

Depression anxiety and attention in adolescents with sickle cell disease and healthy peers.

Kelli R. Long*, Courtney C. Foster¹, Shana W. Schuler², Beth G. Wildman³, & Aimee W. Smith¹

¹Department of Psychology, East Carolina University, Greenville

²Department of Neuro Developmental Science Center, Akron Children's Hospital, Akron, USA

³Department of Psychological Sciences, Kent State University, Kent, USA

Abstract

Sickle cell disease (SCD) is a chronic hematologic condition in which the red blood cells are affected. Individuals with SCD are thought to be at an increased risk for psychosocial or neurobehavioral comorbidities in comparison to healthy individuals, which can impact their coping skills and quality of life. This study examined differences in attention and psychosocial functioning in youth with sickle cell disease and demographically matched healthy peers. The study sample consisted of adolescents 12 to 18 years of age with SCD and demographically matched healthy controls. Measures included a demographic questionnaire, the Spence Child Anxiety Scale, Child Report (SCAS), Center of Epidemiological Studies – Depression, Revised, Child Version (CES-DR), and an adaptive rate continuous performance test (ARCPT). Paired samples t-tests were used to compare groups on sustained attention and psychosocial symptoms. Pearson correlations were used to examine the relationship between sustained attention and psychosocial symptomology for adolescents with SCD and controls. There were no demographic differences between groups. Additionally, and unexpectedly, there were no differences in attention, anxiety, or depression. Performance on the ARCPT was not related to the presence of psychosocial symptoms. The present study found that adolescents with SCD are like healthy peers in terms of sustained attention, anxiety, and depression, providing evidence for resilience in the face of chronic illness. The resilience exhibited by youth in this sample may contribute to their improved pain coping skills and quality of life in comparison to youth with deficits in executive functioning and psychosocial functioning.

Keywords: Chronic illness, Mental health, Resilience, Executive functioning, Pediatrics.

Accepted on 03 December, 2021

Introduction

Sickle Cell Disease (SCD) is a genetic, lifelong condition in which the body produces red blood cells that are sickled. The symptoms of SCD include pain crises due to blocked blood flow, acute chest syndrome, increased risk of infection, decreased red blood cells, and stroke. Youth with SCD are at increased risk of stroke, and psychosocial comorbidities are common in this population, with approximately 40.4% of youth presenting with neurobehavioral comorbidity. Generally, research has identified similar rates of psychosocial comorbidities in healthy youth and youth with SCD [1-6]. However, when children and adolescents with SCD experience psychosocial problems, the consequences are more severe than for youth without SCD. For adolescents with SCD, negative mood and stress have been associated with increased pain, increased health care use, and decreased school and social functioning. Executive functioning has been shown to mediate the relationship between pain and quality of life in youth with SCD, making executive functioning and its related factors important to understand in this population.

Executive functioning is often viewed as having ties to cognitive processes such as attention, memory, and perception [7-10]. Knudson⁹ proposed a framework in which attention is a

process comprised of four working parts—working memory, competitive selection, top-down sensitivity control, and filtering. The framework posits that attention is an on-going process acting in response to competing signals, where working memory evaluates the external competing signals to then determine the signals for which a response should be elicited [11]. There are a variety of measures designed to assess attention, many of which also assess components of executive functioning due to the relatedness of attention to executive function components. By using executive function assessments as a proxy for attentional measures, practitioners can more closely pinpoint where the deficit lies in relation to the four-part framework of attention.

There are many factors known to influence attention in childhood and adolescence, including anxiety and depression. Anxiety impedes sustained attention in individuals. Research is limited as to what types of anxiety or anxiety inducing events cause this decrease in sustained attention. Research supports that trait anxiety is associated with a greater decline in sustained attention than worry. Anxiety experienced in response to a threat improves task performance in adults. There are differences in trait versus state anxiety in participants who are faced with a threat for sustained attention tasks [12-13]. Trait

anxiety impairs attention on tasks and state anxiety improves attention on tasks where there was a threat of shock for incorrect answers. Additionally, there is evidence that clinical severity of depression is linked to sustained attention deficits.

Given the rate of psychosocial comorbidities in SCD, it is reasonable to expect attention may be negatively impacted for these youth. Recent meta-analyses suggest that youth with SCD have significantly lower cognitive abilities across multiple domains including verbal and perceptual reasoning, executive functioning, and processing speed, than demographically matched healthy controls [14]. Further, these analyses found that youth with SCD and a history of cerebral infarction are most impacted in terms of cognitive functioning across domains. Differences in cognitive performance are more pronounced in school-aged children and adolescents than in adults. It is well-established within the literature that children and adolescents with SCD perform more poorly than controls on sustained attention tasks; however, the factors relating to the poorer performance in this population are unknown. Therefore, the present study has two aims: 1) compare adolescents with SCD to demographically matched controls on measures of sustained attention, anxiety symptoms, and depressive symptoms, and 2) determine if sustained attention is related to symptoms of anxiety and/or depression in either the SCD

sample or the matched control sample [15-19]. We hypothesized that 1) youth with SCD would exhibit impaired sustained attention and increased symptoms of anxiety and depression in comparison to healthy controls, and 2) lower endorsement of anxiety and depression symptoms would be related to better performance on the sustained attention task.

Methods and Materials

Participants

Participants included a sample of youth with SCD and a sample of healthy adolescents. The SCD sample has previously been described and included adolescents between 12-18 years old with SCD and their caregivers who received care from the sickle cell program at a midwestern pediatric hospital [20]. Two adolescent participants declined participation in the study for a refusal rate of 7%. The control group consisted of 41 healthy adolescents (no current medical diagnosis) who were recruited from a nearby urban school district. The groups had similar ages ($t(48) = -.43, p > .05$), genders ($\chi(1) = .00, p > .05$), and racial backgrounds ($\chi(2) = 4.93, p > .05$). See Table 1 for complete demographic information for both groups [Table 1].

Table 1. Demographics for youth with SCD and healthy controls.

Variable	M (SD) or %	
	SCD	Controls
Adolescent age	14.4 (2.04)	14.3 (1.41)
Adolescent gender		
Male	48.4	34.1
Female	51.6	65.9
Adolescent Race		
African American	80.6	56.1
Biracial	16.1	17.1
Adolescent medical insurance		
Public	71	70.7
Private	9.7	22
Mother education		
Some high school	9.7	19.5
High school or GED	19.4	19.5
Some college/professional school	35.5	31.7
Associates/Bachelor's Degree	22.6	22
Graduate/Advanced Degree	0	4.9
Father education		
Some high school	3.2	19.5
High school or GED	38.7	43.9

Some college/professional school	16.1	14.6
Associates/Bachelor's Degree	3.2	4.9
Graduate/Advanced Degree	6.5	2.4

Procedures

For the SCD population, research assistants or hematology/oncology staff members recruited potential adolescent participants and their caregivers in the waiting room of the SCD clinic and/or during SCD support group meetings at the hospital [21]. After consent from the parent/legal guardian and assent from the adolescents were obtained, families were given a packet of questionnaires. Research assistants were available to participants for questions during the completion of the questionnaires; specific questions could be clarified, and items could be read to participants as needed [22]. The participants were then scheduled for cognitive screening at a subsequent visit. The cognitive screenings were supervised by a licensed clinical neuropsychologist. This project was approved by the Institutional Review Boards of the researchers' institution as well as the hospital.

The control group was recruited from a system of public charter schools. This school system is demographically similar to the SCD cohort that was used in this study. Adolescents were recruited via letters sent home to families. After assent and consent were obtained in person, graduate and undergraduate research assistants administered the packet of measures and the cognitive screeners in the school setting. For both groups, sample size for the attention variable was attenuated due to limited follow-up with the cognitive screening appointment (scheduled separately from initial data collection due to time restraints) and/or technology difficulties with the computer administering the test [23-24]. Adolescents in both the SCD and control group were given a gift card for their participation in the study

Measures

Demographic Questionnaire

A demographic questionnaire was completed by a caregiver and assessed the adolescent's age, race, gender, and health insurance status and the caregiver's relationship to the adolescent and educational background. Health insurance and educational background of the caregiver were used as a proxy for the adolescent's socioeconomic status.

Attention

We used the computerized adaptive rate continuous performance tests (ARCPT) to measure sustained attention and vigilance.¹⁹ Participants completing the ARCPT are asked to identify the target letter by pressing the spacebar; correct responses as well as incorrect responses are recorded. The primary outcome measure of the ARCPT was a vigilance

decrement score, which measures the decline in overall performance across the task.

Spence Child Anxiety Scale, Child Report (SCAS)

The SCAS assesses anxiety symptoms across six domains (generalized anxiety, panic/agoraphobia, social phobia, separation anxiety, obsessive compulsive disorder, and physical injury fears).²⁰ Respondents rate 38 items on a Likert scale from 0 (never) to 3 (always), (range = 0 to 114). Raw scores are translated to t-scores, which have been standardized for males and females between 8 and 15 years of age. A t-score of 60 or greater reflects elevated anxiety symptoms. While a portion of participants in this study fell outside of the original age range, the SCAS has been used in older adolescents and maintained high internal consistency and correlated with other measures of anxiety.²¹ While specific items on the SCAS assess state anxiety, the overall scores represent trait anxiety.

Center of Epidemiological Studies – Depression, Revised, Child Version [CES-D22; CES-DR23]

The CES-DR is a 20 item self-report measure of depressive symptoms experienced during the past week which participants rate on a scale from 1 (rarely or none of the time, less than 1 day) to 4 (most or all of the time, 5-7 days) (range = 20 to 80). The scale has been previously utilized with African American adolescents.²⁴

Data Analysis Plan

Descriptive analyses were conducted on demographic information and study variables For aim 1, three separate paired samples t-tests compared adolescents with SCD to controls on 1) sustained attention (CPT vigilance decrement), 2) anxiety symptoms, and 3) depression symptoms. For aim 2, Pearson correlations (2-tailed) examined the relationship between sustained attention, anxiety, and depression for youth with SCD and controls. Previous literature examining executive functioning in youth with SCD found medium to large effect sizes, where Cohen's d statistics ranged from 0.5-1.05 across various measures of executive functioning^{8,25}. An a-priori power analysis via G-power software indicated that a large effect (Cohen's d = 0.8) requires 12 matched pairs to yield a power of .8 for the proposed t-tests comparing youth with SCD to controls on sustained attention and psychosocial functioning.^{26,27}

Results

Characteristics of the study sample are presented in Table 1. There were no differences between the two groups on demographic variables (age, race, gender, health insurance).

Comparisons of the study variables are. A paired samples t-test showed no differences in sustained attention between adolescents with SCD (M = .038, SD = .109) and healthy peers (M = .046, SD = .069). Adolescents with SCD (M = 22.93, SD = 13.83) had similar levels of anxiety (M = 28.98, SD = 13.17) and similar levels of depression (M = 38.17, SD = 8.39)

compared to healthy peers (M = 38.29, SD = 10.28). Performance on the sustained attention task was not related to anxiety symptoms (SCAS, $r = .071$, $p = .619$) or depressive symptoms (CESD, $r = -.212$, $p = .134$) shown in [Table 2].

Table 2. Comparisons on sustained attention and psychosocial measures.

Variable	SCD	Controls	p
	n = 13	n = 28	
CPT			
Total Hits	47.08 (5.59)	47.08 (3.66)	0.999
Total False Alarms	9.54 (10.70)	7.00 (5.55)	0.275
Task Sensitivity	.87 (.13)	.90 (.048)	0.237
Final ISI	100.17 (91.67)	109.0 (78.12)	0.732
Inconsistency Index	14.23 (10.81)	11.00 (6.05)	0.187
Vigilance Decrement	.04 (.11)	.05 (.07)	0.765
	n = 29	n = 41	
SCAS	22.93 (13.83)	28.98 (13.17)	0.068
CESD	38.17 (8.39)	38.29 (10.28)	0.959

Discussion

The present study examined sustained attention, anxiety symptoms, and depressive symptoms in adolescents with SCD and matched controls. Previous studies have generally suggested that children with SCD demonstrate lower academic attainment and executive functioning than healthy peers. Overall, the present study found that children with SCD are similar to their healthy peers in terms of sustained attention and symptoms of anxiety and depression. Although unexpected, this finding is strong evidence of resiliency in SCD samples despite their chronic illness. It is possible their resilience may lead to improved pain coping and quality of life compared to youth with SCD who exhibit deficits in executive functioning and psychosocial functioning. Although not statistically significant, the adolescents with SCD responded more variably in the attention task. Therefore, it is important when working with youth with SCD to consider each individual's cognitive strengths and deficits.

Additionally, adolescents with SCD reported similar anxiety and depression symptoms as adolescents in the control group. This finding is consistent with existing literature, suggesting that adolescents with SCD experience similar rates of psychosocial comorbidities in comparison to healthy peers. As the youth with SCD begin to transition into adulthood and begin to plan for and manage their own care, typical levels of anxiety and/or depression symptoms in combination with typical sustained attention (similar to healthy peers) will serve to bolster health related quality of life.

Conclusion

The strength of this study is the use of demographically matched peers in the control group. The control group was matched on age, race, gender, and socioeconomic status. Limitations of this study include a small sample size as well as uneven sample sizes between groups. As a result, the results should be interpreted with caution. On the measure of attention, more youth with SCD responded more variably than their healthy peers. With a larger sample size and even groups, the results may shift to show hypothesized differences between youth with SCD and healthy peers on tasks related to attention, consistent with existing literature. The current study is an important first step in understanding the relationship among anxiety symptoms, depressive symptoms, and attention in youth with SCD. Future studies should aim for a larger sample of youth with SCD.

The present study examined differences in attention and psychosocial functioning between youth with SCD and demographically matched healthy controls. Youth with SCD appeared statistically similar to the healthy controls across a variety of sustained attention measures as well as on depression and anxiety symptomology. While the findings were unexpected, the psychosocial and sustained attention resilience that the youth with SCD in the sample exhibited may enable improved pain coping skills and improved quality of life compared to youth with SCD who exhibit deficits in executive functioning and in psychosocial functioning. It is important for pediatric providers to collaborate with adult providers in order to monitor patients' psychological and

executive functioning, particularly during the vulnerable time of transition to adult care.

References

1. Platt OS, Brambilla DJ, Rosse WF, et al. Mortality in sickle cell disease -- Life expectancy and risk factors for early death. *N Engl J Med.* 1994;330:1639-1644.
2. Anie KA. Psychological complications in sickle cell disease. *Br J Haematol.* 2005;129:723-729.
3. Panepinto JA, Pajewski NM, Foerster LM, et al. Impact of family income and sickle cell disease on the health-related quality of life of children. *Qual Life Res.* 2009;18:5-13.
4. Yang YM, Cepeda M, Price C, et al. Depression in children and adolescents with sickle-cell disease. *Arch Pediatr Adolesc Med.* 1994;148:457-460.
5. Gil KM, Carson JW, Porter LS, Scipio C, et al. Daily mood and stress predict pain, health care use, and work activity in African American adults with sickle-cell disease. *Health Psychol.* 2004;23:267-274.
6. Ludwig NN, Sil S, Khowaja MK et al. Executive functioning mediates the relationship between pain coping and quality of life in youth with sickle cell disease. *J Pediatr Psychol.* 2018;43:1160-1169.
7. Knudsen EI. Fundamental components of attention. *Annu Rev Neurosci.* 2017;30:57-78.
8. Forster S, Nunez Elizalde AO, Castle E, et al. Unraveling the anxious mind: anxiety, worry, and frontal engagement in sustained attention versus off-task processing. *Cereb Cortex.* 2015;25:609-618.
9. Robinson OJ, Krimsky M, Grillon C. The impact of induced anxiety on response inhibition. *Front Hum Neurosci.* 2013;7:69.
10. Grillon C, Robinson OJ, Mathur A, et al. Effect of attention control on sustained attention during induced anxiety. *Cogn Emot.* 2016;30:700-712.
11. Yang X, Ma X, Huang B, et al. Gray matter volume abnormalities were associated with sustained attention in unmedicated major depression. *Compr Psychiatry.* 2015;63:1-79.
12. Prussien, KV, Jordan, LC, et al. Cognitive function in sickle cell disease across domains, cerebral infarct status, and the lifespan: A meta-analysis. *J Pediatr. Psychol.* 2019;44: 948-958.
13. Kawadler, JM, Clayden, JD, Clark, et al. Intelligence quotient in paediatric sickle cell disease: a systematic review and meta-analysis. *Dev Med Child Neurol.* 2016;58(7), 672-679.
14. King AA, Strouse JJ, Rodeghier MJ, et al. Parent education and biologic factors influence on cognition in sickle cell anemia. *Am. J. Hematol.* 2014;89:162-167.
15. Brown RT, Buchanan I, Doepke K, et al. Cognitive and academic functioning in children with sickle-cell disease. *J Clin Child Psychol.* 1993;22:207-218.
16. Buchsbaum MS, Sostek AJ. An adaptive-rate continuous performance test: Vigilance characteristics and reliability for 400 male students. *Percept Mot Skills.* 1980;51:707-713.
17. Spence SH. A measure of anxiety symptoms among children. *Behav Res Ther.* 1998;36:545-566.
18. Essau CA, Anastassiou-Hadjicharalambous X, Muñoz LC, et al. Psychometric properties of the Spence Children's Anxiety Scale (SCAS) in Cypriot children and adolescents. *Child Psychiatry Hum Dev.* 2011;42:557-568
19. Radloff LS. The CES-D scale: A self-report depression scale for research in the general population. *Appl Psychol Meas.* 1977;1:85-401
20. Pittman LD, Chase-Lansdale PL. African American girls in impoverished communities: Parenting style and adolescent outcomes. *J Res Adolesc.* 2003;11:199-224.
21. Berg C, Edwards DF, King A, et al. Executive function performance on the children's kitchen task assessment with children with sickle cell disease and matched controls. *Child Neuropsychol.* 2012;18:432-448.
22. Faul F, Erdfelder E, Buchner A, et al. Statistical power analyses using G*Power 3.1: Tests for correlation and regression analyses. *Behav Res Methods.* 2009;41:1149-1160.
23. Epping AS, Myrvik MP, Newby RF, et al. Academic attainment findings in children with sickle cell disease. *J Sch Health.* 2013;83:548-553.
24. Ladd RJ, Valrie CR, Walcott CM, et al. Risk and resilience factors for grade retention in youth with sickle cell disease. *Pediatr Blood Cancer.* 2014;61:1252-1256

*Correspondence to

Dr. Kelli R. Long
 Department of Psychology
 East Carolina University
 Greenville
 USA
 E-mail: krlong94@gmail.com