UNIVERSITÀ DEGLI STUDI DI TRIESTE

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XXXIII CICLO DEL DOTTORATO DI RICERCA IN

NEUROSCIENZE E SCIENZE COGNITIVE

INHIBITORY PROCESSES IN INDIVIDUALS WITH DOWN SYNDROME AND IN TYPICALLY DEVELOPING CHILDREN

Settore scientifico-disciplinare: **M-PSI/04**

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Abstract

Given the progressive increase in the life expectancy of people with Down syndrome (DS), an increasing number of studies are focusing on neuropsychological developmental trajectories in this population. In particular, executive functions (EFs) plays a crucial role in multiple contexts in which automatic behaviours are not required. The role of inhibition both in typical development (TD) and in individuals with DS has been investigated especially in recent years. Analysing the literature on inhibition in individuals with DS, it reports contradictory results which are also difficult to compare given the lack of reference to a theoretical model and the different types of inhibitory measures used.

The general aim of the present dissertation, which is articulated in seven studies, is to investigate in depth and promote inhibitory processes in individuals with DS matched for a measure of mental age (MA) with TD children. In the first study, a meta-analysis was conducted to investigate if people with DS show more impairments on inhibition abilities, compared to TD children matched on a measure of MA. In the second study, individuals with DS matched for MA with two TD control groups, respectively of 5 and 6 year-olds, were assessed using a battery of tasks tapping on response inhibition and interference suppression (see Gandolfi et al., 2014). The third study aimed to investigate response inhibition, interference suppression, and delay of gratification in a broader sample of individuals with DS matched for a measure of MA with TD children. Furthermore, in order to explore the developmental trajectories of inhibitory abilities in individuals with DS, a cross-sectional analysis of inhibitory strengths and weaknesses was conducted dividing the sample of individuals with DS into two groups basing on their chronological age (i.e., children and adolescents *vs* adults). The fourth study of the present dissertation, aimed to explore in depth interference suppression abilities – less investigated in individuals with DS – with an adapted and computerized version of the Navon task in which the high-familiarity stimuli (i.e., hearts and stars) and the response do not include verbal components in order to reduce language-based difficulties. In the fifth study, the relationship between specific aspects of autonomy in everyday life and tasks measuring response

inhibition, interference suppression, and working memory was investigated. Finally, the studies number six and seven describe the creation and the implementation of a training program, respectively for TD pre-school children aged 4 and for individuals with DS. While the first one – for TD children -– aimed to jointly improve cool EFs, hot EFs, and emotion regulation, the main goal of the second one – for individuals with DS – is to improve response inhibition, interference suppression, and delay of gratification considering also their impact on the general construct of EFs in everyday life. Unfortunately, the seventh study has not been completed due to the Covid-19 pandemic situation and for this reason it will be described only the experimental design and the structure of the intervention. General conclusions will include a discussion of the main findings in light of the current literature and finally clinical and educational implications will be argued.

Abstract (Italian version)

Alla luce di un aumento delle aspettative di vita della persona con sindrome di Down (SD), un numero crescente di studi si è focalizzato sulle traiettorie di sviluppo neuropsicologiche delle persone con SD. In modo particolare, le funzioni esecutive (FE) svolgono un ruolo fondamentale in diversi contesti della vita quotidiana nei quali non è possibile o non è funzionale mettere in atto una risposta automatica. Recentemente, è stata posta maggiore attenzione al ruolo dell'inibizione sia nello sviluppo tipico (ST) che nelle persone con SD. Analizzando la letteratura riguardante gli aspetti inibitori nelle persone con SD, emergono risultati in contrasto tra loro. Alcune ricerche sottolineano infatti che tali difficoltà possano essere legate ad una mancanza di un modello teorico alla base ma anche ai differenti compiti utilizzati per misurare le componenti inibitorie.

L'obiettivo generale di questa dissertazione, che si articola in sette studi, è quello di indagare in profondità i processi inibitori e di individuare specifici programmi per il loro potenziamento in persone con SD matchate per età mentale (EM) con bambini con ST. Nel primo studio, è stata condotta una meta-analisi allo scopo di esaminare se le persone con SD presentano maggiori difficoltà inibitorie rispetto ai bambini con ST (matchati per EM). Nel secondo studio, il gruppo di persone con SD, appaiate per EM con bambini con ST di 5 e 6 anni, sono state testate con una batteria di prove che misurano le componenti di inibizione della risposta e di gestione dell'interferenza (Gandolfi et al., 2014). Il terzo studio, invece, ha lo scopo di analizzare le componenti di inibizione della risposta, gestione dell'interferenza e delay of gratification in un campione più ampio di persone con SD appaiate per EM con un gruppo di controllo con ST. Inoltre, al fine di esplorare le traiettorie di sviluppo delle capacità inibitorie, è stato svolto uno studio cross-sectional per indagare i punti di forza e di debolezza nelle abilità di inibizione dividendo il gruppo in due sotto-gruppi sulla base della loro età cronologica (i.e., bambini e adolescenti *vs* adulti). Il quarto studio presentato in questa dissertazione ha l'obiettivo di porre l'attenzione sulla componente di gestione dell'interferenza, ancora poco indagata nelle persone con SD. È stata perciò creata ed adattata una versione computerizzata del compito proposto da Navon (1977) utilizzando dei simboli ad alta familiarità. Alla

luce delle difficoltà delle persone con SD nelle prove che includono componenti verbali, è stata utilizzata una versione del compito che non richiedeva né stimoli né risposte di tipo verbale. Nel quinto studio, è stata indagata la relazione tra specifici aspetti delle autonomie nella vita quotidiana e compiti che misuravano le seguenti componenti: inibizione della risposta, gestione dell'interferenza e memoria di lavoro. Infine, gli studi numero sette ed otto descrivono la creazione e l'implementazione di programmi di intervento, rispettivamente per bambini con ST in età prescolare dell'età di quattro anni, mentre il secondo per persone con SD. Mentre il primo aveva lo scopo di provare a migliorare congiuntamente le componenti cool e hot delle FE e la regolazione delle emozioni, il secondo aveva lo scopo di migliorare gli aspetti di inibizione della risposta, gestione dell'interferenza e delay of gratification considerando inoltre il loro impatto sulle FE più in generale nella vita quotidiana. Sfortunatamente lo studio numero otto non è stato portato a termine a causa della pandemia di Covid-19 e per questo motivo verranno descritti solo il disegno sperimentale e la struttura dell'intervento che avrebbe dovuto essere svolto. Una discussione generale includerà i risultati principali della presente dissertazione, che verranno discussi sulla base della letteratura più recente. Infine, verranno argomentate le implicazioni cliniche ed educative degli studi svolti ed inclusi in questa dissertazione.

CHAPTER 1

General Introduction

1.5 Down syndrome: the importance to consider all levels

Down syndrome (DS) is the most frequent genetic cause of intellectual disabilities (ID), occurring in 98% of cases with an extra copy of all or even a small part of chromosome 21 (Daunhauer et al., 2014; Pelleri et al., 2019; Roberts & Richmond, 2015). Its average occurrence is one child in 700 births (Mégarbané et al., 2009; Sherman et al., 2007). About 90-93% of the cases are imputed to a maternally derived additional copy of the entire chromosome 21 due to non-disjunction (Ganguly & Kadam, 2017), while in rare cases DS is due to translocation (~2-4%) or mosaicism (~1.3-5%) (Karmiloff-Smith et al., 2016). However, it should be considered that genetics, cellular, neural, behavioural and environmental factors contribute to the heterogeneity amongst individuals in both cognitive abilities and skills phenotype (Karmiloff-Smith et al., 2016; Tsao & Kindelberger, 2009).

The great majority of individuals with DS show ID ranging from mild to severe, with a mean IQ of 50 and a mental age that rarely exceeds 8 years of age, depending on the age, environment and the genotype (Hernandez & Fisher, 1996). It is important to note that while mental age continues to increase over time, intelligence quotient (IQ) decreases (Pulina et al., 2019). A progressive declining trend has been demonstrated in individuals across childhood ranging between 60-70s in the preschool age group with a subsequent decrease to between 40-50s in kindergarten and further decline dropping to between 30-40 in school-aged children (Hodapp et al., 1999). Recently, Toffalini and colleagues (2018) suggested that the most informative score to assess the intelligence structure in ID is age-equivalent scores, which is based on the approach similar to the use of mental age (MA) without sharing its theoretical assumption. They indicated that for example the Wechsler Intelligence Scale for Children – Fourth Edition often produces floor effects in individuals with intellectual disability and that the use of Z or age-equivalent scores can reduce this problem. To this purpose, Channel et al. (2021) investigates cognitive and behavioural variability in a sample of 314 individuals with DS, considering their: a) IQ, b) adaptive and maladaptive behaviour, and c) autism spectrum disorder (ASD) symptomatology (literature estimates that the prevalence of co-occurring autism spectrum disorder is about 5-to-18% in children with DS, see Moss et al., 2013). Channel et al. (2021) identified three profiles: 1) a “normative” profile - the largest one - with a relatively consistent profile of cognition and adaptive behaviour, with low rates of maladaptive behaviour and autism symptomatology; 2) a “cognitive” class with low cognitive scores and adaptive behaviour and more autism symptomatology, but with low rates of maladaptive behaviour; 3) a “behavioural” profile - the smallest one - with higher rates of maladaptive behaviour and autism symptomatology, but with cognition levels similar to the “normative” class. When considering cognitive profile in people with DS, it should definitely be emphasized that in this atypical population there is an increased probability of developing an early and rapid cognitive deterioration. As reported by Akahoshi et al. (2012), even in children with DS as young as 10 years old it could be observed a pattern of some senile changes in the brain MRI such as hippocampal atrophy or ischemic changes of the cerebral white matter. Furthermore, some medical conditions which are typically associated with DS (e.g., depression, sleep apnea, and hypothyroidism) or stressful events in everyday life (e.g., death of a close relative, end of secondary education, difficulties on employment) may lead to early regression and subsequent faster cognitive impairment. This regression has crucial implications for the quality of life of people with DS as it affects more autonomy and daily skills, speech, and psychomotor activity (see Mircher et al., 2017). Individuals with DS have also a greater association with the development of Alzheimer’s disease which is could be due to neuronal loss, neurofibrillary tangles or plaques from the age of approximately 30-35 years old with a significant decline at above 54 years old (Ghezzo et al., 2014).

Overall, the developmental trajectories of individuals with DS seems to be characterized by heterochrony in cognitive, motor, language skills (Karmiloff-Smith et al., 2016). As stated in the guidelines for the diagnosis of ID, these deficits also have an impact on behaviours in daily life, which is why ID also leads to a deficit in adaptive functioning in the conceptual, social and practical domains. In other words, people with ID show different levels of impairment in everyday life levels of autonomy than one would expect on the basis of their chronological age and their culture, involving limitations in one or more activities in daily life, such as communication, social participation and autonomous life, through multiple environments such as home, school, work environment and community (APA, 2013).

1.1.1 Behavioural profiles and autonomies in people with Down syndrome

The term adaptive behaviour (AB) refers to a set of crucial abilities for everyday life aimed to achieve good levels of autonomy and independence. AB includes three sets of skills: conceptual (e.g., language, understanding money, time, and numbers); social (e.g., following rules, interpersonal abilities, social problem solving); and practical (e.g., personal care, handling money, using transports) (Tassè et al., 2012). AB and autonomy are implicated in a future independent life and employment outcomes in people with DS (Tomaszewski et al., 2018). Despite AB is usually impaired in individuals with DS (Steingass et al., 2011), socialization seems to be the strongest the more stable developmental domain in children with DS (Steingass et al., 2011; Cebula & Wishart, 2008). Literature indicates that children with DS have better socialization skills compared to children without DS (Dressler et al., 2010) and even more that some social functioning dimensions such as social orientation, social engagement, and pro-social responsiveness are equally strong (Smith et al., 2017). It should be take into account that about one-third of people with DS show behavioural challenges and social-withdrawal is one of the most important contributors (Will et al., 2016). Literature suggest that make a dual-diagnosis of Attention-Deficit/Hyperactivity Disorder (ADHD) or ASD in individuals with DS is more difficult because some signs of ADHD or ASD and other comorbid disorders may be attributed to the typical DS behavioural phenotype (Palumbo & McDougle, 2018).

Regarding conceptual and practical skills, different authors indicates that people with DS have difficulties especially on conceptual, communication and motor skills (Fidler et al., 2006). Tomaszewski and colleagues (2018) identified as weaknesses the following abilities: managing money, cooking, moving in the community, organizing their time, functional academics, and shopping. It should be highlighted that specific programs aimed at improving autonomy in daily life in people with DS have demonstrated positive effects. For example, O'Neill & Gutman (2020) combined individual and groups interventions using metacognitive strategies (e.g., self-awareness, facilitation of spontaneous generation of problem-solving strategies, facilitation of errors detection) to improve on shopping skills. Other authors indicate specific strategies to improve money skills in people with DS such as: use of calculators or number line, use of prompt cards, provide pre-specified amount of money or using video modelling or video self-modelling (Xin et al., 2005).

1.1.2 Motor and language skills in people with Down syndrome

Regarding motor skills, children with DS show an increased risk of motor delay and coordination skills that may hind children with DS from the basically sensory stimulation that is required for other aspects of learning (Valenti et al., 2014). This gap in motor development may occur around 4 months of age and becomes more manifest as the age advances. For example, fine motor skills are impaired in people with DS with some important implications on both more specifically domains such as writing skills and on more general autonomies in everyday life. In fact, early fine motor skills and writing skills are achieved around the same age range in children with DS and in typical developing (TD) children, nevertheless, with the increasing complexity of tasks, the difference increases between the group with DS and the group with TD (Frank & Esbensen, 2015).

With regard to language and communication, literature suggests that in people with DS the expressive language is more impaired than receptive language and/or language comprehension (Mason-Apps et al., 2018; Næss et al., 2011). As opposed, children with DS develop higher levels of gestural communication than is expected for their developmental age thus placing them in "gestural advantage" (Kumin, 2006). It should be underlined that about two-thirds of individuals with DS may have hearing loss which are related to impairments in phonological memory, grammatical and language comprehension, reading, and expressive language (Martin et al., 2009). They may be related to speech aphasia, dysarthria, and voice quality, plus the fact that individuals with DS may have a smaller oral cavity with an enlargement of the tongue and a more curved palate (Martin et al., 2009).

Difficulties on linguistic abilities and communication have clearly crucial implications for participation in academic, social, and community settings (Abbeduto et al., 2007). However, given the elevated risk for communication impairments detectable since childhood in people with DS, it is of fundamental importance to intervene in a multi-disciplinary way from the first stages of life (Schwower et al., 2021).

1.6 Theoretical background of Executive Functions

Executive Function (EF) refers to a set of self-regulatory cognitive processes involved in goal-directed control of thoughts, behaviours, and emotions (Zelazo & Müller, 2011). EFs support people when they faced with new or complex situations in which it is not possible to implement an automatic response or it is not recommended to act impulsively (Miyake & Friedman, 2012) and significantly improve during the preschool years (Zelazo & Carlson, 2012). In recent decades there has been a progressive increase in interest in the study of EFs given their crucial role in several outcomes such as school readiness, academic achievement, prosocial behaviours, language acquisition (Best et al., 2011; Gandolfi et al., 2021; Shaul & Schwartz, 2014; Traverso et al., 2020), but also self-control, social relationship in adulthood (Campbell et al., 2015; Moffit et al., 2011).

Several model have been proposed to describe EFs in different stages. The literature agrees on the fact that the model proposed by Miyake and colleagues (2000) best describe EFs, considering the following three core components: updating (i.e., information updating and monitoring), inhibition (i.e., inhibition of prepotent responses), and shifting (i.e., mental set shifting). These components support higher-order cognitive processes such as planning and problem-solving (Collins & Koechlin, 2012). Given the different developmental trajectories of EFs throughout the entire life cycle, several authors deeply investigated the development of EFs in different range of ages, highlighting the greater levels of plasticity from early childhood to adolescence (Zelazo et al., 2013). The pre-school and school period are considered crucial moments for the acquisition and the improvement in EFs which appear to be sensitive to early experiences (see Müller et al., 2013). It is important to consider the difficulty in assessing EFs due to tasks impurity (Friedman & Miyake, 2004), which could be mitigated and controlled using a latent variable approach that exclude the possible intrusion of error variance related to the use of a regression with raw scores (Miyake et al., 2000; Usai et al., 2014). Some studies that used a confirmatory factor analysis (CFA), indicated that a unitary construct is more appropriate to describe EFs (Hughes & Ensor, 2007; Wiebe et al., 2011) but some concerns should be highlighted such as the age range of the samples included, the difference in tasks used to assess EFs, and the type of statistical analysis carried out.

In contrast to the above mentioned studies, other authors identified a two-factor model in which inhibition and working memory (WM) are considered distinct but interrelated, as best explain the construct of EFs in pre-school children (Miller et al., 2012; Lee et al., 2013; Usai et al., 2014; Willoughby et al., 2016). In particular, previous study assess EFs with tasks that overlaps inhibitory and WM demands, suggesting the importance to consider tasks that more clearly separate inhibition from WM (Miller et al., 2012). Recently, Scionti and Marzocchi (2021) demonstrate that a strong relation between behaviour and EFs in 3-to-4 years old children, indicating that a two-factor structure better fit to the data and show a more ecological validity than a single-factor structure. In a longitudinal study, Usai et al. (2014) used a CFA to analyse the latent structure of EFs in 5 and 6 years old children indicating that a two-factor structure best fit to the data. Specifically, inhibition was distinguished from WM and shifting that would emerge instead as a unitary component. These researches on developmental trajectories of EFs are also in line with the study of Garon and colleagues (2008) that indicated that assess shifting skills in pre-school children is complex precisely because this component would emerge separately only in later stages of development. Finally, literature suggested that a separated three-factor model could be occur in a protracted period, which start above 11 years olds and reach some stability above at the age of 15 (e.g., Lee et al., 2013).

In recent decades, Zelazo and Müller (2002) pointed out the importance to consider also affective aspects od EFs (i.e., hot EFs) as a continuum of more cognitive EFs (i.e., cool EFs), given the fact that cool EFs are investigated in depth compared to the hot components which are equally involved in several situations with high affective demand. Specifically, while cool EFs are elicited in cognitively demanding situations, hot EFs are required in motivational and emotional contexts. Literature suggested that the distinction between cool and hot EFs can be observed in TD children by the age 24 months (Montroy et al., 2019), while other authors postpone this distinction to the age of 3–4 (Willoughby et al., 2016). A clear example of hot EF is required in tasks assessing the ability to delay gratifications in which subjects have to resolve the conflict to avoid a more salient and immediate reward (i.e., smaller reward) to approach a less salient delayed reward (i.e., larger but delayed reward) (for a review on hot EFs see Garon, 2016). Some studies suggested that the delay of gratification tasks could assess the simpler form of inhibition which is specifically required in tasks such as the Marshmallow task or the Wrap Delay task, or even more the Gift Delay task (Garon et al., 2008; Garon, 2016; Groppe & Elsner, 2014).

1.2.1 The overall impaired profile of executive functioning in individuals with Down syndrome

There is a well agreement on the fact that EFs are a particular area of weaknesses in individuals with ID, however with different degrees of impairment associated with specific profiles. Several studies investigate EFs specifically in individuals with DS, reporting contradictory findings. Recently, Tungate and Conners (2021) published a meta-analysis focusing on EFs in individuals with DS with the aim to better define whether there is a specific profile of strengths and weaknesses EFs' skills. They included studies in which a sample with DS was compared with a TD control group matched on a measure of MA or developmental level and excluded studies in which proxy reports such as the Behavior Rating Inventory of Executive Function (BRIEF, Gioia et al., 2000) were used to assess EFs. Basing on inclusion and exclusion criteria defined by authors, the total number of eligible studies was fifty-seven. Results reported that individuals with DS showed a significantly worse performance on tasks assessing EFs when they are compared to a TD control group both considering the overall EFs profile and the separate EF dimensions (i.e., WM, inhibition, and shifting). In fact, considering separate dimensions, WM and shifting were more impaired compared to inhibition. Authors highlighted the importance to consider the task modality that showed significant results only for WM but not for inhibition and shifting. Their results also suggested that impairments in EFs did not change with chronological age (CA).

An important consideration concerns the fact that only a small number of studies that measured the overall construct of EFs in individuals with DS from a cross-sectional or a longitudinal point of view coincide with studies have used proxy reports such as BRIEF (e.g., Lee et al., 2015; Loveall et al., 2017). Specifically, studies that included only indirect measures reported contradictory findings with a greater agreement on a possible improvement in inhibition in adulthood (see Loveall et al., 2017). These results highlight the current debate in the literature concerning the use of indirect measures for the assessment of EFs. For example, while some researchers argued that indirect measures and performance laboratory tasks measure different aspects of EFs (e.g., Daunhauer et al., 2017; Toplak et al., 2013), other authors suggested the importance to use proxy reports to investigate EFs in more ecological contexts such ad school or home but with a larger sample (e.g., Loveall et al., 2017).

Another crucial issue concerns the fact that emerging literature on EFs suggests the importance to also consider the specific sub-components of the domains of the executive functioning given the results of several studies. For example, considering WM domain which is the most impaired and investigated in individuals with DS, researchers suggest that the WM profile of people with DS is characterized by different performance on verbal *vs* visuo-spatial tasks with a greater impairment on verbal tasks (Brock & Jarrold, 2005; Lanfranchi et al., 2012). Although the overall visuo-spatial profile seems to be less impaired than the verbal one, some authors have investigated different aspects of the visuo-spatial WM component indicating that the spatial-simultaneous component is more impaired than the spatial-sequential one, suggesting that individuals with DS have significant difficulties to manage more than one item at time (e.g., Carretti et al., 2013). The same can be said with regard to the inhibitory construct, which is well-described in the current literature as a multicomponential construct that includes different sub-components (see Gandolfi et al., 2014). The developmental trajectories and the theoretical models for inhibitory abilities will be described in detail in the next paragraph.

1.3 Developmental trajectories of inhibition

Given that the present dissertation focuses in particular on inhibitory aspects in TD children and in individuals with DS, it is fundamental to dedicate the theoretical models that better explain the composition and the development of inhibitory components. Despite there is a well-known agreement on the fact that inhibition is a multidimensional construct (Howard et al., 2015; Rey-Mermet et al., 2017), the majority of studies that assess inhibition in both typical and atypical development did not consider the importance to investigate different inhibitory dimensions (Traverso et al., 2018; St Clair-Thompson & Gathercole, 2006). Rey-Mermet et al. (2017), using a latent variable approach in an adult TD sample, demonstrated that a two-factor model best explain the data. They identified the inhibition of prepotent responses (i.e., the ability to suppress dominant responses) as separate from the resistance to distracter interference (i.e., the ability to ignore distracting information or to suppress competing response tendencies). Nevertheless, as suggested by the literature, differences between inhibitory processes in childhood and adulthood should be take into account (Bunge et al., 2002; Friedman & Miyake, 2004). Starting from these theoretical assumptions, Gandolfi and colleagues (2014) analysed the latent structure of inhibitory processes in children aged 3-to-4, distinguishing the response inhibition dimension from the interference suppression dimension starting from 36-48 months. Traverso and colleagues (2018) suggested that the same pattern of inhibitory dimensions could be detected also in children of 5-to-6 years old. These results indicated that the interference suppression component may emerge after response inhibition, confirming the distinction operated by Garon et al. (2008) between simpler and more complex inhibitory processes related to the WM demand. An increasing number of studies demonstrated that inhibition is strongly related with WM and that this relation has crucial implications in particular in preschool ages (e.g., Miller et al., 2012; Traverso et al., 2020). For instance, paradigms such as the above mentioned *delay of gratification*, *object retrieval*, and *antisaccade* tasks better assess the simpler for of inhibition which require less WM demand, while other tasks such as the *flanker*, *hearts and flower*, *less is more*, *Navon paradigm*, and *knock and tap* could be ascribed to the more complex inhibitory dimension which request to the subject to resolve a conflict between dominant and sub dominant responses (see also Traverso et al., 2020).

1.3.1 The inhibition construct in individuals with Down syndrome

While the greater number of studies on EFs have been analysed performances on WM component in individuals with DS (for a meta-analysis see Tungate & Conners, 2021), an increasing amount of studies are focusing on inhibition in this population given the crucial role of this dimension in different areas of daily life such as adaptive behaviour, daily life autonomies and independence, academic achievements, employment perspectives (Nakamichi, 2017; Sabat et al., 2020; Will et al., 2017). Literature on inhibition in individuals with DS reported contradictory results, but recently Fontana and colleagues (2021a) conducted a meta-analysis to better define the inhibitory profile of individuals with DS. This meta-analysis aimed to explore inhibition in people with DS compared to TD children matched for a measure of MA or general intellectual performance. Given inclusion and exclusion criteria, 8 studies were included in the main meta-analysis. Moreover, an additional analysis to understand potential differences between studies which included *vs* did not include a MA matching was conducted, involved a total amount of 15 studies. Results indicated significant differences on inhibitory tasks performance when a MA matching was not provided (or included) adding to an increase on the level of heterogeneity. In other words, this study is in line with other studies that suggested the importance to match the groups of people with DS with a TD control group when assessing inhibition (see also Roberts & Richmond, 2017). Moreover, significant differences emerged between the performance of individuals with DS and TD children when accuracy was considered as a measure of inhibitory abilities, but the effect was medium. On the other hand, when response time (RT) were considered no significant differences emerged, indicating that RT should be considered with caution (see also Traverso et al., 2016, 2018). Authors also discuss possible reasons for the high levels of heterogeneity highlighting that the majority of studies assess inhibition: a) included a sample with DS with a wide age range, b) used different tasks, c) did not specify the theoretical model which they referred to, d) did not consider inhibition as a multicomponential construct which is also related to both cool and hot components. No significant differences emerged when both the type of stimuli presented (verbal or visuo-spatial) *vs* the response required (verbal or motor) and the CA were included as moderators. These latter results should be considered with caution given the number of studies included. For example, Costanzo and colleagues (2013) suggested that individuals with DS showed worse performance on verbal inhibition than on visuo-spatial inhibition, however this deficit could be considered as a part of a more general impairment or quite associated with a specific EF profile.

As mentioned above for the construct of EFs, only few studies investigated inhibition in a longitudinal or cross-sectional way with laboratory tasks that assess specific inhibitory sub-components (e.g., Fontana et al., 2021b), while other studies analysed inhibitory dimension as a whole using informant-report measure such as the BRIEF to investigate also inhibition (Lee et al., 2015; Loveall et al., 2017; Sabat et al., 2020). Using direct measure of inhibition and considering also different inhibitory aspects (i.e., response inhibition, interference suppression, and delay of gratification), Fontana and colleagues (2021b) found overall worse performance in the sample with DS compared to a TD group matched for MA on response inhibition and delay of gratification while no differences emerged on interference suppression dimension. Dividing the entire sample in two different CA groups, the authors found that older individuals with DS improve their performance on response inhibition and delay of gratification tasks (the simpler inhibitory component), while interference suppression still remain impaired also in adulthood. With regard to studies that assess inhibition with an indirect measure (i.e., BRIEF), different results emerged. While some researches indicated that inhibition may improve with age from 4-to-24 years old (Loveall et al., 2017), other studies suggested that inhibition was consistent from 2-to-18 years of age (Lee et al., 2015).

Moreover, as reported by Sabat et al. (2020), different profiles emerged basing on the raters (e.g., parents *vs* teachers). In fact, when individuals with DS were assessed by teachers, a more impaired profile on inhibition and flexibility emerged, whereas the reverse was true when they were rated by their parents. On the contrary, other studies reported inhibitory impairments when the group with DS was assessed by carers but not by their teachers (Danuhauer et al., 2014; Lee et al., 2011). As suggested by Gross and colleagues (2015), it might be useful to combine direct and indirect assessment methods, also in view of the fact that different assessment methods could identify partially different components. However, a more detailed debate on different studies that assess inhibitory dimensions with different tasks in people with DS is included in each dedicated chapter of the present dissertation related to the specific topic of the studies conducted.

1.4 Intervention programs to improve Executive Functions in typical development and in individuals with Down syndrome

Given the crucial role of EFs in developmental abilities both TD and in individuals with DS (Jacobson et al., 2011; Lanfranchi et al., 2010; Tungate & Conners, 2021), it is clear that an increasing number of studies have been focusing on intervention programs aimed to improve, ameliorate or maintain EFs skills throughout the entire life span (for a review, Diamond & Ling, 2016). As above described (see Paragraph 1.2 of the present Chapter), the developmental trajectories of EFs in TD are characterized by relative plasticity over an extended range of time, from infancy to early adulthood, with greater levels of plasticity in particular from childhood to adolescence (Zelazo et al., 2013). While there is a quite well agreement on theoretical EFs models which researchers and professionals could referred to when examining TD (e.g., Gandolfi et al., 2014; Miyake et al., 2000, Miyake & Friedman, 2012; Miller et al., 2012; Usai et al., 2014), it is not possible to identify any model of executive functioning that refers to people with DS. Given the progressive increase in life expectancy in individuals with DS (Bittles & Glasson, 2004), further studies are necessary to better understand and define developmental trajectories of EFs – considering bot their MA and CA – with specific theoretical models tested for this population. These theoretical models should also have important implications when an intervention program has to be implemented. Furthermore, while on one hand training on cool EFs has been studied in particular in TD pre-schoolers producing significantly positive effects (Scionti et al., 2020), interventions focusing on both cool and hot EFs has been less investigated (for a detailed description of interventions on both cool and hot EFs see Pellizzoni et al., 2019). For instance, Rueda and colleagues (2012), Pellizzoni and colleagues (2020), and Traverso and colleagues (2015) published training programs focusing on both cool and hot EFs, reporting positive or partially positive effects on hot components. Analysing literature it clearly emerged that training on EFs could include several differences on the basis of: a) approaches (e.g., play-based and curricular *vs* physical *vs* technology-based), b) duration (short- *vs* long-term interventions), c) setting (individual *vs* group), d) materials.

Literature on EFs intervention programs in individuals with DS, highlights that the greater number of studies have examined the effect of specific programs on the WM dimension (e.g., Costa et al., 2015; Lanfranchi et al., 2017; Pulina et al., 2015), while only few studies trained also the other components of EFs (e.g., McGlinchey et al., 2019; Ringenbach et al., 2016). Danielsson et al. (2015) conducted a meta-analysis on WM training effectiveness in individuals with ID considering both direct effects and generalization to other EFs components. Their results suggested that the mixed approach in which both verbal and visuo-spatial skills are trained best fit with improvements in WM. Recently, McGlinchey and colleagues (2019) suggested that computerized training programs could be benefit for the improvement of inhibition and planning skills, but not on the adaptive behaviour in everyday life in individuals with DS. The latter mentioned study is of particular importance and shows many innovative aspects, stressing the importance to verify that the effectiveness of EF intervention programs in people with DS is also reflected in everyday life skills. A recent meta-analysis on training programs in atypical development – in particular in children and adolescents with ID – indicated that programs based on physical activities showed the best effects on EFs, however they highlight that CA could influence the results with better results on adolescents and children rather than with adults

(Sung et al., 2020). For a more detailed description of training programs implemented in TD children please see Chapter 7 of the present dissertation, while for depth debate on EFs training implemented in individuals with DS please see Chapter 8 of the present dissertation.

1.5 Aims and structure of the present dissertation

As already broadly underlined in the previous paragraphs, inhibitory abilities in individuals with DS is still underinvestigated and reported contradictory results. Moreover, in most studies that assess inhibition in individuals with DS did not differentiate performance across different inhibitory components, whereas they considered inhibition as a unitary dimension. It should be noted that the greater number of studies used only one task to assess inhibition in individuals with DS.

The main aim of the present dissertation is to examine inhibitory abilities in individuals with DS, trying to shed some light on developmental trajectories of these skills in this population. For this reason, the present dissertation follows a specific theoretical background which considers cool and hot EFs as a part of a continuum (Zelazo & Müller, 2002, 2012). Moreover, in line with the literature, we considered inhibition as a multicomponential construct (Howard et al., 2015; Rey-Mermet et al., 2017) in which response inhibition and interference suppression are distinguished starting from 36-48 months in TD children (Ganfoldi et al., 2014). Given the core role of EFs in everyday life, we considered also other crucial components such as the adaptive functioning and autonomies in everyday life (Daunhauer et al., 2017; Sabat et al., 2020).

Starting from this theoretical background, in the first study (Chapter 2) a meta-analysis was conducted in order to explore and to quantify the overall inhibitory profile of individuals with DS compared to TD children matched for a measure of MA (i.e., on general intellectual performance). Furthermore, in order to examine if significant differences emerged between the group with DS and the TD group when a matching for MA was not documented or when specified details on MA was not provided, an additional analysis was conducted. Given the well documented impaired performance of individuals with DS with verbal tasks rather than on visuo-spatial ones (Brock &

Jarrold, 2005; Costanzo et al., 2013; Lanfranchi et al., 2012), two specific moderators were included: the type of stimuli presented (verbal *vs* visuospatial) and the type of response required (verbal *vs* motor). Finally, given the crucial role of developmental trajectories on inhibitory performance in this population, CA was included as moderator. Unfortunately, given the paucity of studies which could be included in the meta-analysis and given the lack of information on the investigated construct, it was not possible to define and differentiate tasks comprised in the research on the basis of the different inhibitory sub-components.

The second study presented and described in depth in Chapter 3, investigated inhibitory subcomponents with a battery of tasks tapping on response inhibition and interference suppression. To this purpose, 32 individuals with DS were matched for a measure of MA with 35 TD children with a mean CA of 5 years old (5TD) and with 30 TD children with a mean CA of 6 years old (6TD). Therefore, the present study aimed to: a) better understand performance on both inhibitory sub-components in individuals with DS, and b) to verify whether a two-factor model best describes inhibitory performance also in TD children aged 5 and 6. Basing on a CFA, composite scores were calculated in order to partially overlap task impurity problems (Friedman & Miyake, 2004).

Given the importance to jointly consider cool and hot EFs, the third study – presented in Chapter 4 – allowed to expand both the sample of individuals with DS and the battery of tasks used to measure the multidimensional construct of inhibition. In particular, four tasks were used to assess response inhibition, two tasks to assess interference suppression, and two tasks to measure delay of gratification. The main goal of the present study was to investigates these components in a sample of children, adolescents, and adults with DS compared to a TD control group matched for a measure of fluid intelligence. The choice to include a wide age range in the sample with DS was related to the fact that the majority of studies investigated the inhibitory construct in children and adolescents with DS, leaving less investigate these components in adulthood. For this reason, a second analysis was performed to cross-sectionally assess different inhibitory dimensions in individuals with DS divided on the basis of their CA. We expected to find impaired performance in the sample with DS on response inhibition, interference suppression, and delay of gratification tasks. When the group with DS was splitted into two sub-groups on the basis of their CA, we expected to find worse performance on average in children and adolescents with DS – compared to adults with DS – in particular on interference suppression, which is the more complex inhibitory dimension (see also Traverso et al., 2018).

Following an accurate analysis of the literature, it emerged that the less investigated inhibitory dimension in individuals with DS is the interference suppression one. To this purpose, the fourth study (see Chapter 5 of the present dissertation) investigated interference suppression in 51 individuals with DS matched for a measure of MA with 71 TD children with an adapted version of the Navon task (Navon, 1977). It is well known that the Navon paradigm is a measure to assess interference suppression, which requires control over the interference experienced when switching from a global to a local dimension (Navon, 1977; Rey-Mermet & Gade, 2017). As suggested by D'Souza et al. (2016) after using the classic Navon-letter paradigm, results could be influenced by the type of stimuli presented. In order to reduce any difficulties with verbal stimuli for individuals with DS, the classic version of the Navon task was adapted using E-prime software. In fact, the task was administrated in a computerized version presenting a non-verbal Navon-shape task, composed by high-familiarity symbols (i.e., hearts and stars) to reduce language-based difficulties. We expected to find that: a) both groups would perform better in the global condition than when responding to local stimuli (Bellugi et al., 2000; Porter & Coltheart, 2006), suggesting a difficulty on interference suppression of the global information in the latter case; and b) the group with DS would be more impaired than the TD group, and more so in the incongruent than in the congruent condition (Borella et al., 2013; Traverso et al., 2018).

After having thoroughly investigated the inhibitory components in people with DS and on the basis of the emerging literature that stresses the need to jointly consider inhibition, WM, and adaptive behaviour (AB) in order to achieve good levels of autonomy in daily life (Daunhauer et al., 2017; Sabat et al., 2020), the fifth study – included in the Chapter 6 of the present dissertation – aimed to examine the relationship between specific aspects of autonomy (i.e., Socialization, Communication, Ability to choose and proactive behaviour, Orientation and behaviour on the road, Use of public transport, Handling money and using shops, Orientation in time, Handling the telephone, Reading-writing skills, Personal hygiene and self-care, and Unexpected situations) and tasks measuring response inhibition, interference suppression, and WM. Furthermore, for the purpose of investigate possible differences in inhibition and WM domains related to different levels of autonomies, the group of individuals with DS was divided in two sub-groups basing on their autonomy levels (i.e., lower levels of autonomy – LA – *vs* medium-to-high levels of autonomy – MHA –). We expected to find: a) a relationship between performance on tasks tapping on different components of inhibition, WM and specific aspects of autonomy; b) worse performance for the LA group compared with the MHA groups in tasks assessing response inhibition, interference suppression, and WM.

The sixth and the seventh studies included in the present dissertation (see respectively Chapter 7 and Chapter 8) aimed to improve EFs, with a specific focus on inhibition and WM skills, both in TD children and in individuals with DS. It is important to note that most of trainings programs implemented to ameliorate EFs in individuals with DS have been created for children of TD with the same MA. This clearly have many implications both in terms of motivation (e.g., some materials proposed could be excessively childish for the adults with DS) and in terms of effectiveness of the training proposed. To this purpose, two separate trainings have been created, one for children with TD and one for the group of individuals with DS. Starting from the training created for TD children (see Chapter 7), the novelty of this training program lies in the fact that it aims to improve both hot and cool EFs and emotion regulation (ER) in children aged 4. A total of 91 children were involved and then they were randomly assigned to a training group or a control group. The present research aimed to at first assess cool and hot EFs and ER in 4-year-old TD children. Secondly, it aims to implement a training program targeting in particular on inhibitory processes and ER. We expected to see: a) a general improvement in cool EFs because WM and inhibition are closely related in this developmental stage (Diamond, 2013; Miller et al., 2012; Traverso et al., 2015), and b) an improvement in ER and hot EFs (Pellizzoni et al., 2019; Weber-Stratton et al., 2013).

To conclude, the Chapter 8 of the present dissertation is dedicated to a specific training program created on the basis of the peculiar inhibitory profile delineate with previous studies and in line with the current literature. Given the crucial relationship between inhibitory sub-components, AB, and autonomy in everyday life, the present training program jointly considered all these components. Therefore, the present research aims to: a) assess inhibitory sub-components and delay of gratification in a group of adults with DS using both laboratory tasks and proxy reports; b) implement a training program with a series of activities created on the basis of the cognitive and behavioural profile of individuals with DS that focuses on response inhibition, interference suppression, and delay of gratification, to ascertain their effects; c) analyse whether the programme had an impact on levels of EFs in everyday life (e.g., Lanfranchi et al., 2017; McGlinchey et al., 2019); d) examine a possible effect of the following training program on everyday autonomies in mainly five areas such as Communication, Spatial and Temporal orientation, Orientation and behaviour on the road, Use of public transport, and Handling money and using shops (see Contardi, 2016). Unfortunately, our implementation was interrupted due to the Covid-19 pandemic emergency that made the present program impossible to carry out. In fact, in Chapter 8 it will be presented only the experimental design and the structure of the intervention, while data are clearly not yet available.

The ***Table 1.1*** summarizes the main information related to the studies carried out and concluded presented in this dissertation (i.e., title of the study, number of participants involved, mean chronological and mental age of the samples, the investigated construct/s, and the main aims of each specific research). Each research will be described in details in the next chapters.

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Table 1.1 Brief summary of the essential information for each study.

Study	N	Mean CA	Mean MA DS (TD)	Constructs	Aims
1. Meta-analysis on inhibition from childhood to young adulthood in people with Down syndrome **(Chapter 2)**	N(DS) = 161 N(TD) = 160	M_{CA} (DS) = 11.8 years M_{CA}(TD) = 5.0 years	M_{MA} (DS) = 5.3 years M_{MA} (TD) = 5.5 years	• Inhibition	1) Explore the inhibitory profile of people with DS (matched for a measure of MA with the TD control group), quantifying their inhibitory difficulties. 2) Analyse if significant differences on inhibitory performance emerged between the two groups when a matching for MA was not provided. 3) Investigate the role of specific moderators such as type of stimuli presented, type of response required, and CA.
2. Response Inhibition and Interference Suppression in Individuals with Down Syndrome Compared to Typically Developing Children **(Chapter 3)**	N(DS) = 32 N(TD5) = 35 N(TD6) = 30	M_{CA} (DS) = 14.4 years M_{CA}(5TD) = 5.6 years M_{CA}(6TD) = 6.2 years	M_{MA} (DS) = 6.9 years M_{MA}(5TD) = 6.6 years M_{MA}(6TD) = 6.2 years	• Response inhibition • Interference suppression	1) Investigate diverse inhibition components (i.e., response inhibition and interference suppression) in TD children and individuals with DS (Gandolfi et al., 2014). 2) Analyse whether the two inhibitory components can be found in TD children at five and 6 years of age.

3. Inhibitory Dimensions and Delay of Gratification: A Comparative Study on Individuals with Down Syndrome and Typically Developing Children **(Chapter 4)**	N(DS) = 51 N(TD) = 71	M_{CA} (DS) = 23.7 years M_{CA}(TD) = 6.17 years	M_{MA} (DS) = 6.7 years M_{MA} (TD) = 7.1 years	• Response inhibition • Interference suppression • Delay of gratification	1) Investigate response inhibition, interference suppression, and delay of gratification in people with DS compared to TD children matched for a measure of MA. 2) Analyse from a cross-sectional perspective developmental trajectories of inhibitory sub-components and delay of gratification in a sample of people with DS clustered in two different groups on the basis of their CA.
4. An adapted shape-based version of the Navon task for comparing interference suppression in individuals with Down syndrome and typically developing children **(Chapter 5)**	N(DS) = 51 N(TD) = 71	M_{CA} (DS) = 23.7 years M_{CA}(TD) = 6.17 years	M_{MA} (DS) = 6.7 years M_{MA} (TD) = 7.1 years	• Interference suppression	1) Test interference suppression in individuals with DS as compared with a TD control group matched on a measure of MA. We assess interference suppression with an adapted non-verbal version of the Navon shape task in an effort to avoid any confounding influence of language issues.
5. The relationship between different levels of autonomy, inhibition dimensions, and working memory	N(DS) = 22	M_{CA} (DS) = 25.3 years	M_{MA} (DS) = 7.7 years	• Response inhibition • Interference suppression • Working memory	1) Investigate the relationship between specific aspects of autonomy (i.e., Socialization, Communication, Ability to choose and proactive behaviour, Orientation and behaviour on the

in people with Down syndrome **(Chapter 6)**				• Autonomy in everyday life	road, Use of public transport, Handling money and using shops, Orientation in time, Handling the telephone, Reading-writing skills, Personal hygiene and self-care, and Unexpected situations) and tasks measuring response inhibition, interference suppression, and working memory 2) Analyse potential differences in the components of inhibition and in working memory performance between two groups of participants with DS, one with lower levels of autonomy, the other with medium-to-high levels of autonomy.
6. Exploring the effect of cool and hot EFs training in four-year-old children **(Chapter 7)**	N(TG) = 42 N(CG) = 49	M_{CA} (TG) = 4.4 years M_{CA} (CG) = 4.4 years		• Response inhibition • WM • Delay of gratification • Emotion regulation	1) Assess cool and hot EFs in a group of four-year-old children. 2) Implement a training program targeting both cool and hot EFs, with a particular focus on inhibitory processes, together with emotion regulation, to ascertain their effects.

CA = chronological age, MA = mental age, DS = Down syndrome, TD = typically developing, 5TD = typically developing group of 5 years of age, 6TD = typically developing group of 6 years of age, TG = training group, CG = control group, EFs = executive functions

CHAPTER 2

Meta-analysis on inhibition from childhood to young adulthood in people with down syndrome

Fontana, M., Usai, M. C., Toffalini, E., & Passolunghi, M. C. (2021). Meta-analysis on inhibition from childhood to young adulthood in people with Down syndrome. *Research in Developmental Disabilities*, *109*, 103838. https://doi.org/10.1016/j.ridd.2020.103838

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 in- formation 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.

2.1 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, & Valles-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 (Gligorovìc & Buha Đurovìc, 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.

2.1.1 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.

2.1.2 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, Posner, & Rothbart, 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.

2.1.3 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, Happè, & 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 (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 aims 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.

2.1.4 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.

2.2 Method

2.2.1 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.

2.2.2 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).

2.2.3 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.

2.2.4 Analytic strategy

We followed the analytic strategy suggested by Borenstein, Hedges, Higgins, and Rothstein (2009) and Schwarzer, Carpenter, and 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 analyzed separately from the accuracy scores. The variance of the effects was calculated using the formula indicated by Schwarzer, Carpenter, and Rücker, (2015, p. 25).

Following Borenstein, Hedges, Higgins, and Rothstein (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).

2.3 Results

2.3.1 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 2.1 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 2.1. A total of 15 studies were used for the additional analysis including those not reporting details on MA matching.

2.3.2 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, Fidler, Daunhauer, and Gerlach-McDonald (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, $|\Delta B|s < 0.03$).

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 4.3–15.2 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-analyzed. 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 2.2) and funnel plot (Figure 2.3) 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).

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-analyzed 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.

2.3.3 Moderators analysis

2.3.3.1 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).

2.3.3.2 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).

2.4 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 et 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, Viterbori, Traverso, & Usai, 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 pre-schoolers may depend on age, accuracy, and type of task. Individuals with DS, like TD pre-schoolers, 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, Mantini, Usai, & Viterbori, 2016; 2018).

2.4.1 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.

2.4.2 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 (Diamond & Lee, 2011; Garon et al., 2008; Zelazo et al., 2013) 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.

2.4.3 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).

2.4.4 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.

2.4.5 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 behavioural 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.

2.5 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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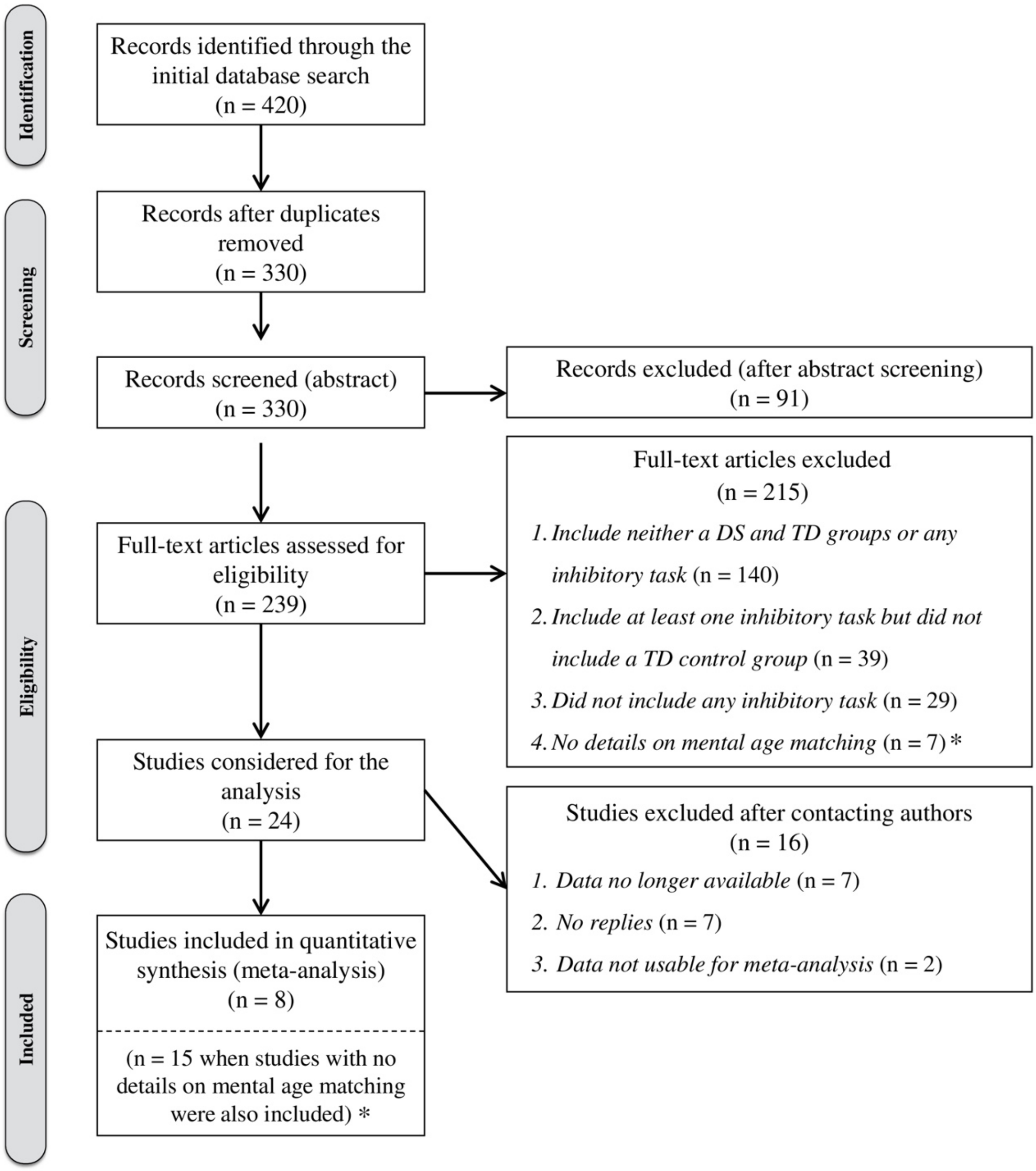
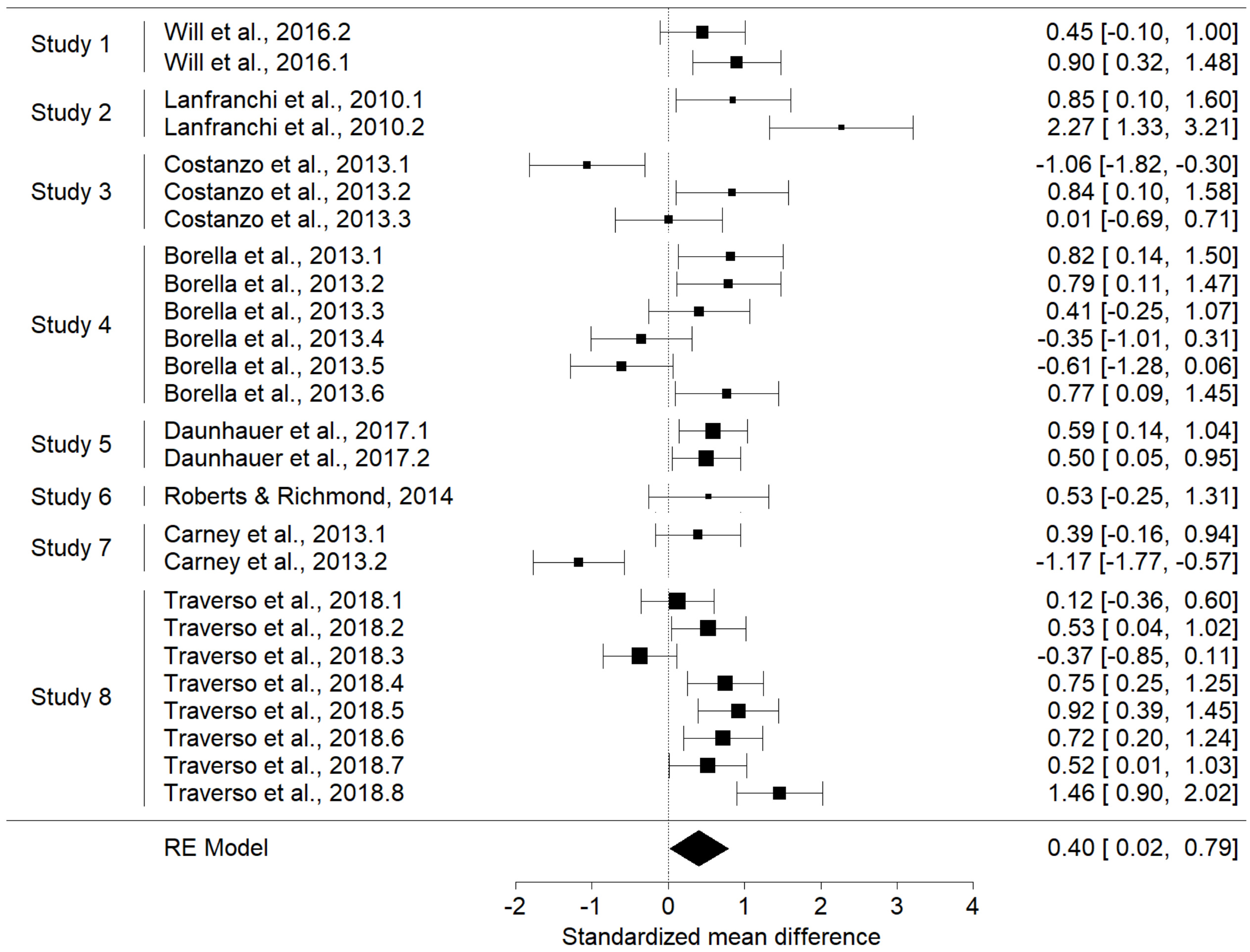
Figure 2.1. Flow chart of the inclusion and exclusion of studies.



* *Studies with no details on mental age matching were subsequently re-included for an additional analysis*

Figure 2.2 Forest plot of the multilevel meta-analytic model for accuracy scores.



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

Figure 2.3. Funnel plot of the multilevel meta-analytic model (all observed effects) for accuracy scores.

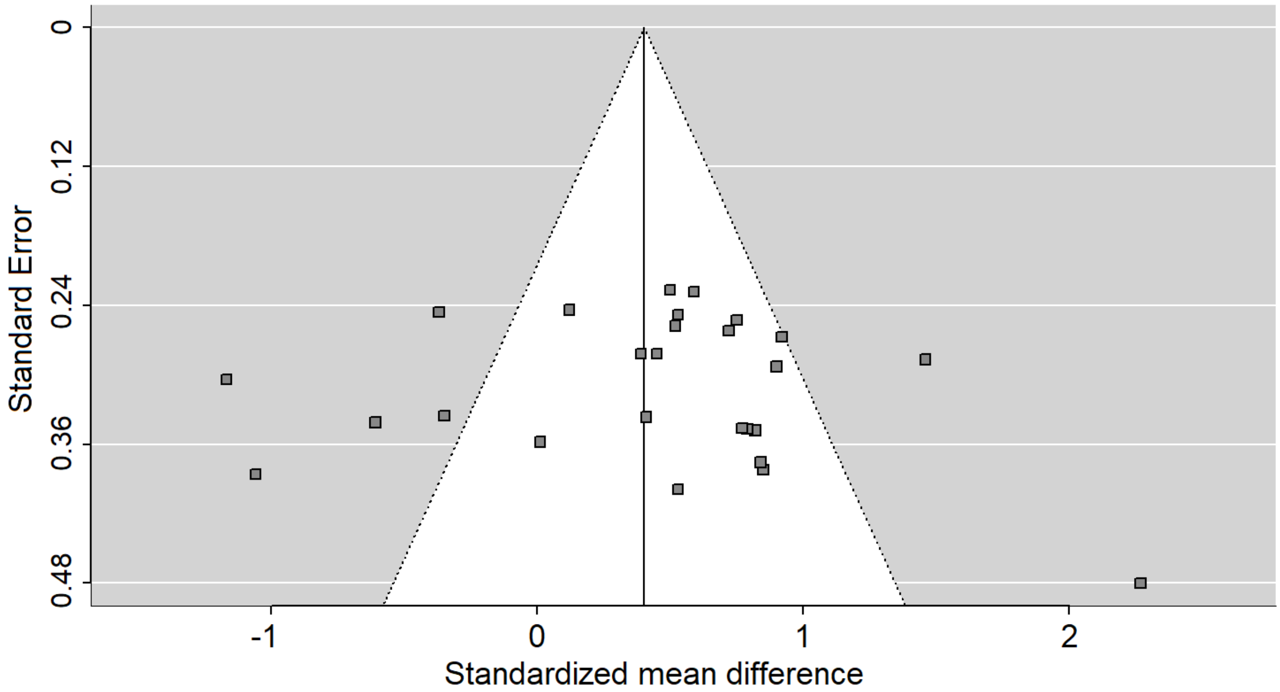


Table 2.1
Characteristics of the studies included in the meta-analysis.

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.

Table 2.2 – supplementary materials
Description of inhibitory tasks provided by authors

Author, year	Inhibitory measures	Description of the tasks
Will et al., 2016	Pony and gator (modified version of the "Bear and Dragon" task - Carlson 2005; Flynn 2007; Garon et al. 2008; Kochanska et al. 1996; Murray & Kochanska 2002-)	*Working memory/inhibition task:* participants were asked to follow motor prompts given by a "nice" pony (e.g., "touch your nose") and to inhibit/ignore instructions from a "naughty" gator (e.g., "cover your eyes"). The task included 10 items randomly assigned. The score was the number of total responses.
	Snack delay (Carlson et al. 2004; Kochanska et al. 2000)	*Inhibitory control task:* the examiner placed a snack under a clear plastic cup. Participants were required to wait until the bell rang to retrieve the snack. Participants had to wait respectively for 5,10, 20 and 15s. The score was the total dysregulated behaviours.
Lanfranchi et al., 2010	Day & Night Stroop (Gerstadt *et al.* 1994)	*Inhibition of prepotent response:* participants were instructed to say "night" when they saw the picture of the sun against a white background, and "day" when they faced with the picture of moon and stars painted on a black card. The task included 16 items and the score was the number of total correct responses.
	Tower of London (Shallice, 1982)	*Planning/inhibition:* participants were in front of a board with three pegs of increasing height. They received three balls (red, blue and green) and coloured pictures of the target that they had to reproduce. Participants were required to recreate the target configuration switching the balls according to the set rules (from a minimum to 3 moves to a maximum of 7 moves). The task included 12 trials and the score was the number of correct responses.

Costanzo et al., 2013	Stroop (Stroop, 1935)	*Inhibition:* in the first neutral condition, participants were instructed to name the colour of 30 circles (blue/green/red), while in the second neutral condition they had to read 30 colour words printed in black. In the third condition (incongruent), participants were asked to name 30 colour word printed in a different colour (e.g., “blue” printed in red colour). The execution time and the error rate for each trial were recorded. An index of interference was also considered as score.
	Go/No-Go (Van der Meere, Marzocchi, & De Meo, 2005)	*Inhibition:* participants were in front of a computer screen and were asked them to press a button as quickly as possible when blue, green and yellow circles appeared but did not press any button when the red one appeared. Response time and correct responses were recorded.
	Tower of London (Shallice, 1982; Italian version: Sannio Fancello et al., 2006)	*Planning/inhibition:* participants were required to solve 12 problems with a maximum of 3 attempts to recreate each trial. The sum of correct responses and the response time were recorded.
Borella et al., 2013	Animal Stroop (adapted from Wright et al., 2003 by Nichelli, Scala, Vago, Riva, & Bulgheroni, 2004)	*Inhibition:* participants faced with a series of animal figures in which the congruency between the head and the body was handled. Participants had to name the animal focusing only on the body. The task included 96 stimuli divided in 4 conditions: 1) the incongruent condition in which the animal’s head was substitute by the head of one of the other animals; 2) the congruent condition in which the stimuli were the same as the prototypes presented to the child during the training phase; 3) the control shape condition in which the head was composed by a geometrical figure; 4) the control face condition in which the head was a caricature of human faces. The response times and the total number of error were recorded. An index was also

		calculated using the following formula: differences between the incongruent and control face condition.
	Proactive Interference (adapted from Borella et al., 2010)	*Resistance to proactive interference:* participants had to listen 16 lists of words regarding 4 blocks of 4 different categories (fruits, animals, body parts, and professions). Each block was composed by 4 word lists of 4 words each, 3 belonging to the same category and 1 to a different category. Participants were required to listen the lists and then to count forward for 16s before the recall phase. Afterwards, they had to recall as many words as possible. The response times and the number of correctly recall words were recorded. An index of proportion of intrusion errors was also considered.
	Directed Forgetting (adapted from Borella, 2006; Borella, Ghisletta, & de Ribaupierre, 2011)	*Response to distracter inhibition:* participants listened 8 unrelated words divided into 2 lists. After hearing the first half of the list, participants received two different instructions: 'Remember All' (the previous list should be remembered for the next test) or 'Forget All' (the previous list should be forgotten in order to concentrate to the relevant list). After a 30s interval in which participants had to draw a sun or a moon, participants had to recall all the items in the two lists. The number of words recalled in the first and in the second half of the list for the two conditions were recorded, while the words recalled in the ''Forget All'' condition were considered as intrusion errors.
Daunhauer et al., 2017	Pony and gator (adapted version of the "Simon Says" task - Carlson 2005; Flynn 2007; Garon et al. 2008; Kochanska et al. 1996; Murray & Kochanska 2002-)	*Working memory/inhibition task:* participants were asked to remember instructions given by a friendly pony and to ignore prompts from the gruff gator. In order to reduce the receptive language demand, authors incorporated familiar actions (e.g., "blow a kiss" and "wave

		goodbye"). The task included 10 experimental trails and the score was the number of total correct responses.
	Snack Task (Carlson, 2005; Carlson et al., 2004; Kochanska et al., 2005)	*Inhibitory control:* participants were sitting in front of a reward (e.g., cheese cracker). The snack was placed under a clear cup and the experimenter asked the participants to wait until a bell was rung to retrieve the reward. Task consists of 4 trials: 5, 10, 20, and 15s delays. The sum of the number of prematurely retrieved or disinhibited behaviours were registered.
Roberts & Richmond, 2014	A-not-B (adapted from Epsy et al., 1999)	*Inhibition/working memory/set shifting:* the experimenter hides a small toy in location A in a box, and then put the box out of sight for 10 seconds. Participants were required to find the toy. If they searched in the correct location for 2 times, the toy will be hided in the location B and so on. The scores were: 1) an index of accuracy (number of trials in which participants correctly searched as a proportion of the total number of 'stay' trials). 2) an index of perseverative responding on switch trials (number of trials where the correctly searched in the new location, as a proportion of the total number of trials in which a post-switch error could have been made).
Carney et al., 2013	VIMI (adapted from Henry et al., 2012)	*Inhibition:* the task was composed of two parts, one verbal and one visuospatial. In the first one the experimenter said either ''doll'' or ''car'' and participants had to repeat the same word for 20 trials. Afterwards, participants had to produce the opposite response for 20 trials (i.e. say ''doll'' if the experimenter said ''car'' and vice versa). The task was the same for the visuospatial task, but the words were replaced by 2 different hand movements: a pointed finger and a clenched fist. The total of errors and the total time were considered.

Traverso et al., 2018	PMFFT (adapted from Kagan, 1966; Traverso et al., 2016)	*Response inhibition:* participants had to find between five options the picture that is the same of the target stimuli. The sum of errors and the latency time were recorded.
	Go/No-Go (adapted from Berlin & Bohlin, 2002)	*Response inhibition:* in this computerized task, participants had to press the space bar when appeared a blue figure, while do not press when it appeared a red figure (24 blue items and six red items). The sum of the correct responses in the "no-go" condition was recorded.
	Fish Flanker (adapted from Ridderinkhof & van der Molen, 1995; Gandolfi et al., 2014; Traverso et al., 2015)	*Interference suppression:* participants was required to respond to a left or right fish presented at the centre of the computer screen by pressing a left or right response button. The fish was flanked by two fishes pointing in the same direction (16 items for the congruent condition) or in the opposite direction (16 items for the incongruent condition). 48 items were randomly presented (16 items per condition, half left and half right). Accuracy and response times in the incongruent condition were recorded.
	Dots (adapted from Diamond et al., 2007; Traverso et al., 2015)	*Interference suppression:* participants had to press on the same side when a heart or a flower appears on the right or left of a computer screen. Participants were told to press on the same side of the heart but on the opposite side of the flower. After a brief training session, in the test session, hearts and flowers were presented randomly. The sum of correct responses and the response time were recorded.

VIMI = Verbal Inhibition, Motor Inhibition Task, PMFFT = Preschool Matching Familiar Figure Task

CHAPTER 3

Response inhibition and interference suppression in individuals with Down syndrome compared to typically developing children

Traverso, L., Fontana, M., Usai, M. C., & Passolunghi, M. C. (2018). Response Inhibition and Interference Suppression in Individuals with Down Syndrome Compared to Typically Developing Children. *Frontiers in Psychology*, *9*. https://doi.org/10.3389/fpsyg.2018.00660

Abstract

The present study aims to investigate inhibition in individuals with Down Syndrome compared to typically developing children with different inhibitory tasks tapping response inhibition and interference suppression. Previous studies that aimed to investigate inhibition in individuals with Down Syndrome reported contradictory results that are difficult to compare given the different types of inhibitory tasks used and the lack of reference to a theoretical model of inhibition that was tested in children (see Bunge et al., 2002; Gandolfi et al., 2014). Three groups took part in the study: 32 individuals with Down Syndrome (DS) with a mean age of 14 years and 4 months, 35 typically developing children 5 years of age (5TD), and 30 typically developing children 6 years of age (6TD). No difference emerged among the groups in fluid intelligence. Based on a confirmatory factor analysis, two different inhibition factors were identified (response inhibition and interference suppression), and two composite scores were calculated. An ANOVA was then executed with the composite inhibitory scores as dependent variables and group membership as the between-subject variable to explore the group differences in inhibition components. The 6TD group outperformed the 5TD group in both response inhibition and interference suppression component scores. No differences were found in both inhibition components between the DS group and 5TD. In contrast, the 6TD group outperformed the DS group in both response inhibition and in the interference suppression component's scores. Summarizing, our findings show that both response inhibition and interference suppression significantly increased during school transition and that individuals with DS showed a delay in both response inhibition and interference suppression components compared to typically developing 6-year-olds, but their performance was similar to typically developing 5-year-olds.

3.1 Introduction

Down Syndrome (DS) is the most common genetic syndrome associated with intellectual disability and affects ~1 in 700 newborns (Sherman et al., 2007; Mégarbané et al., 2009). Individuals with DS seem to have higher psychopathological risk than individuals with other intellectual disabilities (Gath and Gumley, 1986; Collacott et al., 1992; Dykens, 2007; Tassé et al., 2016). Therefore, acquiring more information on the weaknesses and strengths of the neuropsychological profile of individuals with DS is necessary for planning interventions.

Individuals with DS are usually characterized by moderate to severe learning disabilities and relative language impairments, with greater expressive difficulties than receptive ones (Fowler et al., 1994; Abbeduto et al., 2001; Laws and Bishop, 2004; Fidler and Nadel, 2007; Næss et al., 2011). Research on other cognitive abilities has focused mainly on memory resources, particularly working memory (Jarrold et al., 2000; Lanfranchi et al., 2004, 2012; Baddeley and Jarrold, 2007). People with DS have poorer working memory performance than controls, especially on tasks that require verbal processing compared to tasks with visual and spatial stimuli (Jarrold and Baddeley, 1997; Jarrold et al., 1999). This difference seems to be independent of the acoustic deficits typical of DS (Jarrold et al., 2000).

There is widespread agreement about impairments in executive function (Costanzo et al., 2013; Lee et al., 2015), a set of general-purpose control processes that regulate one's thoughts and behaviors (Miyake and Friedman, 2012). However, in the literature examining the cognitive profile of individuals with DS, there is a lack of information about inhibition, one of the core components of executive function (Miyake et al., 2000; Diamond, 2013). Inhibition has been considered to play a central role in cognitive development. Klenberg et al. (2001) claim that the development of basic inhibitory functions may precede the development of more complex cognitive functions. Miyake and Friedman (2012) speculate that inhibition may be a general resource for other executive functions. Because inhibition plays an important role in several cognitive activities, it is reasonable that an investigation into this ability may contribute to explaining cognitive impairments. Nevertheless, to date, only a few studies have examined the diverse inhibition components in individuals with DS, and the results are not consistent.

3.1.1 Inhibition development

Inhibition processes generally refer to the ability to control one's mental processes and responses, to ignore an internal or external prompt and to perform an alternative action (Diamond, 2013). Studies that focus on inhibition have commonly described this ability as a multi-componential construct that includes different dimensions that are useful to perform different tasks (Dempster, 1993; Harnishfeger, 1995; Nigg, 2000; Diamond, 2013). For example, Diamond (2013) argues that inhibition comprises the ability to control irrelevant information at the level of thought and memories (cognitive inhibition), the ability to manage irrelevant data when acquiring information (inhibition at the level of attention), and the ability to control an action at the

level of behavior (response inhibition). The concept of inhibition has been widely used and studied (i.e., Dempster and Brainerd, 1995). However, the psychometric construct of inhibition has been investigated only in recent decades (i.e., Friedman and Miyake, 2004). Using a latent variable approach, Rey-Mermet et al. (2017) demonstrated that a two-factor model in which two components, the inhibition of prepotent responses (the ability to suppress dominant responses) and the resistance to distracter interference (the ability to ignore distracting information or to suppress competing response tendencies), were distinguishable best explained the data observed in young and older adults (see also Stahl et al., 2014). However, this evidence collected with adults may not be applied to the early stages of development. As argued by Friedman and Miyake (2004) and observed by Bunge et al. (2002) in an fMRI study, children and adults may be characterized by different inhibition processes. Although a response inhibition component was not distinguishable in study by Friedman and Miyake (2004), in Bunge et al. (2002) study, different activation patterns for interference suppression and response inhibition were observed in children.

Recently, Gandolfi et al. (2014) proposed an empirical investigation of the latent organization of inhibitory processes in early childhood. They suggested that a unitary model was more useful for describing inhibitory processes in younger children (24- to 32-month-old children), whereas a two-factor model showed the best fit in children aged 36–48 months. Specifically, in 3- to 4-year-old children, Gandolfi et al. (2014) distinguished a response inhibition component from an interference suppression component (see also Bunge et al., 2002; Martin-Rhee and Bialystok, 2008; Cragg, 2016, in which interference at the level of response and interference at the level of the stimulus were considered, corresponding to what we define as the response inhibition and interference suppression components, respectively). The first component, "response inhibition," significantly predicted the children's performance in tasks such as Go-No/Go, in which the child is presented with a stimulus that activates an automatic response that must be suppressed to give the correct response. The second component, "interference suppression," explained performance in tasks such as the Flanker task, in which the child is presented with a stimulus that shows ambivalent data (the target and the flankers). In these tasks, the child must control the interference due to the stimulus characteristic and focus on the relevant information to give the correct response. This evidence may suggest that diverse inhibition components may emerge at different stages of development. For example, interference suppression may emerge after response inhibition, and it may be responsible for the differences between younger and older children in performing tasks in which interference must be controlled.

3.1.2 Inhibition in Down syndrome

Reviewing the literature of the last 20 years, to the best of our knowledge, we were able to identify 10 studies in which at least one inhibition task was proposed to a sample of individuals with DS (Table 3.1).

Although the study designs were comparable, contradictory findings emerged. In some studies, the DS group performed significantly worse on the inhibitory task administered compared to the control group (Lanfranchi et al., 2010; Schott and Holfelder, 2015; Amadó et al., 2016). In other studies, no difference emerged (Pennington et al., 2003; Cornish et al., 2007; Carney et al., 2013).

Finally, in some studies, mixed results were reported (Rowe et al., 2006; Brunamonti et al., 2011; Borella et al., 2013; Costanzo et al., 2013). For example, Borella et al. (2013) found a significant difference in accuracy on all three tasks, although no difference emerged in response time in one of the tasks. In Costanzo et al. (2013), a difference was found for the Stroop task but not for the Go-No/Go task.

These inconsistencies seem to highlight the need to differentiate performance across inhibition components rather than by considering a unitary inhibition dimension. Nevertheless, comparing these results to derive conclusions about the development of the inhibition component in DS is not easy. In most studies, only one task was used. Therefore, contradictory findings may be due to the differences in the tasks used. For example, in both Amadó et al. (2016) and Lanfranchi et al. (2010), accuracy in a Day-Night Stroop task was considered, and in both studies, a significant difference between the DS and the control group was reported. However, these consistent results may involve non-inhibition abilities necessary to perform the task or diverse inhibition components required by the Stroop task that are not assessed with other inhibition tasks. Conversely, in Costanzo et al. (2013) and Borella et al. (2013), a Stroop task was used, and these two studies reported different results using response time and accuracy as indicators. In Costanzo et al. (2013), the DS sample differed from the control group in response time but not in accuracy, whereas the opposite pattern was observed in Borella et al. (2013). As reported by Friedman and Miyake (2004), several problems arise when single and raw inhibition scores are considered. Moreover, although these studies provide useful information about diverse cognitive abilities in DS individuals, the fact that only one task was used to assess inhibition does not allow us to investigate the development of the diverse inhibition components. Only the study by Borella et al. (2013) used three inhibition tasks to assess the three inhibition components initially hypothesized for adults by Friedman and Miyake (2004). In the other studies, the proposed tasks are generally defined as inhibition tasks without providing clarification of the specific component that may be assessed with each task. If we consider the model proposed and verified for children (see Bunge et al., 2002; Gandolfi et al., 2014) in which response inhibition and interference suppression were identified, previous studies on individuals with DS have mostly investigated response inhibition (see inhibition task column in Table 3.1, in which diverse response inhibition tasks were included, such as the Go-No/Go task, the Finger Tapping task, and the Stroop task) rather than the interference suppression component of inhibition. In summary, there is a need for a study that analyses the development of response inhibition and interference suppression components (following the two-factor model proposed and tested with children by Gandolfi et al., 2014) in a DS sample.

3.1.3 The present study

The current study aims to investigate diverse inhibition components in typically developing children and individuals with DS. In agreement with several authors (Friedman and Miyake, 2004; Diamond, 2013), we consider inhibition as having a multicomponent nature, and we hypothesize that at least these two components will be identifiable at this stage of development in TD children (Gandolfi et al., 2014). Specifically, we aim to verify whether two inhibition components, response inhibition and interference suppression, can be found in typically developing children at five (5TD) and 6 years of age (6TD). In addition, considering that inhibition abilities undergo rapid changes in the typical population at the ages considered (Davidson et al., 2006), we investigate whether differences in response inhibition and interference suppression efficiency may be found between TD children aged 5 and 6 years. Moreover, response inhibition and interference suppression are examined in individuals with DS with the same mental age of the two TD groups. Our aims are to investigate whether the DS and the TD groups differ in inhibition performance and to acquire more information concerning inhibition development in DS by comparing this group with two TD groups that may differ in the level of inhibition development.

In contrast to previous studies in which only single task scores were considered, we aimed to at least partially overcome the problems due to task impurity (see Friedman and Miyake, 2004) by creating a composite score for each inhibition component. The difference between typical children of 5 and 6 years and individuals with DS matched for mental age is examined with consideration of these composite scores. Borella et al. (2013) reported general impairment in the diverse inhibition components investigated; thus, we may hypothesize that significant differences will emerge in both components. However, Borella et al. (2013) refer to an adult model of inhibition, whereas we aim to investigate for the first time two inhibition components that have been identified in typical children in a sample of youth with DS.

3.2 Methods

3.2.1 Participants

A final sample of 97 individuals belonging to three groups took part in this study. Thirty-two individuals with Down Syndrome (DS), 22 girls and 10 boys with a mean age of 14 years and 4 months (M_{age} 173.75 in months, *S.D.* 65.17, range: 73–299 months), were included in the DS group. Thirty-five typically developing children, 18 girls and 17 boys with a mean age of 5 years and 6 months (M_{age} 67.37 in months, *S.D.* 2.85, range: 62–71 months), were included in the typically developing control group of 5-year-olds (5TD). Thirty typically developing children, 13 girls and 17 boys with a mean age of 6 years and 2 months (M_{age} 74.40 in months, *S.D.* 4.42, range: 72–84 months), were included in the typically developing control group of 6-year-olds (6TD). Individuals with DS had trisomy 21 without mosaicism and were recruited from two treatment centers in the north of Italy. Typically developing children were recruited from different educational services in the same area. None of the children had a history of neurological impairment or developmental disabilities.

3.2.2 Procedure

A battery of inhibition tasks was administered to the three groups by trained psychologists. All participants were tested individually in a quiet room in two separate testing sessions, each lasting ~20–30min, at an interval of 3–4 days. The DS group was assessed in the treatment center, and the TD children were tested at educational services. The families were previously informed about the aims of the study and about the activities in which the participants were involved. A written informed consent form was completed by the parents before testing began.

All tasks consisted of well-known inhibition paradigms. These tasks have been widely used with children and did not show any floor or ceiling effect in the mental age range of interest (Davidson et al., 2006; Traverso et al., 2015). These tasks minimize the non-executive function abilities required. Basic knowledge (such as colors) and simple responses (such as pointing or pressing) are required to perform the tasks. Finally, all tasks (except for the Go/No-Go) included practice trials before the test began. The examiner gave the instructions and then conducted the practice trials to verify whether the child had comprehended the requirements of the task.

3.2.3 Measures

The Colored Progressive Matrices Test (Raven, 1947; Belacchi et al., 2008) was administered to measure fluid intelligence and was used as a screening measure to match fluid intelligence between the DS group and the two TD groups. It is a multiple- choice test of abstract reasoning in which the child is required to complete a geometrical figure by choosing the missing piece among six possible drawings. The tasks included 36 items. The items varied in difficulty. The score was the number of correct responses (CPM, expected range 0–36).

3.2.3.1 Inhibition Battery

To assess inhibition, the following tasks were administered.

Go/No-Go task (adapted from Berlin and Bohlin, 2002). The Go/No-Go task is a well-known paradigm that tests the abilities of both adults and children to inhibit prepotent responses (Durston et al., 2002; Verbruggen and Logan, 2008). The children were asked to restrain an automatic response. While in front of a computer screen, the child was instructed to press the space bar according to the instructions given by the examiner for the following condition: “Press the space bar when you see a blue figure; do not press when you see a red figure” (24 blue items and six red items). The percentage of go responses was 80%. The stimulus duration was 3,000ms, and the blank page that appeared after each stimulus lasted 1,000 ms. The sum of the correct responses in the no-go condition was recorded (Go/No-Go Accuracy, expected range 0–6). Test-retest reliability (Pearson's r) was calculated in a sample of 75 typically developing children (age range 62–76 months, M_{age} = 68.64; *S.D.* = 3.5) was 0.55, $p < 0.0005$ (unpublished results from the data set used in Traverso et al., 2015). Cronbach's alphas calculated in the present study were 0.71 in the TD group and 0.83 in the DS group.

Preschool matching familiar figure task (PMFFT, adapted by Kagan, 1966; Traverso et al., 2016). This task measures the child's ability to restrain impulsive responses and to compare the target with all of the pictures by shifting attention from the target to each alternative. The children were asked to perform 14 trials, selecting among five different alternatives the figure that was identical to the target picture at the top of the page. The number of errors (PMFFT Errors, expected range 0–56) and the mean latency between the presentation of the item and the child's response (PMFFT Time, expected range 0-no limit) were recorded. Cronbach's alphas calculated in a sample of 174 children (M_{age} = 60.04) were 0.67 for PMFFT Errors and 0.95 for PMFFT Time (Traverso et al., 2016). Cronbach's alpha calculated in the present study for PMFFT Accuracy was 0.76 in the TD group and 0.85 in the DS group. Cronbach's alpha for PMFFT Time was 0.94 for both groups.

Fish flanker task (adapted from Ridderinkhof and van der Molen, 1995; Gandolfi et al., 2014; Traverso et al., 2015). The Flanker task is a well-known paradigm that is used to evaluate the ability to inhibit irrelevant interfering stimuli (Eriksen and Eriksen, 1974; Kramer et al., 1994). The children were required to respond to a left or right fish presented at the center of the computer screen by pressing a left or right response button. The fish was flanked by two fishes pointing in the same direction (congruent condition, 16 items) or in the opposite direction (incongruent condition, 16 items). After a brief training consisting of four items (two of each condition), 48 items were randomly presented (16 items per condition, half left and half right). A warning cross (500 ms in duration) preceded the stimulus. After the response, the screen turned blank for 500 ms. Accuracies (Flanker Accuracy, expected range 0–16) and response times (Flanker Time) in the incongruent condition were recorded. Test-retest reliability (Pearson's r) calculated in a sample of 43 typically developing children (age range 62–75 months, M_{age} = 68.60; *S.D.* = 3.5) was 0.42, $p = 0.002$ and 0.56, $p < 0.001$ for Flanker Accuracy and Flanker Time, respectively (Usai et al., 2017). Cronbach's alphas calculated in the present study for Flanker Accuracy were 0.96 in the TD group and 0.81 in the DS group. Cronbach's alphas for Flanker Time were 0.96 in the TD group and 0.93 in the DS group.

Dots task (adapted by Diamond et al., 2007; Traverso et al., 2015). This task is a high cognitive conflict task (see Diamond et al., 2007; Diamond and Lee, 2011). A heart or a flower appears on the right or left of a computer screen. The child is told that he must press on the same side of the heart but on the opposite side of the flower, which requires inhibiting the tendency to respond on the side where the stimulus appeared and to control the response based on which stimulus appears. After a brief training session with heart and flower items, the test began, and hearts and flowers were intermixed in the test. The sum of correct responses (Dots Accuracy, expected range 0–20) and the response time (Dots Time) were recorded for each child. Test-retest reliability (Pearson's r) calculated in a sample of 43 typically developing children (age range 62–75 months, M_{age} = 68.60; *S.D.* = 3.5) was 0.62 ($p < 0.001$) for Dots Accuracy and 0.72 ($p > 0.\ 001$) for Dots Time (Usai et al., 2017). Cronbach's alpha calculated in the present study for Dots Accuracy was 0.97 in the TD group and 0.80 in the DS group. Cronbach's alpha for Dots Time was 0.89 in the TD group and 0.85 in the DS group.

3.2.4 Statistical Analyses

Descriptive analyses and ANOVAs on CPM and inhibitory measures were conducted to compare the three groups' performance considering both accuracy and response time scores. The relation between accuracy and response time was investigated with bivariate correlations. A confirmatory factor analysis (CFA) was performed using the TD group's inhibitory task scores to verify the characteristics of the inhibition construct in early childhood. Multiple fit indices were considered to compare models (for an extensive description, see, e.g., Schermelleh-Engel et al., 2003): the X^2 statistic, the Comparative Fit Index (CFI), the root mean square error of approximation (RMSEA), the standardized root mean squared residual (SRMR), the Akaike Information Criterion (AIC), and the Bayesian information criterion (BIC). The X^2 test was used to evaluate the appropriateness of the CFA model. Non-significant X^2 values indicated a minor difference between the covariance matrix generated by the model and the observed matrix and thus an acceptable fit. CFI values > 0.97 are indicative of a good fit, whereas values > 0.95 may be interpreted as an acceptable fit (Schermelleh-Engel et al., 2003). RMSEA values ≤ 0.05 represent a good fit, values between 0.05 and 0.08 represent an adequate fit, values between 0.08 and 0.10 represent a mediocre fit, and values > 0.10 are not acceptable (Browne and Cudeck, 1993). The SRMR is the square root of the averaged squared residuals (i.e., the differences between the observed and predicted co-variances). SRMR values < 0.10 are acceptable; however, values lower than 0.05 represent a good fit (Schermelleh-Engel et al., 2003). Based on the CFA results, composite scores were calculated as the mean of the inhibitory z-score to represent the latent inhibitory dimensions. Finally, an ANOVA was conducted with the composite inhibitory scores as dependent variables and group membership as the between-subject variable to explore group differences in the inhibition components.

3.3 Results

Descriptive statistics and ANOVA results for the three groups are shown in Table 3.2. A univariate analysis of variance showed no significant difference in the CPM score. In contrast, significant differences among the groups were found for all the inhibition tasks with the exception of the Dots Time score.

Post-hoc tests using Bonferroni correction revealed that 6- year-olds outperformed 5-year-olds in PMFFT Errors (6TD made fewer errors than 5TD), Flanker Accuracy and Dots Accuracy. The DS group showed high variability in all tasks. This group performed worse than the 6TD group but was similar to the 5TD group in PMFFT accuracy. The opposite was observed for PMFFT time, and the DS group showed a similar response time to the 6TD and a higher response time than 5TD. A significant difference emerged in the Go/No-Go task between the 6TD and DS groups; however, this difference disappeared when a mathematical transformation (exponential function, Kline, 2005) was applied to the Go/No-Go raw score to obtain acceptable skewness and kurtosis parameters. For Flanker Accuracy, the DS group showed similar accuracy scores to the two TD groups and a higher response time than both the 5TD and the 6TD groups. Finally, the DS group showed worse performance in Dots Accuracy than 5TD and 6TD, and no differences emerged in Dots Time.

Zero-order correlations among tasks are reported for the two TD groups (Table 3.3) and the DS group (Table 3.4).

As expected, the inhibition task scores were not highly related (Willoughby et al., 2015). In the 5TD group, a significant association emerged between performance in the PMFFT (Errors) and the Go/No-Go tasks. In the 6TD group, the Dots Accuracy was positively correlated with the Flanker Accuracy, and the Dots Accuracy was related to the Go/No- Go performance. In the DS group, performance in the PMFFT (Errors) and the Go/No-Go tasks were associated, and the Flanker Accuracy was related to both the PMFFT (Errors) and the Go/No-Go Accuracy. Accuracy and response time correlated significantly in both the 5-year-old (r ranged from 0.347 to 0.592) and the 6-year-old (r ranged from 0.391 to 0.754) groups. However, in the DS group, only the Dots Accuracy and the Dots Time scores were related ($r = 0.372$). The CPM performance was associated with the PMFFT Time and the Flanker task (Time and Accuracy) in the 6TD group, no significant association emerged considering the 5TD group, and CPM was related to the PMFFT Time in the DS group. Finally, age was significantly related only to the PMFFT time in the 5TD group.

3.3.1 Identifying the inhibitory components

To verify whether the two-factor model, in which response inhibition and interference suppression were distinguished, would be more useful to explain the observed data than a one- factor model (Figure 3.1), a series of CFAs based on raw data were performed using Mplus software (version 7.4) (Muthén and Muthén, 2007).

The unitary model had mediocre or unacceptable fit indices: $\chi^2 = 5.014$ $p = 0.082$, CFI = 0.872, SRMR = 0.060, RMSEA = 0.152, and 90% CI = [0.000, 0.325]. The two-factor model (Figure 3.1) showed the best fit: $\chi^2 = 0.556$ $p = 0.456$, CFI = 1.000, SRMR = 0.018, RMSEA = 0.000 and 90% CI = [0.000, 0.295]. All the factor loadings were significant (*t* values > 2).

3.3.2 Investigating the inhibitory difference in DS and TD Groups

Two composite scores representing response inhibition and interference suppression were calculated as the mean of the z- scores as follows: the z-score average of PMFFT Errors and Go/No-Go task Accuracy for response inhibition and the z- score average of Flanker Accuracy and Dots Accuracy for interference suppression (Table 3.5). These composite measures can be considered formative indicators of the two inhibitory factors found with the previous EFA (Willoughby et al., 2015). The results of an ANOVA conducted with the two composite inhibitory measures as dependent variables and group membership as the between-subjects variable showed that the three groups differed in both response inhibition, $F_{(2,96)} = 8.363$ $p < 0.001$, and interference suppression, $F_{(2,96)} = 10.530$ $p < 0.001$. The 6TD group outperformed the 5TD group in both the response inhibition ($p = 0.008$, $d_{Cohen} = 0.94$) and interference suppression ($p = 0.001$, $d_{Cohen} = 0.83$) components. No differences were found in either inhibition component between the SD and 5TD groups. In contrast, the 6TD group outperformed the DS group on the response inhibition component score ($p = 0.001$, $d_{Cohen} = 0.96$) and the interference suppression component score ($p < 0.001$, $d_{Cohen} = 1.15$).

3.4 Discussion

The main goal of this study was to investigate diverse inhibition components in children and youth with DS compared to two groups of typically developing children aged 5 and 6 years matched for mental age. Specifically, we aimed to focus on response inhibition and on interference suppression components (see Bunge et al., 2002; Gandolfi et al., 2014). In contrast to previous studies in which only single task scores were examined, we considered both raw scores and composite scores as formative indicators of these two components, referring to a theoretical model of inhibition that was tested in children (Gandolfi et al., 2014).

3.4.1 Inhibition in children with typical development

First, the performance of the two typically developing groups was analyzed. Although inhibition development has been widely documented and investigated in childhood in preschool more than in the transition to school (Carlson, 2005; Romine and Reynolds, 2005; Davidson et al., 2006; Garon et al., 2008), the developmental trajectories of this ability and its components are not yet clear. To acquire more information on atypical development, we argue that it is important to focus on inhibition changes in typically developing children.

Concerning single tasks, our results showed that children 6 years of age were more accurate than 5-year-olds in most of the tasks, although they did not have significant differences in general cognitive functioning measured with CPM. These findings are consistent with previous studies that documented a rapid improvement in accuracy on similar tasks in this age range (Davidson et al., 2006; Traverso et al., 2016). Moreover, the older children significantly increased their response time in the Preschool Matching Familiar Figure Task. In all three tasks in which response time was registered, it was significantly positively related (higher the time, greater the accuracy) to accuracy in both the 6-year-olds and the 5-year-olds. In middle childhood and adulthood, low response time is considered an index of a high level of inhibition. In contrast, Gerstadt et al. (1994) showed that in early childhood, children who took longer to respond were more likely to be correct. Diamond et al. (2002) demonstrated that it is possible to increase accuracy by encouraging children to wait before answering in a Stroop task, and some authors argue that the time is useful because it permits the dissipation of the prepotent response in children (Simpson et al., 2012; Ling et al., 2016). In an investigation of the performance of 3- to 6-year-old children on the Preschool Matching Familiar

Task, in which no instruction to wait before answering was given, Traverso et al. (2016) observed that response time and accuracy were not related until the age of four and a half years. These results suggest that the interpretation of the time response may depend on age, accuracy, and task; consequently, it may not be a valid index of cognitive efficiency when these other parameters are not considered, at least in childhood (see Davidson et al., 2006; but see studies, i.e. Tamm et al., 2012), in which an application of ex Gaussian distribution to response time allowed the achievement of more fine-grained analyses of the distribution and consequently obtained much more information on cognitive profile than using raw response time, which was characterized by high variability and was not normally distributed.

As expected, the inhibition tasks did not correlate with each other (Willoughby et al., 2015; Rey-Mermet et al., 2017) in all three groups. Nevertheless, according to previous studies (see Gandolfi et al., 2014), the CFA demonstrated that a two- factor model in which response inhibition (Go/No-Go task and Preschool Matching Familiar Figure Task indicators) and interference suppression (Flanker Accuracy and Dots Accuracy indicators) were distinguishable best explained the data observed. In the Go/No-Go task and the Preschool Matching Familiar Figure Task, the child is required to focus on one attribute of the stimulus. In the Go/No-Go task, the child must look at the color of the figure and be able to control the response to press the spacebar. In the Preschool Matching Familiar Figure Task, the child must be able to consider the target and then the figure before pointing with the finger. In both tasks, the child is required to press/point or not to press/point according to the stimulus presented. Given the large majority of go stimuli and the diverse figures that need to be compared in the Preschool Matching Familiar Figure Task, in these tasks, the child usually must stop an automatic response or an impulsive tendency. In contrast, in both the Flanker Task and the Dots Task, the child must always give a response (press a computer key). Nevertheless, the child must analyse the type of stimulus that is presented to evaluate what type of response is correct. The stimuli presented are particularly challenging. In the Flanker Task, the child must be able to focus on the central fish; in the Dots Task, the child must focus on the type and side of the stimulus. Whereas, in the first type of tasks the child must decide to respond or not consider the stimulus, in the latter tasks, the child must choose between to different responses by managing the complexity of the stimulus. In these tasks, the child must suppress distracting information as well as competing response tendencies. Following the CFA, two composite scores were calculated as a formative index of response inhibition and interference suppression components. As suggested by Willoughby et al. (2015), formative indices may be a useful method to investigate EF development. However, it must be noted that this conceptual framing is consistent with the characterization of EF as a latent variable that is defined by (rather than giving rise to) individual performance across a set of performance-based tasks. Our results show that older children obtained higher scores than younger children in both response inhibition and interference suppression. These results may suggest that from 5 to 6 years of age, children increase both their ability to control an automatic response and their ability to manage interference. Previous studies have shown that performance on response inhibition tasks such as the Go/No- Go task undergoes significant changes in middle childhood (Brocki and Bohlin, 2004; Cragg and Nation, 2008). Similarly, an increase in performance on tasks that are supposed to require interference suppression was previously observed in middle childhood studies (Hommel et al., 2004). Both components improve during school transition, although Gandolfi et al. (2014) suggested that interference suppression emerges after response inhibition in pre-schoolers, and Cragg (2016) claimed that the improvements in performance on inhibition tasks in middle childhood may be due to development in what we define as interference suppression rather than response inhibition.

3.4.2 Inhibition in individuals with Down Syndrome

With regard to task accuracy, the DS group showed worse performance than the 6-year-olds on the Preschool Matching Familiar Figure Task and worse performance than both groups in the Dots task. No differences were observed in the Go/No- Go task transformed variable (although a difference emerged in the raw score) and in the Flanker Task accuracy. Moreover, the DS group had a higher response time than the 5-year-olds on the Preschool Matching Familiar Figure Task and a higher response time than both control groups on the Flanker task. This inconsistent pattern is in line with the inhibition literature (Rey-Mermet et al., 2017) and with studies that have found high variability on cognitive tasks in the atypical development population (i.e., Tamm et al., 2012; van Belle et al., 2015). With reference to previous studies, as in Costanzo et al. (2013), no differences were observed in the Go/No-Go task, whereas a significant difference emerged in other tasks requiring response inhibition (although in tasks different from the tasks we used; see Lanfranchi et al., 2010; Schott and Holfelder, 2015; Amadó et al., 2016). For interference suppression tasks, to our knowledge, only a study by Merrill and O'dekirk (1994) used a Flanker paradigm, and individuals with DS showed more interference caused by the flankers (and higher response time) than controls. Otherwise, no difference emerged in our study.

One possible explanation for these mixed results may involve the non-executive abilities required by the task. In the Merrill and O'dekirk study, the flankers were letters; therefore, we cannot exclude the possibility that their results were due to the DS group's difficulties in verbal elaboration. Costanzo et al. (2013) explained their mixed results by arguing that the differences were due to the visual vs. verbal stimuli. However, in our study, the DS group performed worse on tasks in which visual stimuli must be processed (i.e., Preschool Matching Familiar Figure Task). In the Flanker Task, in contrast to the other tasks, the examiner used a brief story-telling paradigm to explain what the child was expected to do. Thus, it is possible that the children were more motivated to perform the Flanker task than the other tasks and that they were helped by a practical story rather than arbitrary and abstract rules for the task. Another possible explanation involves the difference in other executive demands of the task. For instance, the Dots task and the Preschool Matching Familiar Figure Task may require higher working memory than the other two tasks. Nevertheless, according to Munakata et al. (2011), the child needs to actively maintain the goal of the task in working memory in all types of inhibition tasks.

To discuss these mixed results, it is helpful to reflect on which variable was considered (accuracy vs. response time). Previous studies considered both accuracy and response time, and, as in our study, mixed results were reported. Nevertheless, it must be noted that in our study, accuracy was unrelated to response time in both the Flanker task and the Preschool Matching Familiar Task. This evidence may suggest that as early pre-schoolers (Traverso et al., 2016), individuals with DS are not able to control response time to be more accurate; thus, response time may not be a useful index of executive control in this population.

We speculate that focusing on single task differences makes it difficult to investigate the efficacy of the inhibition components (see Miyake et al., 2000; Willoughby et al., 2015). Consequently, we prefer to focus on inhibition composite scores as indices of response inhibition and interference suppression. When composite scores were considered, the DS group performed similarly to the younger children using both components. In contrast, a significant difference emerged between the older children and the DS group in both components. These results suggest that individuals with DS show a deficit in both response inhibition and interference suppression components when compared with a TD population that shows more mature inhibition abilities than the younger group of TD children. In previous studies, most of the tasks used required response inhibition. Our studies on the response inhibition component confirmed the evidence provided by Amadó et al. (2016), Lanfranchi et al. (2010), and Schott and Holfelder (2015). However, few studies have examined the interference suppression component. Moreover, to the best of our knowledge, this is the first study in which individuals with DS were compared with two typically developing groups at different stages of development.

In summary, our findings demonstrate that individuals with DS show a delay in inhibition development, but their performance is similar to the typical development of 5-year- old children. This evidence is consistent with the study by Borella et al. (2013), in which individuals with DS showed difficulties in tasks assessing diverse inhibition components. Moreover, it should be noted that even though differences emerged between the groups, the three groups had the same level of general cognitive functioning. These results suggest that significant differences in inhibition abilities may characterize groups with similar levels of general cognitive functioning in typical development.

Consequently, when differences in individuals with DS and typically developing children are investigated, it is possible that mixed results will emerge due to the age of typically developing children with similar cognitive functioning, which may be characterized by diverse levels of inhibition development.

3.4.3 Limitations and future directions

There were some weaknesses in the current study that should be noted. First, although this study aimed to focus on inhibition, it would have been useful to control for other non-executive or executive abilities, such as working memory. Second, although the formative indices may represent a useful methodology to investigate executive functions, in this study, after testing the inhibition model on typical-developmental children with an EFA, we assumed that the inhibition construct was similar in both typical and atypical development. Increasing the sample size would be useful to examine findings observed using reflective and formative inhibition indices (Willoughby et al., 2015) in individuals with DS. Third, the DS group was matched for mental age to the typically developing children. Nevertheless, the DS group showed high variability in chronological age. Consequently, high variability in environmental factors that may have affected inhibition development must be considered. For example, when a large age range is considered, it could be useful to add information concerning the type of treatment and support received and as well as information on differences in treatment that may depend on the cohort to which the subject belongs. To minimize the effect of confounding factors, in future research, it would be useful to consider DS samples with reduced chronological and mental age ranges or to include chronological age-matched TD comparison groups (Godfrey and Lee, 2018).

3.5 Conclusion

To the best of our knowledge, in the last 20 years, only ten studies have examined the inhibition abilities of individuals with DS. These studies reported contradictory results and generally used only response inhibition tasks without referring to a theoretical model of inhibition (see Borella et al., 2013 for the only exception in which an adult model was considered). This is the first study in which different inhibition tasks were used to investigate two inhibition components with reference to a model of inhibition tested in children (Gandolfi et al., 2014). Specifically, in the current study, we refer to response inhibition as the ability to control a predominant response and suppressing interference as the ability to respond to one task attribute and to inhibit the response to another attribute. Our results show that individuals with DS show a delay in both of the evaluated inhibition components. Given the importance of inhibition for other cognitive abilities (i.e., working memory, see Lustig et al., 2001; intelligence, see Lee et al., 2015), this evidence suggests that both the ability to control a response and the ability to manage interference must be supported in individuals with DS. More generally, we argue that investigating inhibition in individuals with DS is preferable to using diverse inhibition tasks to achieve information on diverse inhibition components. As suggested by Morra et al. (2017), it is important to pay attention to the way that inhibition tasks are classified based on theoretical assumptions.

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Table 3.1. Previous studies examining inhibition in individuals with Down syndrome.

Authors & Aims	*Sample*	*Investigated skills*	*Inhibition Tasks*	*Results*
Pennington et al., (2003). Evaluate hippocampal and prefrontal functions in individuals with DS.	N=56 (28 DS and 28 TD) matched for MA. Age: DS average CA=14.7 years; TD average CA=4.9 years.	Inhibition; verbal and visual long-term memory; planning; fluency; spatial and verbal short-term memory.	Inhibition: Stopping task (Logan, Cowan, & Davis, 1984; Logan, Scachar & Tannok, 1997) Accuracy was recorded.	Inhibition: no significant difference between DS group and MA control group in stopping task. Effect size d_{Cohen}= -.63.
Rowe et al., (2006). Investigated EF in adults with DS.	N=52 (26 DS and 26 LD). Age: DS range CA=23-40 years; LD range CA=19-55 years.	Inhibition/perseveration; set shifting; planning/problem solving; working memory; digit span; spatial span; fluency attention; verbal ability; motor speed.	Inhibition/perseveration: Finger tapping (Luria, 1980) Accuracy was recorded.	Inhibition: DS group scored at a lower level than the control group in finger tapping (t=5.74, p=020). After Bonferroni correction the difference was no more significant. Effect size d_{Cohen} = .93.
Cornish et al., (2007). Study 2: Compared the trajectories of different aspects of attention (selective, sustained, inhibition) in three	N=100 (25 DS, 25 FXS, 50 TD) matched for MA. Only boys. Age: DS average CA=11.17 years and average MA=6.09 years; FXS average CA=10.88 years and average MA=6.77 years; TD average	Inhibition; selective and sustained attention.	Inhibition: Walk task-TEA-Ch (Manly Robertson, Anderson, & Nimno-Smith, 1999) Accuracy was recorded.	Inhibition: no significantly differences between DS and control group on Walk task accuracy (Bonferroni correction was used). Effect size d_{Cohen} = .17.

developmental disorders: FXS, DS and WS.	CA=7.78 years and average MA=7.37 years.			
Lanfranchi et al., (2010). Investigating performance on EF tasks on individuals with DS.	N=30 (15 DS and 15 TD) matched for MA. Age: DS average CA=15.2 years and average MA=5.9 years; TD average CA=5.9 years.	Inhibition; working memory; set shifting; conceptual shifting; planning; fluency; sustained attention	Inhibition: Day/Night Stroop Task (Gerstadt, Hong, & Diamond, 1994) Accuracy was recorded.	Inhibition: significant difference between DS and normotypical control group in the experimental condition of Stroop task accuracy ($t = -2.31$, $p = 0.028$). Effect size $d_{Cohen} =.87$.
Brunamonti et al., (2011). Evaluate the profile of cognitive control of movement in DS	N=18 (9 DS and 9 LD) matched for MA. Age: DS average CA=18.2 years; LD average CA=15.3 years; MA= 9.0-9.6 years.	Inhibitory control; cognitive control of the movement.	Inhibitory control: Counterdemanding task (stop signal reaction time - SSRT) (Brunamonti et al., 2011) Reaction time was recorded.	Inhibition: significantly longer reaction time (RT) in DS group compared to normotypical control group in the go process (average 570.9; SE 20.9; t-test; $p < 0.01$), no difference in stop processes. Effects size $d_{Cohen} = -1.62$; $d_{Cohen} = -.14$.
Borella et al., (2013). Investigate whether individuals with DS have any specific or general	N= 38 (19 DS and 19 TD) children matched for MA. Age: DS average CA= 14.5 years and average MA= 5.6 years;	Inhibition (Friedman & Miyake, 2004); working memory.	**Prepotent response inhibition:** Animal Stroop (adapted from Wright, Waterman, Prescott, & Murdoch-Eaton 2003 by Nichelli, Scala, Vago, Riva, &	**Prepotent response inhibition:** no differences between the two groups in RT, participants with DS made more

deficit in inhibitory abilities.	TD average CA= 5.2 years.		Bulgheroni, 2004). Accuracy and reaction time were recorded. **Resistance to proactive interference:** Proactive interference (PI) task (adapted from Borella, Carretti, & Peregrina, 2010). Accuracy was recorded. **Response to distracter inhibition:** Directed forgetting – blocked method (adapted from Borella, 2006; Borella, Ghisletta, & de Ribaupierre, 2011). Accuracy was recorded.	mistakes than TD ($F=6.64$, $p < .05$). Effect size d_{Cohen} =.06, $d_{Cohen=}$-.86. **Resistance to proactive interference:** significant difference between DS and TD groups both in resistance to proactive interference accuracy ($F= 5.86$, $p < .05$). Effect size d_{Cohen} =-.81. **Response to distracter inhibition:** individuals with DS performed less well than TD children considering accuracy, the word recalled in the second half of the list ($F= 8.73$, $p < .05$). Effect size d_{Cohen} =.43.
Carney et al., (2013). Evaluating EF in DS and WS.	N=75 (25 DS; 24 WS, 26 TD). Participants were not individually matched. Age: DS average CA=10.4 - 18.11 years; WS average CA=8.1 - 18.11	Inhibition; working memory; fluency; set shifting.	Inhibition: Verbal Inhibition, Motor Inhibition (VIMI) task (Henry, Messer, & Nash, 2012) Accuracy and time were recorded.	Inhibition: no significant differences between DS and TD group. Effect size, Verbal Errors, d_{Cohen} =0.39; Verbal Time d_{Cohen}=0.06; Visuospatial Errors, d_{Cohen}=1.171.898; Visuospatial Time, d_{Cohen}= .27.

	years; TD average CA=5.0 – 8.0 years.			
Costanzo et al., (2013). Evaluating the aetiological specificity hypotheses pertaining to EF by comparing individuals with intellectual disability of different aetiology (DS and WS).	N= 46 (15 DS; 15 WS; 16 TD) matched for MA. Age: WS: average CA= 17.6 years and average MA= 6.7 years; DS: average CA= 14.5 years and average MA= 6.2 years; TD: average CA= 7.4 years and average MA= 6.9 years.	Response inhibition; attention; short-term and working memory; planning; categorization; shifting.	**Verbal inhibition:** Stroop task (Stroop, 1935) Time was considered. **Visual inhibition:** Go-No-Go (Van der Meere, Marzocchi, & De Meo, 2005) Accuracy and time were recorded.	**Verbal Inhibition:** significant difference in time emerged on Stroop task ($F(2,46) = 7.27$, $p < .01$). Effect size d_{Cohen}= 1.17. **Visual inhibition:** no difference in the Go-No-Go task. Effect size accuracy d_{Cohen} = .87; Response Time d_{Cohen}= .76.
Schott & Holdfelder, (2015). Examine at first motor skills and EF and second the relationship between these two performance domains.	N= 36 (18 DS; 18 TD) matched for sex and age. Age: DS: average CA= 9.06 years; TD: average CA= 8.99 years.	Inhibitory control; motor assessment; executive function; set switching.	**Response suppression and distraction:** Trail-Making Test for young children (Trails-P) Accuracy and time and a composite score were considered.	**Inhibition:** significant differences between DS and TD groups considering number of errors, mean time and efficiency ($p < .001$). Effect size for response suppression accuracy $d_{Cohen} = -1.82$; response time $d_{Cohen} = -2.05$.

Amadò et al., (2016). Investigate the links between EF and social cognition among children with DS.	N= 90 (30 DS; 60 TD). Age: DS: average CA= 8.54 years TD matched: 30 for MA and 30 for LD.	Inhibition; working memory; and cognitive flexibility (EF, Miyake et al., 2000); social cognition.	**Inhibition**: Day-Night stroop task (Gerstadt et al., 1994) Accuracy was recorded.	**Inhibition:** DS group underperformed both CA ($p < 0.001$) and LD groups ($p < 0.01$). Effect size, d_{Cohen} =1.38.

d_{Cohen} with pooled standard deviation.

Table 3.2. Descriptive statistics of measures for the three groups and results of the comparisons among groups (ANOVA) for CPM and inhibition tasks.

	Groups	Mean	S.D.	Min	Max	F	Sig.	Comparisons	Effect Size
CPM	5TD	18.43	2.13	16	24	2.306	.105	5TD=6TD	.69
	6TD	20.33	3.21	16	27			DS=5TD	.31
	DS	19.63	5.03	13	31			DS=6TD	.16
PMFFT Errors	5TD	13.49	5.95	0.00	26.00	8.41	.0001	5TD>6TD**	1.01
	6TD	8.10	3.99	0.00	16.00			DS=5TD	.12
	DS	14.38	8.65	2.00	43.00			DS<6TD**	.89
PMFFT Time	TD5	6.79	5.20	1.93	26.91	8.31	.0001	6TD=5TD	.70
	TD6	10.35	4.52	3.86	24.77			DS>5TD***	.87
	DS	14.27	10.84	5.40	57.26			DS=6TD	.45
Go/No-Go Raw Score	5TD	5.06	1.39	0.00	6.00	5.06	.008	5TD= 6TD	.23
	6TD	5.37	1.22	0.00	6.00			DS=5TD	.52
	DS	4.13	2.09	0.00	6.00			DS<6TD*	.70
Go/No-Go Transformed	5TD	246.60	152.22	1.00	403.43	2.53	.085	5TD=6TD	.30
	6TD	292.23	142.43	1.00	403.43			DS=5TD	.27

	DS	199.76	186.72	1.00	403.43			DS=6TD	.54
Flanker Accuracy	5TD	8.74	4.45	0.00	15.00			5TD<6TD**	.82
	6TD	12.42	4.14	1.00	16.00	6.08	.003	DS=5TD	.35
	DS	10.30	4.08	2.00	16.00			DS=6TD	.50
Flanker Time	5TD	887.26	149.53	513.20	1146.10			5TD=6TD	.68
	6TD	1058.15	322.12	417.60	1932.40	14.91	.0001	DS>5TD***	.99
	DS	3230.11	3332.41	537.69	13822.30			DS>6TD***	.87
Dots Accuracy	5TD	12.83	3.76	4.00	19.00			5TD<6TD*	.50
	6TD	14.80	3.80	8.00	20.00	13.07	.0001	DS<5TD*	.74
	DS	10.63	1.54	8.00	15.00			DS<6TD***	1.41
Dots Time	5TD	1270.70	378.05	570.00	2055.20			5TD=6TD	.23
	6TD	1367.97	439.20	547.70	2254.10	2.37	.099	DS=5TD	.43
	DS	1718.34	1410.30	244.00	5968.30			DS=6TD	.32

*p < .05; **p < .001; ***p < .0001

Note: time is reported in second for the Preschool matching familiar figure task time (PMFFT Time) and in millisecond for the Flanker (Flanker Time) and Dots tasks (Dots Time).

Table 3.3. Zero order correlation through inhibition tasks, CPM and age (in months) in the 5TD group (upper triangle) and in the 6TD group (lower triangle).

	1	2	3	4	5	6	7	8	9	10
PMFFT errors	1	−0.592**	−0.589**	−0.374*	0.156	−0.166	−0.041	−0.096	−0.052	0.133
PMFFT time	−0.543**	1	0.232	0.199	−0.148	0.154	−0.108	0.121	0.134	−0.341*
Go/No-Go raw score	−0.348	0.169	1	0.807**	−0.036	0.264	0.154	0.249	0.081	−0.213
Go/No-Go transformed	−0.198	0.054	0.796**	1	0.008	0.211	0.231	0.23	−0.069	−0.179
Flanker accuracy	−0.247	0.463*	0.14	0.116	1	−0.347*	0.287	−0.047	0.216	0.11
Flanker time	−0.297	0.409*	0.191	0.076	0.391*	1	0.056	0.491**	0.113	−0.059
Dots accuracy	−0.319	0.394*	0.367*	0.34	0.463**	0.347	1	0.557**	0.057	−0.049
Dots time	−0.315	292	0.414*	0.414*	0.408*	0.596*	0.754**	1	0.153	−0.253
CPM	−0.301	0.396*	0.065	−0.037	0.513**	0.436*	0.124	0.322	1	0.171
Age	−0.11	−0.073	0.087	0.053	0.269	0.023	−0.005	−0.087	0.36	1

*$p < 0.05$; **$p < 0.001$.

Table 3.4. Zero order correlation through inhibitory tasks, CPM and age (in months) in the DS group.

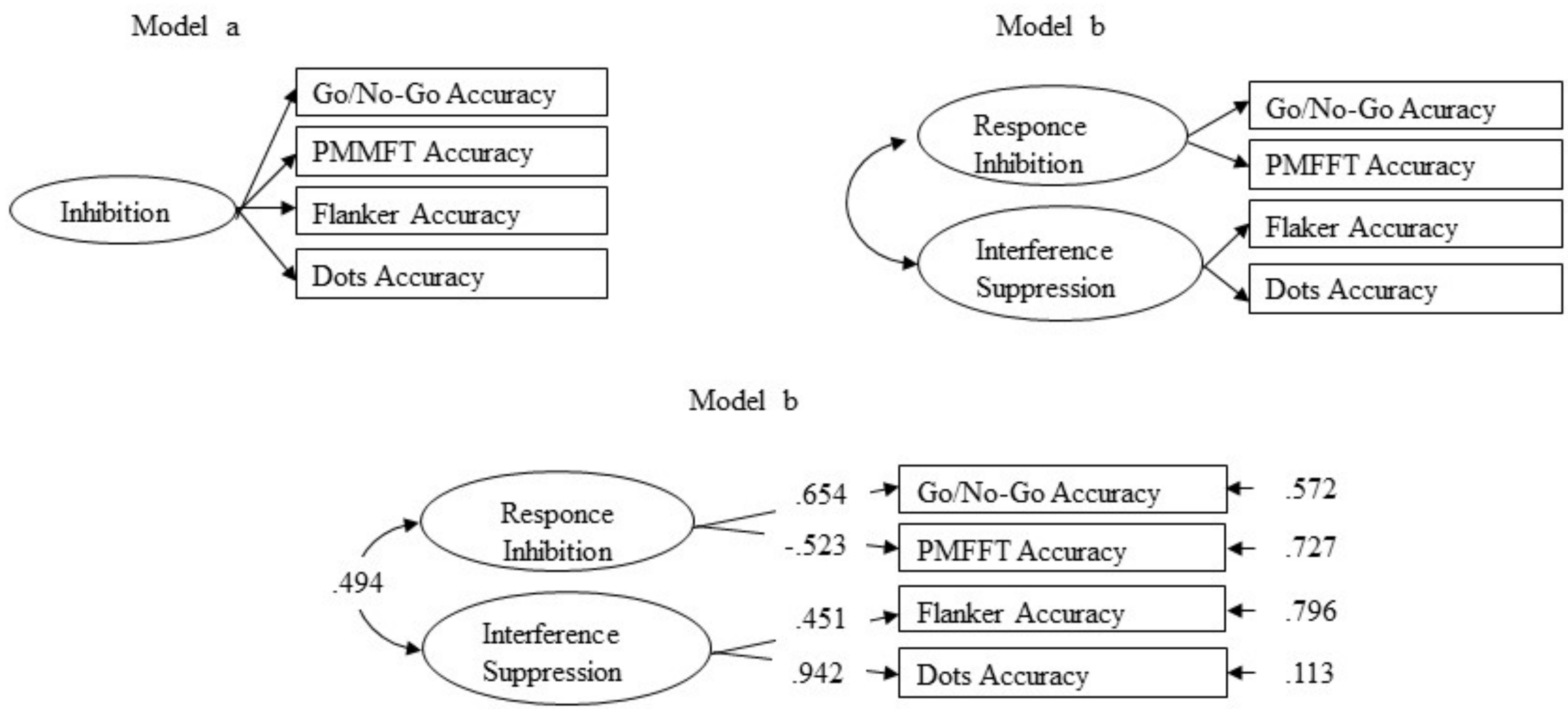
	1	2	3	4	5	6	7	8	9	10
PMFFT errors	1	0.051	−0.360*	−0.348	−0.540**	0.184	−0.154	0.146	−0.583**	−0.267
PMFFT time		1	0.189	0.246	−0.055	0.295	−0.061	0.455**	−0.006	0.147
Go/No-Go raw score			1	0.893**	0.463**	−0.161	0.105	0.206	0.139	0.244
Go/No-Go transformed				1	0.413*	−0.16	0.046	0.155	0.105	0.247
Flanker accuracy					1	−0.246	0.243	−0.007	0.234	0.185
Flanker time						1	0.072	0.575**	−0.189	0.128
Dots accuracy							1	0.372*	0.173	0.113
Dots time								1	−0.084	0.02
CPM									1	0.071
Age										1

**p* < 0.05; ***p* < 0.001.

Table 3.5. Descriptive statistics of inhibitory components in the three groups.

Groups	Response inhibition				Interference suppression			
	Mean	*S.D.*	Min	Max	Mean	*S.D.*	Min	Max
5TD	−0.192	1.11	−2.73	1.78	−0.169	0.820	−2.376	1.278
6TD	0.717	0.782	−1.30	2.21	0.517	0.849	−1.430	1.642
DS	−0.462	1.53	−5.14	1.93	−0.301	0.551	−1.309	0.947

Figure 3.1. Inhibition models. The model b is the endorsed model (standardized parameters are reported).



CHAPTER 4

Inhibitory dimensions and Delay of gratification: a comparative study on individuals with Down syndrome and typically developing children

Fontana, M., Usai, M. C., Pellizzoni, S., & Passolunghi, M. C. (2021). Inhibitory Dimensions and Delay of Gratification: A Comparative Study on Individuals with Down Syndrome and Typically Developing Children. *Brain Sciences*, *11*(5), 636. https://doi.org/10.3390/brainsci11050636

Abstract

While previous research on inhibition in people with Down syndrome (DS) reported contradictory results, with no explicit theoretical model, on the other hand, a more homogeneous impaired profile on the delay of gratification skills emerged. The main goal of the present study was to investigate response inhibition, interference suppression, and delay of gratification in 51 individuals with DS matched for a measure of mental age (MA) with 71 typically developing (TD) children. Moreover, we cross-sectionally explored the strengths and weaknesses of these components in children and adolescents vs. adults with DS with the same MA. A battery of laboratory tasks tapping on inhibitory sub-components and delay of gratification was administrated. Results indicated that individuals with DS showed an overall worse performance compared to TD children on response inhibition and delay of gratification, while no differences emerged between the two samples on the interference suppression. Additionally, our results suggested that older individuals with DS outperformed the younger ones both in response inhibition and in the delay of gratification, whereas the interference suppression still remains impaired in adulthood. This study highlights the importance of evaluating inhibitory sub-components considering both MA and chronological age in order to promote more effective and evidence-based training for this population.

4.1 Introduction

Down syndrome (DS) is the most common neurogenetic syndrome associated with intellectual disability that affects over 1:700 live births (Sherman et al., 2007; Mégarbané et al., 2009). Given the progressive increase in the life expectancy of people with DS, currently reaching nearly 60 years (Bittles & Glasson, 2004), further research is necessary to better understand the neuropsychological developmental trajectories of individuals with DS, considering both their mental age (MA) and their chronological age (CA). Previous studies reported that people with DS show some relatively preserved abilities with respect to visual processing, emotion recognition, and social behavior (Daunhauer et al., 2017; Pochon et al., 2017). On the other hand, relative weaknesses are confirmed in some aspects such as verbal processing, self-regulation, executive functions (EFs), fine and gross motor functioning, motor planning, and adaptive behavior with different degrees of impairment (Daunhauer et al., 2017; Gilmore et al., 2017; Lanfranchi et al., 2010; Will et al., 2017). While there is a widespread agreement on more pronounced difficulties on EFs as a whole (Daunhauer et al., 2017; Gilmore & Cuskelly, 2017; Lanfranchi et al., 2010; Will et al., 2017), contradictory findings emerged when inhibitory skills are investigated. Therefore, the main goal of our research is to analyze inhibitory abilities in individuals with DS in greater depth by elucidating patterns of strengths and weaknesses across the lifespan.

EFs are a complex set of cognitive abilities necessary for emotion regulation, deliberate reasoning, and self-regulation that are required to reach suitable levels of adaptive functioning, quality of life, and wealth, often more than IQ scores and socioeconomic status (Bertollo & Yerys, 2019; Diamond, 2013; Miyake & Friedman, 2012; Moffitt et al., 2011).

In fact, the presence of difficulties in EFs can be considered as a transdiagnostic indicator of atypical development (Zelazo, 2020). The literature agrees on the fact that EFs can be distinguished into three core components: updating, inhibition, and shifting (Miyake et al., 2000), which support higher-order cognitive processes such as problem-solving or planning (Collins & Koechlin, 2012; Miyake et al., 2000). The developmental trajectories of EFs consist of relative plasticity of these functions over an extended range of time (i.e., from infancy to early adulthood) with greater levels of plasticity from early childhood to adolescence (Zelazo et al., 2013).

There is considerable behavioral and neural evidence that EFs vary along a continuum from hot to cool, which typically work together to solve real-world problems (Zelazo & Müller, 2002; Zelazo & Carlson, 2012). While hot EFs are elicited in motivational and emotional contexts, cool EFs are required in cognitively demanding situations. Some studies suggested that the distinction between hot and cool EFs can be observed in TD children's behavior by the age of 3–4 (Prencipe et al., 2011; Willoughby et al., 2016), while others found these two factors as separate in children starting from the age of 24 months (Bernier et al., 2010; Montroy et al., 2019). The evidence clearly highlights the importance to jointly analyze both hot and cool EFs given their importance for some crucial aspects such as daily life, emotion regulation, and academic outcomes both in children (Clark et al., 2010; Garon, 2016; Willoughby et al., 2016) and adolescents (Kim et al., 2013; Prencipe et al., 2011).

4.1.1 Developmental trajectories of inhibition and delay of gratification in typical development

Inhibition, one of the three core components of EFs, is referred to the ability to control one's mental processes and responses, ignoring interfering stimuli, and to perform an alternative action (Diamond, 2013). It is commonly described as a multi-componential construct that includes several types of functions (Rey-Mermet et al., 2018). Evidence suggested that a two-factor model composed by response inhibition (i.e., the ability to suppress automatic behavioural responses in order to give the correct answer) and interference suppression (i.e., the ability to ignore distracting information or to suppress competing response tendencies) best describe inhibition in children of 4 years of age (Gandolfi et al., 2014), 5 to 6 year-old (Traverso et al., 2018), and in young and older adults (Brydges et al., 2014). Interference suppression may emerge after response inhibition and is considered as a more complex dimension that require greater involvement of working memory (WM) (Gandolfi et al., 2014; Traverso et al., 2020). In fact, while response inhibition could be considered as a simpler form of inhibition that is usually assessed with paradigms such as Go/no-go, Day-Night Stroop, Circle Drawing task, and delay of gratification; the more complex interference suppression is significantly predicted in tasks such as the Flanker and the Hearts and flowers (Garon et al., 2008; Gandolfi et al., 2014).

On the other hand, the delay of gratification - that assess the simpler form of inhibition - is considered as a hot dimension (Garon et al., 2008; Groppe & Elsner, 2014; Hongwanishkul et al., 2005) in which individuals have to resolve the conflict to avoid a more salient and immediate reward (i.e., smaller reward) to approach a less salient delay reward (i.e., larger but delayed reward). Delay of gratification skills are usually assessed with tasks such as the Marshmallow task (Mischel et al., 1989) or the Wrap delay task or the Gift delay task (Kochanska et al., 2000). Literature on developmental delay of gratification' trajectories suggested that better performance could be detected by four years of age, coinciding with the development of some cool EFs' skills such as the ability to resolve the conflict and to shift between attention sets (Zelazo & Müller, 2002). Likewise, to reach better waiting time on delay of gratification tasks, subjects have to learn to reduce the salience of the immediate reward using specific strategies such as self-talking and distraction (for a review see Garon, 2016). Literature on typically developing (TD) children reported that who are less capable on delaying gratifications, showed higher levels of behavioural problems such as hyperactivity, impulsivity, and conduct problems (Kim et al., 2016). Furthermore, given the longitudinal stability of the delay of gratification pattern, it seems to be a predictor of worse academic, cognitive, and social future outcomes (Joyce et al., 2016; Watts et al., 2018).

4.1.2. Inhibitory sub-components and delay of gratification in people with Down syndrome

Inhibitory skills in people with DS play a fundamental role in a multitude of crucial abilities such as daily life autonomies, adaptive and social behaviour, academic achievements, and occupational perspectives (Nakamichi, 2017; Sabat et al., 2020; Will et al., 2017). In the last decades, an increasing number of research are focusing on EFs indicating overall poorer performance for people with DS compared to the TD group (Tungate & Conners, 2020), whereas studies on the inhibitory construct in people with DS have been reported contradictory findings. Some cross-sectional studies that examined inhibition using informant-report measure such as the Behavior Rating Index of Executive Function (BRIEF, Gioia et al., 2003) suggested that in individuals with DS aged 4-to-24 inhibition may improve with age (Lee et al., 2015), whereas other indicated that inhibitory abilities were consistent from 2 to 18 years and then declined to about age 30 (Loveall et al., 2017).

Moreover, while some studies have identified inhibitory difficulties in the sample with DS when they were rated by their carers, but not by their teachers (e.g., Daunhauer et al., 2014; Lee et al., 2011), other research reported these difficulties only when teachers were the raters instead of carers (e.g., Sabat et al., 2020), while even other authors reported that both parents and caregivers assessed inhibition as relatively impaired compared to other EFs (e.g., Tomaszewski et al., 2018). As reported by Gioia et al. (2003), only small to medium correlations emerged between parents' and teachers' reports, suggesting that performance on EFs may be interpreted differently by the two raters and that EF demand may vary across the school and home environments.

In a similar way, comparing literature that assessed inhibition in individuals with DS using laboratory tasks, the same contradictory trend appeared. In fact, while in some studies people with DS showed worse performance on inhibitory tasks compared to the TD control group (e.g., Edgin et al., 2010; Lanfranchi et al., 2010; Schott & Holfelder, 2015), in other research, no differences emerged between the group with DS and the TD control group (e.g., Carney et al., 2013; Pennington et al., 2003), while in other studies that used more than one task to assess different inhibitory dimensions mixed results were recorded (e.g., Borella et al., 2013; Daunhauer et al., 2017; Traverso et al., 2018). Moreover, it should be considered that whereas TD children's inhibitory sub-components have been analyzed and assessed referring to a theoretical model (see Gandolfi et al., 2014), the same cannot be said for studies on inhibition in people with DS. Recently, trying to fill this gap, Fontana and colleagues (2021) conducted a meta-analysis on inhibition abilities in people with DS, indicating on average moderately impaired inhibitory performance in this population when they were matched for MA with TD children, whereas when the two groups were not matched for MA, they did not significantly differ from each other. These results highlight the importance of considering the following factors in assessing inhibition: proxies for MA, different inhibitory tasks to assess the diverse inhibitory sub-components (e.g., response inhibition, interference suppression or proactive interference, and delay of gratification), and smaller ranges of CA.

Nevertheless, literature that analyzed the simpler form of inhibition (e.g., response inhibition or prepotent response inhibition) demonstrates high levels of variability. For example, Daunhauer et al. (2017) and Will et al. (2017), using the “Simon says” paradigm, showed significant differences in inhibition performance between the group with DS and the TD control group, while Costanzo et al. (2013) and Traverso et al. (2018), assessing inhibition with the Go/no-go task, reported no significant differences between the two groups in accuracy scores. Otherwise, differences also emerged using the same inhibitory task. For example, considering accuracy score, while some studies reported significant differences in performing the Stroop-like task (e.g., Borella et al., 2013; Lanfranchi et al., 2010), other studies reported comparable performance between the two groups (e.g., Costanzo et al., 2013). Substantial differences with opposite results emerged also in performing the Stroop-like task when response time (RT) were considered (see Borella et al., 2013 and Costanzo et al., 2013).

Regarding tasks tapping on more complex components, Borella et al. (2013), using the Proactive interference task and the Direct forgetting task, reported significant more intrusions in the group with DS, although Traverso et al. (2018), administrating the Fish flanker and the Dots tasks, found no differences in interference suppression’s accuracy score between the group with DS and the TD control group, instead longer RT were recorded for the sample with DS but only for the flanker task.

Finally, there is a widespread agreement on difficulties for people with DS on delaying gratification, reporting overall a shorter waiting time. While Daunhauer et al. (2017) identified no significant differences between children with DS and TD control group in the snack delay task, Daunhauer et al. (2020), using the same task, suggested greater difficulties for people with DS. Moreover, Daunheuer and colleagues (2020) identified a significant negative correlation between the scarce performance on the Delay of Gratification task and academic performance such as letter-word identification and applied problems with potentially far-reaching implications for future academic achievement for students with DS. Other studies that focused on the delay of gratification in children and young adults with DS found that the first group had significantly shorter waiting times and that 45% of the sample waited less than three minutes to receive their reward (Cuskelly et al., 2001; Cuskelly et al., 2003). Furthermore, Cuskelly et al. (2016) registered worse performance on delay of gratification tasks in young adolescents with DS matched for MA to TD children, suggesting an association between the delay of gratification deficit and receptive language.

4.1.3 The present study

The previous paragraph described the state-of-art literature on EFs in typical development and in individuals with DS, showing that studies that assessed inhibitory performance in people with DS: (a) are quite inconsistent; (b) assessed this specific component with a limited number of tasks and without referring to a theoretical model (excepted for Borella et al., 2013 and Traverso et al., 2018); (c) included all measures under the more general label of "inhibition", (d) focused more on children and adolescent with DS, leaving these components in adults with DS less investigated still.

To fill these gaps in literature this study aims to:

1) investigate response inhibition, interference suppression (Brydges et al., 2014; Gandolfi et al., 2014; Traverso et al., 2018), and delay of gratification in people with DS compared to TD children matched for a measure of MA using a specific battery that assess different inhibitory sub-components (Usai et al., 2017; Traverso et al., 2018);

2) try to add some information on cross-sectional developmental trajectories of inhibitory sub-components and delay of gratification in a sample of people with DS clustered in two different groups on the basis of their CA.

Concerning the comparison between the sample with DS and TD children matched for MA, we expected to find worse performance in those with DS in response inhibition, interference suppression, and delay of gratification tasks (Cuskelly et al., 2016; Traverso et al., 2018). Considering instead only the group of individuals with DS, we expected worse performance on average in children and adolescents with DS (DS1) compared to adults with DS (DS2), in particular on interference suppression, which is the more complex dimension (according to Loveall et al., 2017).

4.2 Materials and Methods

4.2.1. Participants

A final sample of 122 individuals took part in this research. The study enrolled 51 individuals with DS (25 females and 26 males) with a mean CA of 23.73 years (SD = 12.24, age range = 5.5–54.5 years) and a mean MA of 6.73 years (SD = 1.73), and 71 TD children (39 females and 32 males) with a mean CA of 6.17 years (SD = 0.72, range = 4.9–8.0 years) and a mean MA of 7.13 (SD = 1.23). We excluded from our sample individuals with DS with: (a) trisomy 21 with mosaicism; (b) a comorbid diagnosis of Autism Spectrum Disorder; (c) severe visual or hearing impairments; (d) neurological impairments or developmental disabilities or a combination of these.

The Coloured Progressive Matrices Test (CPM, Belacchi et al., 2008) was administrated as a screening measure to match the group with DS with the TD control group for nonverbal reasoning ability. A one-way ANOVA on participants' raw CPM scores indicated no significant differences (F = 2.30, p = 0.13) between the group with DS and the TD control group.

To deeply investigate the performances of the group with DS, we split this group by CA considering the CA of 18 years old as cut-off, according to the literature on EFs in TD that show significant changes and improvement until late adolescence (Zelazo & Carlson, 2012) and developmental stability on EFs for people with DS from 2 to 18 years old (Loveall et al., 2017). Therefore, the sample with DS consisted of the following two groups: 21 children and adolescents with DS (DS1) with a mean CA of 12.27 years (SD = 3.71), and 30 adults with DS (DS2) with a mean CA of 31.75 years (SD = 9.35). A one-way ANOVA showed significant differences in participants' CA (F = 81.66, p = 0.0001) between the two groups.

4.2.2 Procedure

Each participant was individually assessed by trained psychologists in a quiet room in three separate sessions, each lasting about 30–40 min with an interval of 3–4 days. According to Carlson and Moses (2001), the task order was maintained constant to better investigate and control individual differences. The group with DS was assessed in two Associations for individuals with DS in northern Italy, while the TD control group belonged to kindergartens and primary schools of northern Italy.

This study was conducted in accordance with the recommendations of the Ethical Code of the Italian Register of Professional Psychologists and of the Ethical Guidelines of the Italian Association of Psychology with written informed consent from all subjects, in accordance with the Declaration of Helsinki. In addition, the administrators at the Associations for people with DS provided their consent to take part in the research and to use their educational institutions for the administration of the test (Prot. n. 1118, April 2017). Regarding the TD control group, consent to involve in the research was obtained both from schools and parents.

4.2.3 Measures

A battery of eight tasks was presented both to the group with DS and to the TD control group to assess inhibition (i.e., response inhibition and interference suppression) and delay of gratification abilities. All measures are well-known inhibitory tasks that have been previously used both with people with DS and with TD children without showing any floor or ceiling effect in the MA included in this study (see Cuskelly et al., 2016; Davidson et al., 2006; Traverso et al., 2018). Moreover, the tasks included in the battery do not require a verbal response and thus reduced confounding language-based influences (Best & Miller, 2010; Mullane et al., 2009).

4.2.3.1 Response inhibition tasks

Circle drawing task (CDT, Bachorowski & Newman, 1985). The CDT assesses response inhibition and the ability to control and slow down a motor response. In this task the participant is required to trace with her/his finger a circle depicted on a cardboard square (17 cm in diameter). The CDT provides for the following two conditions: the first (T1) with neutral instruction (i.e., "Trace the circle with your finger") and the second (T2) with inhibitory instruction (i.e., "Trace the circle again, but this time as slowly as you can"). The score is calculated as the proportion of slowdown with the following formula: T1−T2/T1+T2. The test-retest reliability was .93 (Usai et al., 2017).

Preschool matching familiar figure task (PMFFT, Traverso et al., 2016; adapted from Kagan, 1966). This task evaluates the ability to control impulsive responses, by shifting attention from the target figure to all the other figures stimuli (Gandolfi et al., 2014; Marzocchi et al., 2010). The participant is asked to perform 14 trails, selecting between five alternatives which figure is identical to the target one. The number of errors (PMFFT Errors, expected range 0-56) and RT (PMFFT Time, expected range 0-no limit) were recorded. Cronbach's alpha was .67 for PMFFT Errors and .95 for PMFFT Time for TD children (Traverso et al., 2016), while was .85 for the PMFFT Errors and .94 for PMFFT Time for people with DS (Traverso et al., 2018).

Go/no-go task (GNG, adapted from Berlin & Bohlin, 2002). This task is a well-known paradigm that assess response inhibition both in children and in adults (Verbruggen & Logan, 2008). Sitting in front of a computer screen, the participant has to press the space bar according to specific instructions given from the examiner (e.g., "Press the space bar when blue figures appear, while do not press the space bar when a red figure turn up on the computer screen"). The task is composed by the following three conditions: GNG1 (no-go, 6 red figures), GNG2 (no-go, 6 ball figures), GNG3 (no-go, 8 blue stars). Stimuli duration was 3.000 ms and the blank page after each stimulus lasted

1.000 ms. The sum of the correct no-go responses (GNG1, expected range 0–6; GNG2, expected range 0–6; GNG3, expected range 0–8) and RT of the no-go items (expected range 0- no limits) were recorded for each condition. Cronbach's alphas were .71 in the TD group and .83 in the group with DS (Traverso et al., 2018).

Grass/snow task (adapted from Carlson & Moses, 2001). This Stroop-like task assesses the ability to inhibit a prepotent response to perform an alternative action by pointing instead of speaking. Participant is presented two square cardboards, one coloured green as the grass and one coloured white like the snow. In the first condition, participant has to tap on the green square when she/he listens the word "grass", while to tap on the white square when the word "snow" is pronounced by the experimenter (expected range 0-16). In the second condition, the incongruent one, they had to do the opposite (i.e., to tap on white square for the "grass" and to tap on the green square for the "snow"). In each condition words are presented by the examiner in pseudo-random order. For the scoring the incongruent condition was considered, specifically the number of correct answers (expected range 0-16) and RT. In previous research with TD children, this task showed a good reliability and construct validity with a Cronbach's alphas of 1.00 for accuracy score (Carlson & Moses, 2001).

4.2.3.2 Interference suppression tasks

Fish flanker task (Usai et al., 2017, adapted from Ridderinkhof & van der Molen, 1995). This is a well-known paradigm that assess interference suppression (Eriksen & Eriksen, 1974). Sitting in front of a computer screen, the participant is required to respond to a left- or right-oriented fish by pressing a left or right response button on the keyboard. Two other fishes flank the target central fish and can be directed in the same (congruent condition, 16 items) or opposite direction (incongruent condition, 16 items). After four training items (two congruent and two incongruent), 32 items were randomly presented (16 for each condition, 16 right and 16 left). A warning cross (500 ms in duration) preceded each stimulus and then the screen turned blank after response (500 ms). Accuracy (expected range 0-16) and RT (0-no limits) in the incongruent condition were recorded. Test-retest reliability for accuracy score was .50 (Usai et al., 2017).

Hearts and flowers task (Usai et al., 2017 adapted by Diamond et al., 2007). This task, also labelled as Dots task, is a high cognitive task that assess interference suppression (Diamond & Lee, 2011). A heart or a flower appears on the computer screen and participant has to press on the keyboard the button on the same side when a heart appeared, while to press the button on the opposite side when they saw a flower. After a brief training session, hearts and flowers appear in randomized presentation. Accuracy (expected range, 0- 20) and RT were recorded. Test-retest reliability was .62 ($p < .001$) for accuracy score and .72 ($p < .001$) for RT (Usai et al., 2017).

4.2.3.3 Delay of gratification task

Wrap delay task (Kochanska et al., 1996). This task measures the ability to delay gratification, inhibiting and regulating undesirable behaviours (Carlson & Moses, 2001). The experimenter told to the participant that to have a gift for her/him, but that the gift has not jet been wrapped. The participant is told that she/he should not turn until the examiner has finished. The examiner noisily wraps the gift over 60 s and after that will deliver the gift to the participant. The latency to the first peek (Wrap delay Latecy time, expected range 0-60 s) was recorded. Cronbach's alphas were .95 for latency time (Kochanska et al., 1996).

Marshmallow task (Mischel et al., 1989). This well-known task that evaluate the ability to delay a gratification and to self-regulate behaviours both in TD children and in people with DS (Carlson et al., 2014; Cuskelly et al., 2016). The subject is presented a box which contains treats and she/he has to made their selection. After that, the experimenter place two treats on one plate and 10 treats on another plate to ensure that participants preferred the larger amount. The participant is informed that the examiner has to leave the room to do some works and is told that if she/he will wait – without eating any of the treats – until the experimenter will be back in the room, they could receive the larger pile. If she/he could not wait, the possibility to ring a bell to get the examiner back in the room is given, but in that case she/he will receive the smaller pile of treats. The task ends when participants ring the bell, or eat the treats, or when the time of five minutes lapses and the examiner come back in the room. Waiting time (0- 5 min) was recorded. The test-retest reliability was .99 for latency time scores (Mischel et al., 1989).

4.3 Results

A series of multivariate analysis of variance (MANOVA) were run to assess possible differences between the group with DS and the TD control group matched for MA. We included the groups as a factor and both inhibitory and delay of gratification tasks as dependent variables. Furthermore, to analyze inhibitory and delay of gratification performances in-depth, we split the group with DS into two sub-groups based on CA. For this reason, we conducted a multivariate analysis of covariance (MANCOVA), including CA as a factor, inhibitory and delay of gratification tasks as dependent variables, and the raw CPM score as a covariate. To compare performance differences between groups, η_p^2 was used as a measure of effect size. The criteria of Cohen (1988) were used to classify the effect sizes: small effect: $\eta_p^2 = 0.01$; medium effect: $\eta_p^2 = 0.06$; and large effect: $\eta_p^2 = 0.14$.

Descriptive statistics and differences between the group with DS and the TD control group using MANOVA on inhibitory and delay of gratification tasks are shown in Table 1. The MANOVA results reveal a significant main effect for group factor (Wilks' Lambda = 0.29, $F(17, 104) = 14.78$, $p = 0.000$, $\eta_p^2 = 0.70$) since the two groups significantly differ from each other. With respect to accuracy scores, the TD group outperformed the sample with DS on the following tasks that assess response inhibition: CDT, PMFFT, Grass/snow task, Go/no-go 2 task, Go/no-go 3 task. Moreover, the group with DS showed worse performance compared to TD children in tasks that measured delay of gratification abilities: Wrap Delay task and Marshmallow task. No significant differences in accuracy scores emerged in the Go/no-go1 task and in the two tasks tapping on interference suppression (i.e., Fish Flanker task and Hearts and Flowers task). Regarding RT, the sample with DS showed longer RT compared to TD children on: PMFFT, Go/no-go 2 task, Go/no-go 3 task, Fish Flanker task. No significant differences emerged between the two groups on RT in the following tasks: Grass/snow task, Go/no-go 1 task, and Hearts and Flowers task.

4.3.1 Investigating inhibitory and delay of gratification differences between the two groups with Down syndrome

As shown in Table 2, ignificant mean differences emerged between the group DS1 and DS2 on response inhibition and delay of gratification tasks, while no difference emerged on performances on interference suppression tasks. More specifically, the MAN- COVA results reveal a significant effect of MA (Wilks' Lambda = 0.47, $F(17, 32) = 2.11$, $p = 0.033$, $\eta_p^2 = 0.53$) and CA (Wilks' Lambda = 0.48, $F(17, 32) = 2.00$, $p = 0.044$, $\eta_p^2 = 0.52$) between the two groups. Analyzing accuracy scores, adults with DS (DS2) significantly outperformed children and adolescents with DS (DS1) on both response inhibition and delay of gratification measures: PMFFT, Grass/snow task, Go/no-go 1 task, Go/no-go 2 task, Go/no-go 3 task, Wrap Delay task, and Marshmallow task. No significant differences in accuracy scores emerged in the CPM, indicating substantially the same nonverbal reasoning abilities between the two groups despite different CA, CDT and in interference suppression tasks (i.e., Fish Flanker task and Hearts and Flowers task).

Regarding RT, significant differences between the two groups emerged only in the Go/no-go 1 task and in the Go/no-go 3 task. No significant differences emerged on all others RT tasks.

4.4 Discussion

The present study aimed to assess inhibitory sub-components (i.e., response inhibition and interference suppression) and delay of gratification with a specific battery of eight tasks in a sample of 51 individuals with DS matched with 71 TD children for MA. Moreover, to the best of our knowledge, these results are the first cross-sectional findings that try to evaluate, with specific laboratory tasks instead of rating-based measures, a developmental trend of inhibitory and delay of gratification performance in individuals with DS, considering both their mental age (MA) but especially their chronological age (CA). Furthermore, our research design and our findings are based on a theoretical model tested both in TD children and in people with DS (Gandolfi et al., 2014; Traverso et al., 2018).

Concerning the first aim of our research, our sample with DS showed overall greater difficulties in tasks tapping on diverse inhibitory components and delay of gratification considering accuracy score, while a mixed pattern emerged for response time (RT). Particularly, the sample with DS, compared to TD children with the same MA, performed worse on the Circle Drawing task (CDT), which requires the ability to suppress and control an impulsive motor response. It is salient to stress that people with DS had difficulties in aspects of fine and gross motor functioning and motor planning (Daunhauer et al., 2017, 2011) nd that fine motor control is highly associated with higher-order cognitive control in this population (Chen et al., 2014). Therefore, given the crucial role of such abilities for a variety of everyday life activities, our results agree with the previous studies, which indicate the importance of assessing and monitoring the specific trajectory of motor response inhibition in individuals with DS (see also Daunhauer et al., 2017). Moreover, evidence indicates that there is a specific relationship between EFs and motor skills also in people with DS (Schott & Holfelder, 2015) and that fine motor integration could have important implications also on academic achievement because the brain uses a shared specific neural pathway between the cerebellum and prefrontal cortex (Pitchford et al., 2016).

Concerning the Preschool Matching Familiar Figure task (PMFFT) and the Grass/snow task, results indicated that individuals with DS are less accurate than TD children (Traverso et al., 2018; van Tilborg et al., 2018). While the group with DS showed longer RT on the PMFFT, no differences emerged on the Grass/snow task. This result may suggest that people with DS, as early preschoolers, are not completely able to control RTs even in order to be more accurate and that given that RT may also be subject to greater noise for people with DS, it should be cautiously considered as a reliable index of executive control in this population (Fontana et al., 2021; Smith et al., 2019; Traverso et al., 2016). Furthermore, it is important to consider the fact that both tasks require greater WM skills (compared, for example, to the CDT), and we speculate that the impairments of individuals with DS with both verbal and spatial-simultaneous stimuli could be related to their worse performance on these tasks (Costanzo et al., 2013; Lanfranchi et al., 2010; Yang et al., 2014). For this reason, it would be necessary, in future research, to monitor WM ability and its possible effects on these tasks given the role of WM as a predictor of different inhibitory dimensions (Traverso et al., 2020).

Different results emerged, also, for the three blocks of the Go/no-go task, with significant differences reported for the second and the third block and no differences on the first block on the no-go responses. While Traverso et al. (2018) and Costanzo et al. (2013) found no difference on this task between the group with DS and the TD control group, we considered all the three blocks separately to investigate people with DS performance on this task more in-depth. We think that the last two blocks could be more challenging for people with DS partly because they had to remember to inhibit their impulsive responses and to simultaneously also remember different rules with higher WM and shifting demand (Langenecker et al., 2007). For the Go/no-go task, RTs are in line with the accuracy score reporting no differences on the first block between the two groups.

Considering interference suppression skills, no significant differences emerged between the two groups on accuracy score (see also Traverso et al., 2018). Contrary to our results on the Flanker task, Hauser-Cram et al. (2014) and Merrill and O'dekirk (1994) identified worse performances on the Fish Flanker task accuracy score and longer RT for the group with DS when they were faced with incongruent trials. However, it should be noted that both studies did not match the TD group with the sample with DS for a measure of MA and that the second study also used verbal stimuli. For the Hearts and Flowers task, worse performances were identified in both TD and DS groups, but it should be considered that this task measures complex inhibitory abilities and may require higher levels of WM skills than the Flanker task because subjects had to actively maintain the goal and the rules of the task in WM. However, despite the fact that in children of 5 to 6 years of age, response inhibition is distinguished from interference suppression (Traverso et al., 2018), we speculate that the Hearts and Flowers task could be challenging not only for individuals with DS but also for TD children in this chronological age range. Nevertheless, this mixed pattern of results is in line with studies that highlighted the high variability on cognitive tasks in the atypical population (e.g., van Belle et al., 2015).

Finally, people with DS showed worse performance compared to TD children also on the delay of gratification tasks (i.e., the Wrap Delay and the Marshmallow tasks). Our results are in line with previous research that evidenced difficulties in delaying gratification in individuals with DS (Daunhauer et al., 2020; Cuskelly et al., 2016). Literature suggested that difficulties on the delay of gratification in individuals with DS could be due to: (a) specific language difficulties of people with DS (for a review see Naess et al., 2011) that also impaired the self-talk skills (Cuskelly et al., 2001); (b) poorer response inhibition and cool EFs such as WM (Yu et al., 2016); (c) an overactivation of the hot system as a result of the faster development of the hot system that is not correctly modulated by the immature cool system (Mischel & Ayduk, 2011, pp. 83–105); (d) poor ability to integrate motivation with more abstract concepts and representations (Kable, 2015) such as the concept of time and the ability of time management that is strongly related to low levels of impulse control and poor resistance to distractions (Cabezas & Carriedo, 2019).

As mentioned above, the second aim of our study was to better understand inhibitory and delay of gratification abilities in individuals with DS with the same MA, in light also of their CA. For this reason, we considered the performances of two groups of the sample with DS: children and adolescents (DS1) and adults (DS2). Our results indicated that considering accuracy scores, the group DS1 performed worse—compared to the group DS2—on overall response inhibition and delay of gratification tasks, while no differences emerged between the two groups on the more complex interference suppression dimension. These results suggest that simpler inhibitory components (i.e., response inhibition and delay of gratification) may improve with age, whereas the more complex component (i.e., interference suppression) still remains also impaired in adulthood in people with DS.

Previous studies that assess inhibition with a cross-sectional perspective suggested that these skills may ameliorate with age with a progressive decline after mid-30s (Lee et al., 2015; Loveall et al., 2017). It should be considered that both studies used only rating-based measures instead of laboratory tasks and that inhibition was not investigated considering specific sub-components. Our results are also in line with the Compensation Age Theory (Lifshitz-Vahav, 2015), which postulates that CA could influence and determine the cognitive abilities of individuals with intellectual disabilities beyond their MA. In fact, we think that levels of maturation and cumulative life experiences may explain better performance on inhibitory measures and the acquirement of suitable strategies to cope with new challenges in daily life that require the ability to know how to inhibit, to manage interference, and to wait to receive a reward or to carry out the desired action (see also Numminen et al., 2001). Finally, contrary to Borella et al. (2013), our results suggested the importance of considering different inhibitory dimensions. In fact, while Borella et al. (2013) demonstrated a general inhibition impairment in people with DS, our results indicated specific impairments on the more complex inhibitory dimension that would remain more compromised even in adults with DS.

4.4.1 Limitations and future directions

To the best of our knowledge, our study is the first to assess, with a wide battery of tasks, response inhibition, interference suppression, and delay of gratification in people with DS, at first matching for MA the sample with DS with a TD control group, and secondly cross-sectionally analyzing differences on inhibitory sub-components between younger and older people with DS. Nevertheless, our research also has some limitations, such as the fact that our sample was too small in size to allow us to further divide it into a huge number of clusters with different CA ranges. Moreover, our attempt to cross-sectionally explore the developmental trajectories of inhibitory abilities in people with DS should warrant longitudinal replications. As a third point, it should be mentioned that response inhibition and interference suppression account differently on WM performances in TD children of 5 years of age, but only the interference suppression component served as a significant predictor for all WM tasks administrated. Given the paucity of studies focusing on interference suppression dimension in individuals with DS, future studies should consider the possibility of assessing this dimension using different tasks that capture more complex components taking into account both CA and MA implications and the specific cognitive profile of this population.

Even acknowledging these limitations, we believe that our study: (1) proposed a broad battery of tasks basing on a specific theoretical model (Gandolfi et al., 2014; Traverso et al., 2018) and tapping on response inhibition, interference suppression, and delay of gratification abilities; (2) suggested a developmental perspective of different inhibition abilities analyzing how age/experience could influence inhibitory skills.

Given that inhibition, together with WM, is an important predictor of academic achievement, adaptive behavior, daily life autonomy, and occupational perspectives [8,39], future studies should also jointly consider these dimensions in order to ensure overall better quality of life. Finally, we think that our results, which are in line with previous studies that indicated a growing path of EFs (e.g., Lee et al., 2015; Loveall et al., 2017), raise important issues about how to set training programs or developmental paths for this population. While studies on TD children demonstrated that both cool and hot EFs could be improved (see Marzocchi et al., 2020 and Pellizzoni et al., 2020), to the best of our knowledge, no training programs have yet been created and implemented to improve both components at the same time in individuals with DS. In fact, given the different developmental trajectories of diverse inhibitory sub-components and delay of gratification, we believe that it is important to propose training programs, both as regards the type of materials presented and the activities proposed, which take into account not only the MA of the individuals with DS but also the developmental CA trends of the specific function trained.

4.5 Conclusions

Comparing the group of individuals with DS with a TD control group matched for a measure of MA, our results indicate that the group with DS showed impaired performance in response inhibition, interference suppression, and delay of gratification. However, when younger individuals with DS were compared with older persons with DS, the older group with DS showed greater performance on both response inhibition and delay of gratification, while the interference suppression still remained impaired.

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Table 4.1. Descriptive statistics of measures and results of the comparisons among groups (MANOVA) for the two groups (DS *vs* TD) for CPM, inhibitory tasks, and delay of gratification tasks.

	Groups	N	Mean	SD	Min-Max	F	*p*
CPM	**DS**	51	19.18	5.36	11 – 35	2.30	.13
	TD	71	20.58	3.80	12 – 25		
CDT	**DS**	51	.34	.27	-.61 –.80	49.12	.0001***
	TD	71	.63	.19	.14 –.93		
PMFFT Errors	**DS**	51	12.94	7.55	0 – 30	5.39	.022*
	TD	71	10.25	5.23	2 – 24		
PMFFT Time	**DS**	51	170.46	136.88	30.94 – 636.71	5.12	.025*
	TD	71	128.72	62.62	47.84 – 399.04		
Grass/snow Accuracy	**DS**	51	10.47	5.58	0 – 16	26.50	.0001***
	TD	71	14.10	1.73	8 – 16		
Grass/snow Time	**DS**	51	36.37	10.39	22.25 – 77.02	2.03	.157
	TD	71	34.30	5.45	25.55 – 49.86		
Go/no-go 1 Accuracy	**DS**	51	5.14	1.63	0 – 6	2.34	.128
	TD	71	5.51	1.04	0 – 6		
Go/no-go 1 Time	**DS**	51	835.47	1839.17	0 – 7443.00	.29	.588
	TD	71	658.62	1729.35	0 – 7976.00		
Go/no-go 2 Accuracy	**DS**	51	3.00	1.78	0 – 6	47.75	.0001***
	TD	71	4.94	1.33	0 – 6		
Go/no-go 2 Time	**DS**	51	3348.71	2231.44	0 – 8314.00	33.09	.0001***
	TD	71	1139.31	1986.75	0 – 12186.00		
Go/no-go 3 Accuracy	**DS**	51	4.25	2.29	0 – 8	77.61	.0001***
	TD	71	7.04	1.16	2 – 8		
Go/no-go 3 Time	**DS**	51	3686.24	2602.06	0 – 11264.00	4.18	.043*
	TD	71	4548.96	2054.10	0 – 11571.00		
Fish flanker Accuracy	**DS**	51	13.35	3.77	3 – 16	3.70	.057
	TD	71	14.58	3.23	1 – 16		
Fish flanker Time	**DS**	51	35902.61	16548.86	11307.00 – 86529.00	3.93	.05*
	TD	71	30530.56	12674.24	15683.00 – 72647.00		
Hearts and flowers Accuracy	**DS**	51	5.35	3.41	0 – 10	1.15	.285
	TD	71	4.65	3.70	0 – 10		
Hearts and flowers Time	**DS**	51	20384.86	15145.43	5927.00 – 75480	3.02	.085
	TD	71	16766.06	7518.67	4995.00 – 37842.00		
Wrap delay Latency time	**DS**	51	32.07	23.95	1.14 – 60.00	15.09	.0001***
	TD	71	46.91	18.22	10.00 – 60.00		
Marshmallow Waiting time	**DS**	51	206.19	117.14	11.8 – 300.00	23.86	.0001***
	TD	71	283.91	55.51	60.20 – 300.00		

Note: *p < 0.05; **p < 0.001; ***p < 0.0001. Time is reported in seconds for the Preschool matching familiar figure task Time (PMFFT Time) and in milliseconds for the PMFFT, Fish flanker, and Hearts and flowers task

Table 4.2. Descriptive statistics of measures and results of the comparisons among groups (MANCOVA) for the two groups (DS1 *vs* DS2) for inhibitory tasks and delay of gratification tasks.

	Groups	N	Mean	SD	Min-Max	F	*p*
CDT	**DS1**	21	.26	.32	-.61 –.70	2.77	.073
	DS2	30	.39	.23	-.13 –.78		
PMFFT	**DS1**	21	14.95	8.00	1 – 28	9.02	.0001***
Errors	**DS2**	30	11.53	7.02	0 – 30		
PMFFT	**DS1**	21	126.54	118.82	30.94 – 580.21	2.26	.116
Time	**DS2**	30	201.21	142.10	37.40 – 636.71		
Grass/snow	**DS1**	21	9.10	5.16	0 – 16	5.00	.011*
Accuracy	**DS2**	30	11.43	5.75	0 – 16		
Grass/snow	**DS1**	21	39.03	11.34	26.22 – 77.02	1.92	.157
Time	**DS2**	30	34.51	9.42	25.25 – 64.19		
Go/no-go 1	**DS1**	21	4.19	2.16	0 – 6	9.77	.0001***
Accuracy	**DS2**	30	5.80	.48	4 – 6		
Go/no-go 1	**DS1**	21	1866.43	2538.44	0 – 7443.00	7.98	.001**
Time	**DS2**	30	113.80	282.18	0 – 1104.00		
Go/no-go 2	**DS1**	21	2.33	1.98	0 – 6	6.71	.003**
Accuracy	**DS2**	30	3.47	1.48	0 – 6		
Go/no-go 2	**DS1**	21	3143.27	2115.81	0 – 8314.00	1.39	.260
Time	**DS2**	30	1139.31	1986.75	0 – 12186.00		
Go/no-go 3	**DS1**	21	3.38	2.25	0 – 8	12.19	.0001***
Accuracy	**DS2**	30	4.87	2.15	0 – 8		
Go/no-go 3	**DS1**	21	4346.67	2613.77	0 – 11264.00	6.29	.004**
Time	**DS2**	30	3223.93	2534.79	0 – 11189.00		
Fish flanker	**DS1**	21	12.86	3.60	3 – 16	1.21	.306
Accuracy	**DS2**	30	13.70	3.91	3 – 16		
Fish flanker	**DS1**	21	37921.22	16288.31	16520.00 – 67841.00	1.70	.19
Time	**DS2**	30	34604.93	16879.96	11307.00 – 86529.00		
Hearts and	**DS1**	21	5.52	3.46	0 – 10	1.06	.354
flowers Accuracy	**DS2**	30	5.23	3.42	0 – 10		
Hearts and	**DS1**	21	16618.43	9356.85	5927.00 – 48740.00	1.39	.259
flowers Time	**DS2**	30	23021.37	17822.64	8058.00 – 75480.00		
Wrap delay	**DS1**	21	25.64	22.15	3.08 – 60.00	5.50	.007**
Latency time	**DS2**	30	36.57	24.50	1.14 – 60.00		
Marshmallow	**DS1**	21	152.35	122.12	16.90 – 300.00	4.53	.016*
Waiting time	**DS2**	30	243.87	99.02	11.80 – 300.00		
CDT	**DS1**	21	.26	.32	-.61 –.70	2.77	.073

Note: *p < 0.05; **p < 0.001; ***p < 0.0001. Time is reported in seconds for the Preschool matching familiar figure task Time and in milliseconds for the PMFFT, Fish flanker, and Hearts and flowers task

CHAPTER 5

An adapted shape-based version of the Navon task for comparing interference suppression in individuals with Down syndrome and typically developing children

Fontana, M., Usai, M. C., & Passolunghi, M. C. (submitted[1]). An adapted shape-based version of the Navon task for comparing interference suppression in individuals with Down syndrome and typically developing children.

[1] Submitted to *Developmental Psychology*

Abstract

Inhibition is considered a fundamental skill since early childhood. Literature on inhibitory performances in people with Down syndrome (DS) reported contradictory results. Only a paucity of studies investigated this construct considering inhibitory sub-components. The aim of the present study is to thoroughly investigate interference suppression, through global-local processes, in people with DS matched for mental age with a typically developing (TD) control group. For this purpose, we adapted and administrated a non-verbal Navon-shape task, composed by high-familiarity symbols (i.e., hearts and stars), to remove confounding language-based influences. The final sample included 51 people with DS and 71 TD children. A repeated measure analysis of variance, using mixed model, showed for both groups equal performances on global and local conditions when they had to respond to congruent items, whereas better performances on global condition, compared to local one, when they had to respond to incongruent items. Overall, our results revealed a global-local effect for both groups with grater impairment in incongruent responses, however this deficit on interference suppression was more pronounced in people with DS rather than in TD children matched for a measure of mental age. Our findings suggest the importance of studying global-local and interference suppression abilities in people with DS with important implications for their everyday life. Moreover, this shape-adapted version of the Navon task could be a useful and appropriate tools to assess interference suppression in pre-schoolers and in other atypical populations.

5.1 Introduction

Inhibitory skills are generally considered crucial in various domains, including academic achievement, self-regulation, and everyday life (Oeri, Voelke, & Roebers, 2018). Inhibition becomes organized into a multi-component construct starting from early childhood (e.g., Diamond, 2013). A two-factor model that best describes inhibition in children from 5 to 6 years old distinguishes between response inhibition (the ability to suppress dominant and impulsive responses and behaviors) and interference suppression (the ability to ignore distracting information or suppress competing stimuli) (Traverso, Fontana, Usai, & Passolunghi, 2018). Emerging literature highlights the fundamental influence of interference suppression on attentional processes, response selection, working memory (WM), and also in domains such as language processing (Gandolfi & Viterbori, 2020; Traverso, Viterbori, Malagoli, & Usai, 2020). Studies focusing on individuals with Down syndrome (DS) found clear signs of impairments in more complex inhibitory components like interference suppression and proactive interference (Borella, Carretti, & Lanfranchi, 2013; Palomino, Lòpez-Frutos, & Sotillo, 2019; Traverso et al., 2018). Despite the importance of investigating interference suppression in DS, few studies have considered this component separately from inhibition as a whole. The main goal of the present study was therefore to thoroughly analyze interference suppression in people with DS. To do so, an adapted shape-based version of the Navon task (Navon, 1977; Rey-Mermet & Gade, 2018) was used to compare them with a typically developing (TD) group matched for mental age (MA).

5.1.1 Inhibition and global-local processes in typical development

The Navon paradigm is a well-known method for assessing interference suppression, which requires control over the interference experienced when switching from a global to a local dimension (Navon, 1977). Stimuli typically consist of a large (global) letter made up of smaller (local) letters that may be the same (congruent) or different (incongruent). For instance, in the congruent condition a large upper-case “H” will be made up of repeat copies of a small lower-case “h”, while in the incongruent condition it will be made up of repeat copies of a small lower-case “s”. The experimenter directs participants' attention to either the global or the local condition and asks them what letter they see, and they have to respond as quickly as possible. It has been reported that the global target was normally processed faster than the local one (i.e., there is a 'global advantage'), but a global interference effect emerged when the former differed from the latter (Roux & Ceccaldi, 2001). While most studies used the classical Navon task with letter as stimuli, others proposed an alternative version with hierarchical figures or shapes (Brederoo, Nieuwenstein, Lorist, & Cornelissen, 2017). Whatever the type of stimuli presented, the mechanism underlying global-local processes mainly relies on the ability to suppress local interference when a global response is required, and vice versa (Krakowski, Borst, Vidal, Houdé, & Poirel, 2018). When we need to pay attention to global aspects, interference from local aspects is reduced proportionally with the increase in WM load (Ahmed & Fockert, 2012). Analyzing the processes behind the global-local effect, it is clear that children and adults process such information differently (Poirel, Mellet, Houdé, & Pineau, 2008). Children show a preference for the local components up to 5-6 years old, then gradually shift towards a preference for the global components by around 9-10 years old, after which an adult-like pattern of global precedence is established (Harrison & Stiles, 2009).

5.1.2 Inhibition and global-local processes in Down syndrome

Analyzing the literature comparing inhibition in individuals with DS and TD children, some studies reported an inhibition deficit in DS (Carney, Brown, & Henry, 2013; Edgin et al., 2010), while others found no differences between the two groups (Roberts & Richmond, 2014). Some even described mixed results, with DS and TD groups performing equally well in some inhibition tasks, and the former group faring less well than the latter in others (Borella et al., 2013; Traverso et al., 2018). The few studies that tapped inhibition using interference suppression tasks reported an impaired performance in individuals with DS compared with TD children (Edgin et al., 2010; Hauser-Cram, Woodman, & Hyman, 2014; Traverso et al., 2018). The ability to suppress irrelevant information is crucial to global-local processing (Krakowski et al., 2018), but has rarely been investigated in people with DS, and only in small samples. On the whole, the resulting literature tends to describe this population as "global processors" (Bellugi, Lichtenberger, Jones, Lai, & St. George, 2000). Porter & Coltheart (2006) analyzed global-local processing in a sample of 15 individuals with DS, comparing them with a group with William syndrome, and another with Autism Spectrum Disorder, but without considering a TD control group. The Navon figure they used consisted of a rectangle with crosses that could be congruent or incongruent: in the former condition, participants had to copy the figure, while in the latter they had to name the small shape or the large figure as instructed by the experimenter. The results indicated that the group with DS made more local errors (i.e., they showed a global bias) and, when asked to name an incongruent local condition figure, they wrongly named the global one. As for response time (RT), the group with DS had slower RTs in the incongruent condition, while no differences emerged between the global and local conditions for both groups. In another sample of 15 individuals with DS tested using a Navon task that involved copying letter stimuli, Bellugi et al. (2000) found that participants could reproduce the right letter because they focused on the global configuration, but they made more mistakes when they had to copy the local configuration. D'Souza, Booth, Connolly, Happé, & Karmiloff-Smith (2016) cast doubts on this classification of people with DS as "global processors", however, when they compared 11 participants with DS with two MA-matched groups, one of TD children and the other with William syndrome. Participants were administered a Navon Similarity Judgement task that involved comparing two letter-figures, one with the same global form but different local elements and the other with the same local elements but a different global form. Participants had to point to the figure that was more similar to the standard stimulus. The results showed that the DS group made more local than global matching, though the difference was not significant. In other words, they revealed neither a global nor a local bias. The authors emphasized, however, that a large proportion of the participants with DS withdrew from the task because they found the stimuli too difficult and too quickly to process. In fact, there is clear evidence in the literature that task performance in people with DS is influenced more by language than by visuospatial abilities (Carney et al., 2013).

5.1.3 The present study

Starting with an analysis of the literature regarding the various versions of the Navon task, and the limitations identified by previous studies, the present work aimed first to test interference suppression in individuals with DS as compared with a TD control group matched on a measure of MA. To achieve this aim, we administered an adapted non-verbal version of the Navon shape task in an effort to avoid any confounding influence of language issues.

We expected to find that: a) both groups would perform better in the global condition than when responding to local stimuli (Bellugi et al., 2000; Porter & Coltheart, 2006), indicating a difficulty suppressing the interference of the global information in the latter case; and b) the group with DS would be more impaired than the TD group, and more so in the incongruent than in the congruent condition (Borella et al., 2013; Traverso et al., 2018).

5.2 Method

5.2.1 Participants

The study involved 51 individuals with DS (49% female, M_{CA}= 23.73 years, SD= 12.24, M_{MA}= 6.73, *SD*= 1.73) and 71 TD children (40% female, M_{CA}= 6.17, *SD*= 0.72, M_{MA}= 7.13, *SD*= 1.23). Any individuals with DS who also had trisomy 21 with mosaicism, severe visual or hearing impairments, a comorbid diagnosis of Autism Spectrum Disorder, neurological impairments or developmental disabilities were excluded from the sample.

5.2.2 Procedure

Each participant was assessed individually by a trained psychologist in a quiet room. The group with DS was tested at associations for people with DS in northern Italy, while the TD group was tested at two schools in northern Italy. The study was conducted in accordance with the ethical code of the Italian Register of Professional Psychologists and the ethical guidelines of the Italian Association of Psychology, and with written informed consent from all subjects (for the sample with

DS, both participants and their guardians signed the written consent) in accordance with the Declaration of Helsinki.

5.2.3 Measure

The Colored Progressive Matrices test (CPM, Raven, 1947; Belacchi, Scalisi, Cannoni, & Cornoldi, 2008) was administered to match the group with DS and the TD control group on fluid intelligence. In this multiple-choice test, participants were asked to complete a geometrical figure by choosing the missing piece from one of six possible options. The score was the number of correct answers (range 0–36).

5.2.3.1 The adapted shape-based Navon task

The task was designed using E-prime 2.0 software basing on the global-local version adapted by Andres & Fernandes (2006). All stimuli were presented in a well-lit room on a 17” screen computer. To reduce any difficulties with verbal stimuli for the individuals with DS, we presented two familiar symbols: stars and hearts. The stimuli were presented in black on a white background. The task consisted of two test blocks, each comprising two parts (one requiring a global and the other a local response). Participants first practiced with two items in a given condition (global or local), then they were shown the eight fixed randomized items (four congruent and four incongruent). In the congruent condition there was a large heart made up of small hearts, or a large star made up of small stars, while in the incongruent condition there was a large heart made up of small stars, or a large star made up of small hearts (see Supplementary materials for more details). The two shapes were each associated with a specific button on the keyboard marked with stickers depicting a star or a heart. Before the task items were presented, participants saw a screen with instructions on which condition to consider (global or local) and these instructions were also given orally.

The final score was the number of correct answers (1 point for each correct answer) and ranged from 0 to 8 for each part of a block (0-4 for the congruent and 0-4 for the incongruent condition), for a total score of up to 16 for each test block. Both accuracy and RTs were recorded.

5.2.4 Statistical analysis

All statistical analyses were run with Jamovi version 1.1. A power analysis was conducted, calculating the minimum sample size needed to ensure sufficient sensitivity (Cohen, 1998). The results indicated that a sample size of 51 participants in each group was needed to reliably detect an effect size of 0.5 with a probability greater than 0.8.

A t-test for independent samples on participants' raw CPM scores showed no significant differences (t = 1.69, p = 0.09) between the group with DS ($mean_{MA}$= 7.1 years, *SD*= 1.2 years) and the TD group ($mean_{MA}$= 6.8 years, *SD*= 1.7).

A repeated-measures analysis of variance was performed using a mixed models approach. This enabled us to consider: a) all the factors that might contribute to explaining the results, and the multiple responses from the same individual simultaneously, not as separate from each other; and b) both the fixed- and the random-effect factors, and the statistical control of covariates, avoiding the bias of stepwise regression (see Antonakis & Dietz, 2011). Global-local , congruent-incongruent, and groups were considered as factors, and accuracy and RT scores as dependent variables. A random intercept was also included for the participants. To obtain a single accuracy variable for each condition (i.e., global, local, congruent, and incongruent), the scores were calculated by adding the total number of correct answers in the two test blocks; the means of the RTs for the correct answers in the two blocks were therefore considered. Table 5.1 shows the descriptive statistics and effect sizes according to Cohen's criteria (1988), and adjusted for small sample sizes (Hedges & Olkin, 1985).

5.3 Results

5.3.1 Fixed effect estimates

Using mixed modelling on accuracy scores, the results showed differences in variance when we included the between-subject variable (R^2 marginal = 0.15, R^2 conditional = 0.16), indicating that 1% of the variance could be due to our using repeated measures for each participant. For both groups, the results showed: a significant difference between the global-local and the congruent-incongruent conditions, $F(1, 848) = 5.62$, $p = 0.018$, and a significant interaction between group and congruent-incongruent condition, $F(1,848) = 5.79$, $p = 0.016$. No other significant differences emerged in the interaction between the two groups and global-local condition, $F(1, 848) = 0.07$, $p = 0.78$, or between group, global-local and congruent-incongruent condition, $F(1, 848) = 1.82$, $p = 0.178$.

Regarding the RTs, a considerable amount of variance (55%) was found when the between-subject variable was included (R^2 marginal = 0.069, R^2 conditional = 0.623). The results indicated a difference between the two groups, $F(1, 121) = 11.92$, $p < 0.001$. The implications of this finding are approached in the Discussion.

5.3.2 Post-hoc comparison for significant interactions

Table 5.2 shows the post-hoc results of the mixed model, after Bonferroni's correction, and the respective estimated marginal means. As concerns the interaction between global-local and congruent-incongruent conditions, differences emerged for both groups when participants had to respond to congruent *vs* incongruent items, in both the global ($t = 6.73$, $p < 0.001$) and the local ($t = 10.08$, $p < 0.001$) conditions, with a better performance overall for congruent responses. No other significant differences emerged between the global and local conditions for congruent responses ($t = 0.17$, $p = 1.000$). A difference emerged between the DS and TD groups for the congruent *vs* incongruent conditions ($t = 4.70$, $p < 0.001$): performance was worse in the incongruent condition in both the TD group ($t = 7.33$, $p < 0.001$) and the DS group ($t = 9.37$, $p < 0.001$), but this pattern was more pronounced in the group with DS.

To sum up, both groups performed equally well on the global and local items in congruent conditions, and both performed better on global than on local items in the incongruent condition. Indeed, both groups found the incongruent condition demanding, but their difficulty was more marked in the group with DS.

5.4 Discussion

Given the importance of interference suppression in our daily lives, and its involvement in many cognitive and behavioral processes, the aim of the present study was to use an adapted shape-based Navon task to explore interference suppression on global-local processes in a sample of people with DS, matched for MA with a group of TD children. The adaptation of the task was motivated by the fact that the results may be influenced by the type of stimuli presented (usually letters), as reported by D'Souza et al. (2016). High-frequency, non-verbal stimuli (hearts and stars) were consequently used, also bearing in mind the potential implications of verbal impairments in people with DS. To the best of our knowledge, this is the first study to have used a computerized shape-based version of the traditional Navon task to assess interference suppression in individuals with DS.

A global-local effect emerged in both our study groups (51 individuals with DS and 71 TD children matched for MA): their performance was much the same for global and local stimuli in the congruent condition, and deteriorated in the incongruent condition (Viterbo, Katzir, & Goldfarb, 2020). Focusing on the latter condition, both groups performed better on global than on local stimuli, indicating an interference effect when participants had to process local elements and ignore global shapes. This demands the inhibition of a salient global structure in order to focus successfully on the local level – an ability that seems to develop fully as early as 7 years of age (Krakowski et al., 2018). The difference between the two groups lay in that the individuals with DS were less able to cope with the incongruent condition than the TD control group because they found it more difficult to suppress interfering information (Traverso et al., 2018; Hauser-Cram et al., 2014). As suppressing an interference demands more WM than inhibiting a response in TD children, and this interference suppression dimension seems to be particularly impaired in people with DS (Traverso et al., 2018), we speculate that this mechanism also contributes to the deficit in the ability of people with DS to process information of the WM component.

As for RTs, it should be noted that a broad inter- and intra-individual variability in RTs emerged from our analysis. While the random factor could have an important influence as regards the non-significant fixed factors, people with DS reveal greater inter-individual variability (see Tsao & Kindelberg, 2009). Previous studies also found that people with DS (like TD preschoolers) are unable to control their RT in order to achieve a greater accuracy. Given that RT may also be subject to grater noise for people with DS, they cannot give a reliable indication of executive control in this population (Smith, Hedge, & Jarrold, 2019; Traverso et al., 2018).

Studying interference suppression and global-local processing skills has some important implications for research, and for specialists working with people who have DS (Fisher, Godwin, & Seltman, 2014). The adapted version of the Navon task used in our study, which removes the verbal component in both the presentation of the stimuli and the response required, could be a useful tool for: a) shedding light on which information takes precedence, or prompts a strong interference effect; and b) assessing interference suppression in both TD preschoolers and atypical populations. That said, a limitation of our study lies in that we considered a wide range of chronological ages in our group with DS. Future studies should consider smaller chronological age ranges or longitudinally assess developmental trajectories of global-local processes in people with DS, using tools for investigating sub-components of inhibition that take the specific profile of this population into account.

5.5 Conclusions

Judging from our results, global-local processing in people with DS is in line with that of TD children matched on a measure of MA, with a better performance for global rather than local stimuli, and a worse performance for incongruent rather than congruent conditions. Comparing the performance of our two groups, the individuals with DS had even more difficulty than TD children when having to manage incongruent information and suppress interferences.

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Table 5.1. Descriptive statistics for Navon task in the group with Down syndrome and in typically developing group.

Trials	Groups	N	M(SD)	Effect size (CI 95%)
Global congruent				
Accuracy	DS	51	7.51 (0.68)	0.14 (-0.22 - 0.50)
	TD	71	7.63 (0.99)	
Response Time	DS	51	43.33 (40.75)	0.63 (0.26 – 1.00)
	TD	71	26.17 (9.22)	
Global incongruent				
Accuracy	DS	51	5.73 (1.94)	0.66 (0.29 - 1.03)
	TD	71	6.86 (1.55)	
Response Time	DS	51	44.85 (50.30)	0.41 (0.05 - 0.77)
	TD	71	30.88 (14.22)	
Local congruent				
Accuracy	DS	51	7.33 (1.13)	0.48 (0.11 - 0.84)
	TD	71	7.75 (0.55)	
Response Time	DS	51	48.30 (36.67)	0.72 (0.35 - 1.09)
	TD	71	30.72 (7.92)	
Local incongruent				
Accuracy	DS	51	5.27 (2.73)	0.26 (-0.10 - 0.62)
	TD	71	5.97 (2.70)	
Response Time	DS	51	43.87 (37.58)	0.38 (0.02 - 0.74)
	TD	71	32.67 (21.95)	

G= global, L= local, DS= Down syndrome, TD= typically developing. Time is reported in seconds. Effect size were calculated using Cohen's d (1988) effect size formula, adjusted for small sample size (g, Hedges & Olkin, 1985). An effect size of 0.20 is considered small, an effect size of 0.50 is considered medium, and an effect size of 0.80 is considered large.

Table 5.2. Post-hoc comparisons of the mixed model.

Post-hoc comparison	Interactions (EMM)	*t*	*p*
G-L * C-I	G-C (3.79) * G-I (3.15)	6.73	< 0.001
	L-C (3.77) * L-I (2.81)	10.08	< 0.001
	G-I (3.15) * L-I (2.81)	3.52	0.003
	G-C (3.79) * L-C (3.77)		ns
DS-TD * C-I	TD-I (3.21) * SD-I (2.75)	4.75	< 0.001
	TD-C (3.85) * TD-I (3.21)	7.49	< 0.001
	SD-C (3.71) * SD-I (2.75)	9.57	< 0.001
	TD-C (3.85) * SD-C (3.71)		ns

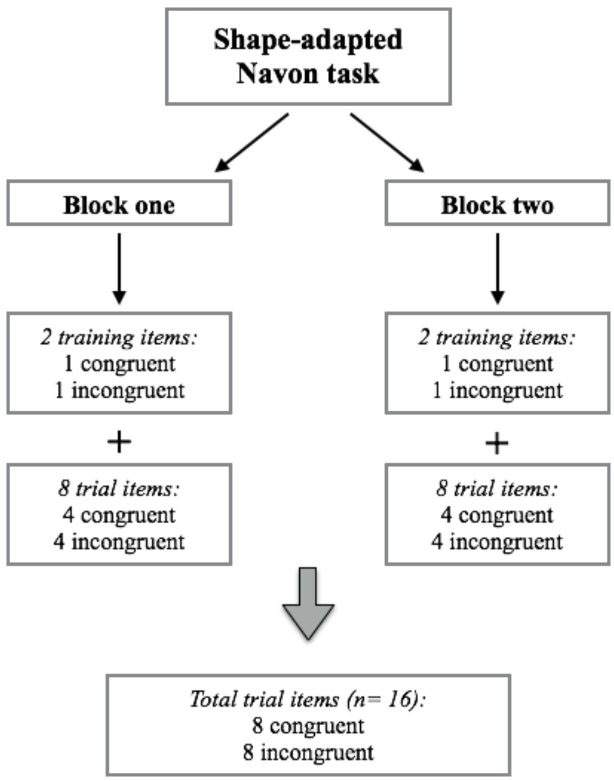
EMM= Estimated Marginal Means, G= Global, L= Local, C= Congruent, I= Incongruent, DS= Down syndrome, TD= typically development

Supplementary materials. Detailed information about adapted-shape Navon tasks' building process.

I. Task design

The task design consists in four components: congruent *vs* incongruent and global *vs* local. The task is structured into two blocks: block one and block two. Each block includes one global condition and one local condition. Each condition (global and local) includes two training items (one that trained the congruent condition and one that trained the incongruent condition) administrated before the eight fixed randomized trials' item, four congruent and four incongruent. To sum up, the block one included a global condition (composed by: two training items, four congruent items, and four incongruent items) and a local condition (composed by: two training items, four congruent items, and four incongruent items). The same is for the block two that replicate the block one structure. A summarizing graphical chart is provided in Figure 5.1 below.

Figure 5.1. Graphical representation of the shape-adapted version of the Navon task's structure.

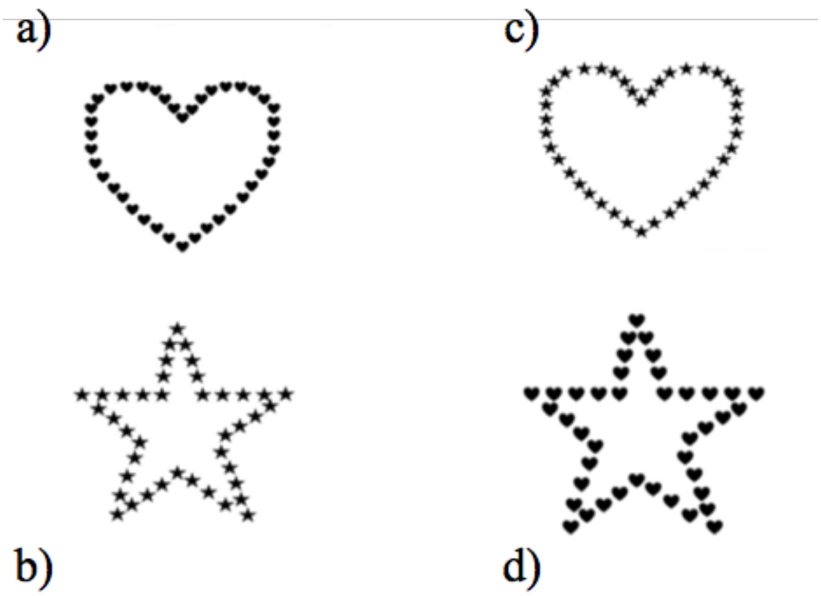


II. Stimuli structure

For this shape-adapted Navon task, we presented two high-frequency non-verbal stimuli: hearts and stars (see Figure 5.2). The local shape was presented in a 24-point font dimension, while the large global form was about 7.15 cm in height and 8.18 cm in width and was positioned in the centre of the computer screen. The congruent items were: a) a big heart composed by 41 little heart or b) a big star composed by 41 little stars. Whereas, the incongruent conditions consisted of: c) a big heart composed by 41 little stars or d) a big star composed by 41 little hearts.

Stimuli were presented in a fixed central location for a duration of 100 ms with a 1000 ms interstimulus interval.

Figure 5.2. Examples of global-local stimuli in congruent condition (left side) and incongruent condition (right side).



III. Shape-adapted Navon task' instructions

Participants received the following instructions before each condition (i.e., global vs local):

For the global conditions: "Now you will see a figure appearing on the screen, I need you to look at the big figure *(the experimenter trace with his finger on the computer screen the big figure)*! If the big figure presented is a heart you have to press the heart button *(the experimenter indicated the heart button on the computer keyboard)*, while if the big figure is a star you have to press the star button *(once again the experimenter indicated the heart button on the computer keyboard)*. Now let's try to do it together and then you'll do it on your own!".

For the local conditions: "Now you will see a figure appearing on the screen, I need you to look at the little figures *(the experimenter point with his finger on the computer screen the little figures)*! If the little figures presented are hearts you have to press the heart button *(the experimenter indicated the heart button on the computer keyboard)*, while if the little figures are stars you have to press the star button *(once again the experimenter indicated the heart button on the computer keyboard)*. Now let's try to do it together and then you'll do it on your own!".

CHAPTER 6

The relationship between different levels of autonomy, inhibition dimensions, and working memory in people with Down syndrome

Fontana, M., Pellizzoni, S., & Passolunghi, M.C. (under review[2]). The relationship between different levels of autonomy, inhibition dimensions, and working memory in people with Down syndrome.

[2] To the *Journal of Disability, Development and Education*

Abstract

Inhibition and working memory (WM) are crucial predictors of everyday life autonomies in people with Down syndrome (DS). We aimed to investigate the possible relationship between different levels of autonomy and tasks tapping on response inhibition, interference suppression, and WM in people with DS. Twenty-two adolescents and adults with DS were enrolled for participation in the study and were assessed with a battery of tasks tapping on inhibitory sub-components and WM. Educators completed and evaluated with a questionnaire levels of autonomy of the sample with DS. Considering levels of autonomy, we divided participants into two groups: one with lower levels of autonomy and one with medium-to-high levels of autonomy. Results showed differences between the two groups in both inhibitory and WM tasks. This study indicates the importance to evaluate the relationship between different inhibitory complexity levels and specific everyday life skills in people with DS. The results are also discussed in terms of possible implementation in training in clinical and educational settings.

6.1 Introduction

Down syndrome (DS) is the most common form of intellectual disability with a prevalence of 1 in 700 newborns (Mégarbané et al., 2009; Sherman et al., 2007). The focus of the literature has shifted, in recent years, from the deficits to the abilities of people with DS, paying more attention to their inclusion, autonomy, community participation, quality of life, and self-determination (Shogren & Wehmeyer, 2017). Di Maggio et al. (2019) reported that the high frequency goals referred with by people with ID consisted on: satisfaction of needs of autonomy, to have economic independence, and build up stable interpersonal relationships. The more balanced observations on the strengths and weaknesses of people with DS, from both the cognitive and the behavioural points of view, suggest difficulties more in specific executive functions, and less in social behaviour and emotional control, when compared with the typically-developing (TD) population (Daunhauer et al., 2017; Will et al., 2017).

Several studies on people with DS investigated the role of working memory (WM), a limited-space memory that enables us to store information and process it while completing cognitive tasks (Baddeley, 1992). According to the multi-componential model proposed by Baddeley and Hitch (1974), WM comprises two "slave" systems involved in retaining verbal and visuospatial information (the phonological loop and visuospatial sketchpad), and a central executive system responsible for controlling and regulating different cognitive activities, and for coordinating the flow of information between the two slave systems. It is generally agreed that people with DS have more pronounced verbal than visuospatial WM impairments (Lanfranchi et al., 2010; Loveall et al., 2017), although several studies found that some aspects of visuospatial WM - such as the spatial-simultaneous component - are less well preserved than others (for a review, Yang et al., 2014).

While findings concerning WM in DS seem to be fairly consistent, those regarding another top-down general-domain function - inhibition - have been more contradictory. Inhibition is defined as a multi-componential construct that enables us to control our mental processes, ignore a given internal or external prompt, and take alternative action (Diamond, 2013). Although they acknowledged the crucial influence of inhibition on academic achievement, self-regulation, emotional control, adaptive social skills, and everyday life activities (Nakamichi, 2017; Will et al., 2017), most studies on people with DS did not distinguish between the various components of this construct. Traverso et al. (2018) recently showed that a two-factor model that distinguished between response inhibition (i.e., the ability to suppress dominant and impulsive responses and behaviours) and interference suppression (i.e., the ability to ignore distracting information or suppress competing stimuli) was better able to describe the inhibitory performance of both 5- to 6-year-old TD children and adolescents with DS. The authors demonstrated that both response inhibition and interference suppression develop later in people with DS than in TD children, and that individuals with DS have more severe impairments in the *more complex* interference suppression dimension, which places a heavier load on WM (for a review, Best & Miller, 2010). Another crucial issue concerns the fact that some studies using inhibitory tasks reported much the same performance between people with DS and TD children (e.g., Carney et al., 2013; Daunhauer et al., 2017), while other studies pointed to a worse performance in the former (e.g., Amadò et al., 2016; Lanfranchi et al., 2010), or found mixed results when tasks tapping different inhibitory dimensions were administered (e.g., Borella et al., 2013; Costanzo et al., 2013; Traverso et al., 2018). The results of studies assessing inhibition with questionnaires were also few and inconsistent due to: the type of matching used, e.g., by chronological or mental age (Loveall et al., 2017); and whether the raters were parents/caregivers or teachers (Gioia et al., 2003). In fact, as reported by Gioia et al. (2003), only small to medium correlations emerged between parent' and teacher' reports, suggesting that EF performance may be interpreted differently by the two raters and the EF's demand may vary across school and home environments.

6.1.1 Autonomy, adaptive behaviour, and inhibition in Down syndrome

Autonomy generally refers to two aspects: independence and volition. While, on one hand, there is considerable congruence between these two concepts, on the other hand autonomy is not only the possibility to act more independently (Wehmeyer et al., 2020) but also to *behave like an adult* and, by working fist on the identity of adolescent and then on that of adult, learning *how to be an adult* (Contardi, 2016).

Adaptive behaviour (AB) is a set of abilities fundamental to everyday life and to our achieving a good degree of autonomy and independence. It is well documented that different levels of autonomy and AB are crucial for both employment outcomes and for a future independent (Contardi, 2016; Tomaszewski et al., 2018). AB demands three sets of skills: conceptual (e.g., language, understanding money, time, and numbers); social (e.g., following rules, interpersonal abilities, social problem solving); and practical (e.g., personal care, handling money, using transports) (Tassè et al., 2012). AB is usually found impaired in individuals with DS (Steingass et al., 2011), who have difficulties especially with managing money, cooking, moving in the community, organizing their time, functional academics, and shopping (Tomaszewski et al., 2018). Most researchers judge socialization and practical skills to be relative strengths in people with DS, and identify conceptual, communication, and motor skills as weaknesses (Fidler et al., 2006). Contradictory findings have emerged, however, the DS population's developmental trajectories have been assessed. For instance, Tomaszewski et al. (2018) reported that social skills remain a strength in adults with DS, while communication and practical skills are relatively weak. Makary et al. (2015) found instead that practical skills remained stable in adolescence and adulthood, while conceptual and social skills declined over time. Other researchers found that abilities gradually declined in the areas of independence, communication, and social skills in adults with DS beyond thirty (Bertoli et al., 2011) or forty (Esbensen et al., 2008; Sabat et al., 2020) years of age.

As mentioned earlier, inhibitory skills and WM play a fundamental part in various crucial abilities needed in daily life (Will et al., 2017; Nakamichi, 2017). Their impairment in people with DS has been thought to be responsible for their social behaviour (Porter et al., 2007), and inhibition is considered a crucial predictor of anyone's ability to adapt their behaviour to their environment. Sabat et al. (2020) recently found in a sample of individuals with DS that WM significantly predicted their conceptual AB, rather than inhibition or flexibility, based on their parents' reports, whereas the reverse was true when they were rated by their teachers. The Authors suggested that WM plays a more important part in the conceptual skills needed in activities at home, while the school environment demands increasing levels of autonomy and the inhibition of inappropriate responses in people's actions and behaviour.

6.1.2 The present study

The present study aimed to investigate: a) the relationship between specific aspects of autonomy (i.e., Socialization, Communication, Ability to choose and proactive behaviour, Orientation and behaviour on the road, Use of public transport, Handling money and using shops, Orientation in time, Handling the telephone, Reading-writing skills, Personal hygiene and self-care, and Unexpected situations) and tasks measuring response inhibition, interference suppression, and WM; and b) differences in the components of inhibition and in WM performance between two groups of participants with DS, one with lower levels of autonomy (LA), the other with medium-to-high levels of autonomy (MHA). We expected to find: a) performance in the tasks measuring the components of inhibition and WM related to specific aspects of autonomy; b) worse performance for the LA group compared with the MHA groups in tasks assessing response inhibition, interference suppression, and WM.

6.3 Materials and Methods

6.3.1 Participants

The study enrolled 22 adolescents and adults with DS (13 females and 9 males) with a mean chronological age of 25.3 years (SD = 10.7, range: 13.3-53.3 years), and a mean mental age of 7.7 years (SD = 1.7). All participants live with their families. Eight go to school, 11 are employed and 3 attend day cares. All individuals had a confirmed diagnosis of DS (based on karyotype). From this sample, we subsequently excluded 4 participants who had a known comorbid psychiatric or neurodevelopmental disorder, and 2 who failed to complete all the required tests.

6.3.2 Procedures

The adults enrolled and the parents of adolescent participants read, accepted, and signed the written informed consent form in accordance with the Declaration of Helsinki. This study was conducted in accordance with the ethical guidelines of the Italian Association of Psychology and the ethical code of the Italian Register of Professional Psychologists. All participants were tested in a quiet room during two separate sessions, each lasting about 20-30 minutes. Professional educators working closely with people with DS completed the Autonomy questionnaire.

6.3.3 Measures

The *Colored Progressive Matrices* test (Raven, 1947; Belacchi et al., 2008) was administered to measure fluid intelligence. This multiple-choice task consists of 36 items that vary in difficulty. Respondents see a target geometrical figure and are asked to choose which one of six items correctly completes the figure. The experimenter awards one point for each correct answer and the sum of the correct answers gives the final score (range: 0-36). Test-retest reliability was .83.

6.3.3.1 Inhibition tasks

The *Preschool Matching Familiar Figure task* (PMFFT, Usai et al., 2017) assesses respondents' ability to inhibit impulsive responses and shift their attention from a target figure to other options. There is a target figures, shown at the top of a page, and respondents have to choose which one of five options underneath it is identical to the target figure, and point their finger at the right one. The task continues until subject identify the right figure. The number of errors (range: 0-56), and the mean latency from the presentation of a figure to a participant's response (range: 0 - no limit) were recorded. Test-retest reliability was .49 (Marzocchi et al., 2010).

The *Fish Flanker task* (Usai et al., 2017), or paradigm is used to assess interference suppression ability. In this computerized version, participants see three fish on screen: the one in the middle is the target fish, and the two fish flanking it may point in the same direction or in the opposite direction.

Participants were asked to press a left or right button on the keyboard depending on the direction of the two flankers. A warning cross appeared for 500 ms before each stimulus, and the screen remained blank for another 500 ms after participant had given their answer. After training with two items for each condition, participants were shown with 48 randomized items (16 for each condition, half with the flanker fish facing right, and the other half with them facing left). The number of correct answers (range: 0-16), and the response times for the incongruent condition were recorded. Test-retest reliability was .50 (Usai et al., 2017).

6.3.3.2 Working Memory (WM) tasks

The *Visuospatial WM task* (Lanfranchi et al., 2004) requires lower levels of WM control. Participants were given a 3X3 or 4X4 chessboard and two small plastic frogs. The experimenter showed a sequence of jumps on the chessboard (more than one jump every 2 seconds) and participants had to repeat it immediately afterwards, moving their frog from cell to cell. The level of difficulty increased, with more jumps to remember and the larger size of the chessboard (i.e., from 3X3 to 4X4). The experimenter awarded 1 point if a whole sequence was repeated correctly and 0 otherwise. Test-retest reliability was .36 (Lanfranchi et al., 2010).

The *Visuospatial dual task* (Lanfranchi et al., 2004) involved stimuli presented on a 3X3 chessboard (with one of the 9 cells colored red). Participants were asked to remember the frog's starting position and also to tap on the table when the frog jumped onto the red cell. The position of the red cell changed from one trial to the next. If participants remembered the frog's starting position and tapped on the table when the frog jumped on a red square, the experimenter awarded one point; if not, they scored 0. Test-retest reliability was .71 (Lanfranchi et al., 2010).

6.3.3.3 Autonomy questionnaire

To assess aspects of autonomy, we used a questionnaire developed by Contardi (2016) for the Italian Association for People with Down syndrome (AIPD) and for people with intellectual disabilities. The questionnaire is composed of 11 scales concerning: Socialization (range: 8-32); Communication (range: 12-48); Ability to choose and proactive behaviour (range: 8-32); Orientation and behaviour on the road (range: 12-48); Use of public transport (range: 6-24); Handling money and using shops (range: 11-44); Orientation in time (range: 4-16); Handling the telephone (range: 7-28); Reading-writing skills (range: 5-20); Personal hygiene and self-care (range: 5-20); and Unexpected situations (range: 4-16). A score of 1 is awarded for the answer "no", a score of 2 if the answer is that the person with DS needs help to perform a given task, a score of 3 if the person with DS performs the task only if expressly asked to do so, and a score of 4 if the answer is "yes". Some examples of the questions are: "Can he/she count money"; "Does he/she communicate his/her needs and wishes"; "Does he/she go to the bathroom by him/herself". Cronbach's alpha for the Autonomy questionnaire calculated in the present study scale was .72.

6.4 Results

All statistical analyses were run with Jamovi Version 1.1. To test our first hypothesis, we conducted a linear correlation analysis using Pearson *r* between inhibitory and WM tasks and the Autonomy questionnaire sub-scales for the whole sample with DS. Further, a series of independent-samples Mann-Whithney *U* tests were run evaluate possible differences in types of inhibition and WM in lower (LA) and medium-to-high (MHA) levels of autonomy.

Correlation analysis (see Table 6.1) on response inhibition, show that PMFFT (errors) correlates with: Communication (*r*= -.45), Fish flanker RT (*r*= .49), Dual task (*r*= -.50), Total score of Autonomy questionnaire (*r*= -.49), Handling money and using shops (*r*= -.54), Handling the telephone (*r*= -.45), Reading-writing skills (*r*= -.43) while PMFFT (RT) positively correlates with: Fish flanker RT (*r*= .57), and Orientation in time (*r*= .53).

Furthermore, Interference suppression (Fish flanker accuracy) positively correlates with Orientation and behaviour on the road (*r*= .44), Handling money and using shops (*r*= .53), Orientation in time (*r*= .53), Reading-writing skills (*r*= .47), Total score of Autonomy questionnaire (*r*= .46) and Interference suppression (Fish flanker RT) negative correlates with WM visuo-spatial task (*r*= -.62), Communication (*r*= -.53), and Use of public transport (*r*= -.43), while correlates in positive direction with PMFFT errors (*r*= .49) and PMFFT RT (*r*= .57).

WM visuo-spatial task, positively correlates with Ability to choose and proactive behaviour (*r*= .68) and negatively with Fish flanker RT (*r*= -.62), while Dual WM task negatively correlates with PMFFT errors (*r*= -.50) and positively correlates with Orientation and behaviour on the road (*r*= .47), Use of public transport (*r*= .70), Handling money and using shops (*r*= .45), and Total score of Autonomy questionnaire (*r*= .56).

Descriptive statistics are reported in Table 6.2. A series of independent-samples Mann-Withney *U* tests for chronological age, mental age, and levels of autonomy for the two groups were conducted. No differences emerged between the LA and the MHA groups for chronological age, (*U*= 51.00, *p= 0.94*), but significant differences emerged for mental age, (*U*= 25.00, *p= 0.05)* and for levels of autonomy (*U*=1.00, *p*= .001).

Mann-Whitney *U*, comparing the group with LA and the group with MHA show differences between the two groups in the following tasks: PMFFT errors (*U*= 15.00, *p*= .009), Fish flanker accuracy (*U*= 11.00, *p*= .001), WM dual task (*U*= 15.50, *p*= .009), while no differences emerged between RT score (see Table 6.3).

6.5 Discussion

Considering the multiple inhibitory dimensions, and its relevance to quality of life for people with DS, this article is one of the first attempts to jointly investigate the influence of specific components of inhibition and WM on the autonomy in everyday life of people with DS. In the correlations between the cognitive measures and levels of autonomy, it emerged that response inhibition, interference suppression, and WM were all linked with total scores for autonomy, indicating the crucial role that all the three components have on autonomy, and on crucial skills such as handling money (Sabat et al., 2020). It is worth emphasizing that interference suppression - a more complex inhibitory dimension that also demands WM - seems to have a major role in the acquisition of important, more structured aspects of autonomy in adolescents and adults with DS such as handling money and using shops, orientation in time and behaviour on the road (also associated with WM), communication, and reading-writing skills. In clinical practice it is well known that people with DS have difficulty with time management, which is a crucial skill in everyday activities. This problem is strongly related to a low impulse control and poor resistance to distractions, both in TD populations and in samples with neurodevelopmental disorders (Cabezas & Carriedo, 2019). Despite their language deficit, many individuals with DS learn to write and read, but they are usually better at word recognition than in reading comprehension (for a review, see Næss, 2012). Furthermore, the ability to understand, manage, and use money is closely associated with arithmetical skills, and that people with DS have more difficulty than TD children in basic mathematical reasoning, and consequently in arithmetic (Belacchi et al., 2014). These aspects have crucial implications for an independent life, such as the possibility to autonomously pay a dinner in a restaurant or to buy a new t-shirt in a shop or even more to pay a train or a bus ticket. An increasing amount of research highlights that is possible to train also money handling and shopping skills with specific programs in adolescents and in adults with DS (e.g., O'Neill & Gutman 2020).

Like interference suppression, response inhibition seems to be linked to crucial aspects of learning, such as reading and writing and handling a telephone. The literature shows that WM and inhibition have a core role in the association between executive functions and academic achievement in people with DS (Will et al., 2017). As regards using the telephone, it has been demonstrated that the ability to communicate with others in social situations (i.e., to use pragmatic language) is strongly related to the ability to follow the rules of conversation, and to monitor and regulate one's behavior (Udhnani et al., 2020). Together with response inhibition, WM is associated with salient aspects relating to orientation and the use of public transport - both of which rely on the ability to remember crucial landmarks in an environment (Meneghetti et al., 2019; Toffalini et al., 2018). Clearly, being able to orient ourselves in time and space, and to use public transport autonomously are fundamental prerequisites for living independently and a good quality of life.

Comparing our two LA and MHA groups of individuals with DS added further detail to the debate on whether different components of inhibition and WM could differently influence autonomy. The MHA group outperformed the LA group on response inhibition, interference suppression, and WM accuracy scores; whereas no differences emerged between the two groups as regards RT on both inhibitory tasks. This divergence between accuracy and RT has been seen in other studies investigating both measures. People with DS, like preschoolers, are unable to control their RT in order to be more accurate - and that is why RT cannot be considered as a reliable indication of executive control in such populations - (Traverso et al., 2018; Smith et al., 2019; Fontana et al., 2020). Our data also seem to corroborate those of other studies examining inhibitory sub-components, which found that people with DS performed worse on the more complex components of inhibition, such as interference suppression and proactive interference (Borella et al., 2013; Traverso et al., 2018). Finally, we deem as important to underline that although the two groups did not differ for chronological age, the group with LA showed an overall impaired profile of cognitive functioning both on levels of mental age and on inhibitory and WM abilities, suggesting further investigations on different individual profiles (Tsao & Kindelberger, 2009).

The present study has some limitations to mention, concerning the small number of participants and the use of only one task to measure specific components of inhibition. Despite these limitations, the study findings have some important implications, partly because the idea of people with DS living independently is becoming an important issue for researchers and clinicians alike. Given the relationships between different dimensions of inhibition and WM that emerged in our sample with DS, parallel studies on daily life autonomy and cognitive aspects would be needed to address specific intervention programs to improve the autonomy of people with DS. Our research identified a crucial role for inhibitory skills, and the more complex interference suppression dimension of inhibition – which require also WM abilities –, in the acquisition of different types of autonomy. Our findings point to the feasibility of training both inhibitory components to increase the level of autonomy of individuals with DS. In fact, from an educational point of view, it is important to consider and understand the levels of inhibitory abilities in each individual with DS with the aim of promoting targeted interventions for the development of autonomy in daily life. For example, the ability of orientation and behaviour on the road requires high levels of inhibitory abilities (e.g., know how to stop before the pedestrian strips, check the traffic light, make sure that vehicles do not arrive from all directions). Therefore, a person with DS that shows significant difficulties in response inhibition and in interference suppression abilities will need to be better supported in crossing the road. It is important to remember that good levels of autonomy requires a long and step-by-step process with a clear beginning in early stages – for example by teaching how to recognize the fundamental road signs for crossing pedestrian and reinforcing simple levels of inhibition such as the ability to control our mental processes and behaviours and to perform an alternative action – and progressively promote more complex learnings (e.g., enhance the ability to manage interfering information and distractions while in parallel work on the ability to cross the road with the monitoring of the educational figure), until finally arriving at higher-order autonomies such as the ability to cross the street by himself and to manage independently some acquired inhibitory abilities.

In considering this possibility, however, we need to bear in mind some issues not strictly related to these individuals' cognitive functioning and abilities. For example, the distance between the place where the person with DS lives (e.g., suburban areas that do not near provide services) and the possibility of using public transport to reach the desired location should not be taken for granted. Moreover, some families may not be ready to embark on a path of growth themselves, along with their children with DS, or there may be logistic constraints (distances that make it difficult to use public transport, or to reach certain places). Be that as it may, we firmly believe that a specific aim of working with people with DS should be to take action simultaneously on the multiple factors that can promote their independence and autonomy, and thereby ameliorate their quality of life, wellbeing, self-esteem, and mental health.

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Table 6.1 Pearson's correlations through inhibitory tasks, working memory tasks, and sub-scales of the Autonomy questionnaire.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Socialization																	
1. Communication	.03																
2. Choose	.22	.26															
3. Orientation	.20	.34	.04														
4. Transport	.02	.25	.26	.76***													
5. Money	-.13	.02	-.04	.56**	.47*												
6. Time	.30	.16	-.01	.72***	.55**	.63**											
7. Phone	.11	.05	.02	.11	-.16	.29	.31										
8. R-W	-.20	.16	.02	.25	.19	.68***	.53*	.39									
9. Care	-.11	-.07	-.16	.04	-.27	.02	-.01	.34	-.10								
10. Unespected	-.11	.02	.33	.13	.41	.17	-.10	-.52*	-.05	-.32							
11. Tot autonomy	.19	.49*	.42*	.78***	.69***	.69***	.70***	.34	.56**	.01	.26						
12. PMFFT rt	.39	-.45*	-.34	.13	.04	.20	.53*	.33	.17	.22	-.25	.08					
13. PMFFT err	-.01	-.19	-.22	-.28	-.35	-.54**	-.34	-.45*	-.43*	-.07	.25	-.49*	-.11				
14. Flanker acc	.25	.18	-.03	.44*	.27	.53*	.53*	.29	.47*	-.01	-.30	.46*	.19	-.32			
15. Flanker rt	.26	-.53*	-.42	-.15	-.43*	-.22	.15	-.01	-.05	.11	-.13	-.34	.57**	.49*	-.16		
16. WM v-s	.18	.06	.68***	.03	.24	.21	-.04	.16	.19	-.16	.08	.33	-.30	-.42	.22	-.62**	
17. WM dual	.07	.19	.19	.47*	.70***	.45*	.39	.04	.32	-.20	.22	.56**	.07	-.50*	.34	-.38	.40

Note. * $p < .05$, ** $p < .01$, *** $p < .001$

Choose, ability to choose and proactive behaviour; Orientation, orientation and behaviour on the road; Transports, use of public transport; Money, handling money and using shops; Time, orientation in time; Phone, handling the telephone; R-W, reading and writing skills; Care, personal hygiene and self-care; Unexpected, unexpected situations; Tot autonomy, total score of Autonomy questionnaire; PMFFT, Preschool Matching Familiar Figure Task; WM v-s, visuo-spatial working memory task; WM dual, working memory dual task.

Table 6.2. Participants descriptives for the two groups.

	Lower levels of autonomy			*Medium-to-High levels of autonomy*		
	M	**SD**	**Range (min-max)**	***M***	**SD**	**Range (min-max)**
Chronological Age	24.6	9.38	13.3 – 38.2	25.7	11.6	13.7 – 53.3
Mental Age	6.9	0.8	5.2 – 7.7	8.1	1.9	4.8 – 11.5
Male	3			6		
Tot autonomy	244	11.00	228 – 259	275	9.59	257 – 295

Note. Tot autonomy, total score of Autonomy questionnaire

Table 6.3. Means, standard deviations, and comparisons for the two groups on tasks.

	Groups	Mean (SD)	Range (min-max)	*U*	Sig.	Cohen's *d*	Comparisons
PMFFT (errors)	LA	1.38 (.63)	.36 – 2.14	15.00	.009	1.50	LA > MHA
	MHA	.60 (.47)	.00 – 1.64				
PMFFT (RT)	LA	12.49 (15.23)	2.21 – 45.50	31.00	.142	.31	LA = MHA
	MHA	16.15 (10.26)	2.90 – 41.40				
Flanker (accuracy)	LA	9.00 (5.10)	3 – 16	11.00	.001	2.15	LA < MHA
	MHA	15.47 (1.36)	11 – 16				
Flanker (RT)	LA	4689.53 (5609.68)	1409.00 – 17264.00	31.00	.142	.76	LA = MHA
	MHA	222.60 (1213.67)	982.00 – 5408.00				
WM v-s	LA	5.57 (1.40)	3 – 7	31.00	.129	.70	LA = MHA
	MHA	6.53 (1.36)	4 – 8				
WM dual	LA	1.57 (1.40)	0 – 4	15.50	.009	1.42	LA < MHA
	MHA	4.80 (2.57)	1 – 8				

Note. LA, group with lower levels of autonomy; MHA, group with medium-to-high levels of autonomy; PMFFT, Preschool Matching Familiar Figure Task; WM v-s, visuo-spatial working memory task; WM dual, working memory dual task; RT, response time. Time is reported in milliseconds for the Fish flanker task.

CHAPTER 7

Exploring the effect of cool and hot executive functions training in four-year-old children

Pellizzoni, S., Fontana, M., & Passolunghi, M. C. (2020). Exploring the effect of cool and hot EFs training in four-year-old children. *European Journal of Developmental Psychology*, 1–16. https://doi.org/10.1080/17405629.2020.1838272

Abstract

Executive Functions (EFs) are crucial top-down processes characterized by cool and hot aspects, required for goal-directed behaviour. Only a few studies evaluated and trained concurrently cool and hot EFs. Therefore, we promote a training aiming to enhance both EFs components. A total of 91 children attending the second year of kindergarten were involved. Forty-two children attended the EFs training, while forty-nine children represented the active control group. The training was proposed twice a week for three months. The twenty sessions were divided as follows: 10 were focused on cool EFs, while the last 10 were related to hot EFs. The children were evaluated before and after the trainings with tasks including inhibition, working memory, delay of gratification, and emotion regulation. The results indicate increased cool and hot EFs abilities in children who attended the EFs training. Data are discussed in terms of developmental implications and highlights the importance to promote training focused also on hot EFs aspects.

7.1 Introduction

Executive functions (EFs) are a set of top-down mental processes implicated in regulating our thoughts, emotions, and behaviour. They are crucial to adaptive and goal-directed behaviour (Garon et al., 2008). It is generally agreed that EFs comprise three core components: 1) working memory (WM), which is the ability to retain, manipulate and update information in our mind; 2) inhibition, or the ability to control our mental processes, emotions and behaviour, and to take alternative actions; and 3) cognitive flexibility, which is the ability to shift between ideas, perspectives and actions (Diamond, 2013; Miyake et al., 2000). Studies on the developmental trajectory of EFs indicate that WM and inhibition emerge and begin to differentiate in preschool age. By the age of five, they allow for the successful performance of tasks that involve either one or both (Usai et al., 2014). Cognitive flexibility, on the other hand, "builds on the other two and comes in much later in development' (Diamond, 2013, p. 149).

The literature also differentiates between cognitive (cool) and motivational (hot) aspects of EFs (Zelazo & Müller, 2002; Zelazo et al., 2005). Cool EFs are implicated in emotionally neutral situations. They require a conscious control of thoughts and actions (e.g., when significant analytical skills, both logical and specific, are used to solve a task at hand), and the type of information involved seems to be processed by neural networks in the lateral part of the prefrontal cortex (PFC). Hot EFs are needed in situations that involve regulation and motivation (e.g., the ability to wait for a reward) and these aspects seem to be processed by the ventral and medial parts of the PFC (Zelazo, 2020). An increasing amount of neurodevelopmental research and neuroimaging studies indicate that cool and hot EFs work together as part of a continuum (Zelazo & Carlson, 2012).

Hot and cool EF processes play an important part in some important aspects of our daily lives, such as emotion regulation (ER) (Garon, 2016; Zelazo, 2020). ER refers to processes that involve experiencing, expressing and modulating emotional experiences (McRae et al., 2012). These processes are linked with limbic regions that interact with other cortical areas (Zelazo, 2020).

Training on cool EFs in preschoolers has been studied extensively producing evidence of its effects (Scionti et al., 2020), while training on hot EFs has been much less investigated. In the last 10 years, to the best of our knowledge, several articles have investigated the effects of EFs trainings in preschoolers (see Pellizzoni et al., 2019), but only three studies have reported positive or partially positive effects on hot EFs. In particular, Rueda et al. (2012) administered a short-term individualized training programme including: (1) tracking/anticipatory; (2) attention focusing/discrimination; (3) conflict resolution; (4) inhibitory control; and (5) sustained attention. In another study, Traverso et al. (2015), proposed 12 play-based training activities for small groups. They required increasing levels of active participation and cognitive control on the children's part. The third study, conducted by Pellizzoni et al. (2019), concerned a school-based training implemented prosed in a severely deprived environmental context. The training focused specifically on inhibition and WM in 10 sessions, and on understanding and controlling emotions in the other 10 sessions. However, none of these studies jointly investigated cool and hot EFs together with ER, which is an important associated factor. Hence our interest in looking at whether a training on EFs and ER might have an incremental effect on hot and cool EFs' components together with ER. The literature suggests that ER and inhibitory control are correlated, and that a greater ability to inhibit impulsive responses is associated with better ER (Nakamichi, 2017). The importance of cool and hot EFs and aspects of ER is well documented in publications that describe associations with developmental outcomes, and particularly with children's school readiness (Blair & Razza, 2007), learning abilities (Clark et al., 2010), and adaptive social skills (Schultz et al., 2011).

7.1.1 Research aims and predictions

Given the core role of EFs in developmental abilities (Jacobson et al., 2011), and the lack of research and training methods specifically targeting hot EFs, the present study had two aims: (a) to assess cool and hot EFs in a group of four-year-old children; and (b) to implement a training program targeting both cool and hot EFs, with a particular focus on inhibitory processes, together with ER, to ascertain their effects. We expected to see: (a) a general improvement in the children's cool EFs because WM and inhibition (assessed with specific and separate tools) are closely related at this developmental stage (Diamond, 2013; Miller et al., 2012; Traverso et al., 2015); and (b) an improvement in the children's ER and hot EFs because our training also focuses on emotional and motivational aspects (Pellizzoni et al., 2019; Webster-Stratton et al., 2013).

7.2 Method

7.2.1 Participants

The study involved four-year-old children attending four different kindergartens in a city of northern Italy. Parents and schools gave their consent to the children's participation. A total of 91 children were randomly assigned to either a cognitive-emotional training group (TG) (*n*= 42, M_{age} = 52.50 months, *SD* = 2.91, 20 girls, age range: 48.20–58.00 months) or to an active control group (CG) (*n*= 49, M_{age} = 53.10 months, *SD* = 2.84, 27 girls, age range: 48.20–59.00 months). From an initial sample of 100 children, nine were excluded for the following reasons: three children exhibited developmental delay, and six attended less than 80% of the training program.

7.2.2 Procedure

At pre- and post-test, the children were assessed individually in a quiet room at the school, and each session lasted about 40 minutes. Two female Master's degree students conducted the training, while a third examiner blinded to the children's grouping was responsible for the pre- and post- training assessments.

7.2.3 Assessment of cool executive functions

7.2.3.1 Inhibition

Circle Drawing task, CDT (Bachorowski & Newman, 1985). This involved tracing a circle (17 cm in diameter) with an index finger. The task was administered twice: the first time (T1), the children were given explicit instructions ('trace the circle') and shown starting and end points on the drawing; the second time (T2), they were given inhibitory instructions (‘trace the circle again but this time as slowly as you can’). Scores were calculated by correlating the times taken to trace the circle using the following formula: T2− T1/T2+ T1. The test-retest reliability was.93 (Usai et al., 2017).

Day and Night Stroop task, DNT (Gerstadt et al., 1994). This task was performed in two conditions, one congruent and the other incongruent. A series of 16 pictures was presented for each condition, eight showing the sun and eight showing the moon. In the congruent condition, children were asked to say ‘day’ when they were shown the sun, and ‘night’ when they were shown the moon. In the incongruent condition, they had to do the opposite, saying ‘day’ when they saw the moon, and ‘night’ when they saw the sun. In each condition, the pictures were presented one at a time and in a pseudo-random order. Scores were based on the number of correct answers given in the incongruent condition (range 0–16). The test-retest reliability in the incongruent condition was .96 (Usai et al., 2017).

7.2.3.2 Working memory

Backward Word Span task (adapted from Lanfranchi et al., 2004). The children were asked to memorize a list of spoken words and then recite them in reverse order. A trial session was run before administering the task to ensure the children understood the instructions. The task consisted of several sets of two lists with the same number of words, with another word added to each successive set to increase the difficulty of the task. The task continued until a child was unable to recall a given set of word lists. A score of one (1) was awarded for each set of two word lists that was recalled correctly (range 0–4). The test-retest reliability was .85.

7.2.4 Assessment of hot executive functions

Delayed gratification task (adapted from Kochanska et al., 1996). This task involved children being asked to wait as long as they could before opening a gift box placed in front of them. Time latency was recorded (range 0 – no limit). The test-retest reliability was .99.

Gift wrapping task (Carlson & Moses, 2001). In this task, the children were told that the examiner would wrap a present, and they were explicitly asked not to peek until the examiner said they could look. The wrapping took 60 seconds and the number of times the child peeked during this time was recorded (range 0 – no limit). The test-retest reliability for the violations was .88.

7.2.5 Assessment of emotion regulation

The Wally Feelings Test (Webster-Stratton et al., 2013) was used to assess the children's understanding and control of emotions. They were shown eight pictures representing positive or negative scenarios, involving a male or female character to match the gender of each child. Participants were examined and scored on the basis of three parameters:

(1) an emotion attribution score, assessing their ability to identify the feeling aroused by the picture correctly (1 point for each appropriate attribution, range 0–8);

(2) an emotion vocabulary score, assessing their identification of other feelings or emotions that could plausibly describe the situations in the pictures. One point for each emotion correctly labelled;

(3) an emotion regulation score, assessing their ability to suggest how to solve the problematic (negative) situations shown in the four negative pictures (1 point if their proposed solution was a pro- social strategy, 0 when they suggested agonistic strategies or could not identify any pro-social strategy at all). The test-retest reliability was .73 (Kayili & Ari, 2015).

7.2.6 Training

The group activities were presented to the children using a game-like approach during 40-minute sessions that took place twice a week, for a total of 20 meetings, for a total period of 5 months, including both pre- and post-evaluation and training.

7.2.6.1 Training group

Activity meetings 1 to 10: the activities were based on the training developed by Traverso et al. (2015), and concern two core aspects of cool EFs. There were five meetings for WM, and five for inhibition.

Activity meetings 11 to 20: the activities were based on cognitive behavioural therapy for children (Ellis & Bernard, 2006; Di Pietro, 2014) and aimed at labelling, understanding, and controlling highly-emotional behaviour and motivational contexts.

7.2.6.2 Active control group

Activity meetings 1 to 10: the activities were based on rearranging a set of pictures and creating a story. Five meetings focused on one character, and the other five on two characters.

Activity meetings 11 to 20: the activities involved reading and drawing classical fairy tales.

Descriptions and examples of the activities are provided in Figure 7.1, and in the supplementary material.

7.3 Analytical strategy

A series of multivariate analyses of covariance (MANCOVA) were run to identify differences between the TG and CG. For the pre-test assessment, we included the groups (TG and CG) as factors, the (cool and hot) EF tasks and the ER task as the dependent variable, and the children's chronological age as a covariate. At post-test, to assess the effects of the training, we examined gains in performance (post-test scores minus pre- test scores) between the pre- and post-test sessions of all tasks (Alloway et al., 2013; Brehmer et al., 2012). A MANCOVA was conducted, including groups as factors, scores for gains in performance as the dependent variable, and pre-test scores as a covariate, to analyse the effects of the training on both groups' performance. To compare pre- and post-test scores obtained in the two different groups, η_p^2 was used as a measure of effect size. Cohen's criteria (Cohen, 1988), suitably adjusted to fit our relatively small sample (Hedges & Olkin, 1985), were used to classify effect sizes as follows: small effect, $\eta_p^2 = .01$; medium effect, $\eta_p^2 = .06$; and large effect, $\eta_p^2 = .14$. Effect sizes (Cohen's *d*, with Hedge's *g* method) for post- hoc pairwise comparisons are also reported as follows: small effect, $d = .20$; medium effect, $d = .50$; large effect, $d = .80$.

7.4 Results

Table 7.1 shows the means and standard deviations of the pre- and post-test scores for the TG and active CG. The two groups did not differ in terms of chronological age, $F(1, 89) = .93$, $p = .34$, $\eta_p^2 = .01$, or gender, $F(1, 89) = .50$, $p = .11$, $\eta_p^2 = .01$, nor was there any significant difference in the number of sessions attended, $F(1, 89) = 2.06$, $p = .16$, $\eta_p^2 = .02$.

7.4.1 Pre-training assessment

To check for any baseline differences in the sample, we ran a MANCOVA with the two groups (TG and CG) as fixed factors, cool EF tasks (CDT, DNT, and Backward Word Span), hot EF tasks (Delayed gratification and Gift wrapping), and ER tasks (emotion attribution, vocabulary and regulation) as dependent variables, and age as a covariate. The MANCOVA revealed no effect of group (Wilks' lambda = .95, $F(8, 82) = .60$, $p = .78$, $\eta_p^2 = .05$), since the TG and CG did not differ at the baseline in any of the measures related to cool EFs, hot EFs, or ER. All parameters and relevant measures for the univariate analysis are illustrated in detail below:

Cool EF tasks: CDT, $F(1, 88) = .75$, $p = .39$, $\eta_p^2 = .01$; DNT, $F(1, 88) = .04$, $p = .84$, $\eta_p^2 = .00$; Backward Word Span task, $F(1, 88) = .10$, $p = .75$, $\eta_p^2 = .00$; Hot EFs tasks: Delayed gratification task, $F(1, 88) = .01$, $p = 0.93$, $\eta_p^2 = .00$; Gift wrapping task, $F(1, 88) = .04$, $p = .83$, $\eta_p^2 = .00$;

Wally Feelings Test: emotion attribution, $F(1, 88) = 2.45$, $p = .12$, $\eta_p^2 = .03$; emotion vocabulary, $F(1, 88) = 0.01$, $p = .93$, $\eta_p^2 = .00$; emotion regulation, $F(1, 88) = 0.98$, $p = .32$, $\eta_p^2 = .01$.

7.4.2 Post-training assessment

We conducted a MANCOVA with group (TG vs CG) as a factor, gains in performance scores as the dependent variable, and pre-test scores as a covariate. Bonferroni's adjusted post-hoc pairwise comparisons were also used for the gains in performance scores. The MANCOVA showed a significant main effect of group after the training (Wilks' lambda = .80, F (8, 74) = 2.31, p = .03, η_p^2 = .20), since the TG significantly differed from the CG. Univariate analysis revealed: significant differences in the DNT, F(1, 81) = 4.54, p = .04, η_p^2 = .05, indicating that the TG's performance was significantly better than the CG's performance in this task, with a greater increase in the number of correct answers in the Stroop condition (M_{diff} = .70, p = .04, d= .27). No differences were observed for the CDT, F(1, 81) = 1.40, p = .24, η_p^2 = .02, or Backward Word Span task, F(1, 81) = .30, p = .59, η_p^2 = .00.

There were significant differences in the Delayed gratification task, F(1, 81) = 5.06, p = .03, η_p^2 = .06. Bonferroni's adjusted post-hoc pairwise comparisons showed that the TG improved significantly in this task after the training, achieving a significantly longer waiting time (M_{diff} = 10.87, p = .03, d= .28). No significant difference was observed between the groups in the Gift wrapping task, F(1, 81) = 1.17, p = .28, η_p^2 = .01.

Significant differences emerged in relation to emotion vocabulary, F(1, 81) = 3.95, p = .05, η_p^2 = .05, with the TG improving significantly after the training, when the number of correctly-identified emotions was higher than in the CG (M_{diff} = 0.67, p = .05, d= .50). As concerns emotion regulation, F(1, 81) = 5.49, p = .02, η_p^2 = .06, the TG again displayed a significant improvement in proposing more prosocial strategies to solve the problems than the CG (M_{diff} = .21, p = .03, d= .49). No differences came to light regarding emotion attribution, F(1, 81) = 1.30, p = .26, η_p^2 = .02.

7.5 Discussion

The present study aimed to assess cool and hot executive functions (EFs) together with emotion regulation (ER) in a group of four-year-old children and to evaluate the effect of a training involved in self-control at both cognitive and motivational level (Diamond, 2013). The training group (TG), compared with an active control group (CG), showed significant differences in EFs: in cool components, particularly referring to Day and Night task, participants increased the number of correct answers in the Stroop condition, and in the hot component preschoolers achieved longer waiting time in the Delay gratification task. Concerning ER, significant improvements emerged in relation to emotion vocabulary and in proposing more prosocial problem solving strategies. To the best of our knowledge, no previous studies examined the effect of a training program designed to enhance hot and cool EFs with specific activities relating to different aspects of ER. In fact, our training program involves a series of games and activities that promote inhibition (Traverso et al., 2015), while also encouraging participants to implement ER strategies (Ellis & Bernard, 2006; Di Pietro, 2014).

As concerns cool EFs, Miller et al. (2012) demonstrated that working memory (WM) and inhibition could still be considered as separate dimensions in children 3 to 5 years old, and the two-factor model show a better fit for this age group (Gandolfi et al., 2014; Usai et al., 2014). Our results indicate that the TG exhibited significant improvements on inhibitory abilities after the training than on the other aspects measured. That said, the TG group's performance improved significantly in the Day and Night Stroop task (with a small effect size), but not in the Circle Drawing task. There may be several reasons for this apparent discrepancy. First of all, fine motor skills are still developing at four years, and this could affect performance in a task that demands specific fine motor competence (Cohen et al., 2018). Second, early preschoolers are typically unable to actively control their response time to improve their accuracy, which is why response time at this age may be less informative than accuracy as a measure of executive control (Traverso et al., 2018, 2016). Then there is the fact that the second part of our training included games relating to hot EFs that do not target motor skills specifically, as they revolve mainly around cognitive inhibition.

No significant changes were observed in the WM component after our training. This could be due to the fact that the training focused more on the inhibitory dimension (with five meetings for cool EFs and 10 for hot EFs) than on WM (five meetings in all). A floor effect was also seen in the WM (Backward Word Span) task, possibly due to the fact that children at this age find this task too difficult (Mammarella & Cornoldi, 2005).

As concern the hot dimension, compared to the cool one's, it should be noted that is still understudied and no theoretical model that clarify sub-components is yet available. The results of our study indicate that our training program improved the TG' hot EFs, as indicated by a better performance in the Delay gratification task (with a small effect size), though this was not confirmed in the Gift wrapping task. One of the main reasons for this difference may relate to the specific measures of each task (Pellizzoni et al., 2019; Traverso et al., 2015). For instance, the amount of time children was able to wait before opening a present (after calling the end of the game by saying 'stop' out loud) is probably a better indication, in our opinion, than how often they tried to peek while a gift was being wrapped. Moreover, what behaviour in children can be construed as a violation is not always clear (e.g., when children fidget on a chair, ask question, search their pockets, ask for a handkerchief).

Alongside an improvement in inhibition-related abilities (e.g., Rueda et al., 2012; Traverso et al., 2015), our training resulted in an increase of EFs' control in saliently motivational and emotional situations (medium effect size), which are designed to promote the ability of thinking before acting and encourage the implementation of pro-social strategies to tackle highly emotionally salient situations (Cole et al., 1994). These outcomes correspond to a significant improvement both in Emotion vocabulary and in Emotion regulation, with some important implications. As reported by the literature, children who are able to understand and successfully manage emotions show significantly higher levels of self-regulation and better academic results with respect to their peers who are less emotion-aware (Eisenberg et al., 2005; Kochanska et al., 2000; McClelland et al., 2007). Moreover, children with better Emotion vocabulary abilities are more likely to develop better social abilities compared to their peers (Joseph & Strain, 2003).

In our study, ER and inhibitory control (hot and cool components) increase during the training, confirming that these abilities are correlated (Nakamichi, 2017). In fact, once children have established a good connection between their inhibitory skills and their ER, their behavioural responses to emotional situations improve (Silkenbeumer et al., 2016). EFs and ER have been studied and trained mostly as separated dimensions. However, further investigations need to jointly consider these components, necessary to fully explained impulsive behaviours in highly motivational context.

We are aware of our study's limitations. First of all, while there was evidence of an improvement in our trained group's inhibitory abilities immediately after the training, it was impossible to test the long-term effects of our training in a follow-up session (because the schools did not renew their consent), or its repercussions on school performance once the trained children moved on to start their formal education. Our study is also only a first, exploratory investigation into the effects of training on cognitive and emotional regulation in terms of improving children's inhibition abilities. More research is needed to examine the effects of specific training programmes aimed at promoting cool or hot aspects of inhibition independently of each other.

Meanwhile, we believe that this study provides a substantial contribution to the literature in numerous ways. It is an unprecedented attempt to train and assess not only cool EFs as already extensively examined in previous studies (Traverso et al., 2015), but also salient aspects of the EFs underlying our ability to regulate emotions and motivation. Our training program was seen to prompt an overall increase in the trained children's level of monitoring (Silkenbeumer et al., 2016).

Given the fundamental influence of EFs on children's learning abilities, academic achievements, and social success among peers, we are convinced that it is crucial to develop evidence-based training methods to include in preschool programs for typically-developing children. Their effects should also be measured in particular social settings characterized by deprivation, migration backgrounds, and neurodevelopmental disorders.

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Figure 7.1. Study design: representation of the training protocols.

Table 7.1. Mean Pre- and Post-test scores in the different tasks.

		Training Group				Active Control Group			
		Pre-Training		Post-Training		Pre-Training		Post-Training	
		M (*SD*)	*Range Min-Max*	*M* (*SD*)	*Range Min - Max*	*M* (*SD*)	*Range Min - Max*	*M* (*SD*)	*Range Min - Max*
Cool EFs	Backward Word Span (accuracy)	0.59 (0.73)	0 - 2	0.67 (0.72)	0-2	0.53 (0.82)	0-3	0.59 (0.81)	0-3
	Circle Drawing (time)	0.42 (0.24)	-.12 - .82	0.51 (0.25)	.03 - .86	0.46 (0.21)	-.18 - .80	0.47 (0.22)	-.04 - .89
	Day and Night Stroop (accuracy)	12.60 (1.98)	10 - 16	14.24 (1.40)	11 - 16	12.67 (2.18)	8 - 16	13.59 (1.54)	10 - 16
Hot EFs	Delay Gratification (time)	25.39 (33.93)	0 - 120	30.33 (26.32)	3 - 119	24.02 (32.08)	0 - 122	20.67 (24.04)	0 - 91
	Gift Wrap (violations)	0.69 (1.48)	0 - 9	0.20 (0.35)	0 - 1	0.65 (1.55)	0 - 9	0.29 (0.53)	0 - 2
Emotion Regulation	Emotion attribution	3.12 (2.12)	0 - 8	5.26 (2.41)	0 -8	3.94 (2.98)	0 - 8	5.14 (2.98)	0 - 8
	Emotion vocabulary	0.43 (0.80)	0 - 3	1.24 (2.17)	0 - 7	0.49 (0.84)	0 - 3	0.47 (1.00)	0 - 4
	Emotion regulation	1.00 (0.70)	0 - 2	1.21 (0.75)	0 - 3	0.86 (0.58)	0 - 2	0.86 (0.57)	0 - 2

CHAPTER 8

Promote and Train Inhibitory skills and Delay of gratification in individuals with Down syndrome in both structured and ecological settings

Abstract

Literature on training programs targeted to improve executive functions (EFs) in individuals with Down syndrome (DS) mainly focused on WM abilities. However, also inhibitory abilities seem to be impaired in people with DS with crucial consequences in every day life. Moreover, literature indicates distinct developmental pattern of inhibitory skills in different age ranges in this population, suggesting the need to create and to implement specific training programs based on the characteristics of individuals with DS, on their mental and chronological age. Overall, previous studies that try to improve EFs in this population – includes inhibitory abilities – reported positive effects. Given the importance to train both hot and cool components (see also Traverso et al., 2015; Pellizzoni et al., 2019, 2020), the present intervention program aimed to: a) foster response inhibition, interference suppression, and delay of gratification skills through a series of game activities proposed to small groups of five individuals with DS both in more structured and in ecological setting; b) analyse whether the programme had an impact on levels of EFs in everyday life; c) examine a possible effect on everyday autonomies in mainly five areas such as Communication, Spatial and Temporal orientation, Orientation and behaviour on the road, Use of public transport, and Handling money and using shops (see Contardi, 2016). Unfortunately, this training program has not been completed due to the Covid-19 pandemic, therefore the present Chapter will describe the procedures provided for the pre- and post-training assessment and the structure of the training itself.

8.1 Introduction

Down syndrome (DS) is associates with specific profiles of strengths and impairments. Specifically, the greater impairments concern: executive functions (EFs), self-regulation skills, adaptive behaviour with different degrees of weakness, motor functioning and planning (Danuhauer et al., 2017; Gilmore & Cuskelly, 2017; Tungate & Conners, 2021). On the other hand, some specific aspects appeared as less impaired in individuals with DS such as emotion recognition, visual processing, and social behaviour (Daunhauer et al., 2017; Pochon et al., 2017; Sabat et al., 2020).

EFs refers to a set of cognitive skills that allow people to control thoughts and actions when they face with novel or complex situations in which an automatic or an impulsive response is not indicated and not useful (Miyake & Friedman, 2012). There is a widespread agreement on a multi-componential nature of EFs and on the fact that there are three main components that include working memory (WM) – updating, monitoring, and manipulating information in the mind –, inhibition – the ability to control one's mental processes and to manage interfering stimuli –, and flexibility – the ability to switch between different tasks or rules. Zelazo and Müller (2002) have proposed a distinction between cool EFs (elicited by abstract and context-free problems) and hot EFs (involved in the regulation of affect and motivation) which typically work together (Zelazo & Carlson, 2012). Both for typically developing (TD) children and for people with DS, EFs play a fundamental role on a multitude of crucial aspects for every day life skills and activities such as academic achievement (Best et al., 2011), social competence (Hughes & Ensor, 2007), adaptive behaviour (AB, Sabat et al., 2020), quality of life (Brown & Landgraf, 2010), and independence skills (Cahn-Weiner et al., 2002). In a recent meta-analysis, Tungate and Conners (2021) suggested overall poorer EFs' performances in individuals with DS compared to TD control group with greater impairment on verbal WM and shifting abilities, while moderate impairment for inhibition and nonverbal WM. Recently, Fontana et al. (2021a) conducted a meta-analysis focusing on the inhibitory construct in individuals with DS that revealed: a) a paucity of studies that distinguished different inhibitory sub-components following a theoretical model (e.g., excepted for: Fontana et al., 2021a and Traverso et al., 2018 that assessed response inhibition separately from interference suppression, and Borella et al., 2013 that distinguished prepotent response inhibition from resistance to proactive interference and from response to distracter inhibition); b) differences on inhibitory results when the group with DS was matched or not for a measure of mental age (MA) with a TD control group, reporting significant lower inhibition abilities when the group with DS was matched on MA with TD children, instead no significant differences when this matching was not provided; c) high levels of heterogeneity that could be due to the different tasks used to assess inhibition and its sub-components. Moreover, given that inhibitory abilities are significant predictors of conceptual and practical AB skills in individuals with DS (Sabat et al., 2020) and given that there is an important relationship between different inhibitory components such as response inhibition and interference suppression (Gandolfi et al., 2014; Traverso et al., 2018) and different levels of autonomy in this population, it is challenging to promote inhibitory abilities especially in those subjects who showed lower levels of autonomy (see Chapter 6 of the present dissertation).

8.1.2 Training programs to improve executive functions in individuals with Down syndrome

Analysing the literature on training programs aimed to improve EFs in people with DS, it emerged that different types of intervention has been implemented, but – given the greater impairment and the number of studies tapping on WM abilities – the majority of training programs focused on the improvement of both verbal WM (e.g., Broadley & MacDonald, 1993; Conners et al., 2008) and visuospatial WM (e.g., Costa et al., 2015; Pulina et al., 2015; Lanfranchi et al., 2017). According to the categorization of different approaches to train EFs proposed by Marzocchi et al. (2020) for TD children, the more recent programs implemented to enhance EFs in people with DS are presented in the following three headings: 1) play-based and curricular approaches, 2) physical approaches, and 3) technology-based approaches. Table 8.1 aimed to summarize the results of more recent interventions to enhance different EFs components in individuals with DS.

Regarding training programs that focused on the improvement of inhibitory abilities in people with DS, an overall positive effect emerged. In particular, to the best of our knowledge no play-based and curricular approached tried to improve inhibition. On the other hand, both physical and technology-based approaches haven been proposed to individuals with DS. For example, Chen et al. (2015) – using a physical approach – found that young adults with DS, assessed with the Knock- Tap task (NEPSY, Korkman et al., 1998), may obtain benefits on inhibitory performance after a simple treadmill walking activity with moderate intensity. Also Ringenbach et al. (2016), assessing inhibition with the same task as Chen et al. (2015), found that the Assisted Cycling Therapy may help to improve impulse control in adults with DS. In fact, motor skills are strongly related to EFs in children with intellectual disabilities (Hartman et al., 2017) and in children with DS (Schott & Holfelder, 2015). Moreover, potentiate inhibitory skills may allow for better control of repetitive and disruptive behaviours that are highly prevalent amongst individuals with DS (Evans & Gray, 2000). More recently, McGlinchey et al. (2019) proposed a computerized training to enhance EFs in people with DS tapping also on inhibitory abilities. Authors assessed inhibition with the following three tasks: the Cats and Dog Stroop task, the Scrambled boxes task, and the Spatial reversal task. Their results suggested that inhibition and planning were the two most improved components, although positive effects reflected in everyday behaviours were not detected using the Behaviour Rating Inventory of Executive Function – Adult Version (BRIEF-A). Finally, the only study that we found in literature that revealed no significant improvement on inhibition is the educational robotic training proposed by Bargagna et al. (2019). It should be noted that authors reported qualitative data only for two children with DS and they reported that these results were due to the high heterogeneity of their sample.

Summarizing, the few previous researches that trained inhibitory skills in individuals with DS showed overall positive effects, suggesting that: a) inhibition could be improve using specific training programs - belonging to different approaches - created or adapted on the basis of the specific cognitive and behavioural profile of people with DS (McGlinchey et al., 2019; Ringenbach et al., 2016), and

b) given the relevant consequences of inhibitory skills also at a behavioural level (Evans et al., 2000), it is necessary to create and to implement adapted but especially new training programs focusing also on other impaired components of EFs such as inhibition and flexibility – rather than only on WM components – and on hot EFs' dimensions such as the delay of gratification skills.

8.1.3 Theoretical background of the present study

Given the above mentioned analysis of the topic, we decide to create a training that specifically enhance inhibitory sub-components in adolescents and adults with DS. Researches reported on average an inhibitory deficit in people with DS when they are matched for a measure of MA with TD children (for a meta-analysis see Fontana et al., 2021a). Examining in more details the inhibitory construct in individuals with DS, it emerges that some cross-sectional studies reported that in this population inhibition may improve with age (Lee et al., 2015) with a greater stability between 2-to-18 years old (Loveall et al., 2017). It should be noted that the two studies mentioned above, used informant-report such as the BRIEF (Gioia et al., 2000) which assess the whole construct of inhibition. Fontana et al. (2021b) used a specific battery of laboratory tasks to assess different inhibitory sub-components jointly with delay of gratification in a sample of 51 individuals with DS, dividing them also in two groups with different chronological age (CA) (i.e., children and adolescents with DS – DS1 group – and adults with DS – DS2 group –). Our results indicated that the group with DS, compared to TD children matched for MA, showed on average impaired performance in response inhibition, interference suppression, and delay of gratification. Nevertheless, when the younger group with DS was compared with the older group with DS, the second one had greater performance on both response inhibition and delay of gratification, while the interference suppression still remains impaired also in adulthood. Moreover, analysing the literature it clearly emerged that: a) consider separately different inhibitory sub-components in individuals with DS play a crucial role in order to investigate in depth their inhibitory profile and to set up specific training programs to potentiate and enhance proper impaired inhibitory skills (Traverso et al., 2018; Fontana et al., 2021b; Borella et al., 2013; Costanzo et al., 2013); b) only few programs trained also inhibitory skills (e.g., Chen et al., 2015; McGlinchey et al., 2019; Ringenbach et al., 2016); c) future researches and training programs for people with DS should also consider hot components such as the delay of gratification (Cuskelly et al., 2016; Daunhauer et al., 2020).

Basing on these considerations and in order to fill this gap, to the best of our knowledge, this is the first training for people with DS aimed to enhance specific inhibitory sub-components (i.e., response inhibition and interference suppression) jointly with delay of gratification skills in both structured and more ecological contexts. According to previous cross-sectional researches mentioned above (e.g., Fontana et al., 2021b; Lee et al., 2015; Loveall et al., 2017), we created a specific training program for adults with DS aimed to potentiate at first the simpler inhibitory components such as response inhibition and interference suppression, and therefore we aimed to try to improve the challenging interference suppression abilities - which are the more complex skills - that appear to be yet impaired also in adulthood in people with DS (Fontana et al., 2021b). Moreover, given the well-known deficit in delay of gratification abilities (e.g., Cuskelly et al., 2016) and given the important implication of this impairment for different future outcomes such as behavioural problems, cognitive, academic, and social outcomes (Joyce et al., 2016; Watts et al., 2018) we focus also on the enhancement of this hot component of EFs.

Despite our hard work of preparing the research design of our training (to create new exercises calibrated according to the specific profile of cognitive and behavioural functioning of individuals with DS) and the effort to create each ecological material, unfortunately our implementation was interrupted due to the Covid-19 pandemic emergency that made the present program impossible to carry out. Therefore, hoping to implement our training as soon as possible, in the present Chapter it will be presented only the experimental design and the structure we organize for our intervention, while data are clearly not yet available.

Therefore, the present research aims to: a) assess cool and hot processes in a group of adults with DS, with a specific focus on inhibitory components; b) implement a training program with a series of activities created on the basis of the cognitive and behavioural profile of individuals with DS that focuses on response inhibition, interference suppression, and delay of gratification, to ascertain their effects; c) analyse whether the programme had an impact on levels of EFs in everyday life (e.g., Lanfranchi et al., 2017; McGlinchey et al., 2019); d) examine a possible effect of the following training program on everyday autonomies in mainly five areas such as Communication, Spatial and Temporal orientation, Orientation and behaviour on the road, Use of public transport, and Handling money and using shops (see Contardi, 2016).

8.2 Method

8.2.1 Participants

Our sample would be composed by adults with DS without: trisomy 21 with mosaicism, a comorbid diagnosis of Autism Spectrum Disorder, severe visual or hearing impairments, neurological impairments or developmental disabilities. According to the literature (Zelazo & Carlson, 2012), we consider as cut-off the CA of 18 years old, given that: a) significant changes and improvement on inhibition occur until late adolescence (Zelazo & Carlson, 2012); b) a developmental stability emerged from 2 to 18 years in people with DS (Loveall et al., 2017); c) older individuals with DS seems to have different performance compared to the younger group on inhibitory abilities (i.e., better performance on response inhibition and delay of gratification, while worse performance on interference suppression) (Fontana et al., 2021b).

Participants are allocated to one of the two conditions considering their CA, nonverbal MA and inhibitory performances. The Colored Progressive Matrices (CPM, Belacchi et al., 2008) are administrated as a screening measure to ensure that there would not be any difference for fluid intelligence at the baseline between groups. The first group (i.e., the training group, TG) receives the training on inhibition and delay of gratification jointly with strategies to enhance these components during activities to improve their autonomies, while the second group (i.e., the active control group, ACG) carries out different activities from the training group for the same amount of time per week.

Participants of the active control group are offered to join a waiting list for subsequent training program.

8.2.2 Procedure

Pre- and post-test assessment are conducted for each subject of the two groups selected (i.e., TG and ACG). Each participant is individually assessed in a quite room in three sessions, each one lasting about 30-40 minutes with an interval of 3-4 days by qualified psychologists, blind to subjects' condition. The task order is maintained constant to better investigate and control individual differences (Carlson & Moses, 2001) both in the pre- and post-test assessment. All tasks of the inhibition battery are administrated twice, excepted for the CPM that is administrated only at the baseline. In addition, in order to obtain a more accurate analysis of the implications of the training programme, we provide a series of pre- and post-test questionnaires to measure both the executive functions and the autonomies in the daily life of individuals with DS.

A follow-up at one month and six months to test maintenance effects is executed (see Lanfranchi et al., 2017; Bennet et al. 2013). This study is in accordance with the recommendations of the Ethical Code of Italian Register of Professional Psychologists and of the Ethical guidelines of the Italian Association of Psychology with written informed consent from all subjects, in accordance with the Declaration of Helsinki.

8.2.3 Measures

8.2.3.1 Inhibitory and delay of gratification battery of laboratory tasks

As mentioned above, all participants complete the baseline assessment to measure non-verbal reasoning abilities with the CPM. All participants complete also baseline measures of inhibition and delay of gratification skills using the battery of tasks presented in depth in the Chapter 4 (see Fontana et al., 2021b). As a reminder, the battery of eight tasks was briefly described in Table 8.2, whereas a detailed description of laboratory tasks is presented in the Chapter 4 of the present dissertation.

8.2.3.2 Executive functions in everyday life

BRIEF2 is used to assess the everyday behaviours of EFs we propose the because it assess EFs from 5-to-18 years old in TD population and therefore it would be more developmentally appropriate for the levels of MA of our participants. The informant report form is used in this study and respondents comprise both parents or carers and Professional Educators that closely work with our sample with DS. This is a pen-and-pencil measure that assess with a total of 63 items the following components: Inhibit, Self-monitor, Shift, Emotion regulation, Initiate, working memory, Plan/Organise, Task Monitor, and Organisation of Materials. Higher scores on the BRIEF represent greater levels of EF impairment. We use raw scores for analysis given the potential for discrepancy between MA and CA for the group with DS (Daunhauer et al., 2017). An adequate test-retest reliability (r's = .78-.90); internal consistency (r's = .80-.97) and concurrent validity with rating scales of attention and behaviour such as the Child Behavior Checklist were reported by Gioia et al. (2000).

Given the important difficulty to complete the self-report form of the BRIEF2 for participants with DS, we created a short questionnaire using a high comprehensibility language with the support of images to qualitative investigate the perception of our sample with DS on their inhibitory and self-regulatory skills before and after the training program. The present questionnaire is composed by 15 items that specific evaluate response inhibition, interference suppression, and delay of gratification abilities. One example of item presented is: "Ho paura quando devo fare una cosa che non conosco." (i.e., "When I have to do something unknown, I'm scared"). Subjects have three emoticon response choice (i.e., a thumbs-up for the "I agree" response, a thumbs-down for the "I don't agree" response, and a person with raised arms for the "I don't know" response). Individuals with DS who have good reading-writing skills complete the questionnaire independently with the possibility to ask for help to the trained psychologist in case of doubt, while for subjects with DS with poorer reading or no reading abilities the trained psychologist read the sentence helping the subject to understand the request.

Finally, to assess different areas of autonomy, we used a questionnaire developed by Contardi (2016) for people with intellectual disabilities and more specifically for people with DS. The questionnaire is composed of 11 scales that assess: Socialization (range: 8-32); Communication (range: 12-48); Ability to choose and proactive behaviour (range: 8-32); Orientation and behaviour on the road (range: 12-48); Use of public transport (range: 6-24); Handling money and using shops (range: 11-44); Orientation in time (range: 4-16); Handling the telephone (range: 7-28); Reading-writing skills (range: 5-20); Personal hygiene and self-care (range: 5-20); and Unexpected situations (range: 4-16). A score of 1 is assigned for the answer "no", a score of 2 if the answer is that the person with DS needs help to perform a given task, a score of 3 if the person with DS performs the task only if expressly asked to do so, and a score of 4 if the answer is "yes". Some examples of the questions are: "Does he/she communicate his/her needs and wishes"; "Does he/she go to the bathroom by him/herself"; "Can he/she count money". Cronbach's alpha for the Autonomy questionnaire is .72 (Fontana et al., under review).

8.2.4 Training program

The intervention program we developed aimed to foster response inhibition, interference suppression, and delay of gratification skills through a series of game activities proposed to small groups of five individuals with DS. It requires progressively higher levels of inhibitory skills and self-regulation control (see Traverso et al., 2015). The groups' activities were performed two times a week for a total of 20 meetings each during approximately one hour over approximately five months, including pre- and post-test assessment (Pellizzoni et al., 2020; Traverso et al., 2015). The reason why we proposed a group-based training program (rather than an individual program) lies in the fact that: a) working with small groups of individuals with DS is not only an organizational choice, but it is mainly an educational experience (Contardi, 2016, pp. 33-35), b) usually people with DS faced mainly with adults without DS (e.g., carers, parents, siblings, educational figures, and therapists), leaving behind the importance to interface and to learn by peers, and c) working in small groups reduce potential factors that influenced the training outcomes (e.g., one to one attention, researcher influence, aware to participating in a training as a part of a study, see McGlinchey et al., 2019).

8.2.4.1 Training group

As mentioned above, our training on inhibition and on delay of gratification includes two meetings a week which take place in a silent room with specific games created on the basis of the battery of tasks developed by Usai et al. (2017). The total of 20 meetings are divided as follow: 8 meetings for response inhibition and delay of gratification in order to consolidate simpler inhibitory components and 12 meetings tapping on the more complex inhibitory dimension of interference suppression. During each meeting, the group is provided simple strategies and meta-cognitive “pills” to enhance their inhibitory abilities. Each activity required that the entire group reach the fixed goals with the aim of creating a climate of collaboration and mutual help and assistance between the participants in order to reach the goal. Each activity started with a brief introduction of the session and ended with a metacognitive activity consisting on asking to colour two thermometers, one that indicate the level of enjoyment perceived and one that evaluate the level of new skills learned during the session. Table 8.3 presents some examples of the activities that would be carry out by the training group.

8.2.4.2 Active control group

The ACG carries out the same total number of activities (n = 20, two meetings per week with a duration of approximate one hour for each one). The 20 meeting would be divided as follows: five activities are focused on watching and discussing five different movies, five activities promote shared reading and discussion of a newspaper article, five activities focus on the discussion of a topic chosen by the group participants, while five activities concern the preparation of recipes from cookbooks or available online.

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Table 8.1. Description of the more recent researches on EFs' training programs in individuals with DS.

Training approach	Author/s (year)	Sample	Function/s trained	Training program	Results
Play-based and curricular	Conners et al. (2008)	N = 16; CA = 6-14 years ($mean_{CA}$ = 10.6, SD = 2.4); IQ = 36-73 (M_{IQ} = 49.9, SD = 11.3)	Auditory memory span	*Duration:* 10-min sessions 5 times a week for 3 months (one or two 3-month periods). *Materials:* rehearsal and auditory training. Group 1 received memory training for the first 3 months, visual activities (a control condition) for the second 3 months, and memory training for the third 3 months. Group 2 followed the inverse schedule. *Setting:* home-based training with parents.	Auditory verbal memory span: positive effect. Distal outcome measure (sentence memory and verbal working memory): no improvement.
Play-based and curricular	Costa et al. (2015)	N = 2 (E.H. = 17 years and 3 months, and A.S. = 15 years and 11 months)	Visuo-spatial STM and WM	*Duration:* 12 training sessions (twice weekly). Training duration was 40 min per session. *Materials:* paper-and-pencil activities and games. *Setting:* individual school-based treatment by trained psychologists.	E.H. showed good direct and transfer effects to passive and active verbal WM tasks, while A.S. only showed direct effects on visuospatial WM.
Physical	Chen et al. (2015)	N = 20 *Attentional group:* $mean_{CA}$ = 20.58 years, SD = 5.74; $mean_{MA}$ = 5.75 years, SD = 1.91. *Exercise group:* $mean_{CA}$ = 23.45 years, SD = 4.86; $mean_{MA}$ = 6.49 years, SD = 2.10.	Choice–response time; Attention shifting; Inhibition	*Duration:* 20 min for both the group that walked on a treadmill and for the group who watched a video. *Materials:* treadmill walking. Ten individuals with DS were assigned to the group who walked on a treadmill for 20 min (excercise group) and ten were assigned to the group who watched a video (attentional group).	Inhibition: positive effect. Choice–response time and attention shifting: no significant improvement.

				Setting: individualized intervention.	
Physical	Holzapfel et al. (2015)	N = 48 *Assisted Cycling Therapy (ACT):* N = 18; $mean_{CA}$ = 19.4 years, SD = 4.9; $mean_{MA}$ = 6.1 years, SD = 3.3 *Voluntary cycling (VC):* N = 16; $mean_{CA}$ = 18.4 years, SD = 3.4; $mean_{MA}$ = 5.2 years, SD = 2.1 *No cycling (NC):* N = 14; $mean_{CA}$ = 17.0 years, SD = 4.0; $mean_{MA}$ = 6.0 years, SD = 1.8	Cognitive planning ability	*Duration:* Those in the ACT and VC groups completed 30 min sessions three times per week on a stationary bicycle. The NC group completed only the pre- and post-testing sessions. *Materials:* modified motorized stationary recumbent bicycle (Exercycle; Franklin, MA). *Setting:* individualized intervention.	Planning: significant improvement.
Physical	Ringenbach et al. (2016)	N = 44 *Assisted Cycling Therapy (ACT):* N = 17; $mean_{CA}$ = 19.4 years, SD = 4.9; $mean_{MA}$ = 5.6 years, SD = 4.3 *Voluntary cycling (VC):* N = 16; $mean_{CA}$ = 18.4 years, SD = 3.4; $mean_{MA}$ = 5.1 years, SD = 2.0 *No cycling (NC):* N = 11; $mean_{CA}$ = 17.2 years, SD = 4.3; $mean_{MA}$ = 6.2 years, SD = 1.9	Set-shifting; Response inhibition	*Duration:* 8 weeks for ACT and VC groups. *Materials:* modified motorized stationary recumbent bicycle (Exercycle; Franklin, MA). *Setting:* individualized intervention.	Response inhibition: positive effect. Set-shifting: no significant improvements.

Technology-based	Bargagna et al. (2019)	N = 9 (6 children, $mean_{CA}$ = 9.5 years, SD = 1.7; 3 children, $mean_{CA}$ = 5.5 years, SD = 0.5). Data were reported only for two children with DS (i.e., S. and F.).	Inhibition; Visuospatial WM	*Duration:* 45-min weekly sessions for 8 weeks. *Materials:* Bee-Bot robot (Bee-Bot Campus Store, TTS Group) that is a black/yellow robot. It has a bee shape and is capable of storing of up to 40 instructions in programmable sequences. Children can control the Bee- Bot by giving it a sequence of simple instructions for movements, using seven buttons positioned on its back. *Setting:* individualized intervention.	Inhibition: no significant effect. Visuospatial WM: positive effect. *N.B.:* authors reported that "due to sample heterogeneity, qualitative results of only two exemplificative children are presented and discussed".
Technology-based	Bennet et al. (2013)	N = 25; CA = 7-12 years ($mean_{CA}$ = 9.6 years, SD = 1.11); MA = 4-7 years ($mean_{MA}$ = 5.5 years, SD = 1.01)	Visuo-spatial WM	*Duration:* 25 training sessions (25 min per session three times a week). Children were encouraged to complete all three training activities for a session on the same day. *Materials:* 7 computerized visuospatial training tasks (4 involved only the storage of visual information, two involved both manipulating and storing visual information, and one incorporated the storage of auditory information alongside visual information). Participants were randomly allocated to one of two groups (intervention or waiting list control). *Setting:* individualized intervention trained by Special Educational Needs Coordinator or Teaching Assistants.	Positive effect on visuospatial STM
Technology-based	Herrero et al. (2019)	N = 26, CA = 7-17 years ($mean_{CA}$ = 9.1 years, SD = 1.5)	Selective attention; Visuospatial STM; Visuospatial processing	*Duration:* at least one hour per week during a period of three months (minimum of three periods of 20 minutes per week of use to each application). *Materials:* Three applications presented as tablet games (i.e.,	Visuospatial STM: significant improvements through training. Selective attention: no significant improvement.

				Bubbles, Pairs and learn, and Tangram). *Setting:* individualized intervention during daily classroom activities supervised by trained teachers.	
Technology-based	Lanfranchi et al. (2017)	N = 61 *Experimental group:* N = 25; $mean_{CA}$ = 148.60 months, SD = 34.29; $mean_{MA}$ = 78.68 months, SD = 14.78 *Active control group:* N = 18; $mean_{CA}$ = 159.0 months, SD = 38.91; $mean_{MA}$ = 77.79 months, SD = 22.39 *Passive control group:* N = 18; $mean_{CA}$ = 138.44 months, SD = 33.36; $mean_{MA}$ = 76.28 months, SD = 11.95	Spatial-simultaneous WM	*Duration:* twice-weekly, 30-min sessions over a period of 4 weeks (with 8 sessions in all). *Materials:* The first group trained on simultaneous components of visuospatial WM adapted from the "visuospatial working memory" (Mammarella et al., 2010); the second served as active control group who completed activities on vocabulary adapted from the "Lexicon and spelling" training program (Bigozzi, Falaschi, & Limberti, 2013); and the third attended the pre-and post-test and follow up assessment. *Setting:* individualized interventions.	Spatial-simultaneous WM passive tasks: positive effect. Spatial-simultaneous WM active tasks: positive effect. Near transfer effects were found on other WM components (i.e., spatial-sequential and verbal WM), but only on active attentional demanding tasks.
Technology-based	McGlinchey et al. (2019)	N = 40; CA = 30-49 years ($mean_{CA}$ = 36.9 years, SD = 5.7). *Intervention group:* N = 20; $mean_{CA}$ = 36.9 years, SD = 5.65; $mean_{IQ}$ = 43.29, SD = 7.70 *Delayed intervention:* N = 20; $mean_{CA}$ = 36.9 years, SD = 5.9; $mean_{IQ}$ = 43.45, SD = 8.10	Inhibition; Planning; Problem solving; Visual attention; visual and spatial WM; Shifting; Processing speed	*Duration:* 20 min per day, 5 days a week, for the duration of the 8 weeks. *Materials:* The online training programme used was Scientific Brain Training Pro. Twelve games were chosen for inclusion, which targeted a range of EFs, including planning, attention, working memory, problem solving and processing speed. *Setting:* individualized interventions.	Inhibition and planning: positive effect (the most improved components). No significant improvements were found for the other components, excepted for the global executive composite score. Positive effects reflected in everyday behaviours were not as expected. Scores on all assessments at T3 (post-intervention) for the delayed intervention group were higher as compared with T2.

Table 8.2. Battery of laboratory tasks for the pre- and post-test assessment.

Task	Component assessed	Description	Scoring
Circle drawing task (Bachorowski & Newman, 1985)	Response inhibition and motor inhibition.	Participants have to trace with the finger a depicted circle on the following two conditions: the first (T1) with neutral instruction and the second (T2) with inhibitory instructions.	The proportion of slowdown with the following formula: T1−T2/T1+T2.
Preschool matching familiar figure task (Traverso et al., 2016; adapted from Kagan, 1966).	Control impulsive responses.	Participants have to select between five alternatives which figure is identical to the target one.	Number of errors (0-no limit) and RT (expected range 0-no limit) are recorded.
Go/no-go task (adapted from Berlin & Bohlin, 2002)	Response inhibition.	Participants have to press or to do not press the space bar according to specific instructions given from the examiner.	The sum of the correct no-go responses (1 point for each correct no-go response) is considered. There are three conditions: the first and the second one range 0-6, while the third rages 0-8. Also RT of the no-go items (expected range 0- no limits) are recorded.
Grass/snow task (adapted from Carlson & Moses, 2001)	Response inhibition.	Participants have to tap on the green square when they hear the word "snow" and to tap on the white square when they hear the word "grass".	Number of correct answers (expected range: 0-16) and RT (expected range: 0-no limits).
Fish flanker task (Usai et al., 2017)	Interference suppression.	Participant have to respond to a left- or right-oriented fish by pressing a left or right	Accuracy (expected range: 0-16) and RT (expected range:

		response button on the keyboard, focusing only on the target fish and not to flankers.	0-no limits) in the incongruent condition are recorded.
Hearts and flowers task (Usai et al., 2017)	Interference suppression.	Participants have to press on the keyboard the button on the same side when a heart appeared on the computer screen, while to press the button on the opposite side when they saw a flower.	Accuracy (expected range: 0-20) and RT (expected range: 0-no limits) are recorded.
Gift wrap task (Kochanska et al., 1996)	Delay of gratification.	The participants are told that they should not turn until the examiner has finished to wrap the gift.	The latency to the first peek (expected range: 0-60 s) is recorded.
Marshmallow task (Mischel et al., 1989)	Delay of gratification.	Participants are informed that the examiner has to leave the room and they have to wait to eat the treat until the experimenter will be back in the room. Only if they follow the rule, they could receive the larger pile of treats.	Waiting time (expected range: 0- 5 min) is recorded.

Table 8.3. Description of some activities proposed in the two settings to the training group.

Name of game	Area of focus	Description
The chest of gold coins	Response inhibition	Subjects have to find the same coins positioned on the table as quickly as possible to collect the major number of golden coins but all participants have to stop when the experimenter lift a red pallet (who does not stop loses and stays still for the rest of the game).
The magic maze	Interference suppression	Participants are sitting in front of a maze that contains some objects use in daily routine (e.g., a phone, a wallet, a watch) and a deck of cards (also composed by elements that are not presented in the maze). Participants have to draw the card and check if the object depicted in the car is presented also in the maze and to place the card on top of the image in the maze (if the figure is not present, they have to move to the next card).
The last one that ends will be the winner!	Delay of gratification	Participants, after having prepared each their own sandwich, have to eat it as slowly as possible (who finishes the sandwich last).
Shopping, shopping, shopping!	Response inhibition. This exercise is also effective for the understanding of the different cuts of money that individuals with DS must use during the activities of autonomy carried out directly in shops.	Each participant brings home 3 objects and during the activity each subject takes turns as a shopkeeper while others have to buy the item at auction. Each participant has at their disposal some not original money with which they can buy the desired object. To be able to book at the auction, however, participants must raise a pallet and wait their turn.
Friendship or love?	Interference suppression and the ability to recognize different emotions and relationship.	Participants are seated in front of a monitor in which images are presented related to different relationships: friendship, love, kinship, or neutral images. Each subject has 4 paddles (one for each condition) and, when requested by the experimenter, they

		all have to raise together the paddle that they think corresponds to the image.
I wait for my friends!	Delay of gratification and the ability to behave adequately within a social context.	During a happy hour activity, one participant at a time have to order what she/he prefers, but she/he can not eat or drink what he ordered until all the friends will be seated at the table.

M1 = meeting which take place in a silent room with specific games created on the basis of the battery of tasks developed by Usai et al. (2017); M2 = meeting carries out during their regular weekly activity to promote their autonomies.

CHAPTER 9

General Discussion

9.1 Discussion

The general aim of the present dissertation was to better understand and promote inhibitory processes in individuals with Down syndrome (DS) with the same mental age (MA) of a typically developing (TD) control group. Given the importance to examine and to assess inhibition as a multicomponential construct (Howard et al., 2015; Rey-Mermet et al., 2017) and to consider hot and cool executive functions (EFs) as a part of a continuum (Zelazo & Müller, 2002), we mainly focused on the following three components which require inhibitory skills: response inhibition, interference suppression, and delay of gratification. Furthermore, given the crucial role of adaptive functioning and autonomies in everyday life (Daunhauer et al., 2017; Sabat et al., 2020), we tested also potential relationship between autonomy in everyday life and inhibitory sub-components. Finally, we developed and implemented two training programs aimed to potentiate EFs – with an attention to both more cognitive and emotional-motivational inhibitory processes –, one specific for pre-schoolers of 4 years of age and one basing on the peculiar inhibitory profile of individuals with DS.

Specifically, the first study (Chapter 2) aimed to meta-analysed studies that assess inhibitory skills in individuals with DS matched or not with a TD control group, considering also some important moderators such as: a) task type of stimuli presented (verbal vs visuospatial) and the type of response required, and b) chronological age (CA). The second study included in the present dissertation (Chapter 3) was created in order to: a) better understand performance on both inhibitory sub-components in individuals with DS (i.e., response inhibition and interference suppression), and b) to verify whether a two-factor model fit the data also in TD children aged 5 and 6 (see Gandolfi et al., 2014). Subsequently, the third research (Chapter 4) was performed with the following goals: a) to extend the sample of the previous research; b) to increase the number of tasks used for the assessment of the inhibitory sub-components (i.e., response inhibition and interference suppression) in individuals with DS matched for a measure of MA with a TD control group; c) to analyse also hot dimensions such as the delay of gratification ability in both samples; d) to cross-sectionally assess different inhibitory dimensions in individuals with DS divided on the basis of their CA. Given that the paucity of studies that focused on inhibitory skills in individuals with DS highlighted an important difficulty on more complex inhibitory aspects such as interference suppression and proactive interference (see Borella et al., 2013; Traverso et al., 2018), the fourth study (Chapter 5) investigated interference suppression with an adapted non-verbal version of the Navon task (Navon, 1977). The main goals of the fourth research were to analyse differences between individuals with DS and TD children matched for a measure of MA on: a) global-local processes, which suggest a difficulty on interference suppression; and b) congruent *vs* incongruent conditions. Basing on previous literature, it emerged that inhibition and working memory (WM) play a crucial role on adaptive behaviour (AB) and autonomies in people with DS (Daunhauer et al., 2017; Sabat et al., 2020). To this purpose, the fifth study (Chapter 6) investigated possible relationships between specific aspects of autonomy in everyday life and response inhibition, interference suppression, and WM in a sample with DS divided in two sub-groups basing on their autonomy levels (i.e., lower levels of autonomy – LA – *vs* medium-to-high levels of autonomy – MHA –). Finally, the sixth and the seventh studies included in the present dissertation (see respectively Chapter 7 and Chapter 8) aimed to improve cool and hot EFs, with a specific focus on inhibitory skills, both in TD children and in individuals with DS with two different training programs. Specifically, the first training program implemented with 91 TD children of 4 years of age aimed to improve both hot and cool EFs and emotion regulation (ER) while the second training was specifically created starting by the peculiar inhibitory profile of people with DS delineate with previous studies and with the previous literature. Therefore, this latter training program aimed to: a) ameliorate response inhibition, interference suppression, and delay of gratification in individuals with DS, and b) analyse a possible impact on levels of EFs in everyday life and on everyday autonomies. Unfortunately, the implementation of the latter training was interrupted due to the Covid-19 pandemic emergency (Chapter 8 presented only the experimental design and data are not yet available for a discussion).

9.1.1 Inhibitory trajectories in individuals with Down syndrome considering different inhibitory sub-components

In the last few decades an increasing amount of studies are focusing on inhibition in individuals with DS for the purpose to delineate a specific profile in this population and to promote intervention programs to ameliorate their inhibitory skills. Given the contradictory findings emerged by the literature, our meta-analysis (Fontana et al., 2021a) presented in the Chapter 2 of the present dissertation, highlighted some critical issues regarding studies that assessed inhibition in individuals with DS such as: a) high levels of variability in the tasks used to assess inhibition; b) lack of reference to a theoretical model of inhibition (see for exceptions Borella et al., 2013; Traverso et al., 2018); c) lack of differentiating the construct on the basis of the specific inhibitory sub-components (see Borella et al., 2018; Gandolfi et al., 2014; Traverso et al., 2018); d) absence of a TD control group matched for a measure of MA in some researches. A clear implication is that contradictory findings emerged. In fact, while some studies reported worse performance on inhibitory tasks compared to a TD control group (e.g., Lanfranchi et al., 2010; Amadò et al., 2016), other studies found no differences on inhibitory performance between the two groups (e.g., Cornish et al., 2007; Carney et al., 2013), whereas in even other studies mixed results were reported (e.g., Borella et al., 2013; Costanzo et al., 2013; Daunhauer et al., 2017; Traverso et al., 2018). It should be noted that the latest studies mentioned assess inhibition with more than one task considering different dimensions such as response inhibition, interference suppression, proactive interference, or delay of gratification (for a more detailed description of differences between these construct see Traverso et al., 2020 and Garon et al., 2016). Recently, Tungate and Conners (2021) published a meta-analysis in individuals with DS, focusing on the overall construct of EFs. The study indicated that groups with DS performed significantly worse on EFs tasks than TD control groups matched for MA both when they considered the overall composites scores for EFs and for inhibition, shifting, and WM. Moreover, the authors identify that WM and shifting are the most impaired component with a large effect, while inhibition seems to be less impaired with a medium effect. However, the inclusion and exclusion criteria for studies included in the meta-analysis in question are not well defined, except for the matching criterion for MA. In line with this research, our meta-analysis (Fontana et al., 2021a) indicated a small-to-medium effect size which would lead to think that inhibition could be considered as moderate impaired. This study, however, also had as its goal to identify any differences in performance when a matching for a measure of MA was included or not. The supplementary analysis indicated that when a matching for MA was not provided, no differences emerged between the group with DS and the TD control group and even more that the overall heterogeneity increased, confirming the importance, whenever possible, to match the group with DS with at least one control group with TD (see also Roberts & Richmond, 2014). Both Fontana et al. (2021a) and Tungate and Conners (2021) suggested the importance to consider also some crucial moderators such as task modality and CA. While CA did not result as a significant moderator in both studies, the task modality emerged as a significant moderator in the second study but not in the first one. It should be noted that it has been possible to include only 8 studies in the specific meta-analysis on inhibitory dimensions and that these results should be considered with caution. Furthermore, regarding inhibition, the tasks used to assess inhibition engage different processes (e.g., Go/No-Go task is used to assess cool components of EFs, while the Delay of gratification task hot EFs). As repeatedly stressed in the course of this dissertation, it clearly emerges the need to consider inhibition as a multi-dimensional construct that includes different components that are implicated in performing different tasks (Nigg, 2000; Diamond, 2013). In fact, as suggested by several studies on TD children of different age stages, a two-factor model in which response inhibition and interference suppression were distinguished, best described data (see Bunge et al., 2002; Gandolfi et al., 2014). Interference suppression – the most complex components that is strongly related to WM (Traverso et al., 2020) – may emerge after response inhibition in pre-schoolers aged 36-to-48 months with a significant improvement during middle childhood (Cragg, 2016). In line with other studies (e.g., Davidson et al., 2006; Traverso et al., 2016), Traverso and colleagues (2018) – presented in Chapter 3 of the present dissertation – showed that children aged 6 years were more accurate than TD children of 5-year-olds in most of the tasks tapping on response inhibition and interference suppression, although there were no differences in terms of fluid intelligence measured with the Coloured Progressive Matrices Test (CPM, Belacchi et al., 2008). On the other hand, concerning the group with atypical development, an inconsistent pattern of performance on inhibitory tasks and a high variability on their performance emerged (see also Rey-Mermet et al., 2017; van Belle et al., 2015). When the group with DS was matched with two TD control groups respectively of 5 and 6 years of age, the group with DS appeared more impaired than the 6-year-olds group on the Preschool Matching Familiar Figure Task (PMFFT) and showed worse performance than both TD control groups in the Dots task (considering accuracy score). However, no differences emerged in the Go/No-Go task and in the Fish Flanker Task. For instance, examining the results of the Go/No-Go task, also Costanzo et al. (2013) did not find any differences between the group with DS and the TD control group. In contrast, Fontana and colleagues (2021b) – described in depth in Chapter 4 – analysed separately all the three conditions of the Go/No-Go task, identifying that the last two blocks were more challenging for people with DS. They explained their results suggesting that this specific difficulty could be due to the fact that they had to remember to inhibit impulsive responses and to simultaneously remember different rules (Langenecker et al., 2007). As indicated by the literature, also delay of gratification tasks – in which individuals had to resolve the conflict to avoid a more salient and immediate reward in order to obtain a less salient but delayed reward – are considered as important measures to assess the simpler form of inhibition as a hot dimension (Garon et al., 2008; Groppe & Elsner, 2004; Hongwanishkul et al., 2005). There is a widespread agreement on the impairments of individuals with DS on delay of gratification abilities and on their shorter waiting time (e.g., Cuskelly et al., 2003; Daunhauer et al., 2017; Fontana et al., 2021b). Previous researches that focused on delay of gratification in individuals with DS suggested that their difficulties could be due to: a) difficulties on self-talk skills and abstract concepts (Cuskelly et al., 2001; Kable, 2015); b) poorer performance also on other inhibitory tasks that assess cool components that required both the ability to control impulses and to manage interferences (Yu et al., 2016).

Examining instead the interference suppression components on the basis of the current literature, contradictory finding emerged suggesting the importance to investigate in depth this more complex component. While Hauser-Cram and colleagues (2014) have found worse performances on accuracy score using the Fish Flanker task when people with DS faced with incongruent items, Traverso and colleagues (2018) and Fontana and colleagues (2021b) did not detected any differences between the group with DS and the TD control groups. It should be noted that the first two mentioned studies did not matched their samples with DS with a TD control group and even more the second study assess interference suppression with a verbal version of the Flanker task. These differences could be due to the fact that both groups were more motivated to perform the Fish Flanker task given the attractive graphics used and the presentation modality, and that they could be helped by the practical story told by the experimenter with respect to abstract rules and more complex to understand and memorize of the other tasks proposed (e.g., the Hearts and Flower task or Dots task). In fact, both the Dots task and the PMFFT may require higher levels of WM in order to actively maintain the main goal of the task (Munkata et al., 2011). The choice to adapt a well-known task such as the Navon task (see Chapter 5), was based by the need to extend the knowledge in the current literature on the interference suppression component, making sure that this task could fits with the specific profile of the persons with DS. For this reason, we adapted this task using non-verbal familiar stimuli (i.e., hearts and stars) and motor responses instead of verbal responses. Our results indicated no differences on global-local processing between the group with DS matched for MA with TD children, with a better performance for global rather than local stimuli, and a worse performance for incongruent rather than congruent conditions. Considering incongruent information and the ability to suppress interferences, individuals with DS showed even more difficulty than TD children. These results are in contrast with those of D'Souza and colleagues (2016) that instead have questioned the classification of people with DS as "global processors", showing more local than global matching, though the difference was not significant, while are in line with those of Bellugi et al. (2000) and Porter and Coltheart (2006) in which when asked to name an incongruent local condition figure, people with DS wrongly named the global one. It should be highlighted that the studies above mentioned that used a classic or adapted Navon task, showed some critical points maybe due to the fact that: a) a large proportion of the sample with DS withdrew from the task because they found the stimuli too difficult and too quickly to process (e.g., D'Souza et al., 2016); b) the choice to use verbal stimuli or verbal responses could influence the performance of people with DS on this task (e.g., Bellugi et al., 2000; Porter & Coltheart, 2006). Finally, another important aspect to consider in the assessment of inhibition is the ability to manage response times (RT) both in children with TD and in people with DS. Overall, literature suggested that, as early pre-schoolers (Traverso et al., 2016), individuals with DS are not able to control response time in order to be more accurate, and that RT may not be a useful index in this population in the evaluation of inhibitory skills (see also Smith et al., 2019; Traverso et al., 2016; 2018).

However, in the panorama of the most recent literature, it could be observed the need to consider alongside the MA also the chronological age (CA) of people with DS in order to outline increasingly specific profiles of cognitive functioning (see Tsao & Kindelberger, 2009) given also the progressive increase in life expectancy of individuals with DS – currently reaching above 60 years of age – (Bittles & Glasson, 2004). In fact, regarding inhibitory developmental trajectories in individuals with DS, only few studies longitudinally or cross-sectionally analysed these components with different measures. For example, the majority of studies cross-sectionally examined developmental trajectories using indirect measures such as the Behaviour Rating Index of Executive Function (BRIEF). For instance, while Lee and colleagues (2015) indicated that inhibitory abilities may improve with age from 4 to 24 years old, Loveall and colleagues (2017) suggested that inhibitory skills could be consistent from 2 to 18 years of age, with a decline around 30-year-olds. Nevertheless, the choice to use rating-based measures leads to some crucial considerations such as: a) the fact that some researches found inhibitory impairments only when individuals with DS were rated by their carer but not by their teachers (e.g., Daunhauer et al., 2017; Lee et al., 2011), while other studies found the opposite results (e.g., Tomaszewski et al., 2018); and, b) only small-to-medium correlations emerged between the two raters (Gioia et al., 2003). Fontana and colleagues (2021b), using a specific battery of tasks to assess response inhibition, interference suppression, and delay of gratification in individuals with DS, cross-sectionally found that simpler inhibitory components (i.e., response inhibition and delay of gratification) may improve with CA, while the interference suppression component – which is the more complex – still remain impaired also in adulthood. In fact, in line with the Compensation Age Theory (Lifshitz-Vahav, 2016), CA could influence cognitive skills in individuals with intellectual disabilities beyond their MA. Furthermore, different levels of maturation and autonomy in everyday life in addition to cumulative life experiences, could influence better performance on inhibition and the ability to cope with suitable strategies in order to learn new challenging skills necessary for daily life (see also Numminen et al., 2001).

9.1.2 The importance to consider adaptive behaviour and autonomy in everyday life in both the assessment and in the improvement of inhibitory skills in individuals with Down syndrome

The most recent literature on individuals with DS highlighted the crucial role to jointly investigate and improve the cognitive and behavioural aspects essential for a more autonomous life. Adaptive behaviour (AB) is usually impaired in individuals with DS (Steingass et al., 2011), with greater difficulties especially with managing money, cooking, moving in the community, organizing their time, functional academics, and shopping (Tomaszewski et al., 2018). Nevertheless, researches that focused on AB in people with DS reported contradictory findings. Whilst most studies observed that socialization and practical skills are relative strengths in this population which remained stable in adolescence and adulthood (Fidler et al., 2006; Tomaszewski et al., 2018), other studies reported that social skills declined over time (e.g., Bertoli et al., 2011; Makary et al., 2015; Sabat et al., 2020). It seems that the greater impaired AB profile in individuals with DS lies in some skills such as conceptual, communication, and motor skills (Fidler et al., 2006). Sabat and colleagues (2020), suggested that WM significantly predicted conceptual AB in a sample with DS, rather than inhibition or flexibility, based on their parents' reports, whereas the reverse was true when they were rated by their teachers. The researchers indicated that it could be due to the fact that WM plays a more important role in the conceptual skills required in home activities, while inhibition and shifting are more requested in the school environment. Basing on the literature, we conducted a research (presented in Chapter 6 of the present dissertation) aiming to better understand the relationship between inhibitory sub-components together with WM and different levels of autonomy in individuals with DS. Specifically, the analysis of correlations between the cognitive tasks and different levels of autonomy, it emerged that response inhibition, interference suppression, and WM were all linked with total scores for autonomy. These results are in line with some recent studies that suggested the crucial role that all the three components have on autonomy, and on crucial skills such as handling money (Sabat et al., 2020). Furthermore, our results highlighted that interference suppression - the more complex inhibitory component that also demands WM - seems to have the greater role in the acquisition of more structured aspects of autonomy in adolescents and adults with DS such as handling money and using shops, orientation in time and behaviour on the road, communication, and reading-writing skills. It is known that the greater number of individuals with DS have difficulties with time management, reading-writing skills, manage and use money which are strongly related to both low impulse control and poor resistance to distractors (Cabezas & Carriedo, 2019) but also with academic performances (Belacchi et al., 2014).

In line with the aim to investigate in depth the relationship between different levels of autonomy in everyday life, inhibitory sub-component, and WM, we divided in two sub-groups basing on their autonomy levels (i.e., lower levels of autonomy – LA – *vs* medium-to-high levels of autonomy – MHA –). Our results suggested that the LA group showed worse performance in accuracy score in all the three components measured with specific laboratory tasks (i.e., response inhibition, interference suppression, and WM). Once more, response time (RT) did not show significant results indicating the importance to consider accuracy score as a reliable index of EFs skills in individuals with DS (see also Traverso et al., 2018; Smith et al., 2019; Fontana et al., 2021b).

9.1.3 Is it possible to improve executive functions both in structured contexts and in everyday life?

Given the importance of inhibitory and WM skills and their relationship with greater levels of AB and autonomies in daily life, some researchers tested different type of training programs to improve these abilities in individuals with DS. Although the greater number of studies aimed to train both verbal and visuo-spatial WM, Danielsson and colleagues (2015) conducted a meta-analysis in order to examine WM training programs effectiveness in individuals with intellectual disabilities. Their results suggested that different type of training programs could lead to different results in terms of effectiveness. In particular, mixed approach – including the enhancement of both verbal and visuo-spatial components, seems to produce better results. Literature on TD children suggested a categorization of different approaches to train EFs (see Marzocchi et al., 2020), dividing them into three categories: a) play-based and curricular approaches, b) physical approaches, and c) technology-based approaches. Analysing literature focusing on training to ameliorate inhibitory abilities in individuals with DS, an overall positive effect emerged (e.g., Chen et al., 2015; McGlinchey et al., 2019). Recently, Sung and colleagues (2021) conducted a meta-analysis to verify the effectiveness of EFs intervention programs in children, adolescent, and adults with intellectual disabilities, suggesting that the physical activity-based interventions on EFs have positive effect but this effectiveness seems to be influenced by different factors, including the CA of the individuals to whom they are targeted, the duration of the intervention, and the specific domain considered. The Chapter 8 of the present dissertation describes our attempt to implement a specific training program for individuals with DS aimed to ameliorate their inhibitory skills – considering specific inhibitory sub-components and delay of gratification – both in more structured environments and in daily life. Unfortunately, it is currently impossible to discuss this intervention because the Covid-19 pandemic did not allow the research already started to be concluded.

Despite the impossibility to carry out the study on the implementation of a specific training program for individuals with DS, it was instead possible to conclude another intervention designed specifically for children with TD in pre-school age. In particular, this training program was created to improve both cool and hot EFs together with emotion regulation (ER) in TD children of 4 years of age. The first 10 activities were proposed to improve inhibitory skills (see Traverso et al., 2015), while the second set of 10 meetings focused on encouraging participants to implement ER strategies (see Ellis & Bernardi, 2006; Di Pietro, 2014). Our results showed that the training group (TG), compared to an active control group (CG), demonstrated significant differences in the overall EFs profile. In particular, cool inhibitory and WM components improved with an increasing amount of correct responses; hot EFs showed an improvement in the delay of gratification waiting time; and ER ameliorate in relation to emotion vocabulary and in proposing more pro-social problem solving strategies. Referring to the literature, usually EFs and ER have been studied and improved separately, whereas in our study all of these components increase during the training program, indicating even more that these abilities are strongly correlated (see also Nakamichi, 2017). Silkenbeumer and colleagues (2016) had in fact highlighted that good levels of connection between inhibitory abilities and ER are indicative of better behavioural responses to emotional situations.

9.2 Clinical-educational implications and future directions

The overall results of the present dissertation may have several implications both for the assessment and for the development of intervention programs for individuals with DS. At first, future studies should consider the importance to select and 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. In fact, some tasks designed for TD children (i.e., using childish cartoons or materials) are not suitable for teenagers and adults with DS. Regarding CA, an important implication is related to the fact that it would be useful to reduce CA ranges or at least to consider the possibility to divide the sample in sub-groups on the basis of their CA considering a developmental perspective of different inhibition abilities and analyzing how age and experience could influence inhibitory skills at different stages of age.

Secondly, future studies should consider the importance to test a specific theoretical model on inhibition also for individuals with DS or at least to include a theoretical model for the selection of tasks and for the discussion of the results. Furthermore, as suggested by the literature, future researches should consider specific inhibitory sub-components in order to better define the inhibitory profile of individuals with DS for each specific developmental stage (e.g., Gandolfi et al., 2014; Traverso et al., 2018). For instance, studying interference suppression through global-local processes is critical for education (Fisher et al., 2014). In fact, Lachman et al. (2014) indicated that global-local processes are implicated for example in word-reading and text-reading processes. Moreover, given the difficulty to suppress interfering local details for people with DS, it should be recommended to avoid overloading the classroom or rooms in which children and adults with DS conduct their actives with irrelevant materials that could confuse and distract. On the other hand, global-local processes are crucial also in every day life. For example, people with DS who lives independently need some guidelines and supports to organize their home, their duties, and responsibilities. It is common to use supports such as tables that delineate their duties (e.g., prepare meals, clean house, do their laundry, go to the supermarket). Again on the inhibition construct, given the behavioural and neural evidence that EFs vary long a continuum from hot to cool (see Prencipe et al., 2011; Zelazo & Müller, 2012), our results also indicate the need to jointly consider inhibitory sub-components and hot aspects in both the assessment and in the intervention program also for individuals with DS (see Fontana et al., 2021b).

Thirdly, from an educational point of view, the possibility to jointly consider both EFs, AB, and autonomies in everyday life in the assessment of the sample with DS could have important implications both to reach an independent life and occupational perspectives (Sabat et al., 2020; Will et al., 2017) and to target individualized interventions considering each specific cognitive and behavioural profile. For example, when they have to cross the street they must focus on the street, inhibit cognitive and behavioural stimuli which are not appropriate, but they have also to select information and stimuli to which is necessary to pay attention, suppressing irrelevant information (e.g., to stop before the pedestrian strips when cars are arriving, check the traffic light or even more do not get distracted when we hear a dog barking across the street). In other words, orientation on the road requires high levels of inhibitory abilities and these components must be taken into account when an educational intervention has to be set up to improve their autonomy. Therefore, knowing that a person with DS has broader difficulties on response inhibition and interference suppression, makes clear the need to: a) consider that any possible difficulties could be related to these impairments in inhibitory abilities; and, b) set learning programs using tools that could be helpful for the person with DS. For example, the use of adhesive labels with a stop symbol that should be sticked on the cover of the smartphone could help the person with DS to understand and remember that messages and calls must be limited in number and in daily time.

Finally, we think that the studies included in the present dissertation, raise critical issues about how to set training programs or developmental paths both for individuals with DS and for TD children. In fact, to the best of our knowledge, no training programs have yet been created to improve both cool and hot EFs and autonomies in individuals with DS. It would be therefore useful to promote paths of EFs improvements that include both specific exercises aimed at strengthening each specific component of executive functioning and more ecological interventions that ameliorate EFs in a transversal perspective considering also the different environments in which the person with DS is included (Daunhauer et al., 2017; Sabat et al., 2020). In addition, as suggested by the emerging literature on intervention in individuals with intellectual disabilities, combined training programs in which also meta-cognitive strategies (e.g., self-awareness, facilitation of spontaneous generation of problem-solving strategies, facilitation of errors detection) were included, leads to positive results in terms of effectiveness and longer life of the training programs (e.g., O’Neill & Gutman, 2020). In conclusion, future studies should consider the importance to promote both individually and groups interventions, given that a group setting may offer an educational experience and through the cooperative learning (Contardi, 2016, pp. 33-35; McGlinchey et al., 2019).

9.3 Conclusions

The results presented in this dissertation contributes to the literature inasmuch as it showed that: a) individuals with DS (matched for a measure of MA with TD controls) show only moderately impaired inhibitory abilities, but it should be considered that the construct was overall assessed without considering specific inhibitory sub-components; b) a two-factor model in which response inhibition and interference suppression are distinguished best fit the data in TD children aged 5-to-6 years of age; c) considering specific inhibitory dimensions (i.e., response inhibition and interference suppression), individuals with DS – matched for MA with a TD control groups – show a delay in both of the evaluated inhibition components; d) individuals with DS showed impaired performance also in the hot component such as the delay of gratification, when they are compared to TD children matched for a measure of MA; e) when younger and older individuals with DS were cross-sectionally compared, the younger group with DS showed worse performance on both response inhibition and delay of gratification, while the interference suppression still remained impaired also in adulthood; f) analysing in depth interference suppression in individuals with DS with an adapted non-verbal version of the Navon task, a global-local effect was observed both in individuals with DS and in TD children matched on a measure of MA, but worse performance for incongruent stimuli – rather than in the congruent condition – were recorded for the sample with DS; g) greater levels of autonomy in every day life are linked with better performance on response inhibition, interference suppression, and working memory; g) given the fundamental influence of EFs on children's learning abilities, academic achievements, and social skills, it is crucial and possible to jointly improve cool EFs, hot EFs, and emotion regulation in TD pre-schoolers.

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