Relationship between Apgar scores and long-term cognitive outcomes in individuals with Down syndrome

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The Apgar scoring system is a comprehensive screening tool performed on a baby at 1 and 5 minutes after birth, which reflects how well the baby tolerated the birthing process and is adapting to life outside the womb. The long-term significance of Apgar scores has been shown for typical developing children and those with neurodevelopmental disorders. However, the significance of Apgar scores on later cognitive outcomes has not been studied for Down syndrome yet. The purpose of this study is to investigate whether Apgar scores at birth are related to long-term memory outcomes in individuals with DS. We analyzed Apgar scores from medical records of 148 individuals with DS (72 females and 76 males, age range: 6 to 25 years). In addition, we directly assessed spatial memory, auditory memory and object-location episodic memory and learning of participants with DS. After controlling for chronological age and sex, Apgar scores at 1 minute were related to all memory outcomes while Apgar scores at 5 minutes were solely related to semantic memory. Implications of our results, indicating that even transient low Apgar scores at 1 minute are linked with poorer long-term memory skills in individuals with DS, will be discussed.

Background

Down syndrome (DS) is the most common known genetic cause of intellectual disability (ID) and it is typically caused by an extra copy of the chromosome 21. It is a complex condition which affects both physical and cognitive development. Although most of the DS phenotypic features are variable, when compared either to typical developing (TD) individuals or individuals with other neurodevelopmental disorders (NDDs), a cognitive profile is generally observed at a group level. However, this cognitive profile can vary from one individual to another. Although genetic and environmental factors certainly affect this variability, associated factors and their underlying mechanisms are not well understood. This variability represents an enormous challenge in providing care for DS at an individual level. Understanding which factors underlie this variability is crucial. In fact, one of the main challenges to an etiology-specific approach to cognitive and behavioral interventions is the lack of understanding of individual variation in the development of cognitive phenotypes both within and across disabilities. Studies in the neonate and the fetus suggest that the perinatal period is of particular importance for the establishment of cerebral blood flow and hemoglobin oxygenation, as patterns of functional activity appear to rapidly increase in spatial complexity during this time (1). Perinatal risk factors have been associated with long-term variability in general cognitive functioning and learning for the TD population (2). In this regard, the Apgar scoring system is

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a comprehensive screening tool performed on a baby at 1 and 5 minutes after birth, which reflects how well the baby tolerated the birthing process and is adapting to life outside the womb. Newborns with DS receive lower Apgar scores, on average, than TD newborns (3). The long-term significance of Apgar scores has been shown for TD children and other neurodevelopmental disorders(4,5). However, the significance of Apgar scores on later cognitive outcomes has not been studied for DS yet.

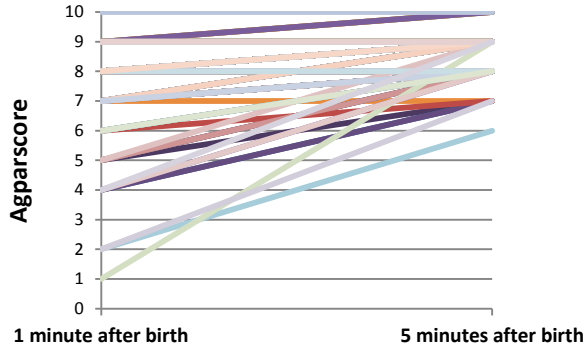

Figure 1: Spaghetti plot representing each participant's trajectory of Apgar scores from 1 minute after birth to 5 minutes after birth.

This study

The purpose of this study is to investigate whether Apgar scores at birth are related to long-term memory outcomes in individuals with DS. Our sample included 148 individuals with DS (72 females and 76 males, age range: 6 to 25 years). Only subjects without other known neurological differences that could influence memory were included. Apgar scores at 1 and 5 minutes of participants with DS were abstracted from medical records using structured forms. We directly assessed vocabulary knowledge (using the test of Verbal knowledge and Riddles; KBIT-II), their immediate spatial memory (using the CANTAB Spatial Span; SSP), immediate auditory memory (using the test Recall of Digits Forward; DAS-II), and visual episodic memory and learning (CANTAB Paired-Associates Learning; PAL) in our participants with DS. See Table 1 for participant's characteristics. Note that Apgar scores significantly improved from 1 minute (range 1-10) to 5 minutes (range 6 to 10) (**Figure 1**). We used multiple regression analysis to examine if Apgar scores at birth predicted individual variability in long-term memory skills for individuals with DS, while controlling for differences in chronological age (CA) at testing and sex. Results showed that higher Apgar score at 1 minute predicted a better performance on all of the memory-related tasks ($p<0.02$), while higher Apgar scores at 5 minutes solely predicted a better performance on the Riddles test ($p=0.02$) (**Table 1**).

Explanatory variable	β	P Value	Adj. R^2
Apgar score at 1 min	0.27	**0.004****	0.09
CA at testing	0.27	0.004	
Dependent variable: **Digits** (total correct)			

Explanatory variable	β	P Value	Adj. R^2
Apgar score at 1 min	0.24	**0.002****	0.18
CA at testing	0.43	<0.001	
Dependent variable: **Riddles** (raw)			

Explanatory variable	β	P Value	Adj. R^2
Apgar score at 1 min	-0.19	**0.02***	0.1
CA at testing	-0.29	<0.001	
Sex	0.18	0.03	
Dependent variable: **SSP** (usage errors)			

Explanatory variable	β	P Value	Adj. R^2
Apgar score at 1 min	0.51	**0.002****	0.1
CA at testing	0.3	<0.001	
Dependent variable: **PAL** (memory score)			

Explanatory variable	β	P Value	Adj. R^2
Apgar score at 1 min	0.19	**0.01***	0.25
CA at testing	0.53	<0.001	
Dependent variable: **Verbal Knowledge** (raw)			

Explanatory variable	β	P Value	Adj. R^2
Apgar score at 5 min	0.17	**0.035***	0.15
CA at testing	0.4	<0.001	
Dependent variable: **Riddles** (raw)			

Table 1: Multiple regression models for explanation of long-term memory outcomes (only significant results $p<0.05$ are represented).
$*p \leq .05$, $**p \leq .01$, $***p \leq .001$

Conclusions

Our results indicate that even transient low Apgar scores at 1 minute are linked with poorer long-term memory skills in individuals with DS, suggesting that acute delivery events may contribute to long-term memory functioning in this population. Apgar scores at 1 minute after birth often reflect acute perinatal events compromising oxygen availability. The hippocampus, which is very sensitive to hypoxic conditions, has been shown to be involved in neurodevelopmental pathways of memory. Nonetheless, the memory tasks performed in this study were not exclusively hippocampal-dependent tasks. Furthermore, we cannot confirm that a low Apgar score at 1 minute was related to low oxygen availability during birth. Therefore, the link between low 1 min Apgar scores and long-term memory outcomes may implicate a variety of pathways. Our next step will be focused on analyzing the link between levels of oxygen at birth (available in medical records), Apgar scores at 1 minute and long term memory outcomes. Future studies investigating how specific perinatal events are linked to long-term variable functionality in individuals with DS are needed to take our findings further. Identification of factors that may explain this variation will potentially lead to the discovery of important underlying biological pathways, which will found the bases for individualized treatments focused in early intervention programs.

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Take home messages

- Our results indicate that even transient low Apgar scores at 1 minute are linked with poorer long-term memory skills in individuals with DS.
- The link between low 1 min Apgar scores and long-term memory outcomes may implicate a variety of pathways.
- Future studies investigating how specific perinatal events are linked to long-term variable functionality in individuals with DS are needed to take our findings further.
- Identification of factors that explain this variation will potentially lead to the discovery of important underlying biological pathways as well as individualized treatments for individuals with DS.