

# Physical Activity and Sleep in 11-Year Old Children With a Familial High Risk of Schizophrenia or Bipolar Disorder. The Danish High Risk and Resilience Study—VIA 11

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**Objective:** People with schizophrenia and bipolar disorder are at increased risk of having comorbid somatic illness. This is partly due to lack of physical activity, which may originate from childhood. Sleep disturbances are associated with schizophrenia and bipolar disorder. We aimed to assess physical activity and sleep in children at familial high risk of schizophrenia or bipolar disorder and population-based controls **Methods:** This study is part of The Danish High Risk and Resilience Study—VIA 11. Children aged 11 born to parents with schizophrenia (FHR-SZ) ( $N = 133$ ), bipolar disorder (FHR-BP) ( $N = 84$ ), or controls (C) ( $N = 150$ ) were assessed by accelerometry for an average of 6.9 days. **Results:** High-intensity physical activity was significantly lower in children at FHR-SZ and FHR-BP compared to controls, (mean hours per day for FHR-SZ: 0.29, SD 0.19, for FHR-BP: 0.27, SD 0.24, and for controls 0.38, SD 0.22,  $P = <.001$ ). Sleep did not differ between the groups. **Conclusion:** Children at FHR-SZ or FHR-BP had less physical activity compared to controls. Our study highlights a research area that reveals a hitherto unexplored

disadvantage of being born to parents with schizophrenia or bipolar disorder. Further research is needed to enhance better understanding of causal pathways and consequences of reduced physical activity in children with FHR-SZ and FHR-BP.

**Key words:** Schizophrenia/bipolar disorder/high risk/children/physical activity

## Introduction

People with schizophrenia or bipolar disorder have an increased lifetime prevalence of somatic diseases compared to the general population<sup>1</sup> and are less likely to incorporate physical activities in their regular daily life routines, and are as such more sedentary compared to the general population.<sup>2,3</sup> This might reflect that people with severe mental illness show lower levels of functioning in general, directly due to their disease or indirectly, as treatment with antipsychotic medication often impairs

mental as well as physical functions.<sup>4,5</sup> Moreover, mental illness implicates impairments in the ability to do physical exercises or activities while negative symptoms impact initiative, pleasure, and energy.<sup>6</sup> Physical activities, sleep problems, and psychiatric disorders are closely related. Previous studies indicate that most patients with schizophrenia or other psychotic disorders at some point during the course of their illness suffer from insomnia and approximately 40 % of the patients meet the criteria for a sleep disorder.<sup>7</sup> Insomnia is the most common.<sup>8</sup> The absence of physical activity affects sleep, and it has been shown that only a few hours of moderate exercise per week (e.g. walking) can significantly reduce insomnia.<sup>9</sup> Schizophrenia and bipolar disorder are highly hereditary, and children born to parents with one of these disorders are at higher risk of developing the same or other psychiatric disorders.<sup>10</sup> Both schizophrenia and bipolar disorder are illnesses with subtle signs, including sleep alterations, that manifest years before the onset of actual psychiatric symptoms.<sup>11–13</sup> Children of parents with schizophrenia and bipolar disorder have been the subjects of several studies that have documented deficits in multiple domains, such as compromised motor, cognitive and social functions and a higher incidence of psychopathology.<sup>14–16</sup> Previous studies have also shown that children with familial high risk of schizophrenia or bipolar disorder have poorer sleep compared to controls<sup>17–19</sup> but to our knowledge, the amount of physical activity is largely unexamined in this population. However, in order to identify predictors for later development of mental and somatic illness, research into the children's physical health, and as such physical activity, might also contribute to our knowledge about aspects of these children's risk profile. In this investigation, we aimed to describe the amount of physical activity, sedentary behavior, and amount of restless and total sleep in children with familial high risk of schizophrenia or bipolar disorder compared to controls, by collecting accelerometric data from children age 11 for a period of 7 days. From comparison analyses of data from our baseline study, The Danish High Risk and Resilience Study—VIA 7, we know that children with familial high risk differ significantly from controls in multiple of the studied areas.<sup>20</sup> We, therefore, included physiological measures of Body Mass Index (BMI) and maximum oxygen uptake the body is able to use during exercise ( $VO_2$  max) as well as contextual information about the children's leisure activities and both the children's and parent's general level of functioning. We hypothesized that children in both familial high-risk groups would be less physically active and have more restless sleep compared to controls. Further, we aimed to investigate any possible differences between the three groups might be reflected in the children's sleep and activity patterns on both weekends and weekdays, and finally, we hypothesized that the amount of sleep and level of activity would be associated.

## Methods

### *Study Design and Participants*

This is the first follow-up study of The Danish High Risk and Resilience Study—VIA 7 (The VIA 7 study), called The Danish High Risk and Resilience Study—VIA 11 (The VIA 11 study). The overall purpose of the studies is to investigate the developmental pathways of children with familial high risk of schizophrenia spectrum psychosis or at familial high risk of bipolar disorder and to identify risk and resilience factors in their development to guide future early interventions. In The VIA 7 Study, we established and examined a cohort of 7-year-old children with no, one, or two parents with schizophrenia spectrum psychosis (FHR-SZ) (defined as ICD-10 codes: F20, F22, F25, or ICD-8 codes: 295, 297, 298.29, 298.39, 298.89, 298.99) or bipolar disorder (FHR-BP) (defined as ICD-10 codes F30 and F31 or ICD-8 codes 296.19 and 296.39) between January 1, 2013 and January 31, 2016. Controls were matched on age, sex, and municipality to children with at least one parent diagnosed with schizophrenia spectrum psychosis in the Danish Register. Parents of PBC's could be registered with any diagnosis except schizophrenia spectrum psychosis and bipolar disorder. Children born to parents diagnosed with bipolar disorder were a non-matched sample but were comparable to the other two groups in terms of sex, age, and urbanity. In the period between March 1, 2017 and June 30, 2020, all families were invited to participate in the VIA 11 Study. A total of 465 families, 89 % of the original cohort, participated in the VIA 11 Study. The Danish Data Protection Agency and The Danish National Committee on Health Research Ethics approved the study protocol (Protocol number H16043682). Adult participants gave written informed consent and the children's custody holders gave written informed consent on behalf of the child.

### *Procedures and Measures*

The study assessors were medical doctors, psychologists, and nurses trained, supervised, and certified in the use of all instruments for assessment of adults and children. The child assessors were blind to the illness status of the parents. The assessment was conducted in child-suitable facilities at hospital clinics in either Copenhagen or Aarhus or in the homes of the participants. We aimed to assess the children's sleep and activity pattern over a period of one week. For this, accelerometry data were collected using SENS motion. SENS motion is a wireless medical device, designed for collecting physical activity data from a large cohort. The SENS motion system consists of a small-sized waterproof sensor (weight 7 g, size 45 x 4.5 x 23 mm) with a tri-axial accelerometer, sampling acceleration at 12 Hz, with a range of  $\pm 4G$ , transferring data wirelessly via a smartphone application to the SENS motion secure cloud for storage and analysis. The sensor was embedded within a hypoallergenic band-aid and attached to the skin

**Table 1.** Background characteristics of the sample of 367 11-year old children at Familial High Risk for Schizophrenia (FHR-SZ) or Bipolar Disorder (FHR-BP) and controls, and of their primary caregiver

	Characteristics of 11-year-old children			Pairwise comparisons			
	FHR-SZ N = 133	FHR-BP N = 84	Controls N = 150	P-value	FHR-SZ versus controls P-value (effect size Cohen's <i>d</i> )	FHR-BP versus controls P-value (effect size Cohen's <i>d</i> )	FHR-SZ versus FHR-BP P-value (effect size Cohen's <i>d</i> )
Age of inclusion mean (SD)	11.9 (0.26)	11.9 (0.20)	11.9 (0.22)	.576 <sup>a</sup>	–	–	–
CGAS score <sup>d</sup> mean (SD)	65.0 (16.1)	69.7 (14.3)	74.7 (14.1)	<.001 <sup>a</sup>	<.001 <sup>b</sup> (0.6)	.042 <sup>b</sup> (0.4)	.072 <sup>b</sup> (0.3)
BMI mean (SD)	19.2	19.0	19.0	.739 <sup>a</sup>	–	–	–
Physical activity in leisure time = yes <sup>e</sup>	91 (68.4%)	54 (64.3%)	124 (82.3%)	.003 <sup>c</sup>	.006 <sup>c</sup>	.002 <sup>c</sup>	.268 <sup>c</sup>
VO <sub>2</sub> max <sup>f</sup> mean (SD)	50 39.82 (6.63)	35 39.44 (6.74)	41 41.47 (7.75)	.329	–	–	–
PSP score <sup>g</sup> primary caregiver <sup>h</sup> mean (SD)	71.0 (16.5)	72.8 (15.5)	83.0 (10.7)	<.001 <sup>a</sup>	<.001 <sup>b</sup> (0.9)	<.001 <sup>b</sup> (0.8)	1.000 <sup>b</sup> (0.1)
Employment primary caregiver = yes	101 (75.9%)	63 (75%)	144 (96.1%)	<.001 <sup>c</sup>	<.001 <sup>c</sup>	<.001 <sup>c</sup>	.964 <sup>c</sup>

P-value <.05. SD = standard deviation.

<sup>a</sup>One-way ANOVA.

<sup>b</sup>One-way ANOVA with post hoc Bonferroni multiple comparison.

<sup>c</sup>Chi-square test.

<sup>d</sup>CGAS: Children's Global Assessment Scale. CGAS is a single score on a scale from 1 to 100 that represent a child's present daily life functioning.

<sup>e</sup>Physical activity in leisure time=yes: The child attends at least one physical activity pr. week.

<sup>f</sup>VO<sub>2</sub> max: The maximum (max) rate (V) of oxygen (O<sub>2</sub>) the body is able to use during exercise. A sub sample of 110/126 children was assessed with VO<sub>2</sub> max.

<sup>g</sup>PSP: The Personal and Social Performance Scale. PSP is a single score on a scale from 1 to 100 that represent a person's present daily life functioning.

<sup>h</sup>Primary caregiver is defined as the parent or foster parent that knows the child best and spends most time with the child.

approximately 10 centimeters from the lateral epicondyle of the knee on the lateral aspect of the thigh. The raw data recorded by the sensor was transmitted when returned to a research assistant. A predefined algorithm integrating the orientation of the sensor and the recorded acceleration to identify the different categories of activity was used. Orientation was defined as the angle of the average acceleration signal over a 5-second interval. The SENS motion system was able to differentiate between amount of time with inactivity and activity. In this study the activities are reported in five categories: “high-intensity activity” (biking and running), “walking”, “low-intensity activity” (light activity such as sporadic walking), “inactivity” (resting), and “steps taken” (walking, running, light activity). It is important to note that the category of “steps taken” is measured with a higher degree of sensitivity by SENS motion and the amounts of steps taken is therefore not comparable to an average measurement of steps taken (e.g. smartphone measure). Sleep was categorized into “total amount of sleep” and “restless sleep”. A more detailed description of data interpretation can be found in appendix one. The child and the caregiver were provided with extra adhesives to keep the sensor on, instructed to—if possible—wear the sensor for seven days. Inclusion criterion was defined as at least 24 assessment hours of either one weekday or one weekend day. When stratifying weekdays and weekends 16 children were excluded from analysis of weekend activities as they did not live up to our inclusion criterion.

The Children’s Global Assessment Scale (CGAS)<sup>21</sup> was used to assess the child’s current level of functioning, and we used the standardized method of measuring the child’s height and weight three times using the median of each to calculate Body Mass Index (BMI). A standardized method was also used to assess the child’s VO<sub>2</sub> max. In collaboration with an external scientific unit from The Department of Nutrition, Sports and Exercise, University of Copenhagen, our portable INNOCOR system was validated against the Douglas bag system.<sup>22,23</sup> The primary caregiver of the child provided information about the child’s leisure time activities and when relevant we also requested information about why the child did not participate in any leisure time activities. Information on physical leisure activity was dichotomized into either “one or more” or “no activity”. The primary caregiver’s social and personal function was assessed by the Personal and Social Performance Scale (PSP)<sup>24</sup> and they were asked if they were employed.

## Statistical Analysis

Differences in continuous variables between the three groups were analyzed with one-way analysis of variance (ANOVA). When relevant, each One-way ANOVA test was followed by post hoc Bonferroni-adjusted tests. Sleep and activity data were then separated into weekdays and weekends and analyzed in the same manner. Differences

between the groups in leisure time and employment status were analyzed with chi-square tests. IBM SPSS Version 22.0 was used for statistical analysis and the level of statistical significance was  $P < .05$ .

## Results

### *Background Characteristics of the Participants*

A total of 367 children participated in the accelerometric study; 133 (36%) children with FHR-SZ, 84 (23%) with FHR-BP, and 150 (41%) controls.

Level of daily functioning based on CGAS scores were significantly lower in children with FHR-SZ (mean 65, SD 16.1) compared to controls (mean 74.7, SD 14.1,  $P < .001$ ) and significantly lower in children with FHR-BP (mean 69.7, SD 14.3) compared to controls ( $P = .042$ ). The groups did not differ in terms of age, BMI, or VO<sub>2</sub> max. Due to practical limitations only children assessed in the research center located in Copenhagen participated in the VO<sub>2</sub> max test, and thus 140 children were assessed. Fourteen children were excluded due to not completing the test, therefore VO<sub>2</sub> max was analyzed for 126 children (FHR-SZ = 50, FHR-BP = 35, and controls = 41) (table 1).

A significantly smaller proportion of children with FHR-SZ and with FHR-BP were reported to attend a physical activity in leisure time compared to controls (68.4%, 64.3%, and 82.3% respectively), and compared to controls a significantly smaller proportion of caregivers to children with FHR-SZ and with FHR-BP were employed (75.9%, 75%, and 96.1% respectively) (table 1). Child’s low level of daily functioning was reported as a reason for lack of participation in leisure activities by 9% of the primary caregivers to controls compared to 20% of primary caregivers to children with FHR-SZ and FHR-BP. The control group was more likely to participate in leisure time activities other than physical activity compared to the two high-risk groups. Ten percent of the controls were not participating in any leisure-time activity while 20% of the children at familial high risk for bipolar disorder and 26% of the children with a familial high risk of schizophrenia did not participate in any leisure-time activity. Current level of personal and social performance in both primary caregivers to FHR-SZ (mean 71, SD 16.5) and primary caregivers to FHR-BP (mean 72.8, SD 15.5) were significantly lower compared with caregivers to controls (mean 83, SD 10.7,  $P < .001$ ) (table 1).

### *Total Amount of Physical Activity*

The three groups did not differ significantly in average time of assessment (children with FHR-SZ were assessed 6.9 days, children with FHR-BP were assessed 7.0 days, and controls were assessed 6.8 days). Hours of high-intensity activity per day was significantly lower in children with FHR-SZ (mean 0.29, SD 0.19) compared to controls (mean 0.38, SD 0.22,  $P = .001$ ) and high-intensity activity was also significantly

**Table 2.** Physical activity and sleep in the sample of 367 11-year old children at Familial High Risk for Schizophrenia (FHR-SZ) or Bipolar Disorder (FHR-BP) and matched controls measured by SENS motion system

	Pairwise comparisons					
	FHR-SZ N = 133 mean (SD)	FHR-BP N = 84 mean (SD)	Controls N = 150 mean (SD)	FHR-SZ versus controls P-value (effect size Cohen's <i>d</i> )	FHR-BP versus controls P-value (effect size Cohen's <i>d</i> )	FHR-SZ versus FHR-BP P-value (effect size Cohen's <i>d</i> )
High-intensity activity <sup>e</sup> hours pr. day	0.29 (0.19)	0.27 (0.24)	0.38 (0.22)	.001 <sup>b</sup> (0.4)	.001 <sup>b</sup> (0.5)	1.000 <sup>b</sup> (0.09)
Walking hours pr. day	2.05 (0.62)	2.09 (0.70)	2.23 (0.60)	.047 <sup>a</sup>	.318 <sup>b</sup> (0.2)	1.000 <sup>b</sup> (0.06)
Low-intensity activity <sup>d</sup> hours pr. day	1.17 (0.37)	1.14 (0.34)	1.22 (0.35)	.184 <sup>a</sup>	–	–
Inactive <sup>e</sup> hours pr. day	10.14 (1.31)	10.30 (1.39)	10.05 (1.24)	.385 <sup>a</sup>	–	–
Steps taken <sup>f</sup> pr. day	14246 (4480)	14219 (4892)	15754 (4451)	.008 <sup>a</sup>	.042 <sup>b</sup> (0.3)	1.000 <sup>b</sup> (0.006)
Total sleep hours pr. night	9.36 (0.77)	9.23 (0.86)	9.22 (0.70)	.251 <sup>a</sup>	–	–
Restless sleep hours pr. night	1.16 (0.31)	1.12 (0.32)	1.10 (0.26)	.305 <sup>a</sup>	–	–

P-value <.05. SD = standard deviation.

<sup>a</sup>One-way ANOVA.

<sup>b</sup>One-way ANOVA with post hoc Bonferroni multiple comparison.

<sup>c</sup>High-intensity activity: Biking and running.

<sup>d</sup>Low intensity activity: Light activity as sporadic walking.

<sup>e</sup>Inactive: Sedentary behavior.

<sup>f</sup>Steps taken is measured with a higher degree of sensitivity by SENS motion and the amounts of steps taken are not comparable to an average measurement of steps taken.

lower in children with FHR-BP (mean 0.27, SD 0.24) compared to controls ( $P = .001$ ). In walking hours per day, the overall analyses showed significant differences between the groups ( $P = .047$ ), whereas significant differences were not found after the Bonferroni-adjusted analysis. Steps taken per day were significantly lower in both children with FHR-SZ (mean 14246, SD 4480) compared to controls (mean 15754, SD 4451,  $P = .018$ ) and in children with FHR-BP (mean 14219, SD 4892) compared to controls ( $P = .042$ ).

After adjusting for primary caregiver’s PSP score (Personal and Social Performance score) and employment status between-group differences in amount of high-intensity activity remained significant (FHR-SZ vs. controls:  $P = .005$  and FHR-BP vs. controls  $P = .011$ ) whereas steps taken did not. Significant differences also remained after adjusting for CGAS (score of child’s current level of daily function) (FHR-SZ vs. controls:  $P = .002$  and FHR-BP vs. controls:  $P = .019$ ). There were no significant differences between the groups in low-intensity activity nor in inactivity (table 2). In figure 1, the significant differences in high-intensity activities during one week is shown, depicting a difference of approximately 36 minutes per week between FHR-children and controls. The total amount of moderate and high-intensity activities come to approximately 16 minutes per day in favor of controls. This means that on a weekly basis, the control children have one hour and 52 minutes more physical activity than the two high-risk groups (16 min times 7 d = 112 min = 1 h and 52 min).

*Physical Activity on Weekdays and in Weekends*

When separating assessment time for weekdays and weekends, the total hours of high-intensity activity on

weekdays in children with FHR-SZ (mean 0.33, SD 0.22) and in children with FHR-BP (0.31, SD 0.26) were significantly lower compared to controls (mean 0.44, SD 0.27  $P = .001$ ). In walking hours per weekday, we did not find significant differences between the groups. Steps taken per weekday in children with FHR-SZ (mean 15566, SD 5101) was significantly lower compared to controls (mean 17136, SD 4697,  $P = .023$ ) and also significantly lower in children with FHR-BP (15498, SD 5058) compared to controls ( $P = .046$ ).

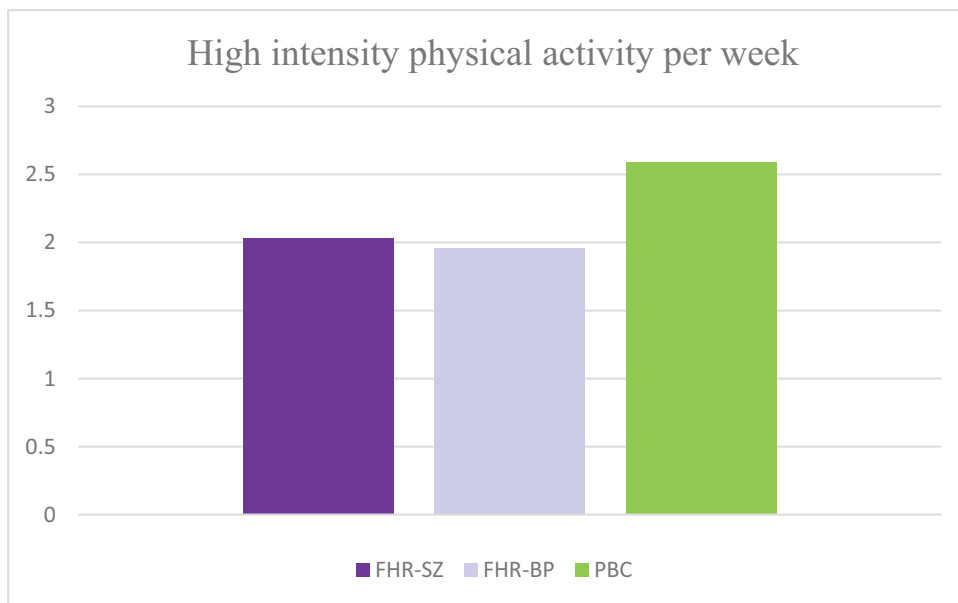
Sixteen children were excluded from weekend analysis, since they did not live up to our inclusion criterion. We did not find significant differences between the groups in amount of activity, as mean of FHR-SZ in high-intensity activity were 0.18, SD 0.19, of FHR-BP 0.17, SD 0.25, and of controls the mean was 0.23, SD 0.21 (overall  $P = .087$ ). In steps taken per day FHR-SZ had a mean of 10960, SD 5412, in FHR-BP 10767, SD 6161, and in controls 12262, SD 5615 (overall  $P = .082$ ). Comparative analyses of the two high-risk groups showed no significant differences (table 3).

*Total Amount of Sleep and Restless Sleep*

In the sleep categories we found no significant differences between the three groups (table 2). We found a small significant correlation ( $P = .024$ ) between the amount of sleep and the total amount of activity.

**Discussion**

In this nationwide cohort study, accelerometric assessment over a period of one week showed evidence of reduced physical activity in 11-year old children with



**Fig. 1.** High-intensity physical activity in the sample of 367 11-year old children at Familial High Risk for Schizophrenia (FHR-SZ) or Bipolar Disorder (FHR-BP) and matched Population-Based Controls (PBC). Hours of high-intensity physical activity per week: FHR-SZ = 2 h and 3 min. FHR-BP = 1 h and 58 min. PBC = 2 h and 35 min.

**Table 3.** Physical activity in the sample of 367 11-year old children at Familial High Risk for Schizophrenia (FHR-SZ) or Bipolar Disorder (FHR-BP) and matched controls separated upon *Weekdays* and *Weekends*

	Physical activity in 11-year in children on Weekdays			Pairwise comparisons		
	FHR-SZ N = 133 mean (SD)	FHR-BP N = 84 mean (SD)	Controls N = 150 mean (SD)	P-value	FHR-SZ versus controls P-value (effect size Cohen's <i>d</i> )	FHR-SZ versus FHR-BP P-value (effect size Cohen's <i>d</i> )
High-intensity activity <sup>c</sup> hours pr. day	0.33 (0.22)	0.31 (0.26)	0.44 (0.27)	<.001 <sup>a</sup>	.001 <sup>b</sup> (0.4)	1.000 <sup>b</sup> (0.08)
Walking hours pr. day	2.23 (0.71)	2.26 (0.72)	2.40 (0.63)	.072 <sup>a</sup>	–	–
Steps taken <sup>d</sup> pr. day	15566 (5101)	15498 (5058)	17136 (4697)	.010 <sup>a</sup>	.023 <sup>b</sup> (0.3)	.046 <sup>b</sup> (0.3)
						1.000 <sup>b</sup> (0.01)
Physical activity in 11-year old children in Weekends						
	FHR-SZ N = 127 mean (SD)	FHR-BP N = 82 mean (SD)	Controls N = 142 mean (SD)	P-value	FHR-SZ versus controls P-value	FHR-SZ versus FHR-BP P-value
High-intensity activity <sup>c</sup> hours pr. day	0.18(0.19)	0.17(0.25)	0.23(0.21)	0.087 <sup>a</sup>	–	–
Walking hours pr. day	1.62(0.77)	1.61(0.88)	1.79(0.79)	0.128 <sup>a</sup>	–	–
Steps taken <sup>d</sup> pr. day	10960(5412)	10767(6161)	12262(5615)	0.082 <sup>a</sup>	–	–

P-value <.05. SD = standard deviation.

<sup>a</sup>One-way ANOVA.

<sup>b</sup>One-way ANOVA with post hoc Bonferroni multiple comparison.

<sup>c</sup>High-intensity activity: Biking and running.

<sup>d</sup>Steps taken is measured with a higher degree of sensitivity by SENS motion and the amounts of steps taken are not comparable to an average measurement of steps taken.

familial high risk of schizophrenia or bipolar disorder when compared to controls. After adjusting for primary caregiver's personal and social performance score, employment status, and score of the child's current level of daily function between-group differences in amount of high-intensity activity remained significant, whereas amounts of steps taken did not. When stratifying the assessment time into weekdays and weekends, differences in physical activity during weekdays were significant, whereas weekend activity showed similar, although not significant, differences.

We interpret that some of the activity differences most likely derived from leisure time, as children in both high-risk groups were significantly less likely to participate in a physical activity during leisure time, and they were less likely to participate in any kind of leisure activity at all. Explorative analyses showed that twice as many of the primary caregivers to children with familial high risk compared to primary caregivers to controls reported, that the child's low level of daily functioning was the reason for lack of participation. Moreover, primary caregivers to children with familial high risk reported their own low level of functioning as a reason, as they considered logistics related to the child's participation in activities too demanding (e.g. accompanying the child), and as such too troublesome to initiate and support. Such difficulties were not reported by any caregivers in the control group. These findings correspond well with the fact that we found significantly lower levels of daily functioning (including unemployment) for both the primary caregivers and the children in the two high-risk groups when compared to the control group. Disadvantages of living in an environment with caregivers with schizophrenia or bipolar disorder are documented,<sup>25</sup> but our study is to our knowledge the first study of this sample size to investigate the amount of physical activity in children at familial high risk compared to controls, and lower amount of physical activity and not being supported in attending physical activities in leisure time, seems to reflect other unrecognized issues. Apart from the potentially unfortunate family constellation of both the child's and primary caregiver's lower level of daily functioning—which itself could make it difficult to handle leisure time activities—findings from The VIA 7 Study showed evidence of impaired motor functions in children with a familial high risk of schizophrenia.<sup>26</sup> Also, delayed motor milestones (unsupported sitting, standing, and walking) are significantly associated with familial high risk of schizophrenia,<sup>27</sup> and it is not unlikely that children with poorer motor functioning show more reluctance towards physical activities, which then again may hinder their motor development. School environment including relations to schoolmates might also contribute to affect the amount of physical activity in children with familial high risk in a negatively manner as children at familial high risk are more likely to report being bullied.<sup>28</sup> Potentially, that could lead to reduced

physical activity during schooltime, as those children might not be invited to participate in free time activities. Moreover, increased social and behavior problems in the children<sup>14-16</sup> could negatively impact both schooltime and leisure time participation. As such, a lower amount of physical activity in children at familial high risk could be an expression of genetic risk variants in combination with a non-supportive or exclusive environment. As the group differences were only marginally significant in weekend activities, we cannot conclude that the children at familial high risk were less physically active during weekends, but based on our knowledge of these children's significantly poorer home environment at age 7,<sup>25</sup> we suspect that it might be the case. Nor did we find differences in the objective measurement of BMI and VO<sub>2</sub> max. BMI in this cohort is within the normal range<sup>29</sup> and since it requires intensive exercise to increase VO<sub>2</sub> max, it is possible, that the magnitude of differences in the level of physical activity between the groups may not be enough to influence VO<sub>2</sub> max which may also be true for BMI. However, in one week's amount of physical activity the distance between controls and children at familial high risk is close to two hours in favor of the controls. Since routines of incorporating physical activities in daily adult life seems to be partly established already in childhood, children at familial high risk might not only be at increased risk of severe mental illness but also at risk of having a sustained low amount of physical activity in the future, and thus elevated risk of somatic illness. Another important aspect is potential psychosocial implications of reduced physical activity, as physical inactivity in children and adolescents is associated with social as well as attention problems and symptoms of depression.<sup>30</sup> Even if the impairments found in children of familial high risk are primarily related to genetic risk factors, it should be considered that in addition these children are at risk of having reduced amount of physical activity which might negatively interact with their genetic predisposition.

In this study, we investigated signs of risk and resilience in children at high risk of schizophrenia and bipolar disorder, and as previous studies have found aberrant sleep patterns prior to onset of those disorders<sup>17-19,31</sup> we expected that our three study groups would also differ in this area. Our hypothesis was not confirmed. However, the accelerometric method does not measure brain activity. By assessing physical activity in 11-year old children at familial high risk of schizophrenia and bipolar disorder this study reveals that further research is required, and further longitudinal studies could contribute with understanding of this area. Currently, attention should also be given to how to support the families to ensure their children's participation in leisure time activities. As such, another future research goal could be an intervention study designed to increase physical activity in children at familial high risk.

This nationwide study is to our knowledge the largest familial high-risk study of physical activity and sleep. An



important strength of the study is the use of the Danish National Register, which ensures high representativity and narrow age range. Furthermore, the large sample size of both participants with familial high risk of schizophrenia and bipolar disorder, the matching of controls, and the assessor's blinding to the groups, is a strength. SENS motion is designed to assess large sample sizes and data was generated over a period of seven days, which contributes to validity of the results reflecting the habits of the children. A limitation of the study is, that SENS motion is not designed to assess sleep and as such might not be sensitive to a degree large enough to differentiate between calm and restless sleep.

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### Declaration of interests

All authors declare no conflict of interest.

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