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LONGITUDINAL ASSESSMENT OF NARRATIVE PROFILE IN A WILLIAMS SYNDROME PATIENT

Introduction

Developmental characterisation of cognitive functioning in different genetic disorders is an important issue in guiding intervention approaches and treatment guidelines. While there are disorders in which an age-associated cognitive decline is evident (Dykens et al., 1989; Fisch et al., 2002) there are others, like Williams Syndrome (WS) that exhibits a stability in cognitive functioning with age (Udwin et al., 1996; Howlin et al., 1998; Searcy et al., 2004).

WS is a neurodevelopmental disorder, with a prevalence of 1 in 7500 (Strømme et al., 2002), characterised by a submicroscopic deletion on chromosome 7 q11.23 (Bellugi et al., 1999). Their typical physical characteristics include facial dismorphology, a specific clinical phenotype together with a remarkable socio-emotional and neurocognitive profile. Specifically, WS individuals display distinct behavioural patterns, characterised by an excessive social behaviour, with a strong impulse towards social contact and affective expression (Bellugi et al., 1999; Jones et al., 2000). They also present a unique cognitive phenotype, with a mild to moderate intellectual disability (mean IQ is 55, standard deviation of 11, and range between 40 and 90) with an uneven pattern of cognitive performance. Specially striking is the initial description of WS as presenting a framework of cognitive dissociation, in which severely impaired visuospatial cognition contrasted with relatively preserved face processing skills and linguistic abilities (Bellugi et al., 1994; Bellugi et al., 2000). However, this notion of spared language abilities was further challenged by studies demonstrating that linguistic function in WS is not only delayed in acquisition, but also impaired in adolescence/adulthood (Semel and Rosner, 2003; Stevens and Karmiloff-Smith, 1997; Thomas et al., 2006). Indeed, abnormal grammatical (syntactic and morphosyntactic), lexico-semantic and pragmatic processes (production of a "cocktail party speech", discourse incoherence, stereotyped conversation and difficulties at initiating and developing conversational rapport) were also found in this syndrome (Gonçalves et al., 2004; Stojanovik, 2006; Garayzábal Heizne et al., 2007; Brock, 2007; Brock et al., 2007; Gonçalves et al., 2010). Several studies failed in showing the hypothesis that verbal skills overcome non verbal skills in WS (Karmiloff-Smith et al., 2003; Porter and Coltheart, 2005; Stojanovik, 2006) with inconsistent findings being reported in several cognitive domains (Greer et al., 1997, Cherniske et al., 2004, Porter and Coltheart, 2005, Sampaio et al., 2008). Thus, studying longitudinally verbal and non-verbal abilities in WS, as well as the impact of intervention in both domains, may be an important approach in understanding the patterns of development and neuroplasticity to cognitive stimulation in WS.

We have previously described a case study of a WS patient (MMP) in 2005 (Gonçalves et al., 2005) in which a detailed characterisation of the cognitive profile was provided. Since 2005, this patient has been engaged in

neurocognitive stimulation sessions and has been continuously assessed. In this article we compared the patient's cognitive profile in two time points (2005 and 2009), analyzing the impact of a cognitive rehabilitation programme in terms of several measures. Again, on our previous evidence that cognitive functioning can improve by general stimulation of the neurocognitive system and the rehabilitation of specific cognitive functions (Gonçalves et al., 2005), we hypothesized that receiving this individually tailored cognitive intervention programme would promote and stimulate neurocognitive and narrative development in MMP.

Method

Participant

MMP is currently 18 years old. This patient is the youngest of three children from a low socio-economic level family. He was born by caesarean section. In terms of developmental milestones, he began to say his first words when he was 18 months old and started walking after 2 years, reading at 6 and began to write when he was 7 years old. At the age of 12 he was diagnosed with WS by fluorescent in situ hybridisation (FISH) (Gonçalves et al., 2005). At the assessment time, he was in 9th grade (adapted curriculum).

Instruments

Wechsler Intelligence Scale for Adults – III (WAIS-III) (Wechsler, 1997) - this scale is one of the most used international system in assessing Intellectual Quotient (Full Scale IQ – FSIQ) allowing the discrimination of two intellectual levels related to verbal and non-verbal abilities (Verbal IQ – VIQ and Performance IQ – PIQ), factorial indexes and performance different subtests. In addition, it is an instrument that has been widely used in our previous studies (Sampaio et al., 2009).

California Verbal Learning Test (CVLT) – Adult version (Delis et al., 2000) – clinical instrument that allows a complete description of memory and learning abilities. This test consists of two shopping lists (A and B) that are read to the participant. List A is presented five times and list B is presented after the fifth trial of A List. In list A, the following measures were analysed: number of words recalled for all five trials. For list B, the total number of recalled items was also reported. Primacy, recency effects and type of strategies as well as short term and long-term delay, recognition performance and discriminability responses were calculated. This instrument has a wide field of application, specifically in children with learning abilities, including Specific Language Impairment, Down syndrome, WS and other etiologies (Nichols et al., 2004; Sampaio et al., 2008).

Rey-Osterrieth Complex Figure Test (Rey, 1959) – recall and copy administration. This test requires a copy of a complex figure without time limit, assessing the use of organization and planning strategies in problem solving and visuo-constructive ability. After a 30 minutes delay, the individual is asked to reproduce the same figure, in order to assess the ability in recalling non-verbal material.

Narrative Induction Task - Frog, Where Are You? - In order to elicit narrative production the pictures book "Frog, where are you?" (Mayer, 1969) was used. This is a storybook without words, composed by a set of images with the aim of eliciting the construction of a story and was coded according Reilly (Reilly et al., 2004) in terms of the following parameters: cognitive inferences; literal description; social commitment; emotional state references; affective states and behaviour references; social attention.

Controlled Oral World Association

(Benton and Hamsher, 1989) – this is a verbal fluency test assessing the speed, verbal spontaneity production and verbal fluency. This test studies oral production of spoken words beginning with a designated letter – F, A, S and a category naming trial (animals) within a time limit (1 minute). Fluency problems may be associated with difficulties in speech, reading and writing and this test is sensitive to frontal executive dysfunctions and slight alterations in semantic memory (Spreen and Strauss, 1991).

Trail Making Test (Reitan, 1958) – this test is used to assess visual conceptual and visuo-motor tracking (Lezak, 1995). It assesses visual search, attention, mental flexibility and motor function. It has two parts, A and B. Part B requires more information processing ability than part A and is clearly the more sensitive part of the test (Spreen and Strauss, 1991). Problems in visual scanning and tracking provide information on how effectively the patient is able to deal with a visual array of any complexity, follows a sequence mentally, deals with more than one stimulus or thought at a time or is flexible in shifting the course of an ongoing activity.

Toulouse Piéron Test (perceptual and attention test) (Toulouse and Pieron, 1986) – this is a cancellation test requiring visual selectivity at fast speed on a repetitive motor response task. This test provides information about concentration and monotony resistance abilities, as well as perceptual speed and continued attention skills. Lower scores can reflect the general response slowing and inattentiveness.

Intervention

MMP was engaged in neurocognitive intervention sessions as described previously (Gonçalves et al., 2005) twice a month between 2005 and 2009. A trained psychologist working at the Galician Williams Syndrome Association (Spain) carried out the intervention sessions that were previously scheduled by the research team. Additionally, several neuropsychological assessment time points were performed in order to assess the patient's evolution and to devise new interventions strategies. The intervention was focused in enhancing several cognitive functions, as described previously (Gonçalves et al., 2005). Specifically, the intervention protocol was designed to promote several dimensions of language (expressive and comprehensive language, pragmatics, conversation, narrative and vocabulary abilities), memory (verbal and visual memory), attention (sustained and divided attention), executive functions (planning and flexibility and generalization of this learning to daily life activities), and spatial orientation (spatial reference and self-reference). The schematic organization of the sessions was as follows: a) the beginning of each session was characterised by an overall assessment of MMP's difficulties during preceding two weeks; b) then, an description of the activities planned for the session, with visual support, was given to MMP; c) the objectives for within and between sessions were alternated between promoting language [expressive language and conversational skills (using verbal/visual stimulli to promote personal interactions and sentence completion), articulatory praxis, reading, writing, narrative, vocabulary, verbal fluency (semantic differentiations) and temporal sequencing abilities], memory [promote verbal and visual memory (structured activities using stimulus (objects and images), structured lists temporally and thematically related] and executive functions [to stimulate reasoning, abstraction, planning and execution abilities (using supervised and structured/directive tasks and day life activities); to improve thought and reflection abilities with implications in daily behaviours]. Taking into account the multidimensional characteristics of all these functions, a top down and bottom up approach was applied and we used play and positive reinforcement as strategies to

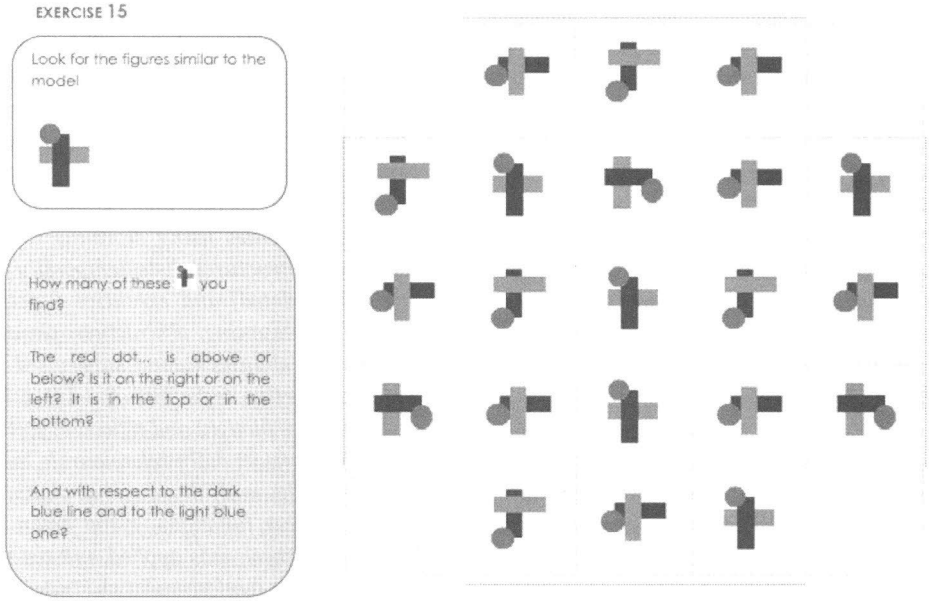
work all dimensions. Attention training was performed in all sessions because this cognitive domain has important implication in all other cognitive tasks (Lens et al., 2009)(FIGURE 1).

Results

Comparing the results collected at the two time points, we observed a heterogeneous profile, characterised by a pattern of either improvement or stability in several cognitive dimensions (see TABLE I for comparison between the two time-points). More specifically, an improvement was found in measures of general intellectual functioning (most evident in full scale IQ and performance IQ) as well as in visual attention (Toulouse-Pierón) and visuo-spatial constructive abilities (Rey-Osterrieth Recall condition). Contrasting with this, stability in verbal domains was also observed, as evident in a small increase in verbal IQ measures and fluency tasks (although fluency in semantic categories was increased). Finally, we observed some variability within the verbal learning and memory task. More specifically, MMP improved in the use of strategies (both semantic and serial) and in recency effect, although there was some decline in the total recalled words in the primacy position of the serial position curve. Consistent with these data, we observed a smaller effect of the interference list and a higher z score in short-term recall. Finally, the ability to discriminate relevant from irrelevant information remained impaired.

In terms of narrative production, we observed that the ability to use social engagement device (such as the use of social modulation, use of sounds, affective prosody, exclamations and reference to emotional sates) as well as reference to affective and emotional states was maintained as a main characteristic

FIGURE 1
Example of an attention training exercise used with MMP



of his narrative. However, in contrast with the first assessment, there were no literal descriptions in the current narrative. Finally, we observed that an absence of cognitive inferences regarding the story characters in narrative collected in 2009.

Discussion

Overall, an improvement on general cognitive functioning (FSIQ) was evident from 2005 to 2009 assessment. This improvement was manly due to a significant increase in performance measures that contrasted with stability in verbal IQ measures. Particularly interesting was the finding of a significant improvement in measures associated with visual attention and visuo-constructive processing. In a different way, we observed either a small increase or overall stability within verbal measures, either in expressive, memory, fluency tasks and narrative. This may have due with the specific nature of language, which is a very complex system demanding integration of different subdimensions. Indeed, when characterisation of specific microlinguistic and

TABLE I
Neuropsychological Assessment in 2005 and 2009

	2005	2009
Full Scale IQ	42	54
Verbal IQ	53	55
Performance IQ	46	61
Toulouse-Piéron	1th Percentile	5th Percentile
California Verbal Memory Test - recall list words (5 trials)	z = -2	z = -3
California Verbal Memory Test - recall interference list (list B)	z = 1,5	z = -1
California Verbal Memory Test - Primacy Effect	z = 4	z = 0
California Verbal Memory Test - Recency Effect	z = -2	z = 2
California Verbal Memory Test - Short-term recall	z = -2.5	z = -2
California Verbal Memory Test - Long-term recall	z = -2.5	z = -3
California Verbal Memory Test - Semantic strategies	z = -1.5	z = -1
California Verbal Memory Test - Serial strategies	z = -0.5	z = 0
Discriminability Index	z = -2.5	z = 4
Rey-Osterrieth Copy condition	10th Percentile	10th Percentile
Rey-Osterrieth Recall condition	1th Percentile	25th Percentile
Trail Making Test B	He was not able to perform the task	122 seconds
Controlled Word Association Test - words	17	16
Controlled Word Association Test - Animals	11	16

macrolinguistic features is performed in the analysis procedures of narrative production in WS, a dissociation between these dimensions was observed (Marini et al., 2010).

Even though previous studies have been reporting difficulties in improving visuo-constructive abilities (Jarrold et al., 2001) our patient seems to be responsive to the cognitive stimulation intervention programme in this domain. This may suggest that although it has been proposed that non-verbal abilities develop at a lower rate, there may exist room for plasticity in WS patients.

The present results are consistent with previous longitudinal reports in WS showing significant increases in general intellectual functioning measures, that were more pronounced in performance IQ measures (51-70 from 34.6% to 100%) than verbal IQ (39.1% to 78.3%)(Udwin et al., 1996). MMP also did not evidence a pattern of cognitive decline over time, which is typical with other developmental disorders like Fragile X or Down syndrome that are characterised by a cognitive decline as the participants age (Dykens et al., 1989; Fisch et al., 2002). Of note, we did not observe this pattern in our case study because he was engaged in the cognitive intervention programme. This data is consistent with results obtained by other studies, showing that IQ remains stable during adulthood with WS (Howlin et al., 1998; Searcy et al., 2004).

Practical Application

The present case study highlights several important implications for WS intervention. First, it emphasises the need to target areas of deficiency, namely to approach visuo-constructive and attentional processing skills, which seem to be responsive the effects of intervention. Indeed, we observed that MMP was able to perform better in orientation, puzzles, with generability to daily life activities, specifically in buttoning up clothes and orientation in strange places. Also, training memory abilities, both short and long-term, with simple instructions, may contribute to the improvement in WS patients memory performance with ultimately impact on their learning abilities (Gathercole and Alloway, 2006). Finally, we observed that intervention in attention had a transversal impact in all domains of cognition, either verbal or non-verbal skills, particularly because these problems are highly present in WS population (Lincoln et al., 2002; Semel and Rosner, 2003; Cherniske et al., 2004).

In this case study, we analysed longitudinally the positive impact of a cognitive stimulation programme in a patient with WS in terms of several neurocognitive measures. We propose that the use of intervention programmes can be generalized to specific populations with cognitive impairment and new studies from our research team have been carried out to assess the neural basis underlying the efficacy of these type if programmes.

Summary

Williams Syndrome is a neurodevelopmental disorder, characterised by a submicroscopic deletion on chromosome 7 q11.23 associated with a particular cognitive and socio-emotional profile. We have previously described a case study of a Williams Syndrome patient in 2005 that has further been engaged in neurocognitive rehabilitaion sessions. In this article, we compared the patient's cognitive profile at two time points (2005 and 2009) analyzing the impact of a cognitive rehabilitation programe, in terms of several neurocognitive measures. Overall, an improvement on general cognitive functioning was evident from 2005 to 2009 assessment that was manly due to a significant increase in performance measures that contrasted with stability in verbal IQ measures. We propose

that the use of intervention programmes can be generalised to specific populations with cognitive impairment.

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