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Behavioral phenotypes of genetic syndromes with intellectual disability: Comparison of adaptive profiles

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ABSTRACT

The study of distinctive and consistent behaviors in the most common genetic syndromes with intellectual disability is useful to explain abnormalities or associated psychiatric disorders. The behavioral phenotypes revealed outcomes totally or partially specific for each syndrome. The aim of our study was to compare similarities and differences in the adaptive profiles of the five most frequent genetic syndromes, i.e. Down syndrome, Williams syndrome, Angelman syndrome, Prader-Willi syndrome, and Fragile-X syndrome (fully mutated), taking into account the relation with chronological age and the overall IQ level. The research was carried out using the *Vineland Adaptive Behavior Scale* (beside the Wechsler Intelligence scales to obtain IQ) with a sample of 181 persons (107 males and 74 females) showing genetic syndromes and mental retardation. Syndrome-based groups were matched for chronological age and mental age (excluding the Angelman group, presenting with severe mental retardation). Similarities and differences in the adaptive profiles are described, relating them to IQs and maladaptive behaviors. The results might be useful in obtaining a global index of adjustment for the assessment of intellectual disability level as well as for educational guidance and rehabilitative plans.

1. Introduction

The differences in adaptive behavior among genetic syndromes with intellectual disability are relevant both for scientific and clinical purposes, since rehabilitation will be enhanced by the knowledge for each specific behavioral phenotype of what behavior can be expected, and of what association with intellectual functioning can be foreseen.

A behavioral phenotype is the characteristic cognitive and psychiatric pattern that typifies a specific disorder (Flynt and Yule, 1994). According to Dykens (1995), a phenotype implies that persons affected by a particular genetic syndrome are more likely to show specific features and abnormal behaviors.

Previous research underlined theoretical and methodological issues arising from the analysis of the behavioral phenotypes of genetic syndromes with intellectual disability, in particular when trying to find consistent behavioral traits differentiating these syndromes in a perspective focused on adjustment, since adaptive behavior (which allows integration in a social and cultural context) is a main part of the phenotype (O'Brien and Yule, 1995; Zigler and Bennet-Gates, 1999; Cassidy and Morris, 2002; Hodapp and Dykens, 2004). Deficits in cognitive abilities and adaptive behavior may increase the risk of psychopathological disorders in children with intellectual disabilities (Tremblay et al., 2010).

Indeed, in the last decades specific adaptive profiles of genetic syndromes have been searched for, with some difficulties due both to the high number of syndromes (more than 750) and to a marked within-profile variability (Dykens, 1999). Dykens et al. (2000) and Hodapp and Dykens (2007) identified the characteristics of people with genetic syndromes, to help parents and professionals understand their behaviors and their needs, so as to be able to provide better interventions and create wider community inclusion. Four major syndromes (Down, Williams, Fragile X, and Prader-Willi) are discussed regarding genetic causes and implications, cognitive profiles, speech and language, and behaviors. Research-based intervention strategies are suggested to improve education, personal relationships, and social interventions.

The relevance to studying the adjustment to the social environment has been stressed by the definition of mental retardation, or more recently intellectual disability (ID), based on the assessment limits both in intellectual and adaptive and social functioning (e.g., Fletcher et al., 2007; Schalock et al., 2007; Salvador-Carulla and Bertelli, 2008).

Many studies focused on adaptive functions of the most common genetic syndromes associated with different levels of ID, but

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addressing the personality factors (e.g., Zigler and Bennet-Gates, 1999) and/or abnormal or deviant behaviors more than the basic skills involved in adaptive functioning.

More specifically, it is well known that adaptation level in Trisomy 21 or Down syndrome is globally higher than cognitive and learning levels, and increases with age (Rondal et al., 1999; Hodapp, 2006). It was hypothesized that adaptive development of persons with Down syndrome is similar to but slower than normal individuals (Loveland and Kelley, 1991).

Chapman and Hesketh (2000), in reviewing evidence for a developmentally emerging behavioral Trisomy 21 phenotype, reported a significant delay in cognitive development with specific deficits in speech and language production, but confirmed fewer adaptive problems than in individuals with other cognitive disabilities. Other studies (Meyers and Pueschel, 1991; Dykens and Kasari, 1997) confirmed the presence of a lower number of maladaptive behaviors and psychopathological correlates in Down syndrome. Temperamental features show a global positive mood (Ratekin, 1996). Hyperactivity and oppositional behaviors may be present, as in other genetic syndromes (Dykens, 1999). Age-related and task-specific emotional and social reactions have been reported (Pitcairn and Wishart, 1994; Kasari and Freeman, 2001).

Williams syndrome was found to be associated with high verbal communication abilities and empathy. The adaptive profile shows points of strength in interpersonal and socialization skills (e.g., skills related to social interaction), but increased anxiety and fears (Einfeld et al., 1997; Mervis and Morris, 2007), and weakness in daily living and motor skills (Udwin et al., 1996; Mervis and Klein-Tasman, 2000; Mervis, 2003). Hypersociability is often reported in persons with this syndrome (Jones et al., 2000; Doyle et al., 2004), but this characteristic may decline with age (Gosch and Pankau, 1997). Independence and self-care are often deficient in adult age (Davies et al., 1997; Greer et al., 1997). Jarvinen-Pasley et al. (2008) pointed out that the social phenotype in Williams syndrome may be considered as a model for elucidating gene–brain–behavior relationships, although personality and social aspects of this diagnostic group remain a considerably less thoroughly studied area.

Angelman syndrome is associated with very low linguistic abilities (Clayton-Smith and Pembrey, 1992), hyperactivity, stereotyped behaviors - e.g., puppet-like movements - frequent and inappropriate laughing, tendency to catch hold of persons and objects, and sleep disturbances (Summers and Feldman, 1999; Clayton-Smith, 2001). Clarke and Marston (2000) also reported restlessness and sleep problems, and fascination with water.

Prader-Willi phenotype has peculiar characteristics relating to compulsive attitudes towards food and non-food situations (Dykens et al., 1996). Along with compulsive hyperphagia, deficits in social behavior are also found: perseverating speech, impulsiveness and temper tantrums, and social withdrawal (Dykens et al., 1992; Dykens and Kasari, 1997; Waters, 1999). Social competence in this syndrome has also been studied in relation to leisure activities (Rosner et al., 2004; Sellinger et al., 2006).

The differentiation between pre-mutation and full-mutation genes in Fragile-X syndrome is still a controversial matter; these different types affect psychological development differently. In the full-mutation phenotype social difficulties have been found, together with autistic features and marked hyperarousal or hyperreactivity (Turk, 1998; Mazzocco, 2000). Higher irritability, avoidance of unfamiliar objects and persons, and resistance to change were reported by Hagerman and Cronister (1996). Also social anxiety and lack of eye contact, have been reported (Turk and Cornish, 1998; Dykens, 1999). For these reasons, some authors have assumed an association between this syndrome and autistic features (Fisch, 1992 firstly challenged this conclusion). According to Cornish et al. (2007) "Children with fragile-X syndrome may be overwhelmed by the demands created by social involvement, novel or unexpected situations, and changes, even by the common transitions of daily life" (p. 83).

Fisch et al. (1999) found that both cognitive and adaptive levels decline with increasing age in fully–mutated Fragile-X males. Results revealed a moderate and significant negative correlation between maladaptive behavior levels and age; adaptive and maladaptive behaviors did not correlate with each other.

Kau et al. (2000) studied preschool males with Fragile-X syndrome using mothers' ratings; deficits in motor skills, increased avoidance and hyperactivity, but also positive mood and low social withdrawal were reported. These characteristics allowed us to distinguish Fragile-X children from a control group with idiopathic developmental delay.

The etiologic approach to cognitive and adaptive effects of different genetic disorders with intellectual disability has been summarized by Hodapp (1997) and Dykens and Hodapp (2001) from three distinct points of view.

(a) *No-specificity*. Syndromes have non-specific cognitive and adaptive effects; mental retardation is the main common outcome. Within-syndrome differences are higher than across-syndrome differences.
(b) *Total specificity*. Cognitive and adaptive outcomes of each genetic syndrome are not common to other syndromes. Differences between syndromes are most relevant.
(c) *Partial specificity*. Outcomes are specific of more than one genetic syndrome. Some genetic disorders' effects differ from those found in mental retardation or in other genetic disorders.

Within-syndrome variability is due to the fact that a very high number of genes within the human genome, together with environmental stimuli, differently affect human behavior besides the common outcome of the specific genetic disorder: "… then, genetic disorders do not have uniform effects on every individual, can change their effects due to developmental and environmental effects, and must not be considered the sum total of any person's overall genetic endowment" (Hodapp, 1997, p. 68).

What is totally specific and what is partially specific among the effects has to be empirically studied, considering also the age and the global intelligence level. Indeed, some methodological issues have to be pursued in etiological research, as Dykens et al. (2000)) pointed out.

Which group should be chosen as control or contrast group? Non-genetic intellectual disability may be inappropriate as a control group, due to the highly variable causes as well as to their direct and indirect effects. A suitable solution might be to contrast groups with genetic diseases, paired according to main variables such as chronological and/or mental age.

Moreover, the approach "similar but different" suggested by Dykens et al. (2000) could be considered, by examining within-group variability together with across-group differences.

The results of this knowledge, based on a proper methodology, are useful for making available information about the expected adaptive behavior patterns to parents and professionals who take care of the persons with a genetic syndrome, fostering more specific and targeted types of interventions (Cassidy and Morris, 2002).

To support this wide applicative framework, empirical studies are needed with circumscribed genetic groups, chosen with respect to their frequency and clinical relevance. Although most cognitive differences between these groups are already known (e.g., Dykens et al., 2000), more knowledge is needed about the differences regarding adaptive behaviors and the relationships between adaptive and cognitive factors, taking into account the subjects' age.

The specific aim of our study was to compare similarities and differences in the adaptive profiles of five most frequent genetic syndromes, i.e. Down syndrome, Williams syndrome, Angelman syndrome, Prader-Willi syndrome, and Fragile-X syndrome (fully