Chapter 4

Offspring of a parent with genetic disease: childhood experiences and adult psychological characteristics

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Abstract

Objective

To investigate childhood experiences and psychological characteristics in offspring of a parent with genetic disease.

Methods

Self-report scales were used to assess adverse childhood experiences (ACEs), adult attachment style, mental health, and psychological symptomatology in offspring of a parent with a neurogenetic disorder (i.e., Huntington's disease, HD; Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy, CADASIL; and Hereditary Cerebral Hemorrhage With Amyloidosis – Dutch type, HCHWA-D), and in offspring of a parent affected with Hereditary Breast and Ovarian Cancer; HBOC. These groups were compared to persons who did not have a parent with one of these genetic diseases. Associations between childhood experiences and adult psychological characteristics were investigated.

Results

Compared with the reference group (*n* = 127), offspring of a parent with a neurogenetic disorder (*n* = 96) reported more parental dysfunction in childhood, and showed more adult attachment anxiety and poorer mental health. Offspring of a parent with HBOC (*n* = 70) reported more parental loss in childhood and showed poorer mental health. Offspring who experienced parental genetic disease in childhood had more attachment anxiety than offspring who experienced parental disease later in life. In the group of offspring, a higher number of ACEs was associated with poorer mental health and more psychological symptomatology.

Conclusions

This cross-sectional study indicates that adult offspring of a parent with genetic disease may differ in attachment style and mental health from persons without one of these genetic diseases in their family, and that this may be related to adverse childhood experiences.

Introduction

Persons at risk for a late onset autosomal dominant genetic disorder, e.g., a neurogenetic disorder or a hereditary cancer syndrome, may have been exposed to the disease process of their affected parent during childhood. The impact on family life of serious neurogenetic disorders like Huntington's disease (HD), Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL), and Hereditary Cerebral Hemorrhage With Amyloidosis - Dutch type (HCHWA-D), and hereditary cancer syndromes like Hereditary Breast and Ovarian Cancer (HBOC) is substantial, with disturbing events and untimely deaths.[1-7]

Clinical characteristics of HD, CADASIL, HCHWA-D, and HBOC are presented in *Table 1*.

Table 1. Clinical characteristics of Huntington's disease, CADASIL, HCHWA-D, and Hereditary Breast and Ovarian Cancer

	Huntington's disease	CADASIL	HCHWA-D	Hereditary Breast and Ovarian Cancer [a]
Symptoms	progressive motor dysfunction, cognitive deterioration, psychiatric disturbances [8]	migraine with aura, multiple strokes, cognitive deterioration, psychiatric disturbances [9]	recurrent hemorrhagic strokes, cognitive deterioration, dementia [10]	breast cancer, ovarian cancer, other cancers
Timing of clinical onset [b]	Mid adulthood	Mid adulthood	Mid adulthood	Early/mid adulthood; later life
Age of death (years), mean	54-55 [11]	65 [12]	60 [10]	Variable
Treatment can alter onset or progression [b]	No	No	No	Yes
Likelihood of development in gene mutation carriers [b]	100%	100%	100%	Variable [c]

CADASIL = Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy; HCHWA-D = Hereditary Cerebral Hemorrhage with Amyloidosis - Dutch type. [a] Due to a *BRCA1* or *BRCA2* gene mutation.
[b] Variables based on Family Systems Genetic Illness Model.[13]
[c] Breast cancer: 48%–58% (females < 60), < 1–7% (males); ovarian cancer: 6%-40% [14]; prostate cancer: 2–7 times higher than general population [15]

Growing up with a parent affected with one of these diseases may negatively affect offspring's development and well-being in later life.[3,5,16] Both the affected parent and the spouse may be less available for offspring and may not be fully able to fulfill parental roles.[3,16] There is an

increased risk for children of having to fulfill parental tasks or becoming a substitute partner in an attempt to fill a vacuum of care within the family.[17] The parent's disease process and associated changes in family life may increase the risk for offspring to experience adverse childhood experiences (ACEs).[18]

The unfavorable changes in family life may affect the formation of attachment styles in offspring.[19] An attachment style is a relatively stable set of mental representations of self and others in close relationships, organizing thoughts, feelings, and behavior.[20,21] Attachment theory assumes that individual differences in adult attachment styles exist, arising from different interaction patterns with parents or other attachment figures during childhood.[22-25] Responsive, sensitive, and consistent behavior of a parent helps the child to develop a *secure* attachment style, characterized by confidence in the availability of others in times of need and by comfort with closeness and interdependence.[21] When a child experiences a parent as unavailable, undependable, rejecting or inconsistently responsive, there is an increased risk of developing low confidence in self and/or others, reflecting an insecure attachment style.[23,26] Various associations have been described between insecure attachment styles in adults and childhood adversity, e.g., sexual abuse, maltreatment, interpersonal trauma, parental divorce, or psychiatric disorders of a parent.[23,26-29] Having an insecure attachment style is a risk factor for poor mental health.[20]

In families with a neurogenetic disorder, where parental dysfunction due to psychiatric problems is relatively common,[18] offspring may have an increased risk of developing *attachment anxiety*, i.e., a tendency to worry about availability and responsiveness of significant others, a fear of interpersonal rejection or abandonment, and an excessive need for approval from others.[30] In families with HBOC, where the odds of losing a parent in childhood was previously found to be 2.5 times higher than in a group of controls,[18] offspring may have an increased risk of developing *attachment avoidance*, i.e., a tendency to feel uncomfortable with interpersonal intimacy and dependency, an excessive need for self-reliance, and reluctance to self-disclose.[30]

The aim of this study is to investigate childhood experiences and adult psychological characteristics in offspring of a parent affected with HD, CADASIL, HCHWA-D, or HBOC. First, childhood experiences and adult psychological characteristics of these groups are described, and compared to a reference group of persons who did not have a parent affected with any of these genetic diseases. It is expected that, compared with the reference group, adult offspring of a parent affected with a neurogenetic disorder ('neurogenetic/offspring') report more parental dysfunction, more attachment anxiety, poorer mental health, and more psychological symptomatology, and that adult offspring of a parent affected with HBOC ('HBOC/offspring') report more parental loss, more attachment avoidance, poorer mental health, and more psychological symptomatology. Second, within the group of offspring of a parent affected with

one of the genetic disorders ('genetic/offspring'), associations between childhood experiences and adult psychological characteristics are investigated. It is expected that exposure to parental genetic disease in childhood (as opposed to later in life) and adversity in childhood (ACEs, parental dysfunction, parental loss) are associated with adult attachment anxiety and/or attachment avoidance, poorer mental health, and more psychological symptomatology.

Methods

Participants

Adults (≥ 18 years) having a parent affected with HD, CADASIL, HCHWA-D, or HBOC were asked to participate in the study when they entered a predictive genetic testing program, in the Leiden University Medical Center in Leiden, The Netherlands (January 2008 – June 2011) or in the Erasmus Medical Center in Rotterdam, The Netherlands (January 2009 – December 2009). A neurological exam was part of the predictive testing protocol for HD, CADASIL, and HCHWA-D; only persons found to be non-symptomatic in this exam were asked to participate. For HBOC, only persons without cancer were asked to participate. These persons' partners, who were not known to have a family history with any of these genetic disorders, were asked to participate as a reference group ('partners').

Procedure

After their first visit for predictive testing, genetic/offspring and partners received oral and written information on the study, and, after informed consent, were given self-report scales. A written reminder was send to non-responders after two weeks; they were reminded by telephone after four weeks. The study was reviewed and approved by the Medical Ethics Committees of both participating hospitals.

Measurement

All instruments were self-report scales. Newly created survey items were used to assess sociodemographic data and, for genetic/offspring, biographic data related to the parent's disease (paternal or maternal transmission of risk, parent's age at participant's birth, participant's age at parent's disease onset and at parent's death). Parent's disease onset was defined as the time at which the parent first manifested signs of the genetic disease, as recalled by offspring.

Adverse childhood experiences (ACEs) were assessed using the Negative Life Events Scale (NLES, 19 items, yes/no-format).[18,31] The NLES measures negative life events concerning self or significant others, such as physical or psychiatric problems in a parent, death of a parent, parental divorce, and abuse experiences, in childhood (defined in the NLES as 'before age 16') and in later life. In this study, only childhood experiences were used. Two thematic clusters of events were composed and analyzed in this study: 'parental dysfunction before age 16' (having experienced, before age 16, psychiatric problems of a parent, domestic violence, alcohol or drug abuse, and/or suicide attempt of a parent), and 'parental loss before age 16' (having experienced, before age 16, death of a parent, and/or divorce of parents). For the purpose of this study, 'exposure to parental genetic disease before age 16' was defined as having experienced physical or psychiatric problems in a parent before age 16, as assessed by the NLES and the survey items related to the parent's disease.

Attachment style was assessed using the Experiences in Close Relationships-Revised (ECR-R; 36 items, 7-point Likert-scale, range 1–7).[32] The ECR-R measures two dimensions of adult attachment, i.e., attachment anxiety (tendency to worry about availability and responsiveness of significant others, 18 items) and attachment avoidance (tendency to feel uncomfortable with interpersonal intimacy and dependency, 18 items). Higher attachment anxiety and/or attachment avoidance scores indicate a more insecure attachment style. Test-retest reliability of the ECR-R over 6 weeks is 86%;[33] α-coefficients in the present study were .91 for attachment anxiety and .91 for attachment avoidance.

Mental health was assessed using the Mental Health Inventory-5 (MHI-5; 5 items, 6-point Likert-scale, range 0–100).[34] A higher total score reflects better mental health. The MHI-5 is a well validated and reliable measure of mental health status;[34] the α-coefficient in the present study was .85. Psychological symptomatology was assessed using the Brief Symptom Inventory (BSI; 53 items, 5-point Likert-scale).[35,36] The BSI measures nine primary symptom dimensions (somatization, obsessive-compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism). The mean of all items results in the General Severity Index (GSI, range 0–4), indicating current level of symptomatology. Validity of the BSI is good; test-retest reliability of the GSI over 2-3 weeks is 90%;[35] the α-coefficient in the present study was .96.

Statistical analysis

Data were analyzed with IBM SPSS Statistics 20 software. Groups were compared using *t*-tests and logistic regression for the occurrence of childhood experiences, and *t*-tests for psychological characteristics. Relationships between childhood experiences and adult psychological characteristics were explored using *t*-tests, Pearson correlations, and crosstabs.

Because this study is exploratory in nature, and some of the groups (especially CADASIL/offspring and HCHWA-D/offspring) were expected to remain small due to the rarity of these diseases, an a priori power calculation was not made. However, an example shows that in a comparison of attachment anxiety of neurogenetic/offspring and partners, using a standard deviation of 1.33,[37] with a power of 80% and an alpha-level of 5%, a sample size of 222 (i.e., 2 x 111) persons is sufficient to identify a 0.5 difference.

Results

Characteristics of participants

A total of 293 persons were included in the study: 74 persons having a parent affected with HD ('HD/offspring'; 111 approached, response rate 67%), 13 persons having a parent affected with CADASIL ('CADASIL/offspring'; 16 approached, response rate 81%), 9 persons having a parent affected with HCHWA-D ('HCHWA-D/offspring'; 14 approached, response rate 64%), 70 persons having a parent affected with HBOC ('HBOC/offspring'; 108 approached, response rate 65%), and 127 partners (214 approached, response rate 59%).

In the telephone call that served as a reminder, non-responders mentioned lack of time, or finding the questions too emotion-laden as reasons for not wanting to participate.

Mean age of non-participants was 37.9 years, and 52% were male. Non-participants did not differ significantly from participants in age or sex.

The proportion of participating partners did not differ significantly among the groups of offspring. As no significant differences were found among partners of the various disease groups in any of the outcome variables, all partners were used as a single reference group. Sociodemographic and biographical data of participants are presented in *Table 2*.

There were significant differences among groups in gender and age. The groups of offspring did not differ from each other in parent's age at birth of participant, or in participant's age at parental disease onset or parent's death. Not all offspring were able to indicate the time of onset of parental disease.

Childhood experiences and adult psychological characteristics of offspring and partners

Comparisons of childhood experiences among groups were adjusted for age, because persons who reported parental dysfunction or exposure to parental genetic disease before age 16

Table 2. Sociodemographic and biographic data of participants (*n* = 293)

Sociodemographic or biographic variable	Partners (*n* = 127)	HD/offspring (*n* = 74)	CADASIL/offspring (*n* = 13)	HCHWA-D/offspring (*n* = 9)	HBOC/offspring (*n* = 70)	*p*-value among groups
Male, *n* (%) [a]	82 (64.6)	36 (48.6)	9 (69.2)	4 (44.4)	10 (14.3)	< 0.001
Age *(years)*, mean; range (SD) [b]	39.8; 18-70 (13.1)	34.1; 18-63 (10.1)	35.7; 20-56 (11.6)	37.4; 27-55 (9.2)	40.9; 19-79 (15.0)	0.01
Married/Common law, *n* (%) [a]	119 (93.7)	58 (78.4)	10 (76.9)	6 (66.7)	55 (78.6)	0.88 [c]
Education ≥ 11 years, *n* (%) [a]	63 (49.6)	34 (45.9)	7 (53.8)	3 (33.3)	28 (40.0)	0.63
Paternal transmission of risk, *n* (%) [a]		36 (48.6)	6 (46.2)	5 (55.6)	28 (40.0) [d]	0.69
Parent's [e] age *(years)* at offspring's birth, mean; range (SD) [b]		29.5; 20-40 (5.0)	29.6; 25-37 (3.8)	30.4; 24-36 (4.3)	29.4; 19-44 (5.8)	0.97
Participant's age *(years)* at parental disease onset [f], mean; range (SD) [b]		20.4; 0-49 (12.2) [g]	18.0; 10-23 (4.4) [h]	20.8; 5-30 (7.6) [i]	22.5; 4-41 (9.7) [j]	0.72
Participant's age *(years)* at parent's [e] death, mean; range (SD) [b]		29.3; 12-48 (10.7) [k]	25.3; 7-49 (12.9) [l]	26.5; 18-38 (7.4) [m]	31.8; 0-57 (14.8) [n]	0.56

HD = Huntington's disease; CADASIL = Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy; HCHWA-D = Hereditary Cerebral Hemorrhage with Amyloidosis - Dutch type; HBOC = Hereditary Breast and Ovarian Cancer.[a] Pearson's Chi-square.

[b] One-way analysis of variance (ANOVA).

[c] Based on groups of genetic/offspring only.

[d] Line of risk transmission unknown in three cases; both paternal and maternal risk transmission in one case.

[e] Risk-transmitting parent.

[f] First symptoms, clinical or genetic diagnosis, as recalled by participant.

[g] Based on *n* = 53.; [h] Based on *n* = 7.; [i] Based on *n* = 9.; [j] Based on *n* = 34.; [k] Based on *n* = 23.; [l] Based on *n* = 7.; [m] Based on *n* = 6.; [n] Based on *n* = 32.

were significantly younger than persons who did not report these childhood experiences. Age was not associated with any of the adult psychological characteristics. No differences in any of the outcome measures were found between males and females, or between offspring of an affected mother and offspring of an affected father. Exposure to parental genetic disease before age 16 was more common among HD/offspring (51%) than among CADASIL/offspring (39%), HCHWA-D/offspring (33%), or HBOC/offspring (36%). Of the partners, 13% reported having experienced chronic or serious disease of a parent before age 16.

Neurogenetic/offspring

Parental dysfunction before age 16 was reported significantly more often by neurogenetic/offspring than by partners *(Table 3)*.

Analysis of the neurogenetic groups separately showed that the higher rate of parental dysfunction was largely due to HD/offspring. Compared to partners, significantly more neurogenetic/offspring had experienced psychiatric problems of a parent before age 16, which was largely due to the group of HD/offspring. The prevalence of parental loss before age 16 in neurogenetic/offspring did not differ from partners. CADASIL/offspring, however, reported parental loss significantly more often than partners. Parental loss was also relatively common in HD/offspring. Neurogenetic/offspring reported a significantly higher number of ACEs before age 16 than partners.

The level of attachment anxiety was significantly higher in neurogenetic/offspring than in partners *(Table 4).*

Attachment anxiety was significantly higher in HD/offspring than in partners. CADASIL/offspring and HCHWA-D/offspring did not differ significantly from partners in level of attachment anxiety. Neurogenetic/offspring did not differ from partners in level of attachment avoidance. Mental health was significantly poorer in neurogenetic/offspring than in partners. Neurogenetic/offspring did not differ from partners in level of psychological symptomatology. However, BSI subscales (*data not shown*) indicated that neurogenetic/offspring had more symptoms of somatization, $t(217) = 2.65$, $p = .009$; depression $t(217) = 2.35$, $p = .02$; and anxiety, $t(217) = 2.22$, $p = .03$, than partners.

HBOC/offspring

Parental loss before age 16 was reported significantly more often by HBOC/offspring than by partners *(Table 3).* The prevalence of parental dysfunction before age 16 or the number of ACEs in HBOC/offspring did not differ from partners. HBOC/offspring did not differ from partners in level of attachment avoidance or attachment anxiety *(Table 4).* Mental health was significantly poorer in HBOC/offspring than in partners. The level of psychological symptomatology was

Table 3. Childhood experiences; genetic/offspring compared with partners

	Partners	**Genetic/offspring**									
		Neurogenetic		**HD**		**CADASIL**		**HCHWA-D**		**HBOC**	
	***n* = 127**	***n* = 96**		***n* = 74**		***n* = 13**		***n* = 9**		***n* = 70**	
Exposure to event < age 16	*n (%)*	*n (%)*	*OR [95% CI]* [a]	*n (%)*	*OR [95% CI]* [a]	*n (%)*	*OR [95% CI]* [a]	*n (%)*	*OR [95% CI]* [a]	*n (%)*	*OR [95% CI]* [a]
Parental genetic disease		46 (47.9)		38 (51.4)		5 (38.5)		3 (33.3)		25 (35.7)	
Parental psych. problems [b]	5 (3.9)	20 (20.8)	**5.47** [1.95-15.37]	18 (24.3)	**6.62** [2.31-18.98]	1 (7.7)	1.86 [0.20-17.50]	1 (11.1)	2.96 [0.30-28.79]	1 (1.4)	0.36 [0.04-3.13]
Parental dysfunction [c]	17 (13.4)	28 (29.2)	**2.24** [1.12-4.48]	25 (33.8)	**2.76** [1.34-5.67]	1 (7.7)	0.43 [0.05-3.65]	2 (22.2)	1.86 [0.34-10.23]	3 (4.3)	0.29 [0.08-1.02]
Parental loss [d]	17 (13.4)	23 (24.0)	1.99 [0.98-4.04]	17 (23.0)	1.80 [0.84-3.86]	5 (38.5)	**4.09** [1.18-14.11]	1 (11.1)	0.80 [0.09-6.83]	20 (28.6)	**2.60** [1.26-5.39]
Exposure to ACEs < age 16	*Mean (SD)*	*Mean (SD)*	*t* [e]	*Mean (SD)*	*t* [e]	*Mean (SD)*	*t* [e]	*Mean (SD)*	*t* [e]	*Mean (SD)*	*t* [e]
Number of ACEs	0.69 (1.30)	1.28 (1.60)	2.98**	1.39 (1.68)	3.12**	0.77 (0.93)	0.23	1.11 (1.70)	0.93	0.87 (1.23)	0.98

HD = Huntington's disease; CADASIL = Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy; HCHWA-D = Hereditary Cerebral Hemorrhage with Amyloidosis – Dutch type; HBOC = Hereditary Breast and Ovarian Cancer

[a] Odds ratios, adjusted for age; 95% Confidence Intervals; genetic/offspring compared with partners.

[b] Psychiatric problems of parent.

[c] Psychiatric problems of parent, domestic violence, alcohol or drug abuse, suicide attempt of parent.

[d] Death of parent, divorce of parents.

[e] t-test; genetic/offspring compared with partners.

** $p < .01$ (2-tailed).

Table 4. Adult psychological characteristics; genetic/offspring compared to partners

	Partners	Genetic/offspring									
		Neurogenetic		HD		CADASIL		HCHWA-D		HBOC	
	n = 127	*n* = 96		*n* = 74		*n* = 13		*n* = 9		*n* = 70	
Psychological characteristic	*Mean (SD)*	*Mean (SD)*	*t* [a]	*Mean (SD)*	*t* [a]	*Mean (SD)*	*t* [a]	*Mean (SD)*	*t* [a]	*Mean (SD)*	*t* [a]
Attachment anxiety (ECR-R)	2.11 (0.75)	2.52 (1.17)	3.00**	2.53 (1.17)	2.78**	2.53 (1.11)	1.82	2.39 (1.31)	0.65	2.12 (0.96)	0.06
Attachment avoidance (ECR-R)	2.22 (0.76)	2.29 (0.92)	0.66	2.35 (0.93)	1.08	2.23 (0.92)	0.06	1.92 (0.82)	-1.15	2.41 (0.94)	1.56
Mental health (MHI-5)	74.58 (13.81)	68.22 (18.77)	-2.76**	68.85 (17.29)	-2.40*	70.46 (16.46)	-1.01	59.00 (31.91)	-1.37	69.33 (13.59)	-2.56*
Psychological symptomatology (BSI) [b]	0.32 (0.36)	0.41 (0.39)	1.73	0.39 (0.35)	1.42	0.29 (0.18)	-0.27	0.67 (0.69)	1.52	0.34 (0.34)	0.43

HD = Huntington's disease; CADASIL = Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy; HCHWA-D = Hereditary Cerebral Hemorrhage with Amyloidosis - Dutch type; HBOC = Hereditary Breast and Ovarian Cancer.

[a] *t*-test; genetic/offspring compared with partners.

[b] General Severity Index, indicating current level of symptomatology.

* $p < .05$ (2-tailed).

** $p < .01$ (2-tailed).

Table 5. Comparison of psychological characteristics of genetic/offspring with or without specific childhood experiences

	Parental genetic disease < age 16			**Psychiatric problems of parent < age 16**			**Parental dysfunction [a] < age 16**			**Parental loss [b] < age 16**		
	no	**yes**		**no**	**yes**		**no**	**yes**		**no**	**yes**	
	***n* = 95**	***n* = 71**		***n* = 145**	***n* = 21**		***n* = 135**	***n* = 31**		***n* = 123**	***n* = 43**	
Psychological characteristic	*Mean (SD)*	*Mean (SD)*	*t* [c]	*Mean (SD)*	*Mean (SD)*	*t* [c]	*Mean (SD)*	*Mean (SD)*	*t* [c]	*Mean (SD)*	*Mean (SD)*	*t* [c]
Attachment anxiety (ECR-R)	2.20 (1.03)	2.55 (1.16)	2.02*	2.29 (1.06)	2.75 (1.29)	1.80	2.29 (1.07)	2.62 (1.18)	1.50	2.31 (1.12)	2.46 (1.03)	0.75
Attachment avoidance (ECR-R)	2.27 (0.85)	2.43 (1.02)	1.10	2.37 (0.93)	2.13 (0.89)	-1.10	2.39 (0.95)	2.14 (0.81)	-1.33	2.28 (0.90)	2.53 (0.98)	1.52
Mental health (MHI-5)	70.06 (17.40)	66.82 (15.76)	-1.22	68.85 (16.50)	67.60 (18.58)	-0.31	69.47 (16.22)	65.33 (18.65)	-1.22	68.91 (17.11)	68.10 (15.72)	-0.27
Psychological symptomatology (BSI)[d]	0.37 (0.38)	0.39 (0.34)	0.38	0.37 (0.36)	0.44 (0.39)	0.78	0.35 (0.34)	0.50 (0.44)	1.71	0.37 (0.37)	0.40 (0.36)	0.46

[a] Psychiatric problems of parent, domestic violence, alcohol or drug abuse, suicide attempt of parent.

[b] Death of parent, divorce of parents.

[c] *t*-test; genetic/offspring with specified childhood experience compared with genetic/offspring without this childhood experience.

[d] General Severity Index, indicating current level of symptomatology.

* $p < .05$ (2-tailed).

not significantly higher in HBOC/offspring than in partners, but BSI subscales (*data not shown*) indicated that HBOC/offspring had more symptoms of somatization, $t(194) = 3.24$, $p = .002$.

Genetic/offspring: Associations between childhood experiences and adult psychological characteristics

Genetic/offspring who had been exposed to parental genetic disease before age 16 showed significantly more attachment anxiety than genetic/offspring exposed to their parent's disease later in life *(Table 5).* These groups did not differ in attachment avoidance, mental health, or psychological symptomatology.

Further analysis showed that genetic/offspring exposed to parental genetic disease before age 16 had experienced a higher number of ACEs before age 16 ($M = 1.97$, $SD = 1.72$) than genetic/offspring exposed later in life ($M = 0.46$, $SD = .77$), $t(164) = 6.91$, $p < .001$. They also more often reported parental dysfunction, $\chi^2(1, N = 166) = 18.70$, $p < .001$ or parental loss, $\chi^2(1, N = 166) = 7.42$, $p = .006$ in their childhood than persons exposed to their parent's disease later in life.

Psychological characteristics of genetic/offspring who had experienced psychiatric problems of a parent, parental dysfunction, or parental loss before age 16 did not differ from genetic/offspring without these experiences before age 16.

There was an almost significant positive association ($p = .06$) between the number of ACEs before age 16 and attachment anxiety *(Table 6).* No association was found between the number of ACEs experienced before age 16 and attachment avoidance. A higher number of ACEs before age 16 was associated with poorer mental health and a higher level of psychological symptomatology, specifically (*data not shown)* more symptoms of somatization, $r(163) = .17$, $p = .03$; obsessive-compulsive, $r(163) = .19$, $p = .01$; depression, $r(163) = .19$, $p = .02$; hostility, $r(163) = .38$, $p < .001$; and paranoid ideation, $r(163) = .16$, $p = .05$. Both attachment anxiety and attachment avoidance were significantly associated with poorer mental health, and with a higher level of psychological symptomatology.

Table 6. Pearson correlations of number of ACEs and psychological characteristics in genetic/offspring

ACEs; Psychological characteristic	Number of ACEs < age 16	Attachment anxiety (ECR-R)	Attachment avoidance (ECR-R)	Mental health (MHI-5)	Psychological symptomatology (BSI) [a]
Number of ACEs < age 16	1				
Attachment anxiety (ECR-R)	.15	1			
Attachment avoidance (ECR-R)	.03	.62**	1		
Mental health (MHI-5)	-.18*	-.41**	-.29**	1	
Psychological symptomatology (BSI) [a]	.22**	.42**	.26**	-.73**	1

[a] General Severity Index, indicating current level of symptomatology.
* $p < .05$ (2-tailed).
** $p < .01$ (2-tailed).

Discussion

This study is a first attempt to systematically describe clinical observations on childhood experiences and adult psychological characteristics in offspring of a parent affected with HD, CADASIL, HCHWA-D, or HBOC. The use of attachment theory to assess psychological characteristics of genetic/offspring is a novel contribution of this study.

In line with expectations, neurogenetic/offspring reported more parental dysfunction in childhood and showed more attachment anxiety and poorer mental health than partners. From this cross-sectional study, no conclusions can be drawn on causal relationships between childhood experiences and psychological characteristics in adulthood. Childhood adversity is known to increase the likelihood of a person developing attachment anxiety or avoidance, but does not necessarily lead to an insecure attachment style. Moreover, self-reported childhood experiences do not necessarily reflect actual experiences. However, this study's findings that neurogenetic/offspring who experienced their parent's disease in childhood show more attachment anxiety and report having experienced relatively many ACEs, including parental dysfunction, yields some support for the theoretical associations.[23,26-29] Parental dysfunction as a result of mental illness is known to increase the likelihood for children of having to fulfill parental tasks or becoming a substitute partner, which is associated with the development of an insecure attachment style.[17,19] Attachment anxiety is thought to develop in childhood when a parent shows inconsistent parenting behavior or a lack of sensitivity to a child's needs.

Longitudinal data and a more in-depth exploration of family dynamics, parent-child interactions, and parenting styles are needed to enhance understanding of relationships between early experiences and adult attachment styles in offspring of a parent affected with a neurogenetic disorder.

The finding that mental health in neurogenetic/offspring was relatively poor is in line with attachment theory, stating that having an insecure attachment style is a risk factor for poor mental health.[20] However, although neurogenetic/offspring were found to be neurologically non-symptomatic, it is possible that prodromal psychiatric symptoms partly explain this finding. Depression and/or other psychiatric disorders may be present in carriers of an HD gene mutation many years before neurological diagnosis of HD.[38] This may also be true in CADASIL and HCHWA-D gene mutation carriers, as clinical observations suggest.

HD, CADASIL, and HCHWA-D have shared features (clinical onset in mid adulthood, full penetrance, no treatment that can alter onset or progression; *Table 1)*. Therefore, the emotional and psychological impact of these neurogenetic disorders on patients and their families is assumed to be similar.[13] The present study indicates that having a parent affected with HD is associated with experiencing psychiatric problems of a parent before age 16, whereas having a parent affected with CADASIL or HCHWA-D is not.

Future research should further explore possible differences among HD, CADASIL, and HCHWA-D, and investigate if these differences are associated with a different impact on family life.

As expected, HBOC/offspring reported more parental loss in childhood and showed poorer mental health than partners. Parental loss is known to increase the likelihood for children of having to fulfill parental tasks or becoming a substitute partner,[17] and is theoretically associated with higher levels of attachment avoidance.[23,26,27] However, and in contrast to expectations, no significant differences in attachment avoidance between HBOC/offspring and partners were found. Likewise, there was no association between parental loss and adult attachment avoidance. More information from studies with larger sample sizes is needed to explore relationships between parental loss and attachment avoidance in HBOC/offspring.

The impact of HBOC on patients and their families is supposed to be different from that of the neurogenetic disorders in this study.[13] Likelihood of development of HBOC in *BRCA1* or *BRCA2* mutation carriers is variable, and there are possibilities for prevention or cure of hereditary cancer, whereas the neurogenetic disorders are fully penetrant and incurable *(Table 1).* This study shows an additional difference: neurogenetic disorders of a parent, in particular HD, may expose offspring to parental dysfunction and psychiatric problems of a parent, whereas HBOC does not.

The findings in this study provide some indications that attachment anxiety is a mediator in the relation between parental genetic disease in childhood and poorer mental health in adulthood. Having experienced parental genetic disease in childhood was associated with adult attachment anxiety, and adult attachment anxiety was associated with poorer mental health in adulthood. Attachment insecurity (e.g., having a high level of attachment anxiety) is associated with an increased susceptibility to stress, with inadequate methods of regulating affect, and with less effective social support seeking,[39,40] thus creating vulnerability for psychological symptomatology.

Serious genetic disease in a mother may have a different impact on the development of offspring, compared to when a father is affected. Fathers and mothers are thought to differ in parental care, due to biological, social, cultural, and historical factors.[41] In this study, no differences in childhood experiences or adult psychological characteristics were found between offspring of an affected mother and offspring of an affected father, but further study is needed to understand in what ways a father's or mother's genetic disease influences family dynamics and child development.

Several limitations of this study should be mentioned, in addition to the ones already discussed. An important limitation is the lack of a control group representing the general population. The results based on comparisons with partners should be interpreted with caution, due to the fact that the psychological characteristics of partners may be affected by their spouses' risk of genetic disease and by their experiences with affected in-laws. The partners in this study may differ from the general population in the percentage that reported chronic or serious disease of a parent before age 16. Moreover, information on how non-participants differ from participants is lacking, making it impossible to generalize this study's findings to the entire population of genetic/offspring. Another limitation is that the sample size of CADASIL/offspring and HCHWA-D/offspring was small, probably leading to insufficient power to find significant differences among groups. CADASIL and HCHWA-D are rare disorders; therefore few eligible persons could be included in this study. However, since little information on the psychosocial aspects of these disorders and their impact on family dynamics and offspring is available, it was considered important to include them in the study. Results are descriptive and should be interpreted with caution.

Furthermore, the HBOC/offspring group differed in gender from the other groups. Logically, females are overrepresented in HBOC/offspring, as it is more medically relevant for females to undergo testing than for males, who have lower risks of cancer when they are carriers of a *BRCA1* or *BRCA2* mutation. This study's results on mental health in HBOC/offspring may reflect a higher impact of HBOC on females than on males; therefore, results may not be generalized to the male population.

Offspring's recollection of parental disease onset may have been biased, since offspring may not know or recall when the parent became symptomatic, especially when they were very young at the time. Moreover, accurate timing of onset of HD or CADASIL may be difficult, because these diseases have an initial phase in which it is uncertain whether or not the disease process has started. Offspring may have indicated as onset the time when the parent started showing symptoms, the time when the parent received a genetic test result (even before symptoms occurred), or the time of the parent's formal neurological diagnosis. Family dynamics may have been affected even before onset of the disease, when parents may have been worried about future disease based on their genetic risk or an unfavorable predictive test result.

A final limitation is that childhood experiences were assessed in the somewhat arbitrary period of 0-16 years of age, without information on when exactly they took place. Assuming that adverse experiences in early childhood have a greater impact than those later in childhood, it would be useful for future studies to assess timing of ACEs and parental disease onset in more detail, to understand their role in development and in the formation of attachment styles.

The results of this study are relevant for clinicians working with offspring of a parent with HD, CADASIL, HCHWA-D, or HBOC. Not only do these populations face the risk of developing the disease they witnessed in their parent, but they may also be relatively likely to have psychological features associated with poor mental health, such as an insecure attachment style. Adopting a life cycle approach may be useful for clinicians who seek to understand how offspring's childhood experiences may be related to their present psychological characteristics and to their perspective on life.

Conclusions

This cross-sectional study indicates that adult offspring of a parent affected with genetic disease (i.e., HD, CADASIL, HCHWA-D, or HBOC) may differ in attachment style and other psychological characteristics from persons without one of these genetic diseases in their family. This may be related to adverse childhood experiences, such as having experienced dysfunction or psychiatric problems of a parent. Longitudinal research is needed to further explore relationships between parental genetic disease and adult psychological characteristics of offspring.

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