Received: 9 April 2021 | Revised: 25 June 2021 | Accepted: 28 June 2021 | Published online: 24 July 2021

DOI: 10.1002/dad2.12225

Alzheimer's & Dementia
Diagnosis, Assessment & Disease Monitoring

RESEARCH ARTICLE

Knowledge assessment and psychological impact of genetic counseling in people at risk for familial FTD

Bonnie Wong[1] | **Diane Lucente**[1,2] | **Samantha Krivensky**[1] | **Erin Krahn**[1] | **Jason Karlawish**[3] | **Bradford C. Dickerson**[1]

[1] Departments of Neurology and Psychiatry, Frontotemporal Disorders Unit and Alzheimer's Disease Research Center, Boston, Massachusetts, USA

[2] Center for Genomic Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, USA

[3] Penn Memory Center & Division of Geriatrics, Departments of Medicine, Medical Ethics and Health Policy, and Neurology, Perelman School of Medicine, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

Correspondence
Bonnie Wong, Frontotemporal Disorders Unit, Massachusetts General Hospital, 149 13th Street, Charlestown MA 02129, USA.
Email: Bonnie.Wong@MGH.Harvard.edu

Abstract

Introduction: The decision to undergo genetic testing for familial frontotemporal dementia (fFTD) is challenging and complex. When counseling individuals, clinicians need to know what individuals understand about the type of fFTD for which they may be at elevated risk. Unfortunately, no tools to measure understanding of fFTD exist, and no study has investigated knowledge gain from fFTD genetic counseling.

Methods: Before and after genetic counseling, 42 asymptomatic individuals from fFTD families completed the newly developed fFTD Knowledge Assessment and Psychological Impact Questionnaire (fFTD KAPI-Q), along with affect and mood questionnaires.

Results: Genetic counseling resulted in substantial knowledge gain on the fFTD KAPI-Q (average gain = 40%); those with lower pre-counseling scores gained the most. Negative affect diminished by 11%. Individuals who gained the greatest knowledge demonstrated the greatest reduction in negative affect.

Conclusions: Genetic counseling was effective regardless of level of baseline knowledge and has an immediate ameliorative impact on negative affect.

KEYWORDS
affect, familial FTD (fFTD), genetic counseling, knowledge assessment

1 | INTRODUCTION

Genetic alterations associated with familial frontotemporal dementia (fFTD) are highly penetrant and follow an autosomal dominant inheritance pattern.[1] In most fFTD families, an alteration is present in the microtubule associated protein tau (*MAPT*) gene on chromosome 17,[2–4] the progranulin (*GRN*) gene on chromosome 17,[5,6] or the chromosome 9 open reading frame 72 gene (*C9orf72*).[7,8] Patients who develop symptoms as a result of an alteration in one of these genes exhibit remarkable heterogeneity in age at onset (ranging from the 20's to the 80's) and clinical phenotype.[9]

As with other autosomal dominantly inherited neurodegenerative diseases, asymptomatic adult members of families with fFTD may choose to obtain genetic testing for a variety of reasons (eg, reproductive decisions; financial, estate, care, or other life planning; long-term care insurance). Individuals deliberating predictive testing under these complex circumstances need a clear understanding of the risks and benefits of learning their genetic status and the uncertainties that would remain if results demonstrate the presence of the genetic abnormality. Because there are no disease-modifying therapies for this debilitating, fatal illness, it would not be surprising for a healthy individual who learns that they are a member of an fFTD family, or that they carry a genetic alteration, to experience a variety of adverse psychological reactions. Research in Huntington's disease (HD) has shown that both positive and negative test results can impact social dynamics and quality of life[10,11]; thus international guidelines for genetic counseling and predictive testing for individuals in HD families have been developed.[12,13] Although these guidelines have informed

the recommendations for genetic counseling and testing for FTD and amyotrophic lateral sclerosis (ALS),[14–16] genetic counselors face potentially even greater challenges when working with fFTD family members owing to the greater heterogeneity in age at onset, clinical phenotypic presentation, and prognosis. The complexities and misconceptions of fFTD can be difficult for lay people to understand, and the implications of genetic testing may lead to substantial distress.

Currently, no tools exist to measure an individual's knowledge about fFTD, and the field lacks evidence to support the efficacy of structured educational and counseling protocols specific to fFTD. Such tools would assist clinicians in evaluating an individual's knowledge of the form of fFTD relevant to them and the issues that may be particularly distressing to that individual, which would then guide additional counseling efforts. The more a clinician is aware of the individual's understanding and appreciation of the illness they may be facing, the better equipped the clinician is to compassionately and effectively deliver potentially devastating news.

To address this need, we developed the fFTD Knowledge Assessment and Psychological Impact Questionnaire (fFTD KAPI-Q) and a structured education and counseling protocol, which we incorporated into our standard procedures for family members in our ongoing longitudinal fFTD cohort study. Using the fFTD KAPI-Q, the goal of the present study was to examine the impact of genetic counseling on gain in knowledge about fFTD, and the relationships between knowledge, counseling, and affect.

We hypothesized that (1) participants would demonstrate an increase in knowledge about fFTD after genetic counseling, and that individuals with less baseline knowledge would improve the most as a result of counseling; (2) individuals with higher baseline anxiety would demonstrate greater baseline knowledge due to proactive information-seeking tendencies prior to participating in genetic counseling, or, alternatively, that individuals with lower baseline knowledge would be more anxious because of a fear of the unknown; and (3) negative affect will decrease after genetic counseling as participants' misconceptions will be corrected, and participants will receive validation that the knowledge they have is accurate.

2 | METHODS

2.1 | Participants and clinical evaluation

The Massachusetts General Hospital (MGH) FTD Unit developed our fFTD Longitudinal Cohort in 2009, collecting a range of data on members of families with autosomal dominant FTD (and in some cases ALS). Participants undergo an extensive annual assessment that involves neurologic, psychiatric, and neuropsychological evaluations, including structured interviews (participant and informant) and research MRI scans.

All participants and study partners undergo genetic counseling with our Genetic Counseling Manager (D.E.L.), and are offered the opportunity to pursue genetic testing. All attempts are made to keep members of the research team blind to genetic status of our participants.

HIGHLIGHTS

- The familial frontotemporal dementia (fFTD) Knowledge Assessment and Psychological Impact Questionnaire (fFTD KAPI-Q) measures fFTD knowledge and efficacy of genetic counseling.
- Genetic counseling results in objective improvement in knowledge about fFTD.
- Genetic counseling for fFTD is not associated with increased negative affect.
- The fFTD KAPI-Q and counseling protocol is a prototype for clinical trials in FTD.

RESEARCH IN CONTEXT

1. Systematic review: The authors present an overview of the existing literature (using PubMed) on the efficacy of genetic counseling for improving knowledge and understanding and its psychological impact on individuals considering predictive testing in neurodegenerative disorders such as familial frontotemporal dementia (fFTD). No tools exist that objectively measure knowledge about fFTD, and there have been no studies that have measured what individuals learn about the condition following genetic counseling or the potential psychological impact that the session has on individuals in the decision-making process to pursue genetic testing.
2. Interpretation: We developed the fFTD KAPI-Q to measure knowledge about fFTD and the psychological impact of genetic counseling, and administered the questionnaire to asymptomatic participants prior to and after genetic counseling and psychoeducation. Our findings indicate that participants show an improvement in knowledge and understanding of fFTD following counseling, with most participants demonstrating a decrease in negative affect associated with increased knowledge of fFTD.
3. Future directions: This study serves as a prototype for other studies that include predictive genetic testing in neurodegenerative disorders (eg, clinical trials that require predictive genetic testing and disclosure of results to participants). The next iterations of the fFTD KAPI-Q will include more complex questions about fFTD to address near-ceiling effects of the current version. Future studies will also examine the longer-term effects on affect and mood following the genetic counseling session and assess for the maintenance of newly learned information that may impact ongoing decision-making related to predictive testing and other future planning.

For the current study, we recruited individuals from the fFTD Longitudinal Cohort who were asymptomatic based on the evaluation described above and multidisciplinary consensus. All participants gave written informed consent in accordance with guidelines established by the Mass General Brigham Institutional Review Boards, which govern human subjects research at MGH.

2.2 | Study assessments

2.2.1 | fFTD Knowledge Assessment and Psychological Impact Questionnaire (fFTD KAPI-Q)

Knowledge of fFTD was evaluated with a questionnaire we developed consisting of 10 multiple-choice or short-answer questions (available upon request). Questions ascertained participants' knowledge of the fFTD-related genetic alteration in their family, symptoms associated with fFTD, age at symptom onset, and inheritance patterns. We based some of these questions on elements of the Capacity Assessment Tool for Genetic Testing, which assesses the understanding and appreciation of apolipoprotein E gene (*APOE*) testing for Alzheimer's disease (AD).[17] The fFTD KAPI-Q score is the percent correct of the 10 questions (primary outcome measure for Hypothesis 1). Additional open-ended questions assessed their understanding and appreciation of the potential impact that this knowledge may have on their psychological and physical well-being and on those within their immediate social network.

2.2.2 | Positive and Negative Affect Scale (PANAS)[18]

This scale comprises 20 items that measure positive and negative affect. Each item is rated on a five-point Likert scale (1 = Very slightly or not at all to 5 = Extremely), reflecting the intensity of affect in the specified time frame. Lower scores reflect lower affect (score range: 10 to 50). We focused only on the negative affect items (PANAS-N) for the current study to capture psychological distress that may develop after counseling. The PANAS-N scale has a normative mean of 14.8 (standard deviation [SD] = 5.4).

2.2.3 | Beck Anxiety Inventory (BAI)[19]

The BAI is a self-report measure of subjective somatic or panic-related symptoms of anxiety. Higher scores reflect a greater level of anxiety.

2.2.4 | Beck Depression Inventory-2 (BDI-2)[20]

The BDI-2 is a self-report instrument that measures the presence and severity of depressed mood. Higher scores reflect greater severity of depressive symptoms.

2.3 | Procedures

Participants first completed study assessment questionnaires immediately before meeting with the genetic counselor (D.E.L.) for comprehensive genetic counseling, which included a review of their responses on the fFTD KAPI-Q, education to correct misconceptions about fFTD, and review of additional possible answers previously generated by the research team for each KAPI-Q question that could have been given by the participant. Participants typically completed the fFTD KAPI-Q and the PANAS again immediately after the counseling session (with some exceptions). Next, participants met with our neuropsychologist (B.W.) for a structured interview exploring participant answers with respect to their own situation and history. Narratives were recorded for future qualitative analyses (beyond the scope of the current article). No new information was shared with the participant during this meeting. No supportive counseling was performed.

2.4 | Data analysis

As the primary variable of interest in hypothesis 1 is change (improvement) in knowledge, participants demonstrating 100% accuracy (n = 11) on the fFTD KAPI-Q prior to genetic counseling were removed from the sample, leaving 31 individuals for the analysis. A repeated-measures analysis of variance (ANOVA) was computed to examine change in percent correct on the fFTD KAPI-Q after counseling.

The percent change in accuracy on the fFTD KAPI-Q was used as the outcome variable in a linear regression analysis to test the hypothesis that those with the least knowledge about fFTD would gain the greatest amount of knowledge as a result of counseling.

For hypothesis 2, a Pearson correlation coefficient was computed to examine the relationship between BAI and percent correct on pre-counseling fFTD KAPI-Q. After excluding cases with missing BAI data, 38 participants were included in this analysis.

For hypothesis 3 (genetic counseling would lead to a reduction in negative affect), we removed participants from the analysis who were at floor (ie, a score of 10 on PANAS-N). With the additional removal of one participant who failed to complete the PANAS after counseling, the sub-sample for this analysis included 33 individuals. A repeated-measures ANOVA was computed, using pre- and post-counseling PANAS-N scores.

To examine the relationship between magnitude of knowledge gain and magnitude of change in negative affect, we removed those individuals from the PANAS-N sub-sample with scores of 100% on the fFTD KAPI-Q prior to counseling (for reasons outlined above), thereby reducing the sample for this analysis to 23 individuals. A percent change score was calculated for PANAS-N scores pre- and post-counseling. A linear regression was computed with percent change in knowledge as the predictor and percent change in PANAS-N as the outcome.

Pearson correlation analyses were computed to identify any effects of gender, age, or education on the outcome measures described above (P's > *.05*).

TABLE 1 Demographic and clinical characteristics of fFTD KAPI study sample

	Genetic alteration in family		
n = 42	*MAPT* (n = 15)	*c9orf72* (n = 25)	*GRN* (n = 2)
Age (years), mean (SD)	47.4 (13.6)	45.0 (12.5)	65.8 (13.8)
Female/male	9/6	17/8	2/0
Education (years), mean (SD)	15.1 (2.2)	16.8 (2.1)	17.0 (1.4)
BDI-2, mean (SD)	6.5 (8.4)	5.6 (5.7)	16 (5.7)
BAI, mean (SD)	4.6 (5.8)	4.1 (5.6)	6.5 (2.1)
Knows own genetic status (carries genetic alteration)	6 (6)	13 (5)	0 (0)

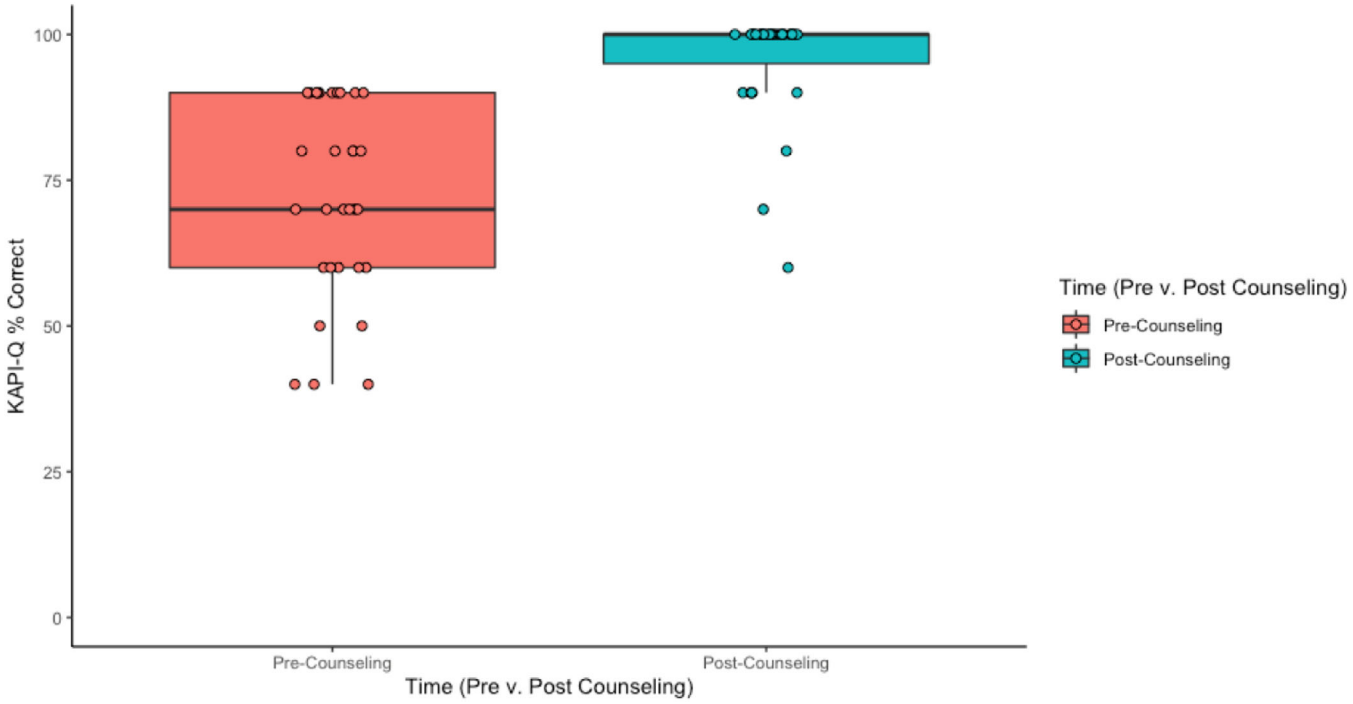

FIGURE 1 The fFTD KAPI-Q demonstrated an improvement in participants' knowledge about fFTD after genetic counseling ($P < .01$). Error bars indicate one standard error of the mean

All analyses were conducted using SPSS software (IBM Corp. Released 2017. IBM SPSS Statistics for Macintosh, Version 25.0. Armonk, NY: IBM Corp.). We used an alpha level of .05 for all statistical tests.

3 | RESULTS

3.1 | Demographics

Demographic and clinical characteristics of participants are shown in Table 1. There were twice as many female as male participants in the sample (28F/14 M). Scores on the BDI-2 and BAI were below cut-off for significant psychopathology for all but one individual in the sample, whose score on both measures fell within the moderate to severe range. Three participants reported symptoms suggesting a moderate degree of depressed mood, with one of these individuals also reporting a moderate degree of anxiety. None reported thoughts of self-harm.

3.2 | Impact of genetic counseling on knowledge of fFTD

Genetic counseling resulted in a measurable gain in knowledge, with a mean pre-counseling fFTD KAPI-Q score of 72.3% (SD = 16.7) and a mean post-counseling score of 95.5% (SD = 9.6) [$F\ (1,30) = 67.1$, $P < .01$)] (Figure 1). On average, participants gained 39.5% in correct answers (with a range of 0% to 150% improvement; SD = 39.3); this was a large effect (Cohen's d = 1.8). Seventy-four percent of participants reached 100% accuracy after counseling. Of the eight participants who did not reach 100% accuracy after counseling, six demonstrated improvement of varying degrees (post-counseling % correct range:

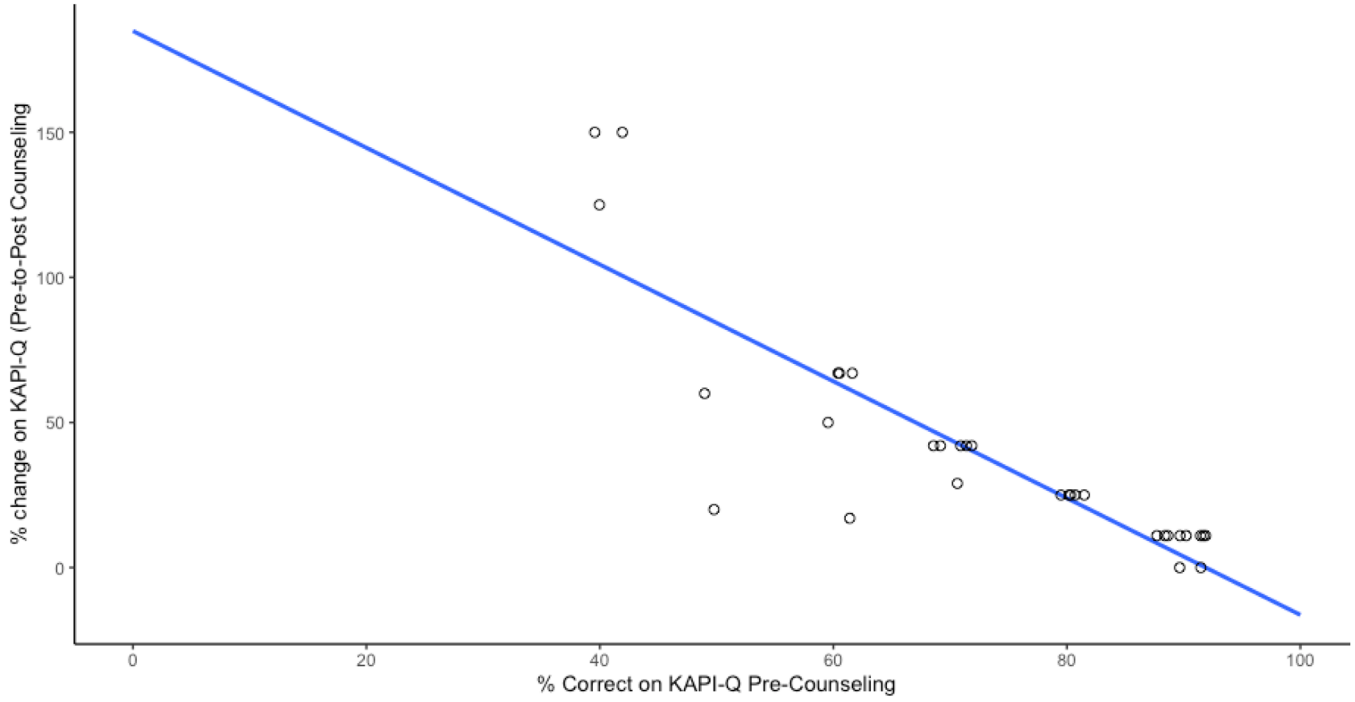

FIGURE 2 Lower baseline knowledge of fFTD is associated with a greater gain in knowledge of fFTD after counseling (r = 0.86, $P \leq .01$)

60% to 90% accuracy). Two individuals showed no change in score, with both participants answering the same question ("If you were identified to have the same genetic alteration as other family member(s) with a neurologic condition, what does this mean about the possible types of symptoms you could develop?") with the same incorrect answer. There was no pattern in their baseline mood or anxiety scores that seemed to account for this unchanged performance, suggesting that factors other than mood interfered with knowledge improvement on this item.

Baseline knowledge predicted the magnitude of knowledge gain after counseling (r = 0.86, $P < .01$); that is, those with less knowledge at baseline gained the greatest amount of knowledge after genetic counseling (Figure 2). This effect was not driven entirely by ceiling effects as not all participants who showed an improvement post-counseling achieved 100% accuracy. The magnitude of change was large for some but not all participants who started with lower baseline scores on the fFTD KAPI-Q.

Our hypotheses about relationships between baseline anxiety and knowledge were supported by the data. There was no significant relationship between BAI and pre-counseling knowledge ($P = 0.1$).

3.3 | Impact of genetic counseling on negative affect

Negative affect diminished after counseling (pre-counseling PANAS-N $\bar{x}$ = 17.5 [SD = 5.0], post-counseling PANAS-N $\bar{x}$ = 15.3 (SD = 5.2) [F(1,32) = 11.65, $P < .01$]) (Figure 3). This is approaching a medium-sized effect, with an average % change (decrease) in PANAS-N score of −11.2% (SD = 18.8; Cohen's d = 0.43). Although the group-average negative affect diminished, a subset of participants showed either no change or an increase in negative affect (11 participants showed either no or only a 1-point change; one showed an increase in negative affect of 6 points).

Due to concerns about distress that genetic counseling may provoke in individuals who have depression or anxiety we examined participants in our sample with a moderate to severe degree of depressed mood and anxiety. Two participants (with BDI-2 and BAI scores in the moderate to severe range) showed no change in negative affect post-counseling. Two participants who reported a moderate level of depression at baseline showed improvement in negative affect after counseling. The individual whose PANAS-N increased from a score of 17 to 23 reported no evidence for baseline depression or anxiety. Overall, baseline mood was not associated with a worsening of (or lack of improvement in) negative affect after genetic counseling.

With respect to the relationship between magnitude of knowledge gain and magnitude of change in negative affect, individuals who gained the greatest amount of knowledge demonstrated the greatest reduction in negative affect: the change in % correct on fFTD KAPI-Q and % change in PANAS-N were inversely correlated (r = -0.49, $P = .02$) (Figure 4).

3.4 | Influence of knowledge of genetic status on primary outcomes

Although the study is not powered to examine differences between participants who knew or did not know their genetic status, a

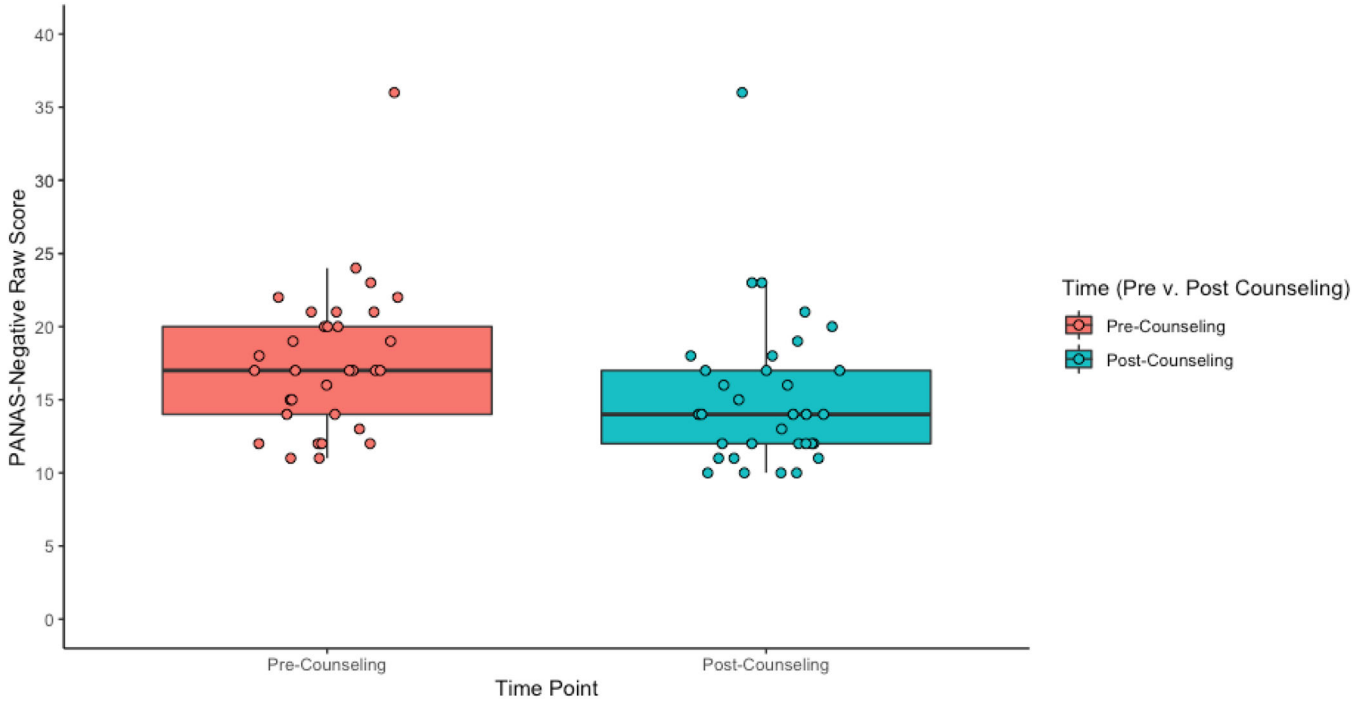

FIGURE 3 Negative affect (PANAS-N) improves after genetic counseling ($P \leq .01$). Error bars indicating one standard error of the mean

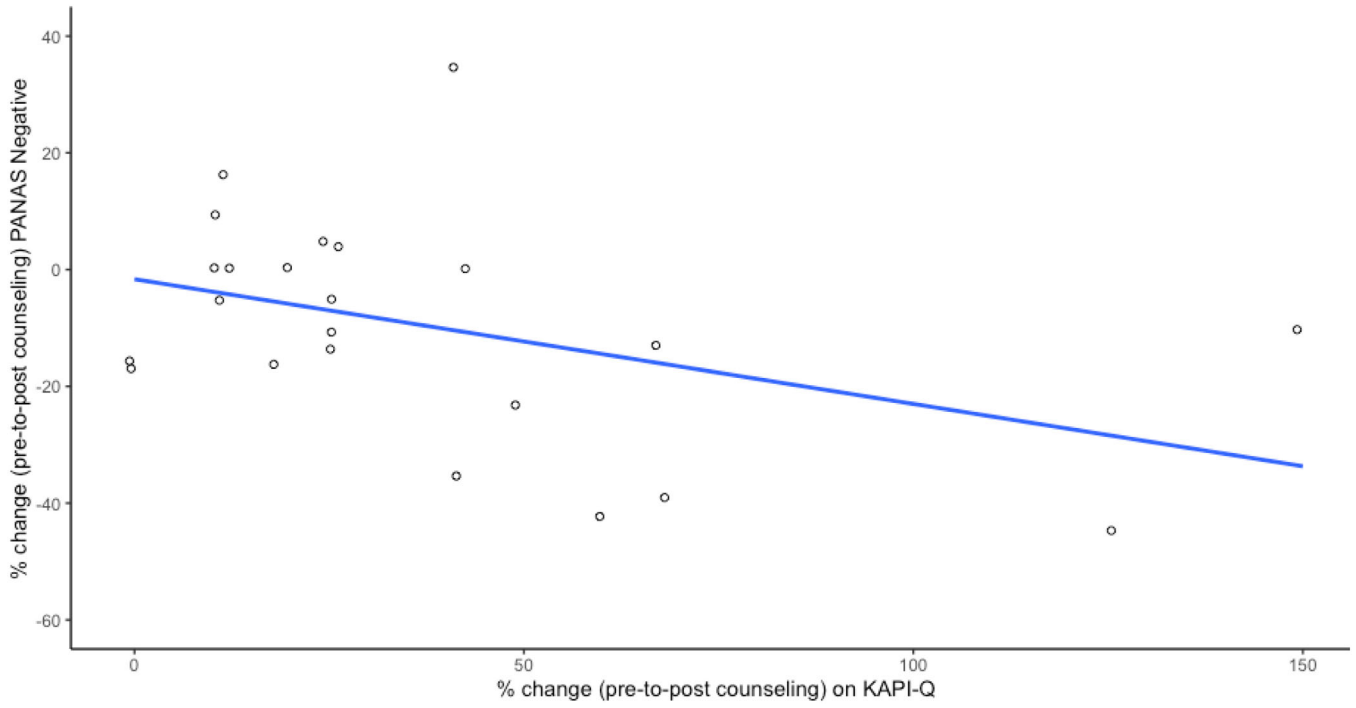

FIGURE 4 Negative affect (PANAS-N) decreases with improvement in knowledge about fFTD after counseling (r = 0.49, $P = .02$)

preliminary analysis revealed no statistical difference between the two groups across any of the primary outcomes (P's > .1); however, trends emerged suggesting that individuals who knew their status tended to have higher baseline knowledge and reported less change in negative affect compared with those who did not know their status. (Table 2).

4 | DISCUSSION

In our experience, asymptomatic family members of patients diagnosed with fFTD often experience substantial distress when discussing their risk of developing the illness and the possibility of undergoing

TABLE 2 Percent change in knowledge (KAPI-Q) and negative affect (PANAS-N) by participants' knowledge of their genetic status

	Knows genetic status (n = 19)	Does not know genetic status n = 23)
Baseline KAPI-Q (% correct), mean (SD)	78 (12.1) (range: 60% to 90%)	66.9 (18.9) (range: 40% to 90%)
% change on KAPI-Q, mean (SD)	29.6 (22.6) (range: 0% to 67%)	48.8 (49.1) (range: 0% to 150%)
Baseline PANAS-N, mean (SD)	16.1 (4.1) (range: 11–13)	18.7 (5.5) (range: 12–36)
% change PANAS-N, mean (SD)	−7.7 (17.6) (range: -39% to 35%)	14.2 (19.8) (range: -45% to 16%)

predictive genetic testing. Some of this distress arises from lack of knowledge or misconceptions about the genetics and the clinical characteristics of the illness. Therefore, we developed the fFTD KAPI-Q to measure individuals' knowledge about both fFTD and the psychological impact of learning the results of fFTD genetic testing. We report here evidence that the fFTD KAPI-Q measured the efficacy of genetic counseling and psychoeducation on asymptomatic family members' knowledge about fFTD. Furthermore, we demonstrate that for most participants in our sample, the knowledge they gain from this intervention was associated with reduced negative affect. These results have important implications for ongoing studies of fFTD, including clinical trials of potential therapies that may require that asymptomatic individuals learn their genetic status in order to participate.

4.1 | Impact of genetic counseling on knowledge gain

Participants showed a substantial improvement in their understanding of facts related to fFTD following counseling. Group results support the notion that the intervention was effective regardless of baseline knowledge, with 74% of participants reaching 100% accuracy. As expected for an effective educational intervention, those who had the lowest level of knowledge of fFTD prior to counseling showed the greatest improvement. Two participants showed no change in their incorrect response to the question regarding types of symptoms one may develop if found to have the same genetic alteration as other affected family members, despite correction during the counseling session. This is likely a result of the participants' personal experiences with affected family members who exhibited similar symptoms, leading them to disregard corrected information. The fFTD KAPI-Q can enable genetic counselors to identify these response patterns to inform ongoing counseling and support around predictive testing decision and life planning.

Although we anticipated one of two possible relationships between baseline anxiety and knowledge about fFTD (ie, individuals with higher baseline anxiety would demonstrate greater baseline knowledge due to proactive information seeking, or individuals with lower baseline knowledge would be more anxious because of a fear of the unknown), we found no relationship between anxiety and baseline knowledge, likely reflecting several factors. First, a subset of participants had undergone clinical genetic counseling prior to participating in our study, contributing to their knowledge about fFTD coming into the study. Second, some participants also knew their genetic status. Information learned about fFTD and their genetic status likely had both mitigating and exacerbating effects on anxiety. Somewhat surprisingly, as shown in Table 2, the primary outcome measures examined in this study did not differ statistically between those who knew their genetic status and those who did not, but there was substantial variability in these measures.

4.2 | Impact of knowledge gain on momentary affect

As a group, participants showed a decrease in negative affect with increased knowledge, likely owing to corrections of misconceptions about the condition that alleviated distress. The gain in knowledge, including discussion of symptoms that may develop, potentially helped individuals regulate emotions and control negative affect, which has been demonstrated in studies of psychotherapy in anxiety disorders.[21] The effect size of our finding, however, was modest, and may have reflected low baseline negative affect (leaving little room for improvement) or the influence of other aspects of the research visit (eg, contact with other providers, exploration of fFTD KAPI-Q responses with respect to their personal histories). Two participants who reported symptoms of a moderate to severe degree of depressed mood and anxiety at baseline showed no change in negative affect after counseling, each experiencing varying levels of negative affect. The two participants who reported only a moderate degree of depressed mood showed improvement in negative affect after counseling. Thus it may be that high state anxiety interferes with the amelioration of negative affect from counseling. The one participant who showed a significant increase in negative affect after counseling (PANAS-N by 7 points) showed no evidence for baseline depressed mood or anxiety. Overall, there appear to be factors unrelated to mood that can lead to worsening of (or no improvement in) negative affect that have yet to be identified and deserve further exploration.

To our knowledge, no study has examined the efficacy of genetic counseling and its impact on affect or mood in fFTD. The majority of

the work involving genetic counseling in neurodegenerative disorders has been in HD and AD [*APOE* studies], focusing mostly on the psychological impact of disclosure of genetic testing results. Although studies exist that examine knowledge improvement in breast cancer genetic counseling,[22] none has been conducted in fFTD.

Our findings have implications for genetic counseling in fFTD. First, individuals benefit from counseling and psychoeducation, which can have a meaningful impact on decision-making processes and future planning. Second, it is unlikely that discussion of the topic will lead to significant emotional distress for most participants (at least those represented by this sample); rather, counseling may have an ameliorative effect immediately following the session. It is unknown, however, if some individuals develop depression or anxiety after the research visit; thus individuals warrant ongoing monitoring even after a counseling session, which we have now implemented in the second iteration of the study at 1-month post-intervention. In general, follow-up interviews with individuals after a counseling session would be important to include in genetic studies to ensure that knowledge and understanding gained from the session is maintained. As seen in the Risk Evaluation and Education for Alzheimer's Disease study,[23] cognitively normal adults can demonstrate variable longer-term retention of information learned from a genetic and psychoeducation session, leaving open the possibility of recalling inaccurate information and impacting predictive testing, decision-making, and life planning.

4.3 | Study limitations

Although no relationship between gender and the outcome variables were found, future studies should attempt to include a greater representation of males. The over-representation of women in this study may reflect a selection bias, and is not typical in large, multicenter studies.[24,25] Our sample includes a self-selected group of individuals who volunteered for a natural history and biomarker study, so it is unclear if our findings would generalize to individuals who do not participate in such a study. Studies that offer predictive testing may attract a self-selected sample of at-risk people who may have better coping skills than people at similar risk who do not volunteer. The decision to participate in a study may be a coping strategy for managing the uncertainties of at-risk status.[26]

Given our participants' high baseline performance on the fFTD KAPI-Q, it is possible that the questionnaire may not have been sufficiently difficult, thereby limiting its sensitivity to detect knowledge gain from counseling. Future versions of the instrument will include questions that are more challenging (eg, details about fFTD not easily found on the internet, in lay literature). Nonetheless, the fFTD KAPI-Q is the first tool of its kind to measure knowledge and understanding of fFTD in this population and may be useful in broader studies of fFTD.

Future studies should also incorporate additional genetic counselors in the protocol to assess the reproduceability of current study results and the validity of the protocol for increasing knowledge gain from counseling; multicenter studies on this topic are being planned. In addition, discussions that may impact affect (eg, personal history, experiences) should be conducted after participants have completed the post- genetic counseling PANAS, as focus on personal situations and histories may have impacted affect ratings to some degree in our sample.

As the field of fFTD makes progress toward the development and launch of clinical trials of potential therapeutics, it will be critical to ensure that participants are fully informed and psychologically supported. We hope this tool and these data provide an example that could be scaled up for use in therapeutic intervention studies currently in the planning stages.

ACKNOWLEDGMENTS

We greatly appreciate the dedication of the participants in this research without whom we would not have been able to perform this study. We appreciate the efforts of the MGH FTD Unit staff whose contributions to data collection and quality control are invaluable. This work was supported by National Institutes of Health (NIH) grants R21 NS084156 and P30 AG062421.

CONFLICTS OF INTEREST

B.C.D. receives research support from NIH, Alzheimer's Drug Discovery Foundation; has consulted for Acadia, Alector, Arkuda, Axovant, Biogen, Eisai, Life Molecular Sciences, Lilly, Merck, Novartis, and Wave LifeSciences; performs editorial duties with payment for Elsevier (Neuroimage: Clinical and Cortex); and receives royalties from Oxford University Press and Cambridge University Press. J.K. receives research support from Generation Program (Novartis), A4 Study (Lily Inc.), AHEAD Study (Esai), ENGAGE, EMERGE, & ADVANCE (Biogen), and NIH; receives royalties from UpToDate; received honoraria for a talk at McGill University; and receives payment for membership on board of the Greenwall Foundation. D.L. received travel support from departmental funds and NIH grant and was paid honoraria for lecturing at the Institute of Health Professionals and the College of the Holy Cross. The other authors report no declarations of interest.

ORCID

Bonnie Wong https://orcid.org/0000-0001-9973-3009

REFERENCES

1. Greaves CV, Rohrer JD. An update on genetic frontotemporal dementia. *J Neurol*. 2019; 266(8): 2075-2086.
2. Hutton M, Lendon CL, Rizzu P, et al. Association of missense and 5'-splice-site mutations in tau with the inherited dementia FTDP-17. *Nature*. 1998; 393(6686): 702-705.
3. Poorkaj P, Bird TD, Wijsman E, et al. Tau is a candidate gene for chromosome 17 frontotemporal dementia. *Ann Neurol*. 1998; 43(6): 815-825.
4. Rademakers R, Cruts M, Van Broeckhoven C. The role of tau (MAPT) in frontotemporal dementia and related tauopathies. *Hum Mutat*. 2004; 24(4): 277-295.
5. Baker M, Mackenzie IR, Pickering-Brown SM, et al. Mutations in progranulin cause tau-negative frontotemporal dementia linked to chromosome 17. *Nature*. 2006; 442(7105): 916-919.
6. Cruts M, Gijselinck I, Van Der Zee J, et al. Null mutations in progranulin cause ubiquitin-positive frontotemporal dementia linked to chromosome 17q21. *Nature*. 2006; 442(7105): 920-924.

7. Renton AE, Majounie E, Waite A, et al. A hexanucleotide repeat expansion in C9ORF72 is the cause of chromosome 9p21-linked ALS-FTD. *Neuron*. 2011; 72(2): 257-268.
8. Dejesus-Hernandez M, Mackenzie IR, Boeve BF, et al. Expanded GGGGCC hexanucleotide repeat in noncoding region of C9ORF72 causes chromosome 9p-linked FTD and ALS. *Neuron*. 2011; 72(2): 245-256.
9. Moore KM, Nicholas J, Grossman M, et al. Age at symptom onset and death and disease duration in genetic frontotemporal dementia: an international retrospective cohort study. *Lancet Neurol*. 2020; 19(2): 145-156.
10. Codori A-M, Brandt J. Psychological costs and benefits of predictive testing for Huntington's disease. *Am J Med Genet*. 1994; 54(3): 174-184.
11. Paulsen JS, Nance M, Kim Ji-In, et al. A review of quality of life after predictive testing for and earlier identification of neurodegenerative diseases. *Prog Neurobiol*. 2013; 110: 2-28.
12. International Huntington Association and the World Federation of Neurology Research Group on Huntington's Chorea. Guidelines for the molecular genetics predictive test in Huntington's disease. *J Med Genet*, 1994;31(7):555-559.
13. Macleod R, Tibben A, Frontali M, et al. Recommendations for the predictive genetic test in Huntington's disease. *Clin Genet*. 2013; 83(3): 221-231.
14. Goldman JS, Wood EMcC. Genetic counseling for FTD. In: Dickerson BC, ed. *Hodges' Frontotemporal Dementia*. Cambridge, UK: Cambridge University Press; 2016.: 153-164.
15. Wood EM, Falcone D, Suh E, et al. Development and validation of pedigree classification criteria for frontotemporal lobar degeneration. *JAMA Neurol*. 2013; 70(11): 1411-1417.
16. Goldman JS. Predictive genetic counseling for neurodegenerative diseases: past, present, and future. *Cold Spring Harb Perspect Med*. 2020; 10(7): a036525.
17. Karlawish J, et al. Using the capacity assessment tool for genetic testing (CAT-GT) to assess the ability of persons with MCI to decide about ApoE testing: the reveal study. *Alzheimer's Dementia*. 2015; 11: P395-P396.
18. Watson D, Clark LA, Tellegen A. Development and validation of brief measures of positive and negative affect: the PANAS scales. *J Pers Soc Psychol*. 1988; 54(6): 1063-1070.
19. Beck AT, Steer RA. *Beck Anxiety Inventory Manual*. San Antonio, TX: Psychological Corporation; 1993.
20. Beck AT, Steer RA, Brown GK. *Manual for the Beck Depression Inventory-II*. San Antonio, TX: Psychological Corporation; 1996.
21. Brooks SJ, Stein DJ. A systematic review of the neural bases of psychotherapy for anxiety and related disorders. *Dialogues Clin Neurosci*. 2015; 17(3): 261-279.
22. Joel E, Brown K, Kim Y, et al. Development and validation of a breast cancer genetic counseling knowledge questionnaire. *Patient Educ Couns*. 2005; 56(2): 182-191.
23. Besser AG, Sanderson SC, Roberts JS, et al. Factors affecting recall of different types of personal genetic information about Alzheimer's disease risk: the REVEAL study. *Public Health Genomics*. 2015; 18(2): 78-86.
24. Fumagalli GG, Basilico P, Arighi A, et al. Distinct patterns of brain atrophy in Genetic Frontotemporal Dementia Initiative (GENFI) cohort revealed by visual rating scales. *Alzheimers Res Ther*. 2018; 10(1): 46.
25. Staffaroni AM, Bajorek L, Casaletto KB, et al. Assessment of executive function declines in presymptomatic and mildly symptomatic familial frontotemporal dementia: nIH-EXAMINER as a potential clinical trial endpoint. *Alzheimers Dement*. 2020; 16(1): 11-21.
26. Gooding HC, Organista K, Burack J, Biesecker BB. Genetic susceptibility testing from a stress and coping perspective. *Soc Sci Med*. 2006; 62: 1880-1890.

How to cite this article: Wong B, Lucente D, Krivensky S, Krahn E, Karlawish J, Dickerson BC. Knowledge assessment and psychological impact of genetic counseling in people at risk for familial FTD. *Alzheimer's Dement*. 2021;13:e12225. https://doi.org/10.1002/dad2.12225