People who need people : an attachment perspective on hereditary disease

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Chapter 1

Introduction

PEOPLE WHO NEED PEOPLE: AN ATTACHMENT PERSPECTIVE ON HEREDITARY DISEASE

Hereditary disorders with onset in adulthood and severe symptomatology may have a life-long impact on offspring of affected parents. When a parent suffers from an incurable disease with progressive physical, cognitive, and psychiatric disturbances, or when a parent is diagnosed with and undergoes treatment for a possibly life threatening disorder, interactions between parents and children may be negatively influenced, and the risk for children of experiencing negative events may be increased. This may interfere with a child's healthy psychological development and may leave traces in adult psychological characteristics.

In this thesis, a perspective of attachment theory is used to investigate hereditary disease with adult onset, in a context of predictive genetic testing. Attachment theory, originally formulated by John Bowlby[1] and Mary Ainsworth,[2] describes how parent-child interactions and childhood experiences influence the development of an individual's personal style of interacting with others and of dealing with emotions in stressful situations. Predictive genetic testing for a hereditary disorder with adult onset is generally experienced as a stressful procedure, in which a person's style of relating to other people may influence how successful they are in regulating unpleasant emotions.

With its focus on the life-long effects of parent-child interactions and childhood experiences, attachment theory offers promising leads for studying psychological aspects of hereditary disorders.

The hereditary disorders studied in this thesis are Huntington's disease (HD), Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL), Hereditary Cerebral Hemorrhage With Amyloidosis – Dutch type (HCHWA-D), and *BRCA1* or *BRCA2* Hereditary Breast and Ovarian Cancer (HBOC) *(Table 1)*.

The disorders studied in this thesis have an autosomal dominant pattern of inheritance, implying that offspring of a person with the disorder have a 50% risk of inheriting the gene mutation. HD, CADASIL, and HCHWA-D are fully penetrant, which means that gene mutation carriers will certainly develop the disease at some point in their lives. These neurogenetic disorders generally start in mid-adulthood, and are progressive, incurable and ultimately fatal. HBOC is partially penetrant, which implies that gene mutation carriers have an elevated risk of developing cancer during their life time. Carriers of a pathogenic *BRCA1* or *BRCA2* gene mutation have options that may prevent cancer (preventive removal of the breasts and/or ovaries); hereditary cancer is treatable and may be cured.

Table 1. 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 [3]	Migraine with aura, multiple strokes, cognitive deterioration, psychiatric disturbances [4]	Severe cerebral amyloid angiopathy, recurrent hemorrhagic and non-hemorrhagic strokes, and dementia [5]	Breast cancer, ovarian cancer, prostate cancer, pancreatic cancer [6]
Timing of clinical onset [b]	Mid adulthood	Mid adulthood	Mid adulthood	Early/mid adulthood; later life
Age of death *(years)*, mean	54-55 [7]	65 [8]	60 [9]	Variable
Treatment can alter onset or progression [b]	No	No	No	Yes
Gene mutation	Expansion of 36 or more CAG trinucleotide repeats in exon 1 of the *HTT* gene [10]	*NOTCH3* gene mutations [4]	Mutation in the *APP* gene on chromosome 21q21.2 [5]	*BRCA1* or *BRCA2* gene mutations [6]
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.[11]

[c] Life time risks in individuals with a mutation in *BRCA1* or *BRCA2* are 40%-80% for breast cancer, 11%-40% for ovarian cancer, 1%-10% for male breast cancer, up to 39% for prostate cancer, and 1% – 7% for pancreatic cancer. There may be an increased risk for melanoma in individuals with *BRCA2* mutations.[6]

Hereditary disorders like HD, CADASIL, HCHWA-D, or HBOC may affect a person's life to a great extent, as the following examples illustrate.

Tom *(20)*
Tom grew up with a mother affected with HD. Tom's mother has been symptomatic for over 17 years, and has been hospitalized for depression and psychosis several times. Tom never perceived his mother as a caring person; he was often frightened by her aggressive and unpredictable behavior. Tom's mother is now permanently hospitalized in a specialized nursing home. Tom sees his father only a few times a year. His parents got divorced not long after the onset of mother's disease process.
Tom has a 50% risk of having inherited the gene mutation associated with HD. If he is a carrier, he will develop HD at some point in his life.

Laura *(36)*
Laura's mother was diagnosed with breast cancer when Laura was 4 years old. She underwent several treatments, but became increasingly ill after she developed a tumor in her other breast. She died when Laura was 14 years old. Laura's father had several episodes of depression during and after the disease process of his wife, and was unable to provide emotional support to Laura and her younger sister. Recently, Laura's sister (33) was diagnosed with breast cancer and was found to be a carrier of a breast cancer gene mutation (BRCA1). Laura has a 50% risk of carrying the same BRCA1 gene mutation, associated with HBOC. If she is a carrier, she has a highly elevated chance of developing breast cancer or ovarian cancer at some point in her life. She could opt for regular surveillance of her breasts, or she could consider preventive measures such as having surgery to remove her ovaries and/or her breasts.

Attachment theory

Attachment in infants

According to Bowlby, human infants have an innate attachment system, that is activated when they perceive a physical or psychological threat to their safety.[12-14] The infant will show behavior that promotes proximity of an adult, who can help restore a situation of safety. This is an important mechanism for the infant's survival, since the infant needs others to stay safe. Infants also need adults to be able to regulate their emotions. In threatening situations, the infant will experience anxiety or distress, and will be able to calm down and feel safe again when a caregiver (father, mother, or other adult) offers protection.

According to Ainsworth, infants differ in the patterns of their behavior towards an attachment figure (mother, father, or other).[2] These attachment patterns may be observed in caregiver-infant interactions and can be understood as strategies for emotion regulation, aimed at the reduction of distress.[2] Thus, through childhood experiences with attachment figures, humans learn which strategies are most effective for regulating their emotions.

When an attachment figure is generally available, sensitive to the infant's needs and sufficiently responsive (e.g., in actions, tone of voice, facial expressions), the infant will regain a state of well-being and perceived security, and internalizes a system of emotional expression that promotes distress reduction. The infant forms a positive image of the caregiver as a reliable source of security, and of itself as an individual who is able to surmount stressful situations. A *secure attachment style* is formed in the infant.[2]

When the attachment figure is insufficiently available, insufficiently sensitive to the infant's needs, or does not respond in ways that help the infant regain a sense of security, the infant will continue to be distressed. It will form a negative image of the caregiver as a source of support, and of itself in relationship to the caregiver. Stress reduction must be achieved by other means than by effective proximity seeking. An *insecure attachment style* is formed in the infant.[2]

In cases where a caregiver is inconsistent in the degree of responsiveness, the infant will be inclined to express high amounts of distress, in an attempt to obtain the caregiver's proximity. This type of behavior is labelled *anxious-ambivalent*.[2] In cases where a caregiver is generally unavailable or irresponsive, the infant will be inclined to show little distress and to minimize its efforts to seek the caregiver's proximity. This type of behavior is called *avoidant*.[2] When the caregiver's behavior is strongly unpredictable and/or frightening, this may result in strongly varying patterns of attachment behavior in the infant. This pattern of behavior is referred to as *disorganized*.[2]

Each of the described patterns of attachment behavior is supposed to reflect a strategy for emotion regulation that is functional within the specific caregiver-infant relationship. Proximity seeking behavior is effective when a responsive caregiver is available; expressing high amounts of distress is useful when there is a chance for the inconsistently responsive caregiver to react as desired, whereas minimizing proximity seeking behavior is functional when the caregiver is not expected to respond adequately to the infant's needs.[15]

A pattern of attachment behavior, or attachment style, is formed in the first months and years of a person's life.[15]

Attachment in adults

Based on early interaction patterns with caregivers (the attachment process), a child develops a *working model* or mental representation of itself and others in a context of intimate relationships. This working model comprises information on attachment figures' availability and responsiveness, and about the degree of worthiness of being loved. Once is has been formed, such a personal attachment style is relatively stable and will serve as a blueprint for social relationships and emotion regulation throughout life.[12,14,16] It is supposed to be activated when a person perceives a situation as threatening and to guide thoughts, feelings, and actions. There are individual variations in adult attachment style.[12,17]

Two traditions for research on adult attachment exist. One research tradition studies adults' memories of childhood experiences with parents, to understand the parent-child relationship and its influence in further life. This line of research uses narrative measures to assess attachment representations, such as the Adult Attachment Interview (AAI).[18] The AAI classifies attachment representations based on how a person discusses childhood relationships with their parents, and the effect of these experiences on their development as an adult and as a parent.[19] An adult is assigned to one of three classifications: *secure (or autonomous)*, when attachment experiences are described as influential and are discussed in a coherent, consistent, and non-defensive manner; *insecure-preoccupied*, when the person is ambivalent about their attachment experiences and discusses them in an incoherent, vague, or inconsistent manner; or *insecure-dismissing*, when childhood experiences with parents are described as unimportant, when the person is unable to recall the experiences, or has a tendency to discuss them in an overly positive way. Additionally, an individual may be classified as *unresolved/disorganized* if they report experiences of unresolved trauma or loss, and show confusion and disorganization when discussing these experiences.[19]

Another research tradition studies adult partner relationships and is based on the idea that a person's attachment experiences in childhood may determine how one approaches and experiences intimate relationships in adulthood.[17] A partner may represent a secure base, just as a parent does for an infant. In stressful circumstances, the partner may provide a sense of security. In this line of research, attachment styles are conceptualized as having two underlying dimensions: attachment anxiety and attachment avoidance.[20] An individual attachment style is characterized by varying levels of attachment anxiety and attachment avoidance. *Attachment anxiety* is the tendency to worry about availability and responsiveness of significant others, to fear interpersonal rejection or abandonment, and to have an excessive need for approval from others.[21] *Attachment avoidance* is the tendency to feel uncomfortable with interpersonal intimacy and dependency, to have an excessive need for self-reliance, and a reluctance to self-disclose.[21] These dimensions can be measured using self-report instruments, such as the

Experiences in Close Relationships – Revised (ECR-R).[22] The ECR-R's two-dimensional way of scoring is based on the idea that individuals differ in the degree of attachment anxiety and avoidance, rather than fit into a distinct category of attachment.[23]

An attachment style is said to be *secure* when a person has low scores on both attachment anxiety and attachment avoidance.[22] In stressful situations, persons with a secure attachment style have optimistic expectations about their ability to cope and about the willingness of their partner or others to support them.[24] They face stressful situations without being overwhelmed by distress and feel comfortable being emotionally close to others and relying on others for support.[25]
An attachment style is said to be *insecure* when a person has high scores for attachment anxiety and/or attachment avoidance.[22] In stressful situations, persons with high attachment anxiety are inclined to keep striving for the proximity and support of their partner or others, which they feel they need for the regulation of their unpleasant emotions.[24] They apprehend that partners will be insufficiently available or supportive, and they fear rejection and abandonment. Conversely, persons with high scores on attachment avoidance are inclined not to seek support from their partner or others in stressful situations, assuming that others' proximity or support will not help them reduce their negative emotions. They prefer staying emotionally distant from others and rely mainly on themselves.[24] Persons with high scores for attachment anxiety as well as attachment avoidance feel they need proximity and support of a partner or others in stressful situations, but emotional closeness makes them feel uncomfortable. They experience a fear of being hurt when becoming close to others.

Attachment insecurity is associated with various negative consequences for social relationships and emotion regulation throughout life, and with various mental health problems, such as depression, anxiety, PTSD, suicidal ideation, and personality disorders.[26] Persons with an insecure attachment style are supposed to have a lack of resilience in coping with stressful life events.[26,27]

Attachment and hereditary disease

HD, CADASIL, HCHWA-D, and HBOC generally start in mid-adulthood. In this period of life, many affected persons are raising one or more children. Parent-child interactions may be negatively influenced by the consequences of the disease to the extent that the attachment process of offspring is disturbed. The affected parent as well as the spouse may be preoccupied with the disease, and may therefore be less available, and less sensitive and responsive to the child's needs. There may be mood or anxiety problems in response to the disease and its prognosis, which will influence parent-child interactions.

Moreover, these diseases may be associated with such disturbances of family dynamics that offspring have a relatively high number of adverse experiences in their childhood. The child's risk of experiencing dramatic losses (e.g., death of the parent) may be increased in families with a neurogenetic disorder or hereditary cancer syndrome, whereas the child's risk of experiencing one or more traumatic events (domestic violence, abuse) may be increased in families with a neurogenetic disorder that often leads to psychiatric problems and changes in personality. When a parent has one of these diseases, there is an elevated risk of parentification and role-reversal, where the child performs adult tasks or has to care for the parent. Negative parent-child interactions and adverse childhood experiences may contribute to the development of an insecure attachment style. Based on the autosomal dominant inheritance pattern of the disease, the affected parent may have experienced a similar background. Therefore, this parent may also have an insecure attachment style, which in itself is a risk factor for insecure attachment in offspring.[28]

The impact of predictive genetic testing

Persons at risk for HD, CADASIL, HCHWA-D, or HBOC who do not have any symptoms of the disease may opt for predictive genetic testing. Through a procedure of DNA testing, the predictive test gives information on whether the person is a carrier of a gene mutation associated with the hereditary disease.

Predictive testing for various late onset hereditary disorders became available in the 1980's and 1990's. Since that time, the psychological impact of predictive testing has been studied, in particular for HD and HBOC. A review shows that most individuals who opt for predictive testing for a neurogenetic disorder report benefits from learning their genetic status.[29] The consequences of predictive testing include transiently increased anxiety and/or depression, but also increased well-being and relief from uncertainty, with few differences between carriers and non-carriers.[29] The level of psychological symptoms (e.g., depression, distress) before the predictive test predicts the level of post-test psychological symptoms, largely regardless of whether the test result is positive or negative.[29] A review on predictive testing for HD shows that distress after testing fluctuates over time, in carriers as well as in non-carriers, with a higher level of distress in carriers.[30] Qualitative studies show that individuals report emotional reactions like shock, fear, and frustration when they learn about their genetic risk, but also when they receive a predictive test result.[30] The fact that most quantitative studies fail to find clinically significant levels of distress after predictive testing may be explained by the use of measures that are not well suited to capturing these emotional reactions.[30]

Most persons who undergo predictive testing for HBOC adapt well to receiving knowledge on their genetic status, although a substantial subgroup (10% – 20%) reports clinically elevated levels of distress.[31] Individuals may be psychologically vulnerable for distress after testing for HBOC if their pretest distress level is elevated, if they have experienced cancer in first-degree relatives or are in a process of complicated grief, or if they have intense emotional representations of HBOC.[31]

Although most people who opt for predictive testing for HD, CADASIL, HCHWA-D, or HBOC may find benefits in learning their genetic status, undergoing predictive testing is generally perceived as stressful by individuals at risk as well as their partners. Even in the absence of psychopathology, persons who present for predictive testing may have a need for psychological counseling and support.[32,33] Various emotions and psychological reactions may occur before, during, and after the predictive testing process.[30] Distress counseling may be needed for worrying about being affected with the hereditary disease or about being stigmatized, for having trouble finding new life goals based on the test result, for dealing with remaining uncertainty after testing, or for difficulties in family communication about the disease.[33] There may be a need for decisional counseling before testing for persons who have difficulty deciding about taking the test. After testing, decisional counseling may also be needed, e.g., when preventive surgery is considered to reduce the risk of cancer, or when reproductive options are considered by persons who do not want to transmit a pathogenic gene mutation to their offspring.

To do justice to the individual needs of individuals who present for predictive testing, a case-by-case approach is advised, preferably taking into account how a hereditary disease may influence persons in various life stages, from one generation to the next.[34] Attachment theory, with its focus on parent-child interactions and resulting individual variations in psychological make-up, may serve to inform such an approach.

The predictive testing procedure

Persons at risk for HD who consider undergoing predictive genetic testing will receive medical and psychological care based on international guidelines.[35] The Leiden University Medical Center (Leiden, the Netherlands) offers a specialized multidisciplinary outpatient clinic for predictive testing for HD. The person at risk is invited to meet with a clinical geneticist, a psychologist, and a neurologist, consecutively. The person at risk is encouraged to bring a companion, such as their partner. The clinical geneticist explores the family history concerning the disorder, and discusses the pattern of inheritance of the disease; the neurologist assesses the person's health status and determines whether there are any neurological symptoms. The psychologist explores the person's experiences with the disease in family members, the

person's emotions, resilience, coping style, and social relationships. The possible test results (favorable or unfavorable) are discussed, and the person is encouraged to reflect on the possible consequences of both results for his or her life. Four weeks later, the person at risk is invited to meet with the clinical geneticist and the psychologist again. The testing procedure and the communication of test results are discussed, and blood for DNA sampling is collected. Four weeks later again, the test result is communicated by the clinical geneticist, after which the psychologist offers support for coping with the test result. Additional psychological support and counseling is available before and after the predictive test.

Persons at risk for CADASIL or HCHWA-D who consider undergoing predictive genetic testing may visit the multidisciplinary outpatient clinic for Cerebral Hereditary Angiopathies (CHA), in the Leiden University Medical Center. The procedure followed is similar to the one for predictive testing for HD, with a multidisciplinary approach (clinical geneticist, psychologist, neurologist), at least two pretest meetings and one meeting in which test results are given, and the possibility of additional psychological support.

Persons at risk for HBOC who present for predictive testing will visit a clinical geneticist, who explores the family history, estimates the person's risk of being a gene mutation carrier, and assesses the person's psychological and social situation. Blood for DNA-sampling may be collected after the first visit. When there is an indication for decisional counseling or distress counseling, the person is referred to a specialized psychologist in the department of Clinical Genetics.

Attachment and predictive testing

Insights from attachment theory and research may be useful to understand individual variations in behavior and adaptation of persons who undergo predictive testing, as insecure attachment styles are associated with maladaptive emotion regulation, inadequate distress reduction in stressful situations, and mental health problems.[26,27] Clinical experience suggest that a personal attachment style plays an essential role in adaptation during and after the emotional and stressful period of predictive genetic testing.

Tom *(20)*
Tom is very nervous when he presents for predictive testing. He feels a need to know whether he will develop HD in the future, but is also afraid of what may happen after the test. He thinks his girlfriend may not want to stay with him if he proves to be a carrier. He is afraid his friends will look at him differently, and will not understand how he feels. Tom feels very vulnerable,

because he thinks he may be unable to cope with this difficult situation alone. He gladly accepts the possibility of discussing the possible consequences of testing with the psychologist.
Tom proves to be a carrier. In the weeks after testing, Tom becomes increasingly hopeless about his future. He avoids visiting his mother with HD, as he sees his own future reflected in her present situation. He has recurrent thoughts of becoming as lonely as she is. Additional psychological counseling is provided as part of the predictive testing protocol.
Tom's attachment style is assessed using the ECR-R; he has an insecure attachment style characterized by attachment anxiety.

***Laura** (36)*
Laura presents for predictive testing. She has not discussed the test with anyone, including her sister, who has breast cancer. Laura is single and has no children. If she would be a carrier of the BRCA1 mutation, she would consider having her ovaries removed, to reduce the risk of getting cancer.
Laura proves to be a carrier. Upon receiving this news, she is more upset than she expected. Psychological support is offered, which she declines.
Over the next two years, Laura increasingly worries about having cancer. The surveillance program with regular mammography and MRI of her breasts offers little reassurance. No one knows how she feels, as she never talks about her feelings. Laura hesitates about having her ovaries removed, fearing the consequences of early menopause. She contacts the clinical geneticist to ask for psychological support with decision making.
Laura's attachment style is assessed using the ECR-R; she has an insecure attachment style characterized by attachment avoidance.

Background of the study

The subject for this thesis and the selection of hereditary disorders was inspired by clinical experience in a setting of predictive testing. Persons who presented for predictive testing for HD, CADASIL, or HCHWA-D frequently described a background with adverse childhood experiences and troubled family relationships. These neurogenetic disorders, with a complex combination of motor, cognitive, and psychiatric symptoms and psychological consequences, often seemed to have influenced family life and parent-child interactions to a great extent. Persons who presented for predictive testing for HBOC often described having a parent with cancer, or having lost a parent due to cancer, but their personal history was in general not marked by dysfunctional parent-child interactions. This led to the hypothesis that attachment style might be different in persons from families with HD, CADASIL, or HCHWA-D, compared to persons from families with HBOC, and compared to persons from a background without such a disease.

Furthermore, clinical experience with predictive testing procedures suggested that persons who showed signs of an insecure attachment style presented with more emotional and psychological problems during and after testing, and had more trouble adapting to the predictive test result. This led to the hypothesis that adult attachment style and emotion regulation strategies were associated with distress before and after predictive testing, in persons at 50% risk for HD, CADASIL, or HCHWA-D.

Aims of this study

This study aims to investigate relationships between adverse childhood experiences, adult attachment style, emotion regulation strategies, and distress before and after predictive testing, in persons from families with HD, CADASIL, HCHWA-D, or HBOC *(Figure 1)*.

The aim of the study described in **Chapter 2** is to investigate whether adult attachment representations of individuals who were brought up by a parent with HD differ from those of a non-clinical population, and to find out if attachment representations are associated with HD-related childhood experiences, especially those leading to trauma and loss. Adult attachment style is assessed using the Adult Attachment Interview (AAI),[18] in order to capture participants' mental representations of attachment during an interview on parent-child interactions, and their perception of the effect of these experiences on adulthood.

In **Chapter 3**, a study is described that aims to explore adverse childhood experiences (ACEs) of adults at 50% risk for HD or HBOC, and to compare the amount and nature of ACEs among these disease groups and to a non-clinical reference group.

The first aim of **Chapter 4** is to compare the prevalence and nature of ACEs and adult psychological characteristics (attachment style, mental health, psychological symptomatology) in offspring of a parent affected with HD, CADASIL, HCHWA-D, or HBOC, to a reference group of persons who did not have a parent affected with any of these genetic diseases. The second aim is to find out whether childhood experiences are associated with adult attachment style and/or mental health. Adult attachment style is assessed using the Experiences in Close Relationships – Revised (ECR-R),[22] in order to detect varying levels of adult attachment anxiety and attachment avoidance in a two-dimensional, non-categorical manner. Using a questionnaire instead of interviews offers the possibility of assessing larger groups of participants.

The aim of the study described in **Chapter 5** is to investigate whether adult attachment style and emotion regulation strategies are associated with distress in persons who present for predictive testing for HD, CADASIL, or HCHWA-D, and whether these psychological traits predict distress after receiving test results.

In **Chapter 6,** we describe how the findings on associations between attachment style, emotion regulation, and distress may be applied in clinical practice, in predictive testing procedures.

The study originated from observations in clinical experience, and intends to inform clinicians working with individuals, couples, and families with HD, CADASIL, HCHWA-D, or HBOC. The results of this study can enhance knowledge on how adult psychological characteristics may be rooted in a childhood with parental hereditary disease, and how these characteristics may influence ways of dealing with distress.

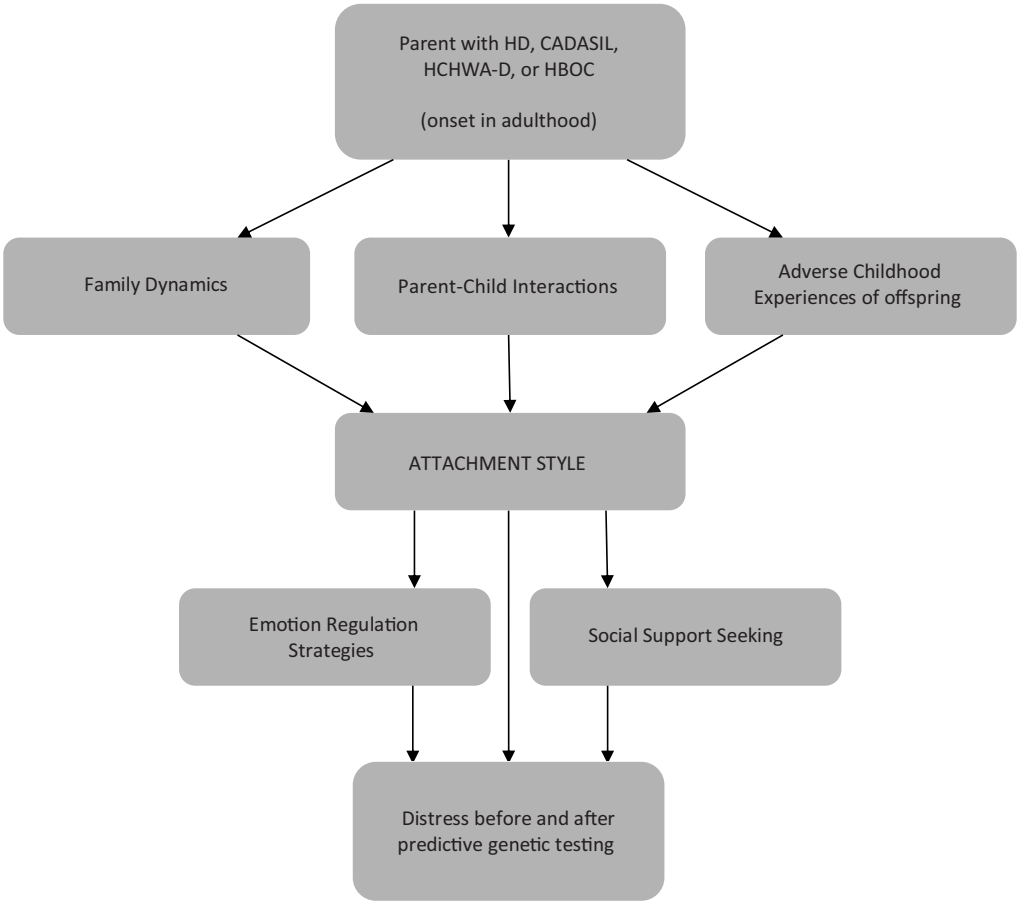

Figure 1. Theoretical precursors and consequences of attachment style in persons with a hereditary disorder.

References

1. Bowlby J. *Attachment and loss. Vol. I: Attachment.* New York: Basic Books; 1969/1982.
2. Ainsworth MDS, Blehar MC, Waters E, Wall S. *Patterns of attachment: A psychological study of the strange situation.* Hillsdale, NJ: Erlbaum; 1978.
3. Ross CA, Tabrizi SJ. Huntington's disease: from molecular pathogenesis to clinical treatment. *Lancet Neurol* 2011; **10**:83-98.
4. Lesnik Oberstein SAJ, Boon EMJ, Terwindt GM. CADASIL *GeneReviews* [Internet, 28-6-2012]. http://www.ncbi.nlm.nih.gov/books/NBK1500/
5. Haan J, Terwindt GM. Hereditary cerebral hemorrhage with amyloidosis, Dutch type. *Orphanet* [Internet, 15-3-2015]. http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Expert=100006
6. Petrucelli N, Daly MB, Feldman GL. BRCA1 and BRCA2 Hereditary Breast and Ovarian Cancer. *GeneReviews* [Internet, 15-3-2015]; 1998-2013.
7. Harper B. Huntington disease. *J R Soc Med* 2005; **98**(12):550.
8. Herve D, Chabriat H. CADASIL. *J Geriatr Psychiatry Neurol* 2010; **23**(4):269-76.
9. Maat-Schieman M, Roos R, Van Duinen S. Hereditary cerebral hemorrhage with amyloidosis-Dutch type. *Neuropathology* 2005, **25**:288-97.
10. Craufurd D, MacLeod R, Frontali M, Quarrell O, Bijlsma EK, Davis M, et al. Diagnostic genetic testing for Huntington's disease. *Pract Neurol* 2015; **15**(1):80-4.
11. Rolland JS, Williams JK. Toward a biopsychosocial model for 21st-century genetics. *Fam Process* 2005; **44**(1):3-24.
12. Bowlby J. *Attachment and loss. Vol II: Separation: anxiety and anger.* London: Hogarth Press; 1973.
13. Bowlby J. *Attachment and loss. Vol. III: Loss: sadness and depression*. London: Hogarth Press; 1980.
14. Bowlby J. *A secure base: parent-child attachment and healthy human development.* New York: Basic Books; 1988.
15. Ainsworth MS, Bowlby J. *An ethological approach to personality development. American Psychologist* 1991; **46**(4):333-41.
16. Bowlby J. *A secure base: clinical applications of attachment theory*. London: Routledge; 1988.
17. Hazan C, Shaver P. Romantic love conceptualized as an attachment process. *J Pers Soc Psychol* 1987; **52**(3):511-24.
18. George C, Kaplan N, Main M. Adult Attachment Interview 3rd edn. Berkeley: University of California; 1996.
19. Crowell JA, Fraley RC, Shaver PR. Measurement of individual differences in adolescent and adult attachment. In: J Cassidy, PR Shaver (Eds.), *Handbook of attachment: theory, research, and clinical applications* (pp 599-634). New York: Guilford Press; 2008.
20. Bartholomew K. Avoidance of intimacy - an attachment perspective. *J Soc Pers Relat* 1990; **7**(2):147-78.
21. Brennan KA, Clark CL, Shaver PR. Self-report measurement of adult attachment: An integrative overview. In JA Simpson, WS Rholes, JA Simpson, WS Rholes (Eds.), *Attachment theory and close relationships* (pp. 46-76). New York, NY US: Guilford Press; 1998.
22. Fraley RC, Waller NG, Brennan KA. An item response theory analysis of self-report measures of adult attachment. *J Pers Soc Psychol* 2000; **78**:350-365.
23. Fraley RC, Waller NG. Adult attachment patterns: A test of the typological model. In: Simpson JA, Rholes WS (Eds.), *Attachment theory and close relationships*. New York: Guilford Press; 1998. p. 77-114.
24. Mikulincer M, Shaver PR, Pereg D. Attachment Theory and Affect Regulation: The Dynamics, Development, and Cognitive Consequences of Attachment-Related Strategies. *Motiv Emotion* 2003; **27**(2):77-102.

25. Mikulincer M, Shaver PR. The Attachment Behavioral System in Adulthood: Activation, Psychodynamics, and Interpersonal Processes. In MP Zanna (Ed.), *Advances in experimental social psychology, Vol.* 35 (pp. 53-152). San Diego, CA US: Elsevier Academic Press; 2003.

26. Mikulincer M, Shaver PR. An attachment perspective on psychopathology. *World Psychiatry* 2012; **11**(1):11-5.

27. Pietromonaco P, Feldman Barrett L, Powers SI. Adult attachment theory and affective reactivity and regulation. In: Snyder DK, Simpson JA, Hughes JN (Eds.), *Emotion regulation in couples and families: pathways to dysfunction and health.* 1st ed. Washington: American Psychological Association; 2006. p. 57-74.

28. Soponaru C, Dirtu MC. Antheus' effect in the intergenerational transmission of attachment styles and its importance for adult education. *Procedia - Soc Behav Sci* 2014; **142**(0):564-9.

29. Paulsen JS, Nance M, Kim JI, Carlozzi NE, Panegyres PK, Erwin C, et al. A review of quality of life after predictive testing for and earlier identification of neurodegenerative diseases. *Prog Neurobiol* 2013; **110**:2-28.

30. Crozier S, Robertson N, Dale M. The Psychological Impact of Predictive Genetic Testing for Huntington's Disease: A Systematic Review of the Literature. *J Genet Couns* 2015; **24**(1):29-39.

31. Van Oostrom I, Meijers-Heijboer H, Duivenvoorden HJ, Brocker-Vriends AH, Van Asperen CJ, Sijmons RH, et al. Prognostic factors for hereditary cancer distress six months after BRCA1/2 or HNPCC genetic susceptibility testing. *Eur J Cancer* 2007; **43**(1):71-7.

32. Gargiulo M, Lejeune S, Tanguy ML, Lahlou-Laforet K, Faudet A, Cohen D, et al. Long-term outcome of presymptomatic testing in Huntington disease. *Eur J Hum Genet* 2009; **17**(2):165-71.

33. Vos J, van Asperen CJ, Oosterwijk JC, Menko FH, Collee MJ, Gomez GE, et al. The counselees' self-reported request for psychological help in genetic counseling for hereditary breast/ovarian cancer: not only psychopathology matters. *Psychooncology* 2013; **22**(4):902-10.

34. Tibben A. Predictive testing for Huntington's disease. *Brain Res Bull* 2007; **72**(2-3):165-71.

35. MacLeod R, Tibben A, Frontali M, Evers-Kiebooms G, Jones A, Martinez-Descales A et al. Recommendations for the predictive genetic test in Huntington's disease. *Clin Genet* 2013; **83**:221-231.