Using a Virtual Classroom environment to describe the attention deficits profile of children with Neurofibromatosis type 1

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A B S T R A C T

The objectives of this study were to describe the nature of the attention deficits in children with Neurofibromatosis type 1 (NF1) in comparison with typically developing (TD) children, using the Virtual Classroom (VC), and to assess the utility of this instrument for detecting attention deficits. Twenty-nine NF1 children and 25 age-and gender-matched controls, aged 8–16, were assessed in a VC. Parents’ ratings on the Conners’ Parent Rating Scales—Revised: Long (CPRS-R:L) questionnaire were used to screen for Attention Deficit–Hyperactivity Disorder (ADHD). Significant differences were found between the NF1 and the control groups on the number of targets correctly identified (omission errors) and the number of commissions (commission errors) in the VC, with poorer performance by the NF1 children (p < 0.005). Significant correlations were obtained between the number of targets correctly identified, the number of commission errors, and the reaction time. Significant correlations were also found between the total correct hits and the cognitive problems/inattention scale, as well as two other indexes of the CPRS-R:L: the DSM-IV Symptoms Subscale and the ADHD Index.

The VC results support the hypothesis that NF1 is marked by inattention and impulsivity and that participants with NF1 are more inattentive (omission errors) and impulsive (commission errors) than normal controls. The VC appears to be a sensitive and ecologically valid assessment tool for use in the diagnosis of attention deficits among children with NF1.

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1. Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant disorder affecting 1 in 2500–3000 individuals (Krab et al., 2008). In addition to the characteristic features, such as café-au-lait spots, neurofibromas, and optic gliomas, patients often have impairments in visuospatial ability, memory, sustained attention, coordination, language, behavior, and intellectual functioning (Levine, Materek, Abel, O’Donnell, & Cutting, 2006). Approximately 30–50% of individuals with NF1 also meet the criteria for the diagnosis of Attention Deficit–Hyperactivity Disorder (ADHD). Although a large body of literature has explored the link between cognitive and learning difficulties and NF1, the relationship between NF1 and attention deficit has only become a focus of investigation in the last decade. The paucity of studies investigating this relationship is surprising.

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considering the high prevalence rates of Attention Deficit–Hyperactivity Disorder (ADHD) in children with NF1 and the reports of attention deficits already evident throughout the literature (Keyhan, Minden, & Ickowicz, 2006).

Due to the lack of biological markers for ADHD, Continuous Performance Test (CPT) and computerized neuropsychological tests have been developed to provide the objective measurement of criteria relevant to the diagnostic process (Greenberg & Waldman, 1993). Studies using CPT on cohorts of children with NF1 have offered inconsistent results. One study reported that children with NF1 and ADHD made more commission errors than children with NF1 alone, children with ADHD alone, and unaffected sibling controls (Mautner, Kluwe, Thakker, & Leark, 2002). In contrast, another study found that children with NF1 demonstrated significantly more errors of omission on a CPT than their unaffected siblings, but did not differ in commission errors or overall response time (Dilts et al., 1996; Mazzocco et al., 1995).

Moreover, CPT are delivered in sterile environments that lack the challenges typically present in the school environment, thus limiting their usefulness in the area of ecological validity. In addition, CPT are tedious and infamious for the negative reactions evoked in children (Adams, Finn, Moes, Flannery, & Rizzo, 2009). Alternatively, Virtual Reality (VR) technology can be employed to immerse a user within a dynamic, three-dimensional ecologically valid stimulus environment for assessment under conditions more similar to the challenges of the “real” world (Rizzo et al., 2006). As such, VR technology delivers results beyond the scope of currently available computerized assessments.

The Virtual Classroom (VC) was developed for the assessment of attention skills in an environment that simulates a real-world classroom. Recent findings have provided initial support for the construct validity of this virtual environment in children with ADHD, demonstrating that the VC effectively differentiates between participants with ADHD and normal control children. Concurrent validity has also been demonstrated by correlating VC results with other widely used ADHD assessment tools. These studies suggest that the VC has good potential for controlled performance assessment within an ecologically valid environment and appears to parse out significant effects due to the presence of distraction stimuli (Adams et al., 2009; Parsons, Bowerly, Buckwalter, & Rizzo, 2007; Pollak et al., 2009; Rizzo et al., 2006).

The present study is the first to use the VC environment to assess attention processes in an NF1 population. The objectives of the study were: (1) to describe the attention deficits profile of children with NF1 as compared to a control group, using the VC; (2) to assess the utility of the VC in detecting attention deficits in a sample of NF1 children, as compared to a widely used ADHD screening questionnaire.

2. Methods

2.1. Participants

The study group consisted of 29 children diagnosed with Neurofibromatosis type 1 (NF1) according to the NIH criteria (9 males, 20 females; mean age 12.2 ± 2.5). Exclusion criteria for the study group were central nervous system (CNS) pathology, such as brain tumors, epilepsy, or hydrocephalus, and significant hearing or visual impairment, as determined by their physician. One child was excluded because of refusal to cooperate. Five children from the NF1 group were previously diagnosed with ADHD (17%), three of whom were using medication for ADHD. The control group consisted of 25 typically developing (TD) children matched to the study group by gender and age (7 males, 18 females; mean age 12.2 ± 2.6). Three children were excluded from the control group because of the presence of ADHD.

All participants used the Hebrew language as their primary means of verbal and written communication. There were no significant differences between the children with NF1 and the controls in the distribution or frequency of age, school year, gender, or handedness. As expected, the IQ scores of the NF1 group were lower (13.0 ± 98.9) than those of the control group (12.3 ± 109.3). However, this gap did not reach significance.

2.2. Materials

2.2.1. Virtual Classroom (VC) (Rizzo et al., 2006)

The Virtual Classroom is a head-mounted display (HMD) immersive VR system. The research version of the VC scenario consists of a standard rectangular classroom environment containing desks, a female teacher, a blackboard across the front wall, a side wall with a large window, and a pair of doorways on the opposite wall. In the Hebrew version of the VC, digits are used instead of letters and the test instructions are in Hebrew.

The task utilized in this study required the participants to tap the mouse button as quickly and accurately as possible, using their dominant hand, when the digit sequence “37” appeared on the VC blackboard. The stimuli remained on the screen for 150 ms, with a fixed inter-stimulus interval of 1350 ms. Participants were instructed to withhold response to any other sequence of digits. The test lasted for 10 min, with five identical blocks of 2 min each. During the 10 min period, 400 stimuli were presented, of which 100 were “37” sequences. These stimuli were accompanied by 20 distractors, including pure audio (e.g., classroom noises); pure visual (e.g., a paper airplane flying across the visual field); and mixed audiovisual (e.g., a car “rumbling” by a window, a person walking into the classroom with hall sounds when the door is opened). Distractors were each displayed for five seconds and presented identically for the entire sample.

The participants’ reaction patterns were recorded and documented using four measures. The first measure was the ability to correctly identify 100 targets out of 400 stimuli (correct and incorrect hits) during the 10-min period, measured as a raw score out of 100. Second was the number of commission errors, that is, incorrect identification of the non-target as the target.
Third was reaction time, which was measured in ms. Finally, head movements were captured and quantified by the inertial tracking system, which is part of the head-mounted display (HMD) that is used to sense head orientation. The head movements were quantified in three orientation axes representing pitch, roll, and yaw.

2.2.2. The Conners’ Parent Rating Scales—Revised: Long (CPRS-R:L) (Conners, 1997)

The CPRS-R:L questionnaire uses a categorical approach to rating symptoms of ADHD. The parents of the participants rated 80 items on a four-point Likert-type scale. The results included seven subscales: (1) Oppositional; (2) Cognitive problems; (3) Hyperactivity; (4) Anxious–shy; (5) Perfectionism; (6) Social problems; and (7) Psychosomatic. The CPRS-R:L contains three additional scales: the ADHD Index, the Conners’ Global Index (CGI), and the DSM-IV Symptoms Subscale. The ADHD Index, which consists of 12 items, is an effective screener for identifying children and adolescents meeting ADHD diagnostic criteria. The CGI is the index with the 10 items found to be most sensitive to treatment effects. The DSM-IV Symptoms Subscale consists of 18 items that directly parallel the DSM-IV criteria for diagnosing ADHD.

2.3. Procedure

All participants in the study group were recruited from the Gilbert Israeli Neurofibromatosis Center (GINFC) at the Pediatric Neurology Unit of Dana Children’s Hospital in Tel Aviv Sourasky Medical Center, Israel. The age- and gender-matched control children were recruited from local elementary and middle schools using “snowball” methodology. The study was approved by the Ethics Review Committee of the Tel Aviv Sourasky Medical Center, and all parents signed an informed consent for their children’s participation in the study.

All parents were requested not to give their children stimulant medication 24 h prior to the assessment. Parents and children were escorted into separate rooms. The HMD was placed on the participants’ heads, and they were allowed to familiarize themselves with the VC by briefly scanning the 360-degree virtual environment using head movements. They then engaged in the VC assessment. While their children were being tested, the parents were asked to fill out a demographic questionnaire and the Conners’ scale for ADHD. Thirty-seven parents answered the questionnaire.

2.4. Data analysis

One-way analysis of variance (ANOVA) and chi-square statistical tests were conducted to compare participants with NF1 and normal controls on all demographic variables. Means and standard deviations of the VC parameters were calculated. A multivariate analysis of covariance (MANCOVA) was used to examine group differences across the dependent variables of the VC on the CPRS-R:L, with group membership as the independent variable and age as the covariate. Pearson correlations were calculated to check for associations between the questionnaire and the VC scores.

3. Results

The results from the assessment of the Virtual Classroom (VC) task are presented in Table 1. As the table shows, the performance of the NF1 group was significantly lower than the controls on the total correct hits and the number of commission

<table>
<thead>
<tr>
<th>Measures</th>
<th>NF1 (n = 29)</th>
<th>TD (n = 25)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total correct hit(^\text{a})</td>
<td>74.37 ± 21.64</td>
<td>87.40 ± 10.48</td>
<td>10.24</td>
<td>.004</td>
</tr>
<tr>
<td>Block 1</td>
<td>15.51 ± 4.38</td>
<td>18.07 ± 2.34</td>
<td>7.03</td>
<td>.01</td>
</tr>
<tr>
<td>Block 2</td>
<td>15.24 ± 4.91</td>
<td>17.50 ± 2.51</td>
<td>4.44</td>
<td>.04</td>
</tr>
<tr>
<td>Block 3</td>
<td>14.82 ± 5.10</td>
<td>17.42 ± 2.51</td>
<td>5.50</td>
<td>.02</td>
</tr>
<tr>
<td>Block 4</td>
<td>14.00 ± 4.44</td>
<td>16.84 ± 3.23</td>
<td>7.21</td>
<td>.01</td>
</tr>
<tr>
<td>Block 5</td>
<td>14.24 ± 4.11</td>
<td>16.61 ± 3.75</td>
<td>4.96</td>
<td>.03</td>
</tr>
<tr>
<td>Commissions errors(^\text{b})</td>
<td>20.27 ± 23.03</td>
<td>5.87 ± 5.34</td>
<td>8.95</td>
<td>.002</td>
</tr>
<tr>
<td>Block 1</td>
<td>4.93 ± 4.43</td>
<td>1.20 ± 1.73</td>
<td>15.57</td>
<td>.00</td>
</tr>
<tr>
<td>Block 2</td>
<td>4.79 ± 6.77</td>
<td>1.36 ± 1.65</td>
<td>6.08</td>
<td>.01</td>
</tr>
<tr>
<td>Block 3</td>
<td>3.13 ± 4.09</td>
<td>1.32 ± 1.28</td>
<td>4.53</td>
<td>.03</td>
</tr>
<tr>
<td>Block 4</td>
<td>3.44 ± 4.54</td>
<td>1.12 ± 1.30</td>
<td>6.12</td>
<td>.01</td>
</tr>
<tr>
<td>Block 5</td>
<td>3.96 ± 4.33</td>
<td>.96 ± 1.01</td>
<td>7.40</td>
<td>.009</td>
</tr>
<tr>
<td>Hit reaction time (ms)</td>
<td>.47 ± .08</td>
<td>.46 ± .06</td>
<td>.07</td>
<td>NS</td>
</tr>
<tr>
<td>Head movement(^\text{c})</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yaw</td>
<td>3.90 ± 7.2</td>
<td>2.72 ± 6.61</td>
<td>.52</td>
<td>NS</td>
</tr>
<tr>
<td>Pitch</td>
<td>−5.14 ± 10.47</td>
<td>−3.52 ± 7.68</td>
<td>.48</td>
<td>NS</td>
</tr>
<tr>
<td>Roll</td>
<td>−3.30 ± 6.28</td>
<td>−1.84 ± 4.88</td>
<td>.92</td>
<td>NS</td>
</tr>
</tbody>
</table>

NF1, Neurofibromatosis type 1.

\(^{a}\) Total correct hit – is raw score (out of 100).

\(^{b}\) Commissions errors – is raw score.

\(^{c}\) Head movement data represent head orientation in space (pitch, roll, yaw axes) and are measures from the inertial head tracking system in the HMD in a given condition.
errors. The NF1 group responded correctly to significantly fewer targets and made more commission errors than the control group for the entire task and for each two-min block (Table 1). Block differences of the total correct hits varied as a function of time according to how much continuous attention was required (Fig. 1). There was no significant difference found in reaction time. Greater head movement was not recorded in participants with NF1, as measured by all three orientation axes (pitch, roll, and yaw) captured from the tracking system of the head-mounted display (HMD).

Significant inter-correlations were found between the VC measures: the total correct hits, the commission errors, and the reaction time (Table 2).

The second analyzed measure consisted of the parents’ questionnaire variables obtained from the Conners’ Parent Rating Scales—Revised: Long (CPRS-R:L). Significant differences were found between the NF1 and the TD groups (Table 3). Univariate ANOVAs indicated that the children with NF1 received significantly higher scores (i.e., performed worse) on the cognitive problems/inattention clinical scale. The children with NF1 also received significantly higher scores (i.e., performed worse) on two indexes of the CPRS-R:L: the DSM-IV Symptoms Subscale and the ADHD Index.

Table 2
Intercorrelations of the Virtual Classroom measures.

<table>
<thead>
<tr>
<th></th>
<th>Commissions errors</th>
<th>Hit reaction time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total correct hits</td>
<td>–.69***</td>
<td>.44**</td>
</tr>
<tr>
<td>Commissions errors</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Correlations
- Correlation is significant at the 0.05 level (2-tailed).
- Correlation is significant at the 0.01 level (2-tailed).

Table 3
Comparison of CPRS-R:L measures between NF1 and controls.

<table>
<thead>
<tr>
<th>CPRS-R:L</th>
<th>NF1 (n = 23)</th>
<th>TD (n = 14)</th>
<th>F</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical scales</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oppositional</td>
<td>54.04 ± 16.01</td>
<td>55.57 ± 10.86</td>
<td>.09</td>
<td>NS</td>
</tr>
<tr>
<td>Cognitive problems/inattention</td>
<td>62.47 ± 11.13</td>
<td>51.64 ± 7.82</td>
<td>10.15</td>
<td>.00</td>
</tr>
<tr>
<td>Hyperactivity</td>
<td>64.04 ± 17.04</td>
<td>56.35 ± 8.31</td>
<td>2.46</td>
<td>NS</td>
</tr>
<tr>
<td>Anxious–shy</td>
<td>53.52 ± 12.12</td>
<td>53.28 ± 7.22</td>
<td>.00</td>
<td>NS</td>
</tr>
<tr>
<td>Perfectionism</td>
<td>46.21 ± 17.35</td>
<td>51.64 ± 17.09</td>
<td>.86</td>
<td>NS</td>
</tr>
<tr>
<td>Social problems</td>
<td>59.76 ± 14.58</td>
<td>59.10 ± 14.55</td>
<td>.00</td>
<td>NS</td>
</tr>
<tr>
<td>Psychosomatic</td>
<td>57.00 ± 14.00</td>
<td>52.21 ± 9.69</td>
<td>1.25</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Indexes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DSM-IV Symptoms Subscale</td>
<td>62.00 ± 13.82</td>
<td>53.28 ± 8.25</td>
<td>4.54</td>
<td>.04</td>
</tr>
<tr>
<td>ADHD Index</td>
<td>60.04 ± 12.79</td>
<td>50.71 ± 6.66</td>
<td>6.34</td>
<td>.01</td>
</tr>
<tr>
<td>Conners’ Global Index</td>
<td>60.60 ± 13.35</td>
<td>54.21 ± 9.19</td>
<td>2.48</td>
<td>NS</td>
</tr>
</tbody>
</table>

CPRS-R:L, The Conners’ Parent Rating Scales—Revised: Long; BRIEF, The Behavior Rating Inventory of Executive Function; NF1, Neurofibromatosis type 1; TD, typically developing.
For the NF1 group, a significant negative correlation was found between the VC's total correct hits and the cognitive problems/inattention clinical scale of the CPRS-R:L ($r = -.42, p < .05$). Thus, a higher number of correct hits was negatively correlated with lower scores, indicating better attention skills on this measure.

4. Discussion

The goal of this study was to describe the attention deficits profile of children with NF1 in an ecologically valid situation. Children with and without NF1 were compared on their performance in a Virtual Classroom (VC). The VC task combined both visual and auditory sensory stimuli, allowing for a more ecologically valid assessment of higher levels of attention (Parsons et al., 2007).

A significant difference was found between the NF1 and the control groups on the number of targets correctly identified in the VC, with the NF1 children performing poorer than the controls (more omission errors). The participants’ difficulties in maintaining continuous attention were demonstrated by their inability to correctly identify 100 targets out of 400 stimuli during a 10-min period. The linear decreasing pattern exemplified in Fig. 1 clearly demonstrates their problems with maintaining continuous attention.

This finding is supported by earlier evidence of deficits in sustained attention skills among children with NF1 (Descheemaeker, Ghesquiere, Symons, Fryns, & Legius, 2005; Hyman, Arthur Shores, & North, 2006; Hyman, Shores, & North, 2005). Further support is also provided in the present study by the finding that a higher number of correct hits was negatively significantly correlated with the cognitive problems/inattention clinical scale of the CPRS-R:L. Thus, more correct hits, as indicated by lower scores on this scale, point to better cognitive/attention skills.

The second significant difference identified in the VC was on the number of commission errors. The participants with NF1 made more commission errors than the normal controls. This finding is consistent with previous research on CPT performance differences between ADHD participants and normal controls (Mautner et al., 2002). The NF1 group responded less accurately to the stimulus as a result of impulsive responding in the absence of a target (Rizzo et al., 2006). The significant negative correlation between reaction time to the targets and commission errors supports this finding. Thus, the children who reacted to target appearance more quickly (short reaction time) committed more errors, and the children who correctly identified more targets made fewer commission errors. These findings lend support to the idea that NF1 is indeed marked by inattention and impulsivity and that participants with NF1 are more inattentive (omission errors) and impulsive (commission errors) than normal controls. The significant negative correlation between these two measures of VC is therefore not surprising.

No significant difference was noted between the two groups on the reaction time to targets. This finding was in contrast to another study, where the performance of 16 NF1 participants and 16 age- and sex-matched controls were compared on computerized tasks and the NF1 participants were found to be significantly slower than controls on a measure of hand responding (Rowbotham, Pit-ten Cate, Sonuga-Barke, & Huijbregts, 2009). Previous studies using the VC have also found that children with Attention Deficit–Hyperactivity Disorder (ADHD) showed slower reaction time compared to controls (Adams et al., 2009; Rizzo et al., 2006). The results of the present study do not indicate that these differences in processing speed (the response time between stimulus and reaction) in children with ADHD (Parsons et al., 2007) are also present in children with NF1. However, due to the contradictory results from an earlier study (Rowbotham et al., 2009), further investigation is needed.

No significant differences were observed in any of the three measures of head movements in the participants with NF1, as compared to the TD group. However, in previous research, children with ADHD showed greater levels of hyperactivity than controls, as measured by their total head and body movements (Parsons et al., 2007). These findings may lead to the conclusion that the attention deficits of children with NF1 do not include more overall hyperactivity. Perhaps this result stems from the fact that the present cohort consisted of both children and adolescents (mean age 12.3 ± 2.6), as it has been suggested that some elements of hyperactivity significantly decrease after puberty (Coude, Mignot, Lyonnet, & Munnich, 2007). Future studies should investigate the presence/absence of hyperactivity separately among children and adolescents with NF1.

The absence of significant group differences in reaction time and head movements may also be attributed to the fact that the groups were characterized by a female majority (21 girls versus 9 boys). Earlier studies have reported gender differences with respect to the prevalence of ADHD, its subtypes, and specific DSM-IV ADHD symptoms. Males are generally more likely to be diagnosed with ADHD than females, with a male/female ratio of approximately 4:1 in community samples (Ramttekkar, Reiersen, Todorov, & Todd, 2010).

The cognitive problems of children with NF1 are well documented (Levine et al., 2006). As expected, the children with NF1 were found to have significantly higher scores (i.e., performed worse) on one clinical scale and two indexes of the CPRS-R:L: the cognitive problems/inattention scale, the DSM-IV Symptoms Subscale, and the ADHD Index. Moreover, the parents' reports on inattention are consistent with the results of the NF1 group in the VC. Thus, we conclude that the VC shows much promise in describing the nature of the attention problems of children with NF1. As such, this tool may be useful in supporting the clinical diagnostic interview, which is essential, among other things, for establishing the presence of impairment from ADHD symptoms.

Some limitations of the present study must be acknowledged. First, the study sample was relatively small, and there were unequal proportions between the genders. Second, only 5 of the 29 NF1 children (17%) had previously been diagnosed with ADHD. This represents a lower rate of attention problems than is usually found. Future investigation should recruit larger cohorts and use more than one screening questionnaire to assess the value of this new tool.
5. Conclusions

The VC results support the hypothesis that NF1 is marked by inattention and impulsivity and that participants with NF1 are more inattentive (omission errors) and impulsive (commission errors) than normal controls. The VC appears to be a sensitive and ecologically valid assessment tool for use in the diagnosis of attention deficits among children with NF1.

References


