try and forget the irrelevant list and concentrate on the upcoming relevant list. Following the inter-list cue, the second part of the list was presented for the two conditions in the same way as for the previous words. After a 30-s interval during which participants were asked to draw a sun or a moon (this task was planned specifically for individuals with DS), a recall test was conducted for each condition, in which participants were asked to recall all the items in the two lists, regardless of which cue had been presented before. Participants had 2 min to answer for each condition, but were given extra time when needed.

The dependent variables were the words recalled in the first and second half of the list for the two conditions (‘Remember All’ and ‘Forget All’). Words recalled in the “Forget All” condition (from the first half of the list) were considered as intrusion errors because they should have been suppressed.

2.3. Procedure

The tasks were administered individually, in a separate quiet room at the school, during three sessions lasting about 30–40 min each; the order of presentation of the tasks was fixed to minimize any error due to participant-by-order interaction. The PPTV-r and Raven’s task were administered in the first session, the verbal WM task and the PI task in the second, and the animal Stroop and directed forgetting tasks in the third.

3. Results

3.1. Working memory

3.1.1. Verbal dual task

One-way ANOVA was conducted on the number of correctly recalled words in the WM. The results showed a main effect of group, F(1, 36) = 8.93, η² = 20, p < .01: the TD children outperforming the individuals with DS (see Table 2).

3.2. Prepotent response inhibition

3.2.1. Animal Stroop task

Repeated-measures ANOVA was conducted on the median RTs using a mixed design with Group (individuals with DS vs. TD children) as the between factor, and condition (incongruent, congruent, control face, control shape) as the within factor. The descriptive statistics are shown in Table 2. Our results indicated that only the main effect of condition was significant, F(3, 108) = 23.31, η² = .39, p < .001. Post hoc analyses with Tukey’s test showed that it took longer to answer in the incongruent condition than in any of the other conditions (p < .001) (incongruent, M = 18.92, SE = 1.07; congruent, M = 13.60, SE = 0.63; control face, M = 15.03, SE = 0.77; control shape, M = 14.77, SE = 0.71).

To assess any presence of an interference effect, a one-way ANOVA was conducted on the animal Stroop interference index on RTs (incongruent condition – control face condition). Our results revealed no differences between the two groups (F < 1)2. The descriptive statistics are presented in Table 2.

The same interference index was also computed for errors; the one-way ANOVA showed a main effect of Group, F(1, 36) = 6.64, η² = .15, p < .05, with the DS group proving more susceptible to interference than the TD children (see Table 2).

3.3. Resistance to proactive interference

3.3.1. Proactive interference task (PI task)

One-way ANOVA conducted on the proportion of intrusion errors in the PI task showed a significant main effect of Group, F(1, 36) = 5.86, η² = .14, p < .05, since the DS group was, on average, more prone to experience the intrusion of already-presented items than the TD children (see Table 2).

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1 Our results did not change when non-parametric analyses were performed. For the inhibitory tasks used, moreover, the results were also unchanged when a relative difference ([experimental condition – control condition]/control condition) was used to check for individual differences in the baseline (control) condition.

2 The results did not change when another control condition was used to calculate the interference index.
A 2 × 4 repeated-measures ANOVA with a mixed design, with Group as the between factor and list (List 1 vs. List 2 vs. List 3 vs. List 4) as the within factor, was conducted on the number of correctly recalled words and showed a main effect of Group, \( F(1, 36) = 5.79, \eta^2 = .14, p < .05 \), with the TD group performing better than the DS group. The main effect of list was also significant, \( F(3, 108) = 8.64, \eta^2 = .19, p < .001 \), since participants recalled more words from List 1 than from List 2 (\( M_{\text{diff.}} = 1.21, p < .01 \)) or List 3 (\( M_{\text{diff.}} = 1.89, p < .01 \)), while there was no difference between the latter two. Fewer words were recalled by all participants in List 3 than in List 4. No other differences were significant.

For the PI index, the repeated-measures ANOVA with a mixed design, with Group as the between factor and Interference (List 2 – List 1 vs. List 3 – List 1) as the within factor, showed a marginally significant main effect of Interference, \( F(1, 36) = 3.46, \eta^2 = .09, p = .07 \). No other effects were significant (see Table 2).

### 3.4. Response to distracter inhibition

#### 3.4.1. Directed forgetting

To investigate the efficient forgetting of items that were to be forgotten (the first half of the list), we examined the number of words correctly recalled: (i) in the first and second half-lists in the ‘Forget All’ condition (4 words); and (ii) in the first half-list in the ‘Remember All’ and ‘Forget All’ conditions (4 words). Efficient inhibition should maximize the difference between the recall of the items to be remembered in: (a) the second half-list vs. the first half-list of words in the ‘Forget All’ condition; and (b) the first half-list in the ‘Remember All’ condition vs. the ‘Forget All’ condition.

Repeated-measures ANOVA with a mixed design, with Group (individuals with DS vs. TD children) as the between factor and list (the first 4 words vs. the second 4 words) as the within factor was conducted on the words recalled by the children (see Table 2 for descriptive statistics). The results indicated that, while the main effect of Group was not significant (\( F < 1 \)), the main effect of list was significant, \( F(1, 36) = 4.62, \eta^2 = .11, p < .05 \), with more words being recalled in the second half-list than in the first half-list (\( M = 0.71, SE = 0.13; M = 1.13, SE = 0.14 \)). The Group × list interaction was also significant, \( F(1, 36) = 8.73, \eta^2 = .19, p < .01 \). Post hoc analysis showed that individuals with DS performed less well than TD children in the second half-list (\( p < .05 \)), and it was only in the TD children that more words were recalled in the second half-list than in the first (\( p < .001 \)).

The 2 (Group: individuals with DS vs. TD children) × 2 (condition: ‘Remember All’ vs. ‘Forget All’) ANOVA on the words recalled in the first half-list revealed that, while the main effect of Group was not significant (\( F < 1 \)), the main effect of condition, \( F(1, 36) = 6.39, \eta^2 = .15, p < .05 \), and of Group × condition, \( F(1, 36) = 4.98, \eta^2 = .21, p < .05 \), were significant. Participants recalled more words in the ‘Remember All’ compared to the ‘Forget All’ condition (\( M = 1.18, SE = 0.14; M = 0.71 \)),
SE = 0.13). The interaction indicated that only the TD children recalled more words in the ‘Remember All’ than in the ‘Forget All’ condition (p < .01).

As for intrusion errors in the directed forgetting task (words recalled from the first list that should have been forgotten in the ‘Forget All’ condition), the main effect of Group was marginally significant, \( F(1, 36) = 3.54, \eta^2 = .09, p = .06 \), with the DS group recalling more words that they should have forgotten than the TD children (\( M = 0.95, SD = 0.91; M = 0.47, SD = 0.61 \), respectively).

4. Discussion and conclusion

Previous studies have identified WM and executive function impairments in individuals with DS (e.g. Lanfranchi et al., 2010; Rowe et al., 2006), but few have analyzed their inhibitory processes (and most of them examined a single function of inhibition, i.e. the ability to control prepotent responses), making it impossible to determine whether or not the other functions of inhibition are impaired in Down syndrome.

Hence the present study aimed to examine whether individuals with DS have a general or specific inhibitory impairment. The efficiency of inhibition-related mechanisms was examined based on the recent distinction drawn in the literature by Friedman and Miyake (2004), according to which inhibition is not a general mechanism, it is characterized by three inhibition-related functions, prepotent response inhibition, resistance to proactive interference and response to distracter inhibition. These inhibitory functions were investigated, together with a test measuring verbal WM.

First, our findings confirm previously reported evidence of significant differences between individuals with DS and TD controls in measures requiring the active manipulation of information; in fact, our DS group performed less well in the WM task (see Lanfranchi et al., 2004).

Turning to the main aim of our study, i.e. to analyze inhibition-related cognitive functions in individuals with DS, our results indicate that DS coincides with a general inhibitory deficit, since our DS group performed less well than TD controls in all the measures considered.

In the animal Stroop task (which measures prepotent response inhibition), participants with DS made more mistakes in the incongruent condition and also proved more susceptible to interference (when the interference index, calculated from the number of errors, was analyzed). These results replicate those obtained by Lanfranchi et al. (2010) and Hippolyte et al. (2009), confirming that individuals with DS are less able to prevent predominant but inappropriate responses, i.e. to block an automatic response (naming the animal based on the head instead of the body in our case). It is worth noting, however, that there was no difference in the response times between our two groups: this could be partly explained by the fact that the RTs also included the erroneous answers, consequently limiting the reliability of this variable, as mentioned by Ludwig et al. (2010).

In the tasks measuring proactive interference and response to distracter inhibition, our participants with DS recalled more off-target words than the TD group, suggesting that the former have more difficulty in resisting the interference of information that was initially relevant to the task in hand but became irrelevant because the requirements of the task were changed.

Curiously, in the ‘Forget All’ condition, only the TD children recalled more words from the second half-list than from the first (which would indicate that they were able to inhibit words from the first half-list), while this was not the case for the group with DS, whose performance was not statistically different in the two conditions (‘Remember All’ and ‘Forget All’). The difficulty individuals with DS experienced in suppressing information that was no longer relevant was apparent from the fact that they did not recall more words (from the first half of the list) in the ‘Remember All’ condition than in the ‘Forget All’ condition. These results indicate that the group with DS had more difficulty in controlling distracting information irrelevant to the task at hand, i.e. words that should have been suppressed, or forgotten, had a “distracting” effect, remaining in their WM, cluttering its limited capacity.

In conclusion, our findings partly reiterate existing results in that they demonstrate deficits in verbal WM and the ability to suppress prepotent responses in individuals with DS, as demonstrated using the animal Stroop task (Hippolyte et al., 2009; Lanfranchi et al., 2010). In addition, we found these individuals less able to suppress non-pertinent information in order to preserve their WM capacity: when compared with TD controls, our participants with DS not only recalled fewer items, they also made more intrusion errors. The latter are usually considered as a measure of the ability to suppress information that has become irrelevant (De Beni, Palladino, Pazzaglia, & Cornoldi, 1998). An increase in the number of these errors would thus indicate a difficulty in keeping the WM free of irrelevant information, with a negative fallout on the individual’s WM capacity. It can be postulated that inefficient inhibitory mechanisms in individuals with DS would contribute to explaining their limited WM capacity, as happens in the normal population (see Robert, Borella, Fagot, Lecerf, & de Ribaupiere, 2009, for example). Based on the present results, we surmise that the impaired inhibitory mechanisms exhibited by individuals with DS are not specific to a particular function of inhibition, but general.

Although it contains a number of insightful findings, we have to acknowledge at least two limitations of the present study, one being the small sample size, and another the use of a single measure for each of the inhibitory functions examined. Concerning the first point, although the size of our sample is in line with other studies in this field, it is somewhat small, and a larger sample would have enabled us, for example, to analyses the relationship between the three measures of inhibition and WM performance. As for the second point (the use of a single measure), multiple indicators of the same inhibitory function would need to be assessed to better elucidate the DS individual’s deficit. Moreover, since all the tasks that we used involve verbal processing, it would be interesting to establish whether the nature of the task (verbal vs. visuospatial, for instance)
affects the DS cases’ performance, given their well-known weakness in verbal skills (e.g., Rondal, 1996). In future studies, it would be useful to analyse inhibitory impairments in DS cases using visuospatial tasks with a view to reducing the influence of modality on the group differences.

From a theoretical viewpoint, our results are nonetheless consistent with an impaired executive functioning (e.g., Lanfranchi et al., 2010; Rowe et al., 2006) in individuals with DS and they shed further light on this deficit in terms of the inhibitory functions involved.

In conclusion, the present study entitles us to claim that the nature of the inhibitory weakness encountered in individuals with DS is not specific to a particular function, but seems to be a general weakness in their ability to control irrelevant, or no longer relevant information.

References


