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Review Article

Neurocognitive Functions in Williams Syndrome Individuals: A Literature Review

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Abstract

Williams syndrome (WS) is a neurodevelopmental disorder with genetic origin due to microdeletion of approximately (28) genes on chromosome (7), individuals with WS have distinctive medical, cognitive, and behavioral characteristics. In this article, many studies have been reviewed to present a neurocognitive profile for these individuals. Cognitive functions in WS individuals in the current study have been classified into (1) executive functions such as, (working memory, cognitive flexibility, planning, attention, inhibition) (2) and non-executive functions such as (memory, intelligence level, expressive vocabularies, face recognition, and visuospatial abilities). Adding to cognitive functions, the study reviewed the neurological aspects that support cognitive abilities and discussed abnormalities in cerebral regions that responsible for these cognitive impairments.

Introduction

Williams Syndrome (WS) is a rare complex neurodevelopmental disorder, caused by a genetic microdeletion of approximately (28) genes on the long arm of chromosome (7), specifically 7q11.23 [1-4]. The syndrome prevalence ranged between 1 in 7500 live births to 1 in 20,000 [5-7]. The disorder affects both males and females equally [8]. Recently WS has attracted more attention due to its unique aspects, individuals with WS exhibit specific physical, cognitive, medical, and behavioral characteristics [8-10]. They have some medical problems such as supravalvular aortic stenosis, connective tissue abnormalities including hernias or diverticula of the bladder or colon, also they have distinctive facial morphology [10]. They suffered from reduced brain size in the parietal lobe and occipital gray matter. these results are indicated by structural magnetic resonance imaging (MRI) [11]. Despite the wide variation in intellectual functioning, the majority of WS individuals diagnosed with mild to moderate cognitive impairments [12] also indicated that infants and young children displayed developmental delay, and older children in most cases showed learning or intellectual disabilities. Despite the aforementioned intellectual impairment, WS individuals have relatively preserved verbal skills [13,14]. But they have more severe visuospatial impairments [15,16] have collected major Williams Syndrome Features as the following:

(1)Neurological

- Average IQ 55(range 40-90)
- Poor coordination
- hypersensitivity to sound
- hoarse voice

(2) Cardiovascular

- Supravalvular aortic stenosis
- peripheral pulmonary artery stenosis
- plumonric vavular stenosis
- ventricular/ atrial-septal defects

(3) Facial features

- Full prominent lips
- Stellate iris pattern
- Prominent ear lobes
- Wide mouth
- Medial eyebrow flare
- Flat nasal bridge
- Short nose/ anteverted nares (4)other
- Elastin deletion probe (FISH)
- Transient infantile hypercalcemia
- Developmental delay (infants height and weight <5th percentile)

WS and Executive functions

Executive functions (EF) is a broad term referring to a variety of higher cognitive abilities associated with planning, controlling, and regulating other functions to achieve successful adaptation [17,18]. Executive

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functions are associated with the frontal lobe especially prefrontal circuits that adjust social, cognitive, and emotional behaviors [8]; so individuals with frontal lobe damage exhibit social disinhibition and simultaneously executive functions impairments [19]. Executive functions appear in the first years of childhood, and continue to develop into adulthood [20,21]. Executive functions include a set of wide cognitive abilities such as working memory, cognitive flexibility, planning, attention, inhibition, fluency (generation of new responses), and self-monitoring [14,22-24]. Executive functions are critical for adaptive behavior because they play a vital role in starting and stopping actions, observing (keeping track of) and changing actions, and in delineation future actions [17]. Generally, WS individuals reveal executive functions deficits, in attention, flexibility, and inhibitory control [25]. Meyer-Lindberg et al, [26] assumed a probable explanation for these findings by amygdala dysfunction and abnormalities in connections within prefrontal regions. Functional magnetic resonance imaging (FMRI) indicated that while WS individuals completed a Go No Go inhibition task, they appeared low activity in the striatum, dorsolateral, and dorsal anterior cingulate cortices, these regions are involved in behavior inhibition [27]. In a study by Rhodes et al, [9] they compared individuals with WS (mean age 18 years) to TD (typically developing individuals). the two groups were matched for (1) chronological age and (2) verbal mental age, the two groups completed tasks of attention set-shifting, planning, and working memory. results indicated that WS individuals exhibited impairments in frontal lobe-related executive functions that included working memory, planning, and attention set-shifting.

In a study by Costanzo et al, [17] they examined executive functions (attention, short-term memory, working memory, categorization, inhibition, shifting, and planning) in two different intellectual disabilities groups, one of them is the WS group, the other is Down syndrome (DS) group, the aforementioned EF tasks were applied on (15) children, adolescents and adults with WS. (15) Children, adolescents, and adults with Down syndrome, and finally (16) mental age-matched typically developing children. The results indicated that both WS and DS groups revealed impaired functions in visual selective attention, visual categorization, working memory, and auditory sustained attention, they also showed preserved auditory selective attention, visual inhibition, and visual sustained attention. On the other hand, individuals with DS performed worse than their peers with WS in shifting, inhibition, and verbal aspects of memory, at the same time WS was poor in palnning.

In a study by Menghini et al, [28] Inhibition abilities were impaired in individuals with WS in both verbal and non-verbal tasks, also WS individuals revealed both verbal and visual-spatial deficits in selective and sustained attention, deficits in short-term memory, working memory, planning, and inhibition, although shifting and categorization abilities are relatively unimpaired in tasks that depend on verbal materials.

Atkinson et al, also indicated that children with WS aged (4-15) years; compared with peers typically developed children whose chronological age (CA) matched the WS children with WS's vocabulary age on the British picture vocabulary scale, have better performance on verbal inhibition tasks (Day-Night Stroop task) than on the two motor inhibition task. In addition, their performance on the verbal inhibition task was at or above the expected level for vocabulary age, but most of WS children's performance on the spatial inhibition was poor and underlaid below the vocabulary expected level.

From previous studies, we can conclude that most executive functions are impaired in WS individuals especially when tasks used in measuring depend on visual materials, and the executive functions are relatively unimpaired in tasks that depend on verbal materials. This conclusion is supported by many other findings extracted from multiple studies for example Greer et al, [25] found that individuals with WS have deficits in maintaining sustained attention under conditions of automaticity they explained this by the effect of irrelevant stimuli that caused difficulty in task engagement. Although some studies suggested that, there are deficits in both verbal and visuospatial working memory [29,30]. But Meyer-Lindenberg et al, [11] assumed that verbal short-term memory is relative strength. Because visuospatial abilities are complex and, need a wide range of sub-components to achieve the task such as selective attention, inhibition of multiple irrelevant stimuli, synthesizing parts into whole construction, and temporarily storing some stimuli while manipulating simultaneously; this causes load on visuospatial working memory, so the performance of WS individuals on such visuospatial tasks is poor and impaired. The complexity of visuospatial tasks, causes the engagement of multiple brain regions in visuospatial processing, such as the posterior parietal cortex, a special activation has been recorded in the intraparietal sulcus, which is a part of the dorsal visual system [31,32]

In addition, WS individuals have problems with multiple abilities related to inhibitory control and, tasks that depend on attention because of this they display inattention and distractibility [33]. So many individuals with WS meet the diagnostic criteria for comorbid attention hyperactivity disorder (ADHD) [34]

Finally Best et al, [35] concluded that generally, individuals with WS have deficits in principle components of executive functions such as cognitive or attentional flexibility, planning, and inhibition control.

WS and Non-executive functions

WS individuals have relatively preserved social interaction abilities, verbal abilities, and spared face recognition [13][36]. Memory span deficits and, short-term delayed memory are also observed. [9].

Individuals with WS show better performance on verbal memory than visual memory [37,38].

In the field of visuospatial abilities, WS individuals show significant delays in comparison to the overall level of intellectual abilities [16,39]. In addition, WS individuals have obvious weaknesses in visuospatial construction tasks in comparison to typically developing peers [40].

Although WS individuals are likely to have the normal ability in the visual whole pattern processing, they suffer difficulties at processing on micro-levels and segmenting that pattern into sub-components [41].

The Functional MRI studies showed that individuals with WS have structural abnormalities in visuospatial brain areas, specifically the posterior-occipital sulcus, also they appeared hypoactivation in the intraparietal sulcus. [32,42].

Many studies confirmed that WS individuals show preserved verbal memory skills particularly grammatical and vocabulary abilities [43-45].

Many studies compared expressive vocabularies of young children with WS and Down Syndrome, the findings revealed

that the WS performance group was significantly better than the DS group in case of matching between the two groups in chronological age. although when the two groups were matched for developmental level, the performance differences between the two groups was disappeared [14]. Major of WS individuals are classified as mild to moderate mentally retarded, their global standard scores on IQ tests locate between 40 to 90 with a mean of around 55 [46].

WS individuals generally show difficulties in mathematics and its application in daily life [16].

WS individuals have great difficulties in problem-solving, these difficulties may be a result of emotional reactions that disrupt their skills [47].

Surprisingly Teenagers and adults with WS speak clearly and most times, they tend to be gossipy [16].

Conclusion

The current review study showed that research on executive functions among individuals with Williams syndrome has received more attention compared to research on non-executive cognitive functions in the same group. The results on WS Executive functions revealed that they in general have impairments in most executive functions, such as planning, working memory, sustained attention, inhibitory control, cognitive flexibility, selective attention, and, shifting specially when measuring tasks depend on visual material, on the other hand when measuring tasks depend on verbal materials the performance in general is relatively unimpaired. Neurological findings indicated that they appear low activity in brain regions that support executive functions like the stratum, dorsolateral and dorsal anterior cingulate, prefrontal cortex, posterior parietal cortex, and, intraparietal sulcus.

In the field of non-executive cognitive functions, there is a scarcity of research and, the few research revealed that WS individuals also showed better performance on verbal memory than visual memory, also they showed relatively preserved social interaction, but they have memory span deficits, short-term memory delaying, problem solving and mathematics difficulties. Most of WS individuals classified as mild to moderate mentally retarded.

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