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MULTITASKING ABILITIES IN ADOLESCENTS WITH 22Q11.2 DELETION SYNDROME: RESULTS FROM AN EXPERIMENTAL ECOLOGICAL PARADIGM

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KEYWORDS: *adolescents; 22q11.2 deletion syndrome; multitasking; negative symptoms; real-world functioning*

ABSTRACT

The 22q11.2 deletion syndrome (22q11.2DS) is associated with cognitive and functional impairments and increased risk for schizophrenia. We characterized multitasking abilities of adolescents with 22q11.2DS using an experimental naturalistic setting and examined whether multitasking impairments were associated with real-world functioning and negative symptoms. Thirty-nine adolescents (19 with 22q11.2DS and 20 controls) underwent the Multitasking Evaluation for Adolescents. Real-world functioning and clinical symptoms were assessed in participants with 22q11.2DS. Adolescents with 22q11.2DS performed poorly in the multitasking evaluation. Our data also suggest that multitasking abilities are related to adaptive functioning in the practical domain and negative symptoms. This study shows that adolescents with 22q11.2DS are characterized by multitasking impairments, which may be relevant for several aspects of the clinical phenotype.

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The 22q11.2 deletion syndrome (22q11.2DS) is a neurogenetic condition affecting at least one in 4,000 live births, and most cases are caused by a hemizygous 3-megabase microdeletion on the long arm of chromosome 22. Frequently associated conditions include conotruncal cardiac defect, velopharyngeal insufficiency, and intellectual disability (Bassett et al., 2011). The 22q11.2DS is also one of the highest known risk factors for the development of schizophrenia; 30%-40% of adults with this syndrome meet diagnostic criteria for a schizophrenia spectrum disorder (Schneider et al., 2014a). In the past decade, a large number of studies have described the cognitive profile of people with 22q11.2DS and have notably shown that executive functioning is a particular weakness (Campbell et al., 2010; Gur et al., 2014; Niklasson & Gillberg, 2010; Shapiro, Wong, & Simon, 2013). For example, Campbell et al. (2010) observed that children with 22q11.2DS have impaired planning abilities and limited cognitive flexibility.

Despite the well-acknowledged presence of executive dysfunctions in 22q11.2DS, little is known about their effect on daily-life functioning; and studies have yielded mixed results (Kiley- Brabeck & Sobin, 2006; Shashi et al., 2012). This may be due to the fact that classical executive tasks, such as the Wisconsin Card Sorting Test or the Verbal Fluency Test, are known to poorly detect executive dysfunctions in the daily-life environment (e.g., Burgess, 2000). Indeed, many case studies have revealed that some patients with acquired prefrontal brain injuries have intact scores in classical executive tasks but display marked executive dysfunctions in their daily-life environment (Burgess, 2000; Damasio, 1995). These observations stress the need for studying executive functioning by means of more ecological paradigms. According to Burgess (2000), such investigations could be achieved through the use of tasks involving multitasking (i.e., the coordination of multiple and simultaneous goal-directed activities), which is a characteristic of the majority of daily-life activities.

Several tasks have been developed to assess multitasking abilities in naturalistic experimental settings, such as the Multiple Errand Test or the Executive Secretarial Task (Lamberts, Evans, & Spikman, 2010; Shallice & Burgess, 1991), and in virtual environments, such as the Computerized Shopping Task (Laroi, Canlaire, Mourad, & Van Der Linden, 2010). These tasks have shown robust associations with real-world functioning measures in different populations, including adults with schizophrenia (Laroi et al., 2010), bipolar disorder (Laloyaux et al., 2013) or acquired brain injury (Lamberts et al., 2010). Recent conceptualizations suggest that multitasking abilities rely on the integration of multiple cognitive functions, including planning and memory (prospective memory, working-memory, and long-term memory) (Burgess, 2000; Logie, Trawley, & Law, 2011). Burgess, Simons, Du- montheil, and Gilbert (2005) have also argued that source switching is a key element involved in multitasking and relates to the ability to switch flexibly between internal information (e.g., goals, actions plans) and external information (information provided by the environment).

Although multitasking has not been investigated thus far, there are several reasons to believe that adolescents with 22q11.2DS would display significant impairments in this domain. Indeed, Campbell et al. (2010) have shown significant impairments in planning and cognitive flexibility in adolescents with 22q11.2DS, two domains that are likely to affect multitasking abilities (Logie et al., 2011). Further, neuroimaging studies have observed an atypical trajectory of brain

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development in 22q11.2DS, characterized by an accelerated cortical thinning in the frontal regions during adolescence (Schaer et al., 2009). This finding indicates that brain regions critically involved in multitasking (i.e., frontal regions and especially the rostral prefrontal cortex; Burgess, Veitch, de Lacy Costello, & Shallice, 2000) are altered during the course of development in 22q11.2DS. Finally, several studies have observed that some individuals with 22q11.2DS have lower adaptive skills than what would have been expected based on their intellectual level (Angkustsiri et al., 2012; Butcher et al., 2012). Cognitive abilities other than those directly assessed in typical intelligence scales may thus be better predictors of adaptive functioning.

Multitasking impairments could also be related to specific aspects of the 22q11.2DS clinical phenotype. Recent studies have shown that the severity of negative symptoms (i.e., decreased emotional expressiveness and motivation) is an important characteristic of adolescents and young adults with 22q11.2DS (Armando et al., 2012; Schneider et al., 2012; Schneider et al., 2014b). In particular, negative symptoms have been described in the literature as a ''pathology'' of goal-directed activities (Brown & Pluck, 2000) and are known to influence outcome in individuals with 22q11.2DS (Schneider et al., 2012; Schneider et al., 2014b). Within this framework, it is likely that cognitive deficits critically involved in the accomplishment of goal-directed behaviors, such as multitasking, would underlie the clinical expression of negative symptoms in this population. In support of this hypothesis, Semkovska, Bedard, Godbout, Limoge, and Stip (2004) showed that multitasking impairments were associated with the severity of negative symptoms, but not positive symptoms, in adults with schizophrenia. Moreover, Esposito et al. (2010) have shown that multitasking impairments are an important predictor of apathetic manifestations in adults diagnosed with Alzheimer disease. This gives further support to the involvement of multitasking in the development of negative symptoms, especially amotivation.

The present study aims at investigating multitasking abilities in a sample of adolescents with 22q11.2DS. To the best of our knowledge, multitasking has never been explored in adolescents with intellectual disability using a naturalistic experimental setting. For this reason, we developed the Multitasking Evaluation for Adolescents, a new paradigm appropriate for use with adolescents with intellectual disability. In particular, the level of difficulty was carefully examined, and the content of the task was chosen to match the adolescents' environment (school vs. work environment). We hypothesized that adolescents with 22q11.2DS would show significant impairments on the Multitasking Evaluation for Adolescents compared with typically developing individuals. We also explored the associations between intellectual functioning and multitasking impairments in the 22q11.2DS group. In accordance with Burgess (2000), we made the hypothesis that intellectual functioning would not be strongly associated with multitasking abilities. The second goal of this study was to explore the associations between multitasking abilities, real-world functioning and negative symptoms in adolescents with 22q11.2DS.

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Material and Methods

PARTICIPANTS

A total of 19 participants with 22q11.2DS and 20 typically developing individuals between 11 and 20 years of age were included in the study. Both groups were matched for age (t = —0.061, p = 0.951) and gender distribution (v = 0.244, p = 0.62i) (see Table 3). Six (31.58%) participants with 22q11.2DS were receiving psychotropic medication at the time of testing: three were on antidepressant medication, four on methylphenidate, one on antipsychotics, and one on anticonvulsant medication.

Individuals with 22q11.2DS were recruited through advertisements in patient association newsletters. The presence of a 22q11.2 microdeletion was confirmed using Quantitative Fluorescence Polymerase Chain Reaction (QF-PCR). Typically developing individuals were recruited among the siblings of the participants with 22q11.2DS or through the local school system. Written informed consent was obtained from participants and their parents under protocols approved by the local Institutional Review Board.

MATERIALS

THE MULTITASKING EVALUATION FOR ADOLESCENTS. This is the first presentation of this paradigm in the literature. It was designed to examine multitasking abilities in a situation closing resembling daily life. To ensure that performing the requested actions in a serial manner was impossible in the given amount of time, the task was pretested with several healthy control adults. During the task, the participants were settled in a large conference room containing several tables and a dozen chairs. The following items were available in the room: An electric kettle filled with water, a thermos flask, a toaster, and a large plastic box containing relevant and irrelevant items. Four edible (e.g., stock cubes) and four nonedible (e.g., hand cream), irrelevant items were included in the box. Before the beginning the task, the participants received a copy of the instruction sheet (see Table 1) and had the opportunity to ask questions. One examiner (M.S. or S.M.) was present in the room to monitor the proceedings of the task. However, the participants were explicitly told not to interact with the examiner (except during the question break). If the participants broke the rule and asked a question, the examiner could use predefined answers, depending on the type of question (see Table 2).

The participants were instructed that the maximum duration of the task was 30 min, but that they were allowed to stop it before the end, if they thought that everything was prepared according to the instruction sheet. At the beginning of the task, the examiner activated a digital timer that was visible and accessible to the participants. Fifteen minutes after the beginning of the task, the examiner informed the participants that one of their school friends was unable to come because he was feeling sick.

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The task was videorecorded and subsequently scored by two independent and trained raters (M.S. and J.B.). First, the two raters assessed the participants' performance using a scoring grid developed by the authors. The four main actions (tea, sandwiches, placement on the table, and folders) were further divided into smaller goals (units), each of them being worth 1 point. For example, the ‘‘tea'' action was divided into the five following units: turning on the kettle (1 point); letting the kettle boil until it stopped (1 point); pouring boiled water into (a) the thermos or (b) the cups (1 point); brewing tea bag(s) in (a) the thermos or (b) the cups (1 point); removing the tea bag(s) from (a) the thermos or (b) the cups (1 point). A total of 33 points could be attributed to the four actions. In addition, two general items were scored: (1) whether the additional information given by the examiner 15 min after the beginning of the task (i.e., one school friend is sick) was taken into account (yes = 1 point; partially = 0.5 point; no = 0 point), and (2) whether the participants took into account that they should include themselves (five school friends and the participant = six persons) (yes = 1 point; partially = 0.5 point; no = 0 point). Finally, 1 point was attributed for each irrelevant item correctly left out (8 irrelevant items left out = 8 points). One point was removed for each irrelevant item used during the task (e.g., putting on hand cream). Half a point was removed if the participants deliberately placed the irrelevant item on the table but did not use it. A total of43 points could be awarded for the whole task, corresponding to the total performance score. The intraclass correlation coefficient (ICC) between the two raters for the total performance score was 0.995, indicating almost perfect agreement.

Second, the two raters independently assessed the timing and sequencing of the different actions for each participant. The whole recording was split into different sequences, each sequence referring to a set of behaviors related to one of the four main actions (tea, sandwiches, placement on the table, or folders). All the behaviors not directly related to one of the four main actions (e.g., waiting, cleaning) were rated into a fifth ‘‘other'' category. For example, if a participant performed a series of behaviors related to the ‘‘tea'' action during 156 s and then a series of behaviors related to the ‘‘placement on the table'' action during 27 s, this was considered as two sequences of 156 and 27 s, respectively. The time spent before the first action was recorded and considered as the initial planning time. The two raters also examined the starting and ending time of each sequence. A consensus between the two raters' evaluations was reached after a common viewing of the sequences if its duration differed by more than 3 s. The ICC between the two raters for the total number of sequences was 0.830, indicating strong agreement.

Finally, the two raters assessed the participants' behavior during the task. Specifically, they rated the number of questions asked by the participants (excepting those formulated during the question break), as well as the number of glances toward the examiner (glances were not accounted for when the participants were talking to the examiner). Both were considered as helpseeking behaviors. The time spent by the participants to read the instruction sheet was also recorded.

COGNITIVE ASSESSMENT. Full-scale IQ was calculated for all participants using the Wechsler Intelligence Scale for Children 3rd edition (WISC-III; Wechsler, 1991) or the Wechsler Adult Intelligence Scale 3rd edition (WAIS-III; Wechsler, 1997). This was used as a general measure of

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intellectual functioning. The cognitive assessment was performed by trained master's level psychologists.

FUNCTIONAL ASSESSMENT. Real-world functioning was measured using the Adaptive Behavior Assessment System 2nd edition (ABAS-II; Harrison & Oakland, 2003). The participants' caregiver completed this questionnaire based on the actual level of adaptive functioning. In the present study, we used the three domain-specific scores (Conceptual, Practical, and Social; m = 100 [SD = 15]).

CLINICAL ASSESSMENT (22Q11.2DS GROUP). Finally, the severity of positive and negative symptoms was rated using two evaluation scales administered by a child and adolescent psychiatrist (S.E.): the Structured Interview for Prodromal Syndromes (SIPS; Miller et al., 2003) and the Positive And Negative Syndrome Scale (PANSS; Kay, Fiszbein, & Opler, 1987). The SIPS evaluates positive, negative, disorganization, and general prodromal symptoms, using a 7-point severity scale (ranging from 0 to 6). The PANSS is composed of a positive, negative, and general psychopathology subscale. All symptoms are rated on a 7-point severity scale (ranging from 1 to 7). For more direct comparison with the results obtained with the PANSS, the SIPS items were rescored on a scale ranging from 1 to 7. Interrater reliability for the SIPS and the PANSS was previously examined based on a random selection of filmed interviews and appeared to be excellent (ICC > 0.9 for all SIPS and PANSS subscales) (Schneider et al., 2012).

In a previous study (Schneider et al., 2012), a factor analysis using the PANSS and the SIPS items identified one positive and two negative dimensions (i.e., expressive and amotivation dimensions). We used the same dimensions and computed three symptom scores as followed: Positive score (mean of SIPS P1, P2, P3, P4, and D2 and PANSS P1, P2, P3, P4, P5, P6, and P7), emotional expressiveness score (mean of SIPS N3, N4 and PANSS N1, N2, N5, N6, N7, G7), and amotivation score (mean of SIPS N1, N2, D4 and PANSS N4, G16).

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***Table 1**. Instructions for the Multitasking Evaluation for Adolescents*

You have decided to invite 5 school friends to your house to prepare a project for school. You have 30 minutes to organize everything before they arrive.

Here is the list of the things you need to do before they arrive.

1. **Prepare a picnic for everyone**
   The picnic is made of two things
   Tea
   The tea must be hot when your friends arrive
   The tea must have enough taste when your friends arrive
   Sandwiches
   The sandwiches must be warm when your friends arrive
   You will find everything you need in the box next to you.
2. **Prepare the table for the afternoon**
   Place on the table all the things you will need during the afternoon.
   You will find everything you need in the box next to you.
3. **Prepare a folder for each person with the photocopies of the chapter from the history book about your project.**
   All the chapters must be stapled and the folders ready before you start working.
   You will find everything you need in the box next to you.

10 minutes after the beginning of the exercise, I shall come and see if you have any questions.

***Table 2.** Types of Questions and Defined Answers for the Multitasking Evaluation for Adolescents*

Content of Question	Answer
A) The participant asks if he is doing correctly	"Do as you think"
B) The participant asks if he/she needs to use everything that is in the box	
The participant expresses verbally that he doesn't know how to perform an action (e.g., make tea)	"Do the best you can"
The participant expresses verbally that he doesn't know how to use one of the items (e.g., open the thermos flask)	"Try to look at the device and find out by yourself'
The participant asks if he has to perform all the actions "for real"	"Yes, try to do everything that's written on the instruction sheet"
The participant asks for specific help due to fine motor difficulties (e.g., opening the cheese wrapping)	The examiner encourages the participant to try at least once by himself. If he doesn't succeed, the examiner performs the action

STATISTICAL ANALYSES

Group differences on the Multitasking Evaluation for Adolescents were tested using Mann- Whitney U tests for continuous variables and Chi Square comparisons for nominal variables. Nonparametric tests were chosen for group comparisons because normality and homogeneity of variance were not met for some variables of the task and because of the small sample size. Specifically, group differences were examined for the following continuous variables: number of

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questions, number of glances toward the examiner, number of instruction reading, total performance score, total amount of time, planning time, total number of sequences, and percentage of sequences allocated to the main actions (tea, sandwiches, placement on the table, and folders) versus ''other'' activities. The following nominal variables were also compared: percentage of individuals who ignored one or more actions, percentage of individuals who took the additional instruction into account (i.e., one school friend is sick) and percentage of individuals who included themselves in the task (five school friends and themselves). A Benjamini- Hochberg (B-H) correction was applied to account for multiple comparisons (Thissen, Steinberg, & Kuang, 2002).

In the 22q11.2DS group, Spearman correlations were performed to examine the associations among multitasking performance, general intellectual functioning, real-world functioning, and clinical symptoms. Again, a Benjamini-Hochberg (B-H) correction was applied to account for multiple comparisons. To test the hypothesis that multitasking impairments were specifically associated with negative symptom severity, robust regression models with positive and negative symptoms as independent variables (IV) were performed to predict multitasking performance. We also conducted robust regression models in order to examine whether some areas of real-world functioning were more consistently associated with multitasking impairments. Robust regressions were chosen over classical multiple linear regression models because our data were not normally distributed. Hence, it was likely that influential observations would bias our results. In a robust regression, weights (ranging between 1 and 0) are attributed to each observation based on the value of the absolute residuals. This has the advantage of reducing the impact of influential observations on the final result.

All the analyses were performed using SPSS version 21, except for the robust regression models that were computed using the ''rreg'' command in STATA version 13.

Results

GROUP DIFFERENCES IN COGNITIVE AND REAL- WORLD FUNCTIONING

Group comparisons revealed significant differences in general intellectual functioning between adolescents with 22q11.2DS and controls ($t = 11.224, p < 0.001$; see Table 3). Caregivers also reported significantly lower scores on all the ABAS-II domains in the 22q11.2DS group (all $p < 0.001$).

GROUP DIFFERENCES IN THE MULTITASKING EVALUATION FOR ADOLESCENTS

Behavior during the task. Participants with 22q11.2DS had a tendency to ask more questions, but the significance level was just above the threshold for multiple comparison correction (see Table 4). There was no significant group difference in the number of glances toward the examiner or in the amount of instruction reading.

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PERFORMANCE. There was a significant difference between the two groups in the total performance score (see Table 4). Post-hoc comparisons revealed that participants with 22q11.2DS obtained a significantly lower score for the four main actions (tea, sandwiches, placement on the table, and folders) (all $p < 0.01$). Seven participants completely ignored one or more of the main actions (i.e., no performance point was obtained for an action and no time was allocated to this particular action). All seven belonged to the 22q11.2DS group.

Between-group differences on two general items were also examined (see Table 4). The number of participants who took into account that one of the school friends was sick (i.e., who observed the ongoing instruction) was higher in the control group. However, this comparison did not survive multiple comparison correction. Second, the rate of participants who included themselves in the task (five school friends and themselves) was significantly higher in the control group.

Finally, the two groups did not differ regarding the use of distractors during the task (see Table 4).

TIMING AND SEQUENCES. There was no significant difference in the total amount of time spent on the task or in the initial planning time (i.e. time spent before the first action) between the two groups (see Table 4).

On average, adolescents from the 22q11.2DS group accomplished significantly fewer sequences than the control group during the whole task (see Table 4). In addition, the percentage of sequences allocated to “other” activities compared to the four main actions (tea, sandwiches, placement on the table, and folders) was significantly higher in the 22q11.2DS group.

Table 3. *Demographic, General Intellectual Functioning, and Real-World Functioning Scores in the 22q11.2DS and the Control Group. If not otherwise specified, mean (SD) values are displayed.*

	22q11.2DS	Controls	Test
Age	16.17 (2.80)	16.12 (2.17)	n.s.
Gender (% males)	57.9%	50%	n.s.
Full-Scale IQ	70.53 (9.88)	112.90 (13.34)	$p < 0.001$
ABAS-II Conceptual SS	79.00 (11.96)	106.40 (11.60)	$p < 0.001$
ABAS-II Practical SS	84.21 (11.53)	102.75 (11.78)	$p < 0.001$
ABAS-II Social SS	74.42 (14.65)	100.15 (12.84)	$p < 0.001$

Note. SS = Standard score; ABAS-II = Adaptive Behavior Assessment System - II.

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Table 4. *Performance and Behavior During The Multitasking Evaluation for Adolescents in Participants With 22ql 1.2DS and Controls. If not otherwise specified, mean (SD) values are shown. Correlations with full-scale I (fare displayed in the last column.*

	22qll.2DS	Controls	Mann Whitney U	x^2	Test[a]	Correlation with FSIQ[b]
Number of questions	5.16 (6.05)	2.00 (2.18)	275.50	—	p = 0.015	0.298
Number of glances	6.90 (7.57)	5.50 (8.99)	223.00	—	p = 0.365	-0.058
Number of instruction reading	5.32 (3.71)	4.95 (2.91)	202.50	—	p = 0.728	0.391[c]
Total performance score (max = 43)	28.16 (6.41)	37.10 (2.94)	26.50	—	p < 0.001	0.148
At least one action ignored (% individuals)	36.84%	0%	—	8.980	p = 0.003	—
Ongoing instruction observed (% individuals)	Yes: 68.42% / Partially: 5.26% / No: 26.32%	Yes: 100%	—	7.464	p = 0.024	—
Participant includes him/herself (% individuals)	Yes: 21.05% / Partially: 5.26% / No: 73.67%	Yes: 90% / No: 10%	—	18.896	p < 0.001	—
No use of distractors (max = 8)	6.84 (1.52)	7.30 (0.82)	165.00		p = 0.496	0.303
Total time (seconds)	1677.80 (190.25)	1607.68 (268.40)	183.00		p = 0.857	0.437[c]
Planning time (seconds)	65.00 (59.37)	57.00 (53.05)	201.50		p = 0.749	0.198
Number of sequences	35.45 (6.22)	26.68 (11.83)	87.50		p = 0.003	-0.001
% sequences allocated to "other" activities	40.30 (8.36)	33.79 (7.56)	278.50		p = 0.011	-0.092

Note. FSIQ_= Full-scale IQ.
[a]Significant group differences after correction for multiple comparisons with the Benjamini-Hochberg (B-H) procedure (i.e., where p < 0.0125) are displayed in bold.
[b]Spearman correlation coefficients.
[c]0.05 < p < 0.10.

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ASSOCIATIONS BETWEEN TASK-RELATED VARIABLES IN ADOLESCENTS WITH 22Q11.2DS

In adolescents with 22q11.2DS, we examined which task-related variables significantly differentiating the two groups (total number of sequences and percentage of sequences allocated to ‘‘other’’ activities) were associated with the total performance score. The total number of sequences ($r_s = 0.694$, $p = 0.001$) and the percentage of sequences allocated to ‘‘other’’ activities ($r_s = —0.826$, $p < 0.001$) were both significantly associated with the total performance score.

ASSOCIATIONS BETWEEN MULTITASKING AND INTELLECTUAL FUNCTIONING IN ADOLESCENTS WITH 22Q11.2DS

To examine the associations between general intellectual functioning and multitasking abilities, we performed Spearman correlations between fullscale IQ and all the continuous measures extracted from the Multitasking Evaluation for Adolescents. None of the correlations was statistically significant (see Table 4).

ASSOCIATIONS AMONG MULTITASKING, REAL- WORLD FUNCTIONING, AND CLINICAL SYMPTOMS IN ADOLESCENTS WITH 22Q11.2DS

Finally, the task-related variables that significantly differentiated the two groups (total performance score, total number of sequences, and percentage of sequences allocated to ‘‘other’’ activities) were correlated with real-world functioning measures and symptom severity. A few correlations were below the $p < 0.05$ threshold but did not survive multiple comparisons correction (Benjamini-Hochberg correction) (see Table 5). It was the case for: the correlations between the total performance score and the three ABAS- II domains (conceptual, practical, and social); the correlations between the total performance score and the severity of amotivation symptoms; the correlation between the total number of sequences and the ABAS-II practical domain; and the correlation between the percentage of sequences allocated to ‘‘other’’ activities and the severity of expressive symptoms.

To examine the hypothesis that multitasking impairments are specifically associated with negative symptom severity in adolescents with 22q11.2DS, robust regression models were performed to predict the total performance score, the total number of sequences, and the percentage of sequences allocated to ‘‘other’’ activities. To avoid multicollinearity issues (i.e., $r > 0.600$ between two independent variables), the amotivation and the expressive symptom scores were combined to create a negative symptom score. Hence, the negative and positive scores were used as independent variables (IV). We also conducted robust regression models to examine whether some areas of real-world functioning (ABAS-II conceptual, practical, and social domains) were more consistently associated with multitasking impairments. Again, to avoid multicollinearity issues, the ABAS-II conceptual and social scores were combined to create an ABAS-II communication and

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social score. Hence, the ABAS-II practical and the ABAS-II communication and social scores were used as independent variables (IV). The results of the robust regression models are displayed in Table 6.

Discussion

The present study examined multitasking abilities in a group of adolescents with 22q11.2DS compared to a group of typically developing controls using a naturalistic experimental setting. In accordance with our hypotheses, we observed that individuals with 22q11.2DS performed poorly on the Multitasking Evaluation for Adolescents and that the severity of intellectual disability was not significantly associated with multitasking impairments. We also observed that some indicators of impaired multitasking abilities in adolescents with 22q11.2DS were predicted by a higher severity of negative symptoms and lower adaptive skills in the practical domain.

MULTITASKING ABILITIES IN ADOLESCENTS WITH 22Q11.2DS

Consistent with our hypothesis, adolescents with 22q11.2DS significantly differed from the control group on several aspects of the Multitasking Evaluation for Adolescents. First, they had a significantly lower performance score than controls (65% of the total number of points vs. 86% in the control group). Their scores were significantly lower for the four main actions, indicating that the difficulties were not circumscribed to one specific activity (e.g., making tea). They also experienced more difficulties in general aspects of the task. Specifically, they had an increased tendency to ignore instructions not explicitly stated in the instruction sheet (i.e., the participant has to include himself in the task), suggesting that adolescents with 22q11.2DS benefit from very explicit instructions. Additionally, participants with 22q11.2DS often ignored additional instructions (i.e., one school friend is sick); and some of them completely overlooked one of the main actions during the task. These two results, which were not observed in controls, are suggestive of prospective memory difficulties in individuals with 22q11.2DS. Indeed, prospective memory difficulties may lead to not taking into account an instruction after having heard it. It may also lead to forgetting to read the instruction sheet and verify that all the actions have been performed. According to Burgess (2000), prospective memory is one of the key cognitive processes involved in multitasking and is rarely examined in classical neuropsychological assessments.

The second variable on which participants with 22q11.2DS differed from controls was the number of behavioral sequences accomplished during the task. On average, they performed significantly fewer behavioural sequences than controls and spent a longer period of time on the same action before switching to another one. In the 22q11.2DS group, the number of sequences accomplished during the task was significantly associated to the total performance score, indicating that participants who performed more behavioral sequences during the task (i.e., more switches) also had a higher performance score. Interestingly, this finding is similar to previous observations by Burgess et al. (2005) on patients with cerebral lesions involving the rostral prefrontal cortex.

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Indeed, they observed that these patients performed fewer switches during a multitasking evaluation and tended to stay longer on each task in comparison with the control group. On the opposite, Semkovska et al. (2004) observed that participants with schizophrenia made frequent and irrelevant switches during a cooking task, which also led to poor task performance. Results from these different studies suggest that too little and too many switches between the tasks can both lead to impaired multitasking abilities. Based on previous work by Burgess et al. (2005), source switching is a key element involved in multitasking and relates to the ability to switch flexibly between internal information (e.g., goals, actions plans) and external information (information provided by the environment). Therefore, it is possible that insufficient switching (as observed by Burgess et al. [2005] and in the present study) and inappropriate switching (as observed by Semkovska et al. [2004]) are both the result of source switching difficulties. Future studies should examine source switching abilities using experimental paradigms to examine the integrity of this cognitive process in individuals with 22q11.2DS (see Dumontheil, Gilbert, Burgess, & Otten, 2010; Gilbert, Frith, & Burgess, 2005).

Finally, the third variable that distinguished participants with 22q11.2DS and controls was the percentage of sequences allocated to non-goal- directed activities (‘‘other'' activities). Indeed, participants with 22q11.2DS allocated a significantly greater percentage of sequences to non-goal-directed activities (40% vs. 34%). In the 22q11.2DS group, this variable was significantly related to the total performance score, indicating that participants who allocated more sequences to non-goal-directed activities were also those who had a poorer performance score. The increased rate of nongoal-directed sequences in adolescents with 22q11.2DS may be due to the use of inefficient planning strategies. Indeed, planning difficulties have been previously observed in children with 22q11.2DS using a modified version of the Tower of London test (Campbell et al., 2010). In that study, children with 22q11.2DS spent more time thinking, but still made significantly more moves to succeed the task, which is suggestive of inefficient planning strategies. In the present study, the two groups did not differ regarding the length of the initial planning time (i.e., time before starting the first action). This finding suggests that participants with 22q11.2DS developed an inefficient strategy during this period.

Interestingly, the two groups did not differ regarding the use of distractors. Indeed, adolescents from both groups were confused by the presence of irrelevant items; and the majority used at least one distractor during the task. The ability to successfully inhibit irrelevant information critically involves regions of the prefrontal cortex (Wright, McMullin, Martis, Fischer, & Rauch, 2005), which are known to mature late compared to the majority of the remaining regions of the cortex (Teffer & Semen- deferi, 2012). This may explain why both groups did not adequately inhibit irrelevant items. The performance of adults on this multitasking paradigm should be examined in future studies to explore the development of several abilities involved in complex multitasking situations, and notably the inhibition of irrelevant items.

In accordance with our hypothesis, none of the variables extracted from the Multitasking Evaluation for Adolescents was significantly associated with general intellectual functioning (i.e., full-scale IQ) in adolescents with 22q11.2DS. This finding suggests that intellectual disability does

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not contribute to the presence of multitasking impairments in this population, which is consistent with previous observations by Burgess (2000).

Indeed, he observed the presence of severe multitasking impairments in eight individuals following frontal lobe damage, despite aboveaverage intellectual functioning.

Table 5. *Correlations Between Multitasking Variables, Real-World Functioning (ABAS-II Scores) and Clinical Symptoms*

	ABAS-II Conceptual	ABAS-II Practical	ABAS-II Social	Amotivation symptoms	Expressive symptoms	Positive symptoms
PERF	0.493[a]	0.511[a]	0.478[a]	—0.477[a]	-0.408	-0.255
SEQ	0.184	0.476[a]	0.027	-0.394	-0.426	-0.059
%SEQ ‘‘other’’	-0.115	-0.390	0.053	0.303	0.473[a]	-0.065

Note. Spearman correlation coefficients are displayed. PERF = total performance score; SEQ = total number of sequences; %SEQ‘‘other’’ = % of sequences allocated to ‘‘other’’ activities.
[a]$p < 0.05$, uncorrected.

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Table 6. *Robust Regression Models to Predict Multitasking Performance in Adolescents With 22q11.2DS*

Dependent variables	Model		Coefficients	
Independent variables (significant variables in bold)	*F(2,16)*	*p*	*t*	*p*
Total performance score	1.78	0.201		
Negative symptoms[1]			-1.83	0.086
Positive symptoms			0.63	0.537
Total number of sequences	11.23	0.001		
Negative symptoms[1]			**-4.23**	**0.001**
Positive symptoms			**4.14**	**0.001**
% sequences allocated to "other" activities	3.95	0.040		
Negative symptoms[1]			**2.75**	**0.014**
Positive symptoms			-2.01	0.062
Total performance score	2.43	0.120		
ABAS-II practical			0.95	0.354
ABAS-II comm. and soc.[2]			1.39	0.183
Total number of sequences	3.03	0.077		
ABAS-II practical			**2.37**	**0.031**
ABAS-II comm. and soc.[2]			-1.62	0.125
% sequences allocated to "other" activities	3.05	0.076		
ABAS-II practical			**-2.44**	**0.027**
ABAS-II comm. and soc.[2]			1.38	0.185

Note. ABAS-II — Adaptive Behavior Assessment System 2nd edition.
[1]Negative score — mean of amotivation and expressive scores.
[2]ABAS-II communication and social score — mean of ABAS-II conceptual and ABAS-II social scores.

ASSOCIATIONS AMONG MULTITASKING, REAL- WORLD FUNCTIONING, AND NEGATIVE SYMPTOMS IN 22Q11.2DS

None of the correlations between multitasking abilities and real-world functioning or between multitasking and clinical symptoms survived multiple comparison correction in the 22q11.2DS group, probably due to the relatively small sample size. However, robust regressions that more specifically targeted our hypotheses revealed that adaptive functioning in the practical domain (but not in the communication and social domains) was a significant predictor of two variables extracted from the Multitasking Evaluation for Adolescents: the total number of sequences and the percentage of sequences allocated to "other" activities. This finding suggests that multitasking impairments are associated with specific areas of functioning. In the ABAS-II, the practical domain covers skills needed for personal care (e.g., bathing, dressing), basic care of a home setting (e.g., cleaning, food preparation), functioning in the community (e.g., shopping skills), and health

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protection (e.g., using medicine). Therefore, it is likely that multitasking abilities are particularly important for areas of functioning that are crucial for achieving independent living. This association between multitasking and daily-life functioning is also consistent with previous studies, including adults with schizophrenia, bipolar disorder, and acquired brain injury (Laloyaux et al., 2013; Lamberts et al., 2010; Laroi et al., 2010). However, to the best of our knowledge, this is the first time that this association is highlighted in an adolescent population with intellectual disability. In the present study, real-world impairments were not significantly associated with the severity of intellectual disability, consistent with the results of a previous study in the field of 22q11.2DS (Angkustsiri et al., 2012). This finding suggests that multitasking impairments may be a greater contributor of functional impairments than intellectual disability in this population and should be a target for specific interventions.

Robust regressions also revealed that the total number of sequences and the percentage of sequences allocated to ‘‘other'' activities were predicted by the severity of negative symptoms. Unfortunately, we could not examine the specific contribution of amotivation and expressive symptoms because of the strong correlation between these two variables. This finding is consistent with the study of Semkovska et al. (2004) that found a significant correlation between multitasking performance and the severity of negative symptoms in adults with schizophrenia. It is also in line with the previous report of Esposito et al. (2010), who showed that multitasking performance was one of the best predictors of apathetic manifestations in individuals with Alzheimer disease. In light of these findings, it seems that the inability to deal with multitasking situations underlies the clinical expression of negative symptoms in different populations, including adolescents with 22q11.2DS and adults with schizophrenia or Alzheimer disease. We believe that investigating the cognitive bases of clinical manifestations across diagnostic categories is critical to improve the efficacy of psychosocial interventions. Indeed, this will help to better understand general cognitive mechanisms leading to the expression of symptoms in psychiatric and neurological disorders.

The results of the present study should be interpreted in light of the following limitations. First, only adolescents were included in this study, which prevented us from examining the development of multitasking abilities over time in individuals with 22q11.2DS. Indeed, a previous study has shown that adaptive functioning declines in at least part of individuals with 22q11.2DS (Schneider et al., 2014a). For this reason, it may be important to examine whether an atypical developmental trajectory of multitasking abilities could partly explain this finding. Second, and because the sample size was relatively small, the obtained results should be confirmed and extended in independent samples. Third, the external validity of the Multitasking Evaluation for Adolescents was not examined. Future studies should compare the results of this ecological paradigm with other existing measures of multitasking, such as the Six Elements Test. In addition, associations with cognitive tests that target specific components of multitasking (e.g., prospective memory) should also be examined. Finally, the inclusion of a control group matched for intellectual functioning may add important information as to whether multitasking impairments are a specific characteristic of adolescents with 22q11.2DS.

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In conclusion, this is the first study to examine multitasking abilities in adolescents with 22q11.2DS, a neurogenetic condition associated with a high risk of schizophrenia and increased rates of negative symptoms. We observed significant multitasking difficulties in adolescents with 22q11.2DS compared to typically developing controls. Our data also suggest that multitasking abilities are related to adaptive functioning in the practical domain and may underlie the clinical expression of negative symptoms. In light of these preliminary findings, we believe that efforts should be invested to better understand the cognitive mechanisms underlying multitasking abilities in individuals with 22q11.2DS, such as prospective memory or source switching. Such research may ultimately help to develop multitasking rehabilitation techniques specifically adapted to this population.

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