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ORIGINAL ARTICLE

Illness perceptions, risk perception and worry in SDH mutation carriers

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Abstract Succinate dehydrogenase (SDH) mutation carriers are predisposed for developing paragangliomas. This study aimed to explore illness perceptions, risk perception and disease-related worry in these individuals. All consecutive *SDHB* and *SDHD* mutation carriers followed at the Department of Endocrinology of the Leiden University Medical Center (LUMC), a tertiary referral center, were eligible for inclusion. Illness perceptions were assessed using the validated Illness Perception Questionnaire-Revised and compared to reference populations. Risk perception and worry were measured by two items each and associations with illness perceptions explored. Twenty *SDHB* and 118 *SDHD* mutation carriers responded. Compared with various reference groups, SDH mutation carriers perceived less controllability of their condition. *SDHB* mutation carriers considered their condition to be less chronic in nature ($p = 0.005$) and perceived more personal ($p = 0.018$) and treatment control ($p = 0.001$) than *SDHD* mutation carriers. Mutation carriers with manifest disease reported more negative illness perceptions and a higher risk perception of developing subsequent tumors than asymptomatic mutation carriers. Illness perceptions, risk perception and disease-related worry were strongly correlated. Risk perception and disease-related worry may be assessed through illness perceptions. The development of interventions targeting illness perceptions may provide tools for genetic counseling.

Keywords Illness perceptions · Paraganglioma · Risk perception · SDH mutation · Worry

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Introduction

Germline mutations in subunits B and D of the succinate dehydrogenase (SDH) gene are significant causes of inherited paragangliomas (PGLs); neuroendocrine tumors of the paraganglia [1, 2]. *SDHD* mutation carriers typically present with multifocal head-and-neck paragangliomas (HNPGLs), whereas *SDHB* mutations are more frequently associated with pheochromocytomas, extra-adrenal non-HNPGLs and malignant disease [3–6].

Considering the potential fatal course of (untreated) pheochromocytomas and malignant PGLs, at the LUMC biochemical screening for the presence of PGLs is performed at intervals of 1 (*SDHB* mutation carriers) or 2 years (*SDHD* mutation carriers), and radiological screening every 2 years (*SDHB* mutation carriers).

To date, an increasing number of SDH mutation carriers are identified through (presymptomatic) molecular genetic testing of family members of SDH mutation carriers with manifest disease, i.e. index cases. Because of the age dependent penetrance of the *SDHB* and *SDHD* mutations and incomplete penetrance of the *SDHB* mutation, the risk of a mutation carrier to develop PGLs later on in life can only be estimated [3, 5, 7]. In other words, genetic testing provides SDH mutation carriers with probabilistic rather than deterministic information. Several studies have demonstrated that

decision-making concerning genetic testing, screening and risk-reducing behavior is guided through an individual's perceived risk and disease-related worry rather than his or her objective risk [8–10]. Therefore, it is of vital interest to explore how mutation carriers perceive and respond to this probabilistic information and how affect (e.g. worry) and cognitions (e.g. beliefs about the disease) influence perceptions of genetic risk information [11]. To assess risk perception and worry in persons at genetic risk for a disease, Leventhal's common-sense model (CSM) can be used [12–14], which describes how both cognitive and emotional processes influence illness perceptions and coping strategies when a patient faces a health threat [14]. Besides emotional representations of the illness (e.g. worry and anxiety), five features of cognitive representations have been identified: identity, timeline, cause, controllability and consequences of the disease. These dynamic, simultaneous emotional and cognitive processes mutually affect each other.

Previous research has proven that illness perceptions affect quality of life (QoL). Positive beliefs regarding the controllability of the disease positively influence well-being, whereas stronger beliefs about the chronicity, negative consequences and the number of symptoms attributed to the disease negatively affect well-being [15–17]. Furthermore, illness perceptions affect self management and coping behavior [18]. They can be influenced by targeted interventions; two in-hospital intervention studies designed to alter patients' perceptions after myocardial infarction resulted in a quicker return to work in the intervention group [19, 20]. Knowledge of a patient's representations of the illness may therefore serve as a tool through which QoL, self management and coping behavior can be influenced.

At present, there are no studies assessing illness perceptions in SDH mutation carriers. With this study, we aimed to explore the representations of inherited PGLs in *SDHB* and *SDHD* mutation carriers, both those with manifest disease and asymptomatic mutation carriers. To put these illness perceptions into perspective, we compare them to those of several reference populations. The second objective of this study was to assess associations of these illness perceptions with perceived likelihood and worry of developing PGLs in *SDHB* and *SDHD* mutation carriers. Knowledge of the way this risk is perceived may be instrumental in developing interventions to help mutation carriers and their relatives cope with genetic risk information.

Materials and methods

Study protocol

Subjects were recruited from the outpatient clinic of the department of endocrinology of the LUMC; a tertiary referral center for patients with PGLs. Screening for SDH mutations was performed in patients who agreed to genetic testing. In index cases, the SDH genes were scanned for the presence of mutations at the laboratory for DNA diagnostics at the LUMC. All exonic and adjacent intronic regions of these genes were tested by direct sequencing using the Sanger method on an ABI 377 Genetic Analyser (Applied Biosystems, Carlsbad, CA, USA) and multiplex ligation-dependent probe amplification (MLPA) was carried out with the P226 MLPA kit (MRC Holland, Amsterdam, the Netherlands) [21]. Family members of index patients were tested for the family-specific mutation.

All consecutive *SDHB* and *SDHD* mutation carriers were included. In February 2012, a total of 250 mutation carriers were sent an envelope containing questionnaires assessing illness perceptions, risk perception and worry. Subjects were asked to voluntary complete these questionnaires and return them in a prepaid envelope. Non-responders were encouraged by a reminder letter to complete and return questionnaires. In case of missing data, patients received the missing questions by mail with a request to complete them. All questionnaires received before May 1st 2012 were included in our study.

The study protocol was approved by the medical ethics committee of the LUMC. All persons returning completed questionnaires gave written consent for participation in the study.

Clinical characteristics

Illness related and demographic variables of all participants were collected, including age, gender, genetic status and the presence of manifest disease.

Illness perceptions

Illness perceptions were assessed using the Dutch version of the Illness Perception Questionnaire-Revised (IPQ-R) [22]. With this validated questionnaire, a quantitative assessment of the five components of illness representation in Leventhal's CSM can be made. It consists of three parts; the first is the illness identity scale and comprises 14 commonly experienced symptoms (e.g. nausea and fatigue). As proposed by the authors of the questionnaire, we modified the illness identity scale in order to suit the illness under investigation and added seven PGL-associated symptoms, i.e. tinnitus, impaired hearing, problems swallowing, palpitations, perspiration, pallor and fainting. Subjects are asked whether or not they have experienced each symptom (yes/no) and whether or not they believe the symptom is attributed to their disease (yes/no). The illness identity scale is calculated by summing up the number of "yes" responses on the second items. A higher score

represents higher beliefs of the number of symptoms attributed to the disease.

The second part consists of 38 statements representing cognitive and emotional representations of the disease. Individuals are asked to rate each statement on a 5-point Likert type scale, ranging from "strongly disagree" to "strongly agree". The cognitive representations are subdivided into six dimensions (subscales): timeline acute/chronic, timeline cyclical, consequences, personal control, treatment control and coherence. High scores on the timeline acute/chronic, timeline cyclical and consequences subscales, indicate strong beliefs about the chronicity and cyclical nature of the disease and negative consequences of the condition. High scores on the personal control, treatment control and coherence subscales indicate positive beliefs about the controllability of the illness and a good understanding of it.

The third part assesses the causal dimension and uses the same 5-point Likert type scale. It comprises 18 statements representing possible causes of disease. Individuals are asked to rate whether or not they think each concerning cause has contributed to their condition. In addition, in an open ended question they are asked to list up to three (other) causes which in their opinion have contributed the most to their condition.

Reference populations

Normative IPQ-R scores of the general (healthy) population are not available, since they are not assumed to have an illness. IPQ-R scores of PGL patients were compared to those of several reference groups derived from literature, which were chosen based on availability and comparability. Although an ideal reference group would comprise persons with a susceptibility to hereditary disease, no such IPQ-R reference group was available in the literature.

The first reference group comprised 80 newly diagnosed vestibular schwannoma patients. These patients are similar to SDH mutation carriers with HNPGLs in that they suffer from a benign tumor in the head-and-neck area which can cause similar bothersome symptoms, e.g. tinnitus. This group comprised 36 men and 44 women, with a mean age of 57.7 years [23]. The second reference population consisted of 48 male and 20 female recently diagnosed head and neck cancer patients with a mean age of 60 years [15]. This sample represents patients who also suffer from an illness located in the head-and-neck area.

To compare SDH mutation carriers with individuals also suffering from a chronic condition, the third reference group consisted of 63 patients with chronic pain, i.e. longer than 3 months and unexplained by medical signs alone; 26 men and 37 women with a mean age of 54 ± 11 years [22]. The final two reference populations comprised, respectively, 81 patients with long-term biochemical control of acromegaly (47 men and 34 women, mean age 60 ± 12 years) [16] and 52 patients with long-term remission of Cushing's syndrome (7 men and 45 women, mean age of 54 ± 11 years) [17]. These populations were chosen because they comprised patients suffering from a neuroendocrine disease, as does our study population.

Risk perception and disease worry

To assess perceived risk of developing PGLs, two items were used that derived from Cameron et al. [13, 24]: (1) How likely do you think it is that, in some point in your life, you will develop (subsequent) PGLs? (2) How vulnerable do you think you are to developing (subsequent) PGLs at some point in your life? These items were scored on a 7-point Likert scale, with scores ranging from 1 ("not at all") to 7 ("almost certain or extremely"). Ratings from both items were added to calculate a total score (ranging from 2 to 14) for risk perception.

To assess PGL-related worry, again, two items were used that derived from Cameron et al. [13, 24]: (1) To what extent are you worried about developing (subsequent) PGLs? (2) To what extent are you concerned about developing (subsequent) PGLs? These items were also scored on a 7-point Likert scale, with scores ranging from 1 ("not at all") to 7 ("extremely"). Ratings from both items were added to calculate a total score (ranging from 2 to 14) for PGL-related worry.

Statistical analysis

Data were analyzed using SPSS for Windows version 17.0 (SPSS Inc., Chicago, IL, USA). For all measures, means ± SD were calculated. To test for normality the Kolgomorov–Smirnov test was used. The unpaired t test or, when necessary, Mann–Whitney *U* test was used to compare *SDHB* with *SDHD* mutation carriers and mutation carriers with manifest disease with asymptomatic mutation carriers. Differences were considered statistically significant at $p \leq 0.05$.

Cronbach's α coefficients were calculated to establish internal consistency of the subscales of the IPQ-R. To compare IPQ-R results of the study population with those of reference groups, the unpaired *t* test was used. Because multiple comparisons were performed, differences were considered statistically significant at $p \leq 0.01$. To detect relationships between perceived risk, worry and subscales of the IPQ-R, Spearman's rank-order correlations were calculated.

Results

Clinical characteristics

A total of 147 mutation carriers (59 %) responded. The mean age of responders was significantly higher than that of non-responders (51.8 ± 13.8 vs. 47.6 ± 15.2 years, $p = 0.03$) and a significantly higher percentage of women was found in the responder-group (56 vs. 43 % in the non-responder group, $p = 0.03$).

Nine questionnaires were incomplete and discarded from our analyses. Therefore, the study population consisted of 138 individuals: 61 men and 77 women with a mean age of 51.8 ± 13.6 years. The study population comprised 20 *SDHB* and 118 *SDHD* mutation carriers. In this latter group, eight individuals were not genetically tested but they were considered to be obligate *SDHD* mutation carriers, since they had a positive family history with a proven *SDHD* mutation and a personal history of PGLs.

In *SDHB* mutation carriers, 10 (50 %) were diagnosed with one or multiple HNPGLs and two with extra-adrenal non-HNPGLs. In *SDHD* mutation carriers, 106 (90 %) were diagnosed with one or multiple HNPGLs, 11 with pheochromocytoma and eight with extra-adrenal non-HNPGLs.

Five patients (one *SDHB* and four *SDHD* mutation carriers) suffered from malignant PGL, i.e. the presence of chromaffin tissue in nonchromaffin organs or tissues distant from the primary tumor.

Eight persons in the *SDHB* group (40 %) and eight in the *SDHD* group (7 %) were asymptomatic mutation carriers, i.e. persons without manifest disease, as determined after biochemical and radiological screening for PGLs.

There were no significant differences in number or localization of PGLs between responders and non-responders.

Illness perceptions in *SDH* mutation carriers

None of the asymptomatic mutation carriers filled in the first part of the IPQ-R, which assesses illness identity, as they have no PGL-associated symptoms to report. Sixty-four percent of 122 SDH mutation carriers with manifest disease experienced symptoms, which they attributed to inherited PGLs. The most frequently reported symptoms were tinnitus (39 %), impaired hearing (29 %) and problems swallowing (25 %) (Table 1).

On the causal attributions scale, the most frequently reported causes (the ones SDH mutation carriers agreed or completely agreed on) were "hereditary" (mentioned by 94 % of the study population), "chance or bad luck" (49 %) and "stress or worry" (11 %). On the open-ended question, the most frequently mentioned causes fell into the same categories: "hereditary" (91 %), "chance or bad luck" (20 %) and "stress" (9 %).

Table 1 Symptoms attributed to inherited paragangliomas

Symptoms	SDH mutation carriers with manifest disease ($n = 122$)
Tinnitus	48 (39 %)
Impaired hearing	35 (29 %)
Problems swallowing	31 (25 %)
Dizziness	27 (22 %)
Fatigue	24 (20 %)
Pain	20 (16 %)
Breathlessness	16 (13 %)
Sleep difficulties	14 (12 %)
Perspiration	13 (11 %)
Loss of strength	13 (11 %)
Palpitations	12 (10 %)
Wheeziness	11 (9 %)
Headaches	10 (8 %)
Sore throat	8 (7 %)
Sore eyes	8 (7 %)
Fainting	7 (6 %)
Stiff joints	7 (6 %)
Weight loss	5 (4 %)
Pallor	3 (3 %)
Nausea	2 (2 %)
Upset stomach	2 (2 %)

Comparison of IPQ-R scores of *SDHB* mutation carriers with those of *SDHD* mutation carriers revealed several significant differences (Table 2). *SDHB* mutation carriers considered their condition to be less chronic in nature ($p = 0.005$) and perceived more personal ($p = 0.018$) and treatment control ($p = 0.001$).

Compared with asymptomatic mutation carriers, mutation carriers with manifest disease held stronger beliefs about the chronicity ($p = 0.000$) and negative consequences of their condition ($p = 0.050$) (Table 2). They experienced less personal ($p = 0.025$) and treatment control ($p = 0.001$).

Illness perceptions in SDH mutation carriers compared with reference groups

Since we used a modified version of the IPQ-R in which we added seven PGL-associated symptoms to the "Identity" subscale, no comparative analyses with scores of reference groups on this subscale could be made. Scores of SDH mutation carriers on the other subscales of the IPQ-R differed from those of the reference groups in various ways (Table 3). Compared with vestibular schwannoma patients,

Table 2 IPQ-R scores, risk perception and worry in SDH mutation carriers

IPQ-R subscale	SDH mutation carriers ($n = 138$)	*SDHB* ($n = 20$)	*SDHD* ($n = 118$)	p value (*SDHB* versus *SDHD*)	Mutation carriers with manifest disease ($n = 122$)	Asymptomatic mutation carriers ($n = 16$)	p value (manifest versus asymptomatic)
Identity[a] (total score 0–21)	2.6 ± 3.1	2.0 ± 2.3	2.7 ± 3.2	0.602	2.6 ± 3.1	–	–
Timeline acute/chronic[a] (total score 6–30)	24.9 ± 5.1	21.6 ± 6.0	25.5 ± 4.7	0.005**	25.8 ± 4.6	18.7 ± 4.2	0.000***
Timeline cyclical[a] (total score 4–20)	9.6 ± 3.6	10.0 ± 3.4	9.5 ± 3.6	0.528	9.5 ± 3.6	10.0 ± 3.6	0.507
Consequences[a] (total score 6–30)	15.4 ± 5.2	15.2 ± 5.3	15.4 ± 5.3	0.857	15.7 ± 5.3	13.0 ± 4.3	0.050*
Emotional representations[a] (total score 6–30)	14.7 ± 5.1	15.4 ± 5.6	14.5 ± 5.0	0.489	14.8 ± 5.1	13.4 ± 4.9	0.304
Personal control[b] (total score 6–30)	13.7 ± 4.5	15.9 ± 4.7	13.4 ± 4.3	0.018*	13.4 ± 4.4	16.1 ± 4.5	0.025*
Treatment control[b] (total score 5–25)	14.4 ± 3.9	17.0 ± 3.0	13.9 ± 3.9	0.001***	14.0 ± 3.8	17.4 ± 3.1	0.001***
Illness coherence[b] (total score 5–25)	16.2 ± 4.0	15.4 ± 3.6	16.4 ± 4.1	0.287	16.4 ± 4.0	14.9 ± 3.9	0.170
Risk perception (total score 2–14)	10.1 ± 3.3	8.7 ± 4.0	10.3 ± 3.1	0.100	10.6 ± 3.1	6.4 ± 2.8	0.000***
Worry (total score 2–14)	7.8 ± 3.6	6.8 ± 4.1	8.0 ± 3.5	0.162	8.0 ± 3.6	6.3 ± 3.4	0.083

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$

[a] A higher score on this subscale negatively influences well-being [15–17]

[b] A higher score on this subscale positively influences well-being [15–17]

SDH mutation carriers believed their condition to be more chronic in nature, and perceived less personal and treatment control (all $p < 0.001$).

Compared with patients with head and neck cancer, SDH mutation carriers again perceived less personal and treatment control and held stronger beliefs about the chronicity of their condition. However, they perceived fewer negative consequences and emotional representations (all $p < 0.001$). Also, they perceived fewer negative consequences and emotional representations than patients with chronic pain and reported less belief in the cyclical nature of their condition and less personal control. They experienced more illness coherence (all $p < 0.001$).

Compared with patients with long-term biochemical control of acromegaly, SDH mutation carriers thought their condition to be more chronic in nature and experienced more emotional representations (both $p < 0.01$). They perceived less controllability ($p < 0.001$).

Finally, when compared with patients with long-term remission of Cushing's syndrome, SDH mutation carriers considered their condition less cyclical in nature and experienced fewer negative consequences (both $p < 0.001$). Again, they experienced less personal ($p < 0.001$) and treatment control ($p < 0.01$).

Risk perception and worry in SDH mutation carriers

SDH mutation carriers reported risk perception and worry scores of 10.1 ± 3.3 and 7.8 ± 3.6, respectively (Table 2). There were no significant differences in risk perception and worry between *SDHB* and *SDHD* mutation carriers. However, mutation carriers with manifest disease reported higher risk perceptions for developing subsequent PGLs than asymptomatic mutation carriers for developing a primary PGL (10.6 ± 3.1 vs. 6.4 ± 2.8, $p = 0.000$). Worry did not differ significantly between these two groups.

Associations between illness perceptions, risk perception and worry

Correlations between illness perceptions, risk perception and worry scores are shown in Table 4. All subscales showed an acceptable to good internal consistency (α ranging from 0.73 to 0.88).

Table 3 Comparison of IPQ-R scores of *SDH* mutation carriers to various reference populations

IPQ-R	SDH mutation carriers ($n = 138$)	Vestibular schwannoma ($n = 80$) (23)	Head neck cancer ($n = 68$) (15)	Chronic pain ($n = 63$) (22)	Acromegaly ($n = 81$) (16)	Cushing ($n = 52$) (17)
Identity[a,c] (total score 0–21)	2.6 ± 3.1	2.2 ± 2.4	2.3 ± 2.5	6.2 ± 2.8	2.5 ± 2	3.8 ± 3
Timeline acute/chronic[a] (total score 6–30)	24.9 ± 5.1	20.6 ± 4.0**	17.1 ± 4.4**	23.1 ± 4.4	22.9 ± 6*	23.6 ± 7
Timeline cyclical[a] (total score 4–20)	9.6 ± 3.6	10.6 ± 3.8	9.9 ± 3.1	12.9 ± 3.9**	10.1 ± 4	11.9 ± 4**
Consequences[a] (total score 6–30)	15.4 ± 5.2	16.4 ± 2.1	19.4 ± 4.3**	23.5 ± 3.9**	16.9 ± 5	20.4 ± 5**
Emotional representations[a] (total score 6–30)	14.7 ± 5.1	15.3 ± 3.9	19.2 ± 5.5**	19.8 ± 4.2**	12.6 ± 4*	15.3 ± 5
Personal control[b] (total score 6–30)	13.7 ± 4.5	19.1 ± 2.6**	18.8 ± 3.8**	18.4 ± 4.0**	17.5 ± 5**	16.9 ± 6**
Treatment control[b] (total score 5–25)	14.4 ± 3.9	16.9 ± 3.0**	17.5 ± 2.9**	14.2 ± 3.4	18.1 ± 3**	16.7 ± 5*
Illness coherence[b] (total score 5–25)	16.2 ± 4.0	18.1 ± 3.6[d]	15.8 ± 3.8[d]	13.4 ± 4.8**	17.5 ± 3[d]	17.0 ± 3[d]

* $p < 0.01$; ** $p < 0.001$

[a] A higher score on this subscale negatively influences well-being [15–17]

[b] A higher score on this subscale positively influences well-being [15–17]

[c] No comparative analysis was made on the "Identity" subscale

[d] In the Dutch version of the IPQ-R, one item of the illness coherence subscale appeared to be incorrectly translated. As a result, this item would be wrongly reversely scored when using the original syntax. We corrected this error in our study, but consequently no comparative analyses on this subscale were done with other studies which made use of the Dutch version of the IPQ-R

Our findings illustrate that individuals who perceived a higher risk of developing PGLs, perceived more signs and symptoms, negative consequences and emotions of their condition, experienced less personal and treatment control and believed their condition to be more chronic. Individuals who worried more about developing PGLs reported a less clear understanding of their condition, perceived more signs and symptoms, negative consequences and emotional representations. They believed their condition to be more chronic and cyclical in nature and less controllable by treatment.

Risk perception and worry were positively correlated ($\rho = 0.54$).

Discussion

SDHB and *SDHD* mutation carriers are genetically at risk for developing PGLs [1, 2]. Their perceived risk and disease-related worry may be influenced by their representations of the illness, of which knowledge is currently lacking. Information regarding this process is needed to guide genetic counseling and the development of interventions to help mutation carriers cope with genetic risk information. For this purpose, we assessed illness perceptions, risk perception and worry in *SDHB* and *SDHD* mutation carriers.

The most remarkable difference in illness perceptions of SDH mutation carriers compared to various reference groups was that they perceived less controllability of their condition. This may be explained by the hereditary, "unchangeable" component of their disease: the development of PGLs cannot be prevented by any medical treatment or by protective behavior. An additional explanation may be that a large part of patients with HNPGLs are conservatively treated in our center; since most HNPGLs are indolent in nature [25] and surgical treatment may lead to neurovascular complications [26], a "wait and scan" policy is followed in appropriate cases. This conservative treatment may lead to a sense of uncontrollability in these patients. It has to be noted that SDH mutation carriers perceived less personal and treatment control than vestibular schwannoma patients, although a "wait and scan" policy is also often followed in this latter group [27]. However, the vestibular schwannoma reference group comprised newly diagnosed patients in whom illness perceptions were assessed before treatment proposal, which may account for this difference [23].

Our results indicate that *SDHB* mutation carriers considered their condition less chronic in nature and perceived more personal and treatment control than *SDHD* mutation carriers. This difference may be attributable to the larger percentage of asymptomatic mutation carriers amongst *SDHB* mutation carriers (40 vs. 7 % amongst *SDHD* mutation carriers), since our study shows that asymptomatic mutation carriers held less strong beliefs about the chronicity of their condition and experienced more personal and treatment control than mutation carriers with

Table 4 Spearman's rank order correlations between the IPQ-R subscales, risk perception and worry

	Identity	Timeline acute/ chronic	Consequences	Personal control	Treatment control	Illness coherence	Timeline cyclical	Emotional representations	Risk perception	Worry
Identity	–	0.34**	0.54**	−0.18	−0.28**	−0.09	0.43**	0.31**	0.23*	0.31**
Timeline acute/ chronic		–	0.14	−0.40**	−0.51**	0.23**	−0.06	0.11	0.45**	0.26**
Consequences			–	0.03	−0.16	−0.15	0.39**	0.54**	0.25**	0.40**
Personal control				–	0.45**	−0.15	0.15	0.02	−0.20*	−0.11
Treatment control					–	−0.05	0.05	−0.10	−0.26**	−0.23**
Illness coherence						–	−0.23**	−0.29**	0.09	−0.22**
Timeline cyclical							–	0.33**	0.03	0.27**
Emotional representations								–	0.18*	0.63**
Risk perception									–	0.51**
Worry										–
Cronbach's α		0.87	0.85	0.78	0.73	0.82	0.85	0.88		

* $p < 0.05$; ** $p < 0.01$

manifest disease. The large percentage of asymptomatic mutation carriers in the *SDHB* group is probably due to the reduced penetrance of the *SDHB* mutation in our cohort [7]. As a consequence, *SDHB* mutation carriers in our cohort are being confronted with severely affected family members to a lesser extent. Since the experiences of other family members can be modifiers of how mutation carriers conceptualize their own risk [28], hypothetically, *SDHB* mutation carriers may perceive a lower risk of developing PGLs and worry less. However, no differences in risk perceptions and worry between *SDHB* and *SDHD* mutation carriers were found.

SDH mutation carriers with manifest disease reported significantly higher risk perceptions than asymptomatic mutation carriers. This is in concordance with findings of a study assessing risk perception and worry in individuals with a genetic predisposition to venous thrombosis by Kaptein et al., in which perceived risk was significantly higher in individuals with a history of venous thrombosis than in subjects without a history of venous thrombosis [13]. In SDH mutation carriers with manifest disease the probabilistic risk to develop PGLs has inevitably become deterministic, which may lead to a higher perceived risk.

Several studies have demonstrated that decision-making concerning genetic testing, screening and risk-reducing behavior is guided through an individual's perceived risk and disease-related worry [8–10]. Knowledge of this framework is of vital interest to improve health communications on genetic testing. Therefore, we calculated correlations between this risk perception, worry and illness perceptions. The positive correlation between worry and risk perception indicates that people who worried more about inherited PGLs experienced a higher risk perception and vice versa. This is in accordance with findings in recent literature on risk perceptions, in which it is demonstrated that an individuals' subjective illness risk is discrepant from his or her objective illness risk [29, 30]. Apparently, individuals base their perceived risk on their emotional and cognitive perceptions of the target illness rather than on objective medical information. Therefore, illness perceptions may be used as tools to influence risk perceptions and worry, which in turn may influence decision-making concerning genetic testing, screening and risk-reducing behavior.

A possible limitation of our study might be the presence of non-response bias, considering the non-response rate of 41 %. However, the significance of this potential bias is unclear. Possibly, more distressed persons were more likely to respond, which could have led to an overestimation of our results. Reversely, individuals with high levels of distress may avoid being confronted with their condition through research studies, which could have led to an underestimation of our results.

A significantly higher age and larger percentage of women was found among respondents than among non-respondents. We do not know how this may have influenced our results, since, to our knowledge, possible effects of age and gender on illness perceptions have not been explored. However, our study clearly demonstrates correlations between illness perceptions, risk perception and worry. Previous research has proven that cognitively based interventions, such as targeted psychological interventions specifically structured to change highly negative perceptions, can change illness perceptions [20]. Considering the

rapid advances in genetic testing for disease susceptibility, more and more individuals at a genetic risk for a disease will be identified. Efforts should be made to assess illness perceptions in these individuals, in order to identify the ones who could benefit from such interventions and to be able to target risk-perception and worry.

Conflict of interest The authors declare that they have no conflict of interest.

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