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Title: Meta-analysis on inhibition from childhood to young adulthood in people with Down syndrome

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Abstract

Background: Few studies have investigated inhibition in people with Down syndrome (DS), indicating contradictory results.

Aim: This meta-analysis investigated if people with DS show more severe difficulties on inhibition, compared to typically developing (TD) children matched on a measure of mental age (MA).

Methods and procedures: Literature search included studies conducted before March 2019, combining the following keywords: “Down syndrome” with “Inhibition”, “Interference control”, “Effortful control”, “Impulsivity”, “Self-regulation”, and “Executive functions”. Descriptive information was coded, according to inclusions criteria. Meta-analysis of standardized differences between DS and TD groups’ means was performed. Relevant moderators were also considered.

Outcomes and results: Eight studies were included in the meta-analysis, including 161 people with DS and 160 TD children. The results indicated that people with DS showed significantly lower inhibition abilities when they are matched on MA with TD children, instead no significant differences emerged when this matching was not provided. A high heterogeneity across studies was estimated.

Conclusions and implications: This meta-analysis indicates that people with DS show, on average, an inhibition deficit compared to TD matched children, albeit not a severe one. These results suggest the importance of investigating in depth inhibition processes in people with DS from childhood to young adulthood.

Keywords: Down syndrome; Meta-analysis; Inhibition; Interference control; Executive Functions; Self-regulation

What this paper adds?

Inhibition is a multi-componential construct that includes different abilities, such as controlling impulsive responses and suppressing interferences, both in cognitive and in behavioural ways. Inhibitory abilities play a central role in everyday functioning (e.g., successful academic, job outcomes and social skills). Studies that investigated inhibition processes in people with Down syndrome (DS) demonstrated contradictory findings: some studies indicated that people with DS showed worse performance on inhibitory tasks than typically developing (TD) children, while other studies reported mixed results. This study contributes to the literature by conducting a meta-analysis of studies on inhibitory abilities in people with DS. The results suggested that people with DS, matched on mental age with TD control group, showed significantly weaker inhibitory abilities. Nevertheless, the small-to-medium effect size indicated that the inhibitory deficit in people with DS could be considered moderately impaired. Contrary, when match for mental age is not provide, results indicated no differences on inhibitory performance between the group with DS and the TD control group. Specifically, these outcomes support the importance of matching people with DS with TD control groups on more general abilities, to better compared their inhibitory processes. The high heterogeneity across studies, emerged from this meta-analysis, gave the opportunity to discuss some possible moderators as sources of the high variability on inhibitory abilities in people with DS (i.e., different tasks or chronological age range).

1. Introduction

Down syndrome (DS) is the most common form of intellectual disability (ID), with an incidence of 1 in 691 live births (Parker et al., 2010). People with DS are characterized by different degrees of ID, with highly variable cognitive profiles (Tsao & Kindelberger, 2009). It is well known that individuals with DS have specific weaknesses in executive functions (EFs), but some studies have reported that this atypical population exhibits different levels of impairment in any given EF component (Amadò, Serrat, & Vallès-Majoral, 2016; Carney, Brown, & Henry, 2013; Lanfranchi, Jerman, Dal Pont, Alberti, & Vianello, 2010; Rowe, Lavender & Turk, 2006). These functions are needed in several everyday activities, such as learning processes or social skills, and they correlate significantly with adaptive behavior (Gligorović & Buha Đurović, 2014). Although EFs play a key role in everyday life, inhibitory abilities in people with DS have yet to be thoroughly investigated, and the findings in the literature are not always consistent. This meta-analysis is an attempt to: 1) provide a comprehensive picture of the inhibitory abilities of people with DS; 2) establish whether their abilities might be considered as strengths or weaknesses for this population.

1.1 Executive functions in typical development

We use EFs when we cannot use automatized routines or scripts, and when we are faced with novel situations (Diamond, 2013). It is generally agreed that cognitive flexibility, inhibition, and working memory are core EFs (Miyake et al., 2000). These constructs, defined as "cool" EFs, are invoked in situations that are cognitively demanding and emotionally neutral. Recently, an increased number of studies have pointed to the importance of considering "hot" affective-emotional aspects of EF as well, such as the ability to delay gratification, and affective decision-making (Zelazo & Carlson, 2012; Zelazo & Müller, 2002). As Zelazo and Cunningham (2007) reported, "cool" EFs are implicated in abstract and context-free tasks, while "hot" EFs are involved in situations demanding the regulation of emotions and motivation.

1.2 Inhibitory components in typically developing children

Inhibition is an important component of EF that could affect both "hot" and "cool" tasks, as well as everyday life functioning and processes, such as self-regulation (see Rueda et al., 2005; Riggs, Greenberg, & Rhoades, 2011). Diamond (2013) defined inhibition as our ability to control our mental processes and responses, to override some internal or external stimuli and focus instead on others more consistent with our goals, and to carry out an alternative action that is consistent with goal achievement. It is also generally agreed that inhibition is a multi-component construct (Diamond, 2013), but it is only in recent decades that it has been analyzed as a psychometric construct, in its various aspects and developmental trajectories. For instance, a two-factor model best explains inhibition processes in young and older adults, distinguishing between two components: the *inhibition of prepotent responses* (or being able to suppress habitual or impulsive behavior or representations) and *resistance to distracter interference* (or coping with competition from recently-presented information, and suppressing distracting or incongruent information) (Rey-Mermet, Gade, & Oberauer, 2017). These two inhibitory components may have different neural activation patterns in children and adults (Bunge, Dudukovic, Thomason, Vaidya, & Gabrieli, 2002). Gandolfi, Viterbori, Traverso, and Usai (2014) demonstrated that the inhibition construct is not differentiated before 36 months of age, and a single-factor model best describes these processes in younger children. The two-factor model, in which *response inhibition* is distinguishable from *interference suppression*, better explains the inhibitory processes of children from 36 to 48 months old. Inhibitory components may actually emerge in different stages of development as sequential processes (response inhibition being acquired before interference suppression). *Response inhibition* significantly explains performance in tasks in which subjects have to choose between two conflicting options of the same stimulus, one a habitual and prepotent response, and the other non-dominant (e.g., the *Go/No-Go task* involves participants pressing the space bar on a keyboard when they see a blue figure on the computer screen, and doing nothing when a red figure appears).

Interference suppression significantly predicts performance in tasks that require a greater degree of cognitive control, and also involve selecting an item of information as irrelevant, and disregarding an interfering stimulus. In the *Fish Flanker task*, for example, a fish is flanked on either side by two other fishes moving in the same or the opposite direction (congruent and incongruent flankers, respectively), and respondents are asked to indicate which way the central fish in the middle of the computer screen is going, right or left, by pressing a right or left response button on the keyboard.

1.3 Inhibition in people with Down syndrome

Despite the growing number of studies on inhibition in the typically developing (TD) population, there is still a paucity of information about the development of inhibition in some atypical populations, and especially in people with DS. Analyzing the literature of the last 30 years, it appears that only a few studies investigated this specific topic, producing contradictory findings. Some researchers reported that people with DS had a worse performance in inhibitory tasks than TD controls, exhibiting weaker overall inhibitory skills (D'Souza, Booth, Connolly, Happé, & Karmiloff-Smith, 2015; Edgin et al., 2010; Johns, Homewood, Stevenson, & Taylor, 2012; Lanfranchi et al., 2010). Others found no differences on inhibition between groups with DS and TD control groups (Carney et al., 2013; Cornish, Scerif, & Karmiloff-Smith, 2007; Pennington, Moon, Edgin, Stedron, & Nadel, 2003; Roberts & Richmond, 2014). Others still reported mixed findings, including differences in the inhibitory performance of people with DS in terms of accuracy and response time (RT) (Borella, Carretti, & Lanfranchi, 2013; Costanzo et al., 2013; Daunhauer Gerlach-McDonald, Will, & Fidler, 2017; Traverso, Fontana, Usai, & Passolunghi, 2018). To give an example, Traverso et al. (2018) found the performance of people with DS significantly worse as regards their accuracy and RT in two tasks measuring inhibition, but not in two other tasks. Such mixed results might relate at first to the small sample size characterizing the majority of the studies. In addition, it could be due to the inhibitory dimension assessed, such as "cool" and "hot" processes. Daunhauer et al. (2017) found that people with DS had significantly worse accuracy scores than TD controls on a "cool" inhibitory task, while no such differences emerged in a "hot" task tapping participants' ability to delay gratification. Referring to these mixed results, it is noteworthy that all of the above-mentioned studies used more than one task to measure the inhibition construct, but only Traverso et al. (2018), and Borella et al. (2013) referred to a specific theoretical model, and clearly stated which aspect of inhibition they were assessing. It therefore seems clear that some crucial issues remain in the literature on inhibition in people with DS. For a start, as mentioned earlier, authors generally did not refer to a specific theoretical model, opting instead to consider all the tasks they administered under the same broad label: *inhibition*.

Several differences come to light when we look at the samples analyzed in these few studies. First, not all the studies included a TD control group, or a control group matched on a measure of mental age (MA), or on an age-equivalent cognitive ability score. MA matching is crucial in research involving people with ID and can be more useful than matching by chronological age (CA) (Flanagan, Russo, Flores, & Burack, 2008), or intelligence quotient (IQ). This is especially true for people with DS, who show an apparent decline in IQ over time (for a review, see Patterson, Rapsey, & Glue, 2013). In short, the core reason why matching with a TD control group is so important lies in the fact that a crucial improvement in core EFs occurs between 3 and 6 years old, in preschool age, although EFs continue to develop during adolescence too (Diamond & Lee, 2011; Garon, Bryson, & Smith, 2008). Even an age difference of one year in TD children can have an important influence on their performance in EF tasks, and on the results of a study, particularly when the TD children serve as a control group (Traverso et al., 2018).

A second issue concerns the much-debated topic of the type of stimuli presented *vs* the type of response required. As confirmed by the literature, it is generally agreed that people with DS show more severe impairments when assessed using tasks that involve processing verbal rather than visuospatial information (Brock & Jarrold, 2005; Lanfranchi, Baddeley, Gathercole, & Vianello, 2012). This tendency can be seen for tasks measuring inhibition too. Costanzo et al. (2013) reported that people with DS performed less well on verbal inhibition tasks than on visuospatial inhibition tasks that demanded a motor response. Task modality may not be the main reason for their worse performance, however, because it is reasonable to consider their difficulties in some EF domains as part of a "general impairment", or associated with a specific EF profile for people with DS.

The third source of diversity arises from the very variable ranges of CA for the samples with DS. In particular, in studies on inhibition that reportedly matched groups with DS and TD control groups by MA, it emerged that the CA range considered spanned through different developmental stages. For example, Costanzo et al. (2013) included in their sample people with DS that ranged from 8.6 years to 21.2 years, Carney et al. (2013) considered a sample that spans from 10.3 years to 23.1 years, or even Traverso et al. (2018) included people with DS starting from 6.1 years to 24.9 years. Clearly, with such wide ranges of CAs involved, it could be difficult to clearly ascertain when inhibition and its subcomponents emerged, and how this construct developed across different ages.

This brief literature review aimed to show that, for people with DS too, inhibition has an important role not only in their cognitive development, but also in their academic or occupational achievements, social skills, and everyday life (Amadò et al., 2016; Daunhauer et al., 2017). Inhibition is considered as a general resource needed for other EFs to be effective (Miyake & Friedman, 2012). We see that, when the EFs of people with ID are challenged in their everyday life, this can affect their ability to generate effective compensation (Tarazi, Mahone, & Zabel, 2007). It is therefore plausible that further investigating inhibition in people with DS may contribute to explaining their cognitive difficulties and identifying appropriate intervention programs to support their inhibitory abilities.

1.4 The present study

To the best of our knowledge, this is the first meta-analysis focusing on inhibition in people with DS. The primary goal was to explore the inhibitory profile of people with DS, and to quantify their difficulties in tasks tapping their inhibitory abilities vis-à-vis a TD control group matched on a measure of MA (i.e., on general intellectual performance). Furthermore, we conducted an additional analysis including studies without specified details on MA matching in order to analyze if significant differences on inhibitory performance emerged between the two groups. Moreover, considering tasks previously used to assess inhibitory performance in such groups, this study also aimed to investigate whether the type of stimuli presented (verbal *vs* visuospatial) and the type of response required (verbal *vs* motor) could influence performance in inhibition tasks in people with DS. We included also CA as a moderator to test whether differences in the developmental stage of our sample with DS affected their performance in inhibition tasks.

2. Method

2.1 Literature search

For this meta-analysis, we used three electronic databases - PsycInfo, ERIC, and EBSCO - because they include the relevant literature, both grey literature and peer-reviewed (Lipsey & Wilson, 2001). We also used ProQuest to search for unpublished "dissertations & theses". Our literature search included studies written in English and conducted before March 2019. As suggested by Nigg (2017), we combined the following keywords: "Down syndrome" with "Inhibition", "Interference control", "Effortful control", "Impulsivity", "Self-regulation", and "Executive functions". The EBSCO system also generates all the literature that is congruent with the constructs sought (e.g., "Down's syndrome" or "Downs syndrome"). These variants of the keywords were also added manually in ProQuest.

2.2 Inclusion and exclusion criteria

The following criteria were adopted to select studies for inclusion in this meta-analysis. We *included* only studies that:

1. compared children, adolescents and adults with DS (and with no additional diagnoses) with a TD control group;
2. matched the group with DS with at least one TD group on a measure of MA (reporting means and standard deviations). In an additional analysis, we also included studies with no explicit matching on MA in order to test for potential differences;
3. included at least one task tapping different aspects of inhibition, and both the group with DS and the TD group had completed all the inhibition tasks.

We *excluded* studies that:

1. involved a DS group that was not human (i.e., mouse models);
2. concerned a mixed group of people with different types of ID, unless the authors provided specific details about the types of ID involved, and provided data separately for the subgroup with DS;
3. were not original articles (e.g., editorial prefaces, reviews, meta-analyses and book chapters).

2.3 Screening and coding

All abstracts were reviewed in detail independently by two authors (MF & MCU), based on our inclusion and exclusion criteria. When abstracts provided incomplete information, full papers were checked to reach a final decision. After comparing their results, the two authors discussed any inconsistencies with one another and, if necessary (if they failed to reach an agreement), with a third reviewer (MCP). The proportion of studies in which there were inclusion disagreement was about 1% (5 out of 420 studies). Authors were contacted by e-mail for clarification in the event of missing data or unclear information.

For each paper included in the meta-analysis, the following information was encoded for the groups with DS and the TD groups: number of participants; means and standard deviations for both

CA and MA; means and standard deviations (or an overall index measure) for all inhibition tasks administered, in terms of accuracy and/or RT; type of stimuli presented (verbal *vs* visuospatial); and type of response required (verbal *vs* motor) involved in the inhibition measures administered.

2.4 Analytic strategy

We followed the analytic strategy suggested by Borenstein, Hedges, Higgins, & Rothstein (2009) and Schwarzer, Carpenter, & Rücker (2015). All analyses were performed using the R software, version 3.5.2, with the “robumeta” (Fisher, Tipton, & Zhipeng, 2017), and the “metafor” (Viechtbauer, 2010) packages.

We meta-analysed between-group comparisons (DS vs TD) in performance, namely standardized differences between group means indicating the disadvantage of DS vis-à-vis TD groups (Cohen’s d with the Hedge’s g correction). Measures of accuracy scores were available for all studies. RT were analysed separately from the accuracy scores. The variance of the effects was calculated using the formula indicated by Schwarzer et al. (2015, p. 25).

Following Borenstein et al. (2009), we adopted a random effects approach, which allows to account for the heterogeneity of the effects across studies. The heterogeneity was estimated using the I^2 index (Borenstein et al., 2009), which expresses its percentage over the total variability. High heterogeneity suggests that there could be strong moderating factors.

Most studies reported measures from multiple tasks, and thus multiple between-group standardized differences. To deal with the resulting dependencies among effects, we fitted multilevel random-effects models implemented in the “metafor” package. As a further robustness check, we employed the “robumeta” package, which computes meta-regression models using the robust variance estimation (RVE) method, also allowing to implement small-sample adjustments (Hedges, Tipton, & Johnson, 2010). The “hierarchical” model weighting scheme (Tipton, 2015) was employed.

We tested the type of stimuli presented (verbal *vs* visuospatial), the type of response required (verbal *vs* motor), and the CA as moderating factors. Significance of the moderators was tested via meta-regression coefficients in “robumeta”, and via likelihood ratio test in the “metafor” package.

Finally, to assess publication biases we used the funnel plot and the “trim-and-fill” method (Duval, 2005). As the latter could not be directly used for multilevel models, we applied it to the funnel plot based on the estimated random effects (i.e., one per study) extracted with “metafor”. The trim-and-fill method directly estimates the potential bias, imputing missing studies to compensate for asymmetry observed in the funnel plot (this assumes that the observed asymmetry is entirely due to publication bias, but note that there may be other sources of asymmetry, Borenstein et al., 2009).

3. Results

3.1 Outcome of the literature search and screening

Electronic database searchers found 420 articles of which 90 were removed as duplicates. All the abstracts were screened according to inclusion and exclusion criteria. After abstract screening, 91 articles were dismissed, according to exclusion criteria, and the remaining 215 studies were excluded after reviewing in full text (see Figure 1 for Flow Chart and the reasons of exclusions). Eight studies were included in this meta-analysis, fulfilling all the inclusion criteria. Their characteristics are presented in Table 1. A total of 15 studies were used for the additional analysis including those not reporting details on MA matching.

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3.2 Overview and meta-analysis of the group with Down syndrome *vs* typically developing control group differences in inhibitory performance

After contacting the authors of Daunhauer et al. (2017), they stated that about 70% of their DS sample and 60% of their TD sample overlapped with the study by Will et al. (2016). Therefore, we assumed that Daunhauer et al. (2017) included all participants tested by Will et al. (2016) plus others. Thus, we corrected to avoid double counting of their participants. The reported measures of EFs, however, were different and independent. We chose to present the two studies separately for any descriptive purposes (e.g., forest plots), but in the meta-analytic models we treated them as sharing the same random effect (this was equivalent to considering them as one study when fitting models; nonetheless, even if they were considered as separate studies, the estimates changed negligibly, $|\Delta B|$s < .03).

Across the eight studies, an estimated total of 161 individuals with DS and 160 children with TD were involved. The mean CA and MA were calculated by averaging the ages reported by different studies, weighted by sample size. Children with DS had a mean CA of 11.8 years (range of mean CA across studies was 4.3 to 15.2 years), and a mean reported MA of 5.3 years (range of mean MA between 1.9 and 6.9 years). TD children, by comparison, had a mean CA of 5.0 years (range of mean CA between 1.9 and 7.4), and a mean MA of 5.5 years (range of mean MA between 1.9 and 6.9).

For accuracy scores, a total of k = 26 effects from eight studies were meta-analysed. A significant standardized difference was estimated, Hedges' g = .403, p = .039, 95% CI (.020, .786), suggesting a small-to-medium inhibitory deficit of individuals with DS vis-à-vis matched TD children. Heterogeneity was high, I^2 = 77.89%. To provide the reader with more detailed information, we reported the forest plot (Figure 2) and funnel plot (Figure 3) referred to the multilevel model (i.e., they provide a visual overview of all effects included). The identical estimate obtained via the RVE estimation method was nearly the same, Hedges' $g = .435$, $p = .033$, 95% CI (.060, .809).

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The trim-and-fill procedure did not suggest any substantial asymmetry in the funnel plot, thus it did not adjust the above results. Regarding RT, only four studies were available, involving k = 12 effects calculated in an estimated total of 91 children with DS and 94 TD children. A quantitatively similar effect (but in the opposite direction) was found, albeit non-significant, Hedges' g = -.321, p = .121, 95% CI (-.726, .084). Heterogeneity was once again high, $I^2 = 74.72\%$.

The model fitted with RVE suggested a slightly larger between-group difference, albeit characterized by an extremely large uncertainty, Hedges' g = -.481 p = .121, 95% CI (-1.330, .367). The trim-and-fill procedure was not adopted for RT due to the small number of studies.

In order to analyze whether significant differences in inhibitory performance emerged when the group with DS and the TD group are not matched on a measure of MA, we conducted an additional analysis including studies without specified details on MA matching. Such analysis included 15 studies, involving a total of 345 individuals with DS and 396 TD children. Children with DS had a mean CA of 12.6 years (range of mean CAs 2.2-18.7 years), whereas children with TD had a mean CA of 5.6 years (range of mean CAs 1.1.-8.4 years).

For accuracy scores, a total of 36 effects were meta-analysed from the 15 studies. The between-group difference was non-significant and small, Hedges' $g = .163$, $p = .331$, 95% CI (-.166, .493). With RVE, the estimate was just slightly higher, but still non-significant, Hedges' $g = .298$, $p = .131$, 95% CI (-.008, .605). Heterogeneity was high, $I^2 = 77.92\%$. The trim-and-fill procedure suggested no evidence of a publication bias and it did not adjust the estimate.

For RT, a total of k = 14 effects from six studies were available. The effect was only slightly larger than in the previous analysis, and it reached significance, Hedges' $g = -.439$, $p = .004$, 95% CI (-.737, -.142). Heterogeneity was moderate to high, $I^2 = 71.00\%$. Once again, the trim-and-fill procedure did not adjust the estimate.

3.3 Moderators analysis

3.3.1 Type of stimuli presented *vs* type of response required

Regarding the type of stimuli presented (i.e., verbal *vs* visuospatial, which however coincided with type of response required in 73% of cases), from the main analysis it emerges that tasks requiring verbal responses mostly presented verbal material, while tasks requiring motor responses mostly presented visuospatial material. Out of 26 reported effects across eight studies, there were only seven exceptions (three effects from tasks requiring verbal responses but presenting visuospatial stimuli, and three effects from tasks requiring motor responses but presenting verbal stimuli). Therefore, testing the type of stimuli presented as a moderator of the group with DS *vs* TD standardized difference in accuracy showed no evidence of a moderating effect and the difference in effect was negligible, $\chi^2(1) = .707$, B = .179, p = .400 (B coefficient indicates the estimated difference in Hedge's g between the two conditions). The same effect estimated with RVE was slightly larger, but still non-significant, B = .281, p = .358 (the direction of the effect indicated slightly larger between-group difference when tasks presented visual as compared to verbal stimuli).

Concerning the type of response required (verbal *vs* motor), three studies reported effects from both tasks requiring verbal and tasks requiring motor responses, one study reported effects only from tasks requiring verbal responses, four studies reported effects only from tasks requiring motor ones. Therefore, testing the type of response required as a moderator of the group with DS *vs*

TD standardized difference in accuracy showed virtually the same results as the type of stimuli presented, $\chi^2(1) = .334$, B= .138, $p = .563$. With RVE estimation, B = .359, p = .213.

Regarding the additional analysis performed on studies that not report a MA matching between the two groups, the estimates remained practically the same as before. Concerning type of stimuli presented, $\chi^2(1) = 2.020$, $B = .283$, $p = .155$ (with RVE estimation, $B = .321$, $p = .348$). Concerning type of response required, $\chi^2(1) = .001$, $B = -.009$, $p = .971$ (with RVE estimation, $B = .124$, $p = .658$).

3.3.2 Chronological age

CA of the group with DS was also tested as a possible moderating effect for the group with DS *vs* TD difference in accuracy in the main analysis with a MA matching, but it was found non-significant, $\chi^2(1) = .124$, $p = .725$, and virtually zero in terms of the effect size, $B = -.016$. With RVE estimation, B = -.014, p = .675. As studies reporting information of RT where very few, we decided not to test any possible moderating factor. The additional analysis that included accuracy scores of studies that did not provide data for MA matching brought practically the same results (CA was available for 13 studies), $\chi^2(1) = .451$, $B = .020$, $p = .502$ (with RVE estimation, $B = .018$, $p = .635$).

4. Discussion

This meta-analysis investigated the inhibitory abilities of people with DS, considering studies that investigated children, adolescents and young adults with DS, comparing them with TD controls on at least one task tapping different aspects of inhibition. Eight studies met all our inclusion criteria (including matching on MA) and were the object of our main meta-analysis.

Although several authors stressed the importance of matching their group with DS with their TD control group on MA, our literature search identified another seven studies in which inhibition tasks had been administered but this matching on MA had not been documented. The results of our separate meta-analysis on these latter studies indicate that, when studies provided no detailed information on MA matching, or when the group with DS was not matched with a TD control group on a cognitive measure: a) the average deficit of individuals with DS may range from around zero to no more than a medium effect (i.e., .50; Cohen, 1988) and this result did not change in a significant way the meta-analytic estimations of the main analysis; and b) the level of heterogeneity remained high as well in studies that had matched DS and control groups in terms of MA. Nevertheless, matching groups on a measure of general cognitive functioning is important for any purpose of comparing groups of people with DS and TD on any more specific measure, such as inhibition, as it excludes an important confounding factor. Therefore, to establish whether there is a disability-specific deficit in inhibition, future studies should consider proxies for MA, including receptive language and/or non-verbal ability, and match it with an equivalent level of performance in TD control populations (Roberts & Richmond, 2014).

Examining the results of our main meta-analysis, a significant difference between the group with DS and the TD controls emerged, when accuracy was considered as a measure of inhibitory abilities. The group with DS scored lower than the TD controls in the inhibition tasks, but the effect was medium, as a large effect could be excluded from the confidence interval. Our analysis also reveals a high heterogeneity, however, which suggest important moderating factors across studies.

One of the reasons for this heterogeneity may lie in the different tasks used to assess inhibition. As expected, most of the studies included tasks tapping response inhibition using various paradigms: the ‘Simon says’ paradigm (Daunhauer et al., 2017; Will et al., 2016); Stroop-like tasks (Borella et al., 2013; Carney et al., 2013; Costanzo et al., 2013; Lanfranchi et al., 2010); motor inhibition task (Carney et al., 2013); the Go/No-Go paradigm (Costanzo et al., 2013; Traverso e al., 2018); the Delay task (Daunhauer et al., 2017); the A-not-B task (Roberts & Richmond, 2015); and the Matching task (Traverso et al., 2018). The Tower of London task (ToL, Costanzo et al., 2013; Lanfranchi et al., 2010) has also been used because it is a complex task that requires response inhibition and the ability to suppress prepotent moves (Miyake et al., 2000; Usai, Viterbori, Traverso, & De Franchis, 2014). Although the EF component being considered, i.e., response inhibition, was apparently the same, the tasks used to test it were by no means equivalent. For example, Go/No-Go tasks or Delay tasks engage different processes that refer to *cool* and *hot* aspects of EF, respectively. We might expect the level of impairment in people with DS to be influenced by the emotional-motivational component (Lee et al., 2011) when this interacts with their inhibition processes. As suggested by Borella et al. (2013), the studies focused mainly on one aspect of inhibition - the control of prepotent response - rather than on other components, such as interference suppression (Gandolfi et al., 2014). Only two studies in our meta-analysis considered tasks tapping cognitive inhibition or interference suppression. In one, Borella et al. (2013) used the Proactive Interference and Direct Forgetting tasks; and, in the other, Traverso et al. (2018) used the Fish Flanker and the Dots tasks. In the Proactive Interference task, individuals with DS were generally more prone than TD children to experience the intrusion of already-presented items. In the Direct Forgetting task, the group with DS confirmed a general inhibitory deficit. As concerns accuracy, individuals with DS did not differ from two TD groups in the Fish Flanker task, whereas both TD groups outperformed the DS group in the Dots task. We speculate that a possible reason for these mixed results lies in the different amounts of irrelevant, or no longer relevant, information to be controlled. Summarizing, most of the studies included in our analysis considered only the response inhibition component, so we can only surmise that individuals with DS and TD controls matched for a measure of MA show similar patterns of development as concerns this particular component of inhibition.

Finally, when RT was considered as a measure of inhibition abilities, the estimated effect size was roughly similar, albeit it did not reach significance (it should be noted that only four studies used this indicator, however). RT in preschoolers may depend on age, accuracy, and type of task. Individuals with DS, like TD preschoolers, may be unable to control their RT in order to be more accurate. That is why RT should be considered with caution as a measure of inhibition in this population (Traverso et al., 2016, 2018).

4.1 Type of stimuli presented *vs* type of response required

A task-related source of heterogeneity may concern the type of stimuli presented (verbal *vs* visuospatial). However, when we considered this moderator, our multilevel model did not produce evidence of any relevant moderating effect of verbal *vs* visuospatial type of presentation of the stimuli. The same trend emerged when the task type of response required (verbal *vs* motor), as the tasks differed, eliciting either a verbal or a motor response. However, we should consider this result with caution because the number of studies included in our meta-analysis is not large enough to exclude with certainty a moderating effect of the way in which the stimuli are presented or the type of response elicited.

4.2 Chronological age

Another source of heterogeneity may be the wide range of CAs of the individuals with DS considered in the studies. It is well known that inhibitory abilities develop from early childhood though adolescence (Zelazo et al., 2013; Diamond & Lee, 2011; Garon et al., 2008) in the TD population, and age affects performance in inhibitory tasks (see, for instance, Best & Miller, 2010). We can assume that the same applies to the population with DS, albeit in different age ranges. The studies included in our main meta-analysis considered individuals with DS whose ages ranged from 36 months (Roberts & Richmond, 2014) to 25 years (Traverso et al., 2018).

Unexpectedly, when the CA of the group with DS was tested as a possible moderator of the difference between the DS and TD groups' accuracy in the tasks, the effect was nearly exactly zero. This would suggest that the severity of the impairment in the inhibitory abilities of people with DS is only low-to-moderate in children as in young adults, but such a conclusion should be considered with caution. It should be noted, however, that we were only able to analyze three studies with a sample of young adults, so this lack of any significant moderating effect of age might also be attributable to a lack of statistical power.

4.3 Implications

Even though it was only moderate, the difference found between the group with DS and the TD group suggests that promoting and training the "cool" and "hot" inhibitory abilities of people with DS right from the early stages of their development could have important implications for their future autonomy. Inhibition is fundamental to the learning of new and more complex skills, such as those needed to move autonomously in different environments. It is crucial, for example, when we need to cross a street. We use our inhibitory abilities to acquire and make use of important social skills, and also to regulate our own impulsive behavior. For instance, individuals with weak inhibitory skills often have difficulty controlling their appetites and experiencing satiety, with important implications for their health (for a review, see Bertapelli, Pitetti, Agiovlasitis, & Guerra-Junior, 2016).

4.4 Limitations

This study has some limitations, the most significant being the small number of studies that we were able to find with a specific focus on inhibition in the literature on individuals with DS. In addition, none of the moderators considered were able to explain the high degree of heterogeneity emerging from these studies. Specifically, no differences were found as regards: the type of stimuli presented (verbal *vs* visuospatial), the type of response required (verbal *vs* motor), and the CA. It also proved impossible to cluster the tasks used by inhibitory dimension (i.e., response inhibition *vs* interference suppression) because only two studies provided details about the construct measured and the theoretical model taken for reference.

4.5 Future directions

Despite the above-mentioned limitations, this study provides some useful pointers for further research aiming to better understand the functioning of inhibition abilities in the population with DS. It would be helpful if future studies could provide more information about the sample considered and the daily activities of the participants with DS (e.g., whether they work or go to school; to what degree they are integrated in the environment in which they live; whether they engage in activities such as cognitive and behavioral training programs, speech therapy, occupational therapy, or specific programs to improve their autonomy levels in everyday life). It would also be advisable to consider more restricted ranges of CA for samples with DS, or to differentiate between subgroups at different developmental stages. Longitudinal studies on people with DS are also warranted. As emerged from the results of our meta-analysis, future research should also take into account the importance of: 1) comparing groups with DS with TD control groups, providing detailed information on the cognitive measures used to matched the two groups; and 2) referring to a theoretical model of inhibition abilities.

Moreover, in future research it should be considered the feasibility of analyzing in depth each dimensions of the inhibitory construct (e.g., cool and hot aspects with their specific components), rather than the inhibition construct as a whole. We believe that using an approach that separately examines the different components of inhibition could generate a more exhaustive picture of the inhibitory profile of individuals with DS.

Given the clinical and educational implications, it is important to administer tasks and materials that are appropriate for the MA of participants with DS, and for their general level of functioning, without disregarding their CA. Tasks designed for children (i.e., using childish cartoons or materials) are not suitable for teenagers and adults with DS. Finally, we support the conviction that the choice of tasks, and of the settings in which they are administered should take into account not only the specific weaknesses, but also and especially the strengths of people with DS.

5. Conclusions

To the best of our knowledge, this is the first meta-analysis to focus on the inhibitory skills of children, adolescents, and young adults with DS. The present study contributes to the literature inasmuch as it showed that, when matched with TD controls on a measure of MA, people with DS show only a moderately impaired inhibition. In other words, it suggested that this particular population does not have any serious inhibitory difficulties. That said, the majority of the studies analyzed only assessed response inhibition abilities, so a more severe impairment in other components of inhibition – such as interference suppression – cannot be ruled out.

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Figure captions

Figure 1. Flow chart of the inclusion and exclusion of studies.

Figure 2. Forest plot of the multilevel meta-analytic model for accuracy scores.

Note to Figure 2: Study 1 and study 5 had partial overlapping on the sample and were treated as sharing the same random effect in the analysis.

Figure 3. Funnel plot of the multilevel meta-analytic model (all observed effects) for accuracy scores.

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Table 1
Characteristics of the studies included in the meta-analysis.

Author, year	N DS (TD)	Mean CA DS (TD)	Mean MA DS (TD)	Investigated skill	Inhibitory measures	Effect size *(Hedges' g)*	95% CI
Will et al., 2016	29 (23)	6.6 (3.3)	3.9 (3.9)	Inhibitory control	Snack delay	0.45	-0.10, 1.00
				Working memory/inhibition	Pony & Gator	0.90	0.32, 1.48
Lanfranchi et al., 2010	15 (15)	15.2 (5.9)	5.7 (5.7)	Inhibition of prepotent response	Day & Night Stroop	0.85	0.10, 1.60
				Planning/inhibition	Tower of London	2.27	1.33, 3.21
Costanzo et al., 2013	15 (16)	14.5 (7.4)	6.2 (6.9)	Inhibition	Stroop	-1.06	-1.82, -0.30
				Inhibition	Go/No-Go	0.84	0.10, 1.58
				Planning/inhibition	Tower of London	0.01	-0.69, 0.71
Borella et al., 2013	19 (17)	14.6 (5.2)	5.2 (5.9)	Inhibition	Animal Stroop	0.82	-0.14, 1.50
				Resistance to proactive interference	Proactive Interference	0.79	0.11, 1.47
				Response to distracter inhibition	Directed Forgetting _ RA1	0.41	-0.25, 1.07
				Response to distracter inhibition	Directed Forgetting _ RA2	-0.35	-1.01, 0.31
				Response to distracter inhibition	Directed Forgetting _ FA1	-0.61	-1.28, 0.06
				Response to distracter inhibition	Directed Forgetting _ FA2	0.77	0.09, 1.45
Daunhauer et al., 2017	42 (38)	7.6 (3.4)	4.2 (4.2)	Working memory/inhibition	Pony & Gator	0.59	0.14, 1.04
				Inhibitory control	Snack Task	0.50	0.05, 0.95
Roberts & Richmond, 2014	13 (13)	4.3 (1.9)	1.9 (1.9)	Inhibition/working memory/set shifting	A-not-B	0.53	-0.25, 1.31
Carney et al., 2013	25 (26)	13.6 (6.1)	6.0 (6.5)	Inhibition	VIMI (verbal)	0.39	-0.16, 0.94
				Inhibition	VIMI (motor)	-1.17	-1.77, -0.57
Traverso et al., 2018	32 (35)	14.5 (5.6)	6.9 (6.5)	Inhibition of prepotent response	PMFFT	0.12	-0.36, 0.60
				Inhibition of prepotent response	Go/No-Go	0.53	0.04, 1.02
				Interference suppression	Fish Flanker	-0.37	-0.85, 0.11
				Interference suppression	Dots	0.75	0.25, 1.25
				Inhibition of prepotent response	PMFFT	0.92	0.39, 1.45
				Inhibition of prepotent response	Go/No-Go	0.72	0.20, 1.24
				Interference suppression	Fish Flanker	0.52	0.01, 1.03
				Interference suppression	Dots	1.46	0.90, 2.02

DS = Down syndrome; TD = typically developing; CA = chronological age (months), MA = mental age (months), RA = "Remember All" condition, FA = "Forget All" condition, VIMI = Verbal Inhibition, Motor Inhibition Task, PMFFT = Preschool Matching Familiar Figure Task

Note. The reported effect sizes express the deficit of the DS group vis-à-vis the matched TD group in standardized terms, independently from the metric of the variables used in the study. Some signs were thus inverted. Negative values indicate better performance in the DS group vis-à-vis the TD group.