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Genetics and mathematics: Evidence from Prader-Willi syndrome

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Abstract

Mathematical abilities were tested in people with Prader-Willi syndrome (PWS), using a series of basic mathematical tasks for which normative data are available. The difference between the deletion and the disomy variants of this condition was explored. While a wide phenotypic variation was found, some basic findings emerge clearly.

As expected from previous literature, deletion and disomy participants were found to differ in their degree of impairment, with disomy being overall the most spared condition. However, the tasks selectively spared in the disomy condition are not necessarily the easiest ones and those that discriminate less the PWS group from controls. It rather seems that disomy patients are spared, with respect to deletion, in tasks entailing transcoding and comparison of numbers in the Arabic code.

Overall a particular difficulty was detected in reliably performing parity judgments. This task has been shown to be very frequently spared after a brain injury, even in severe aphasic conditions. The most interesting result is the sparing in analog number scale, whereby PWS seem, overall, to outperform controls. This finding may help in understanding previously reported, surprising results about cognitive skills in PWS. Elevated performances in PWS may result from life-long hyper-reliance on one visuo-spatial system in presence of underdevelopment of the other.

Keywords: Prader-Willi syndrome; Genetic disorders; Numbers; Calculation; Visuo-spatial system

1. Introduction

Prader-Willi syndrome (PWS) is a genetically based disorder characterized by muscular hypotonia, hyperphagia, obesity, hypogonadism, short stature, maladaptive behavior and mental retardation. PWS affects males and females equally and is caused by the paternal deletion within 15q11–q13 (70–75% of cases), maternal uniparental disomy of chromosome 15 (UPD15) (20–25%), or by a defect in the imprinting centre (2%) (Butler & Thompson, 2000). It has a prevalence estimated at about 1:8000–1:16,000 live births (Burd, Vesely, Martsolf, & Korbeshian, 1990; Whittington et al., 2001). On average symptom severity seems to be dampening in UPD cases with respect to deletion cases (Dykens, Cassidy, & King, 1999).

All PWS patients suffer some degree of intellectual impairment. Language milestones are usually delayed. Cognitive abnormalities become evident as the child reaches school age. Most subjects fall in the mildly mentally retarded range (mean IQ: 60–70), with approximately 40% having borderline retardation or low normal intelligence and about 20% having moderate retardation (Cassidy, 1997; Molinari, 2002).

Regardless of measured IQ, most PWS children have multiple severe learning disabilities, and their academic performance is poor for their mental abilities (Curfs, Wiegers, Sommers,

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Borghgraef, & Fryns, 1991; Curfs, Hoondert, van Lieshout, & Fryns, 1995; Dykens, Hodapp, Walsh, & Nash, 1992). State and Dykens (2000) showed a distinctive, although not necessarily unique, profile of cognitive strengths and weaknesses of PWS patients compared to controls with mental retardation. Some PWS patients have relative strengths in spatial–perceptual organization and visual processing and, as a group, they score on a par with normal subjects on word searches: a surprising finding (Dykens, 2002) is that, overall, children with PWS outperform age-matched normal peers with jigsaw puzzles, placing more than twice as many pieces as the typically developing group.

Weaknesses have been noted in sequential processing and short-term memory tasks, including visual, motor, and auditory short-term memory; academically, reading/decoding and comprehension may exceed arithmetic skills (Holm, 1981; Masheim, 1981). Indeed, disproportionate difficulties with mathematical tasks have been systematically reported (Sulzbacher, Wong, McKeen, Glock, & MacDonald, 1981). Until very recently, however, this finding was only anecdotally portrayed in the majority of available studies and was mostly based on the administration of rather generic tasks which could only broadly tap mathematical abilities. The first and only systematic investigation has been so far reported by Bertella et al. (2005) where the main components of mathematical cognition were separately considered in the context of a complete neuropsychological examination.

Bertella et al. (2005) study could indeed confirm previous reports: PWS patients show a systematically worse performance in arithmetic tests than in tasks tapping other cognitive skills. This finding first emerged in the administration of WAIS, whereby the lowest graded scores were found on the arithmetic subtest (only Digit Span was disturbed almost as much). The WAIS arithmetic subtest was also found disproportionately disturbed in PWS with respect to a group of IQ-matched intellectually disabled subjects: thus a low IQ could not be the only explanation for the PWS group's selective impairment of mathematical abilities. The disproportionate impairment in mathematical skills became however more evident when patients were administered a wide battery of specific neuropsychological tasks (Spinnler & Tognoni, 1987).

Bertella et al. (2005) then provided, on a lesser number of PWS patients, a systematic assessment of a number of more specific mathematical tasks: dots counting, knowledge of counting sequences, parity judgements, comparison of Arabic numerals and written verbal numerals, reading and writing of Arabic numerals, transcoding from written verbal numerals to Arabic numerals and vice versa, recognition and comprehension of arithmetical signs, retrieval of arithmetical facts, verification of multiplication facts, mental multi-digit calculation and written multi-digit calculation. None of these tasks resulted unaffected in PWS.

The case by case analysis seemed to reveal a wide phenotypic variation: PWS does not necessarily affect all specific mathematical functions, since ceiling or close to ceiling performance was shown by at least one subject in every single task. However, what could be a specific pattern of deficit seemed to emerge. Number transcoding difficulties were found especially in cases where a syntactic frame has to be generated in order to produce Arabic numbers starting from a verbal numeral: as a result syntactic errors tended to prevail. Another specific weakness was found in multiplication facts: more specifically PWS subjects tended to miss considering one of the two operands and hence proceed in multiplying one of the operands by a different number (operand errors). Finally PWS patients also appeared to perform poorly using calculation procedures. An analysis of their errors did not reveal consistent and systematic "bugs" or faulty strategies. It rather showed inconsistent and unsystematic errors, reflecting no strategies, all sub-procedures being occasionally correct. Thus, according to the criteria expressed by Semenza, Miceli, and Girelli (1997), their deficit seems to lie in a monitoring defect rather than in a distorted or missing knowledge of procedures. A spatial component to the deficit could not be safely excluded, since misalignment of numbers in their appropriate columns and spatial number inversion were observed. The study, possibly due to the limited number of subjects, could not detect any reliable difference between the two PWS groups, the deletion and the UPD patients.

Overall Bertella's et al. (2005) findings suggest how some portions of chromosome pair 15 may play a pivotal role in the genetic transmission of capacities that can be potentially recruited for mathematical tasks. However, Bertella's et al. study constituted only a preliminary, though systematic, exploration, that cannot by any means be considered a exhaustive one. The present investigation is meant to further explore mathematical abilities in PWS by using a much more complete testing battery on a larger number of participants. One important aim of the study is to assess the difference for the first time between the deletion and the UPD conditions.

2. Subjects and methods

Twenty-three adult PWS patients (10 males and 13 females), aged 29.61 ± 6.53, range 19–44, were included in the study. Most of them belonged to a group of PWS people that have been followed up and extensively studied for at least 3 years at the Ospedale S. Giuseppe, Piancavallo di Verbania, Italy, a section of the Istituto Auxologico Italiano. The entire study protocol was approved by the ad hoc Ethical Committee of the Istituto Auxologico Italiano. Written informed consent was obtained by the parents and, where applicable, the patients.

All patients showed the typical PWS clinical phenotype (Holm et al., 1993). Cytogenetic analysis was performed in all participants: 15 of them had interstitial deletion of the proximal long arm of chromosome 15 (del15q11–q13); it was also possible to determine that three subjects had a type 1 (i.e. large as opposed to small) deletion; uniparental maternal disomy for chromosome 15 (UPD15) was instead found in eight individuals. All participants were living with their families: this is customary in Italy for PWS who are not affected by additional incapacitating pathological conditions. Years of education received were 9.04 ± 1.72: 16 participants had completed lower secondary school (8 years) with special educational support and seven participants had attended higher secondary school (10–13 years).

IQ was measured in each participant via the WAIS-R (Wechsler, 1981) battery with the following results: whole group: mean verbal IQ 60.26 ± 15.21, range 45–117, performance IQ 67.22 ± 10.57, range 46–84, total IQ 59.70 ± 11.68, range 45–99; deletion group: mean verbal IQ 56.87 ± 8.30, range 45–78, performance IQ 66.27 ± 12.54, range 46–84, total 57.33 ± 9.01, range 45–76; UPD group: mean verbal IQ 66.63 ± 22.78, range 52–117, performance IQ 69.00 ± 5.58, range 57–75, total 64.13 ± 15.22, range 54–99.