Received: 1 September 2022 | Accepted: 14 January 2023

DOI: 10.1111/head.14484

RESEARCH SUBMISSIONS

Patient-reported experiences with migraine-related cognitive symptoms: Results of the MiCOAS qualitative study

Maya T. Gerstein DrPH[1] | R. J. Wirth PhD[2] | Alyssa A. Uzumcu BA[1] | Carrie R. Houts PhD[2] | James S. McGinley PhD[2] | Dawn C. Buse PhD[2,3] | Kelly P. McCarrier PhD[1] | Alexis Cooke PhD[1] | Nancy M. Touba MPH[1] | Tracy K. Nishida PhD[2] | Peter J. Goadsby MD, PhD, FAHS[4,5] | David W. Dodick MD[6,7] | Richard B. Lipton MD[3,8]

[1]Patient Centered Outcomes, OPEN Health Group, Bethesda, Maryland, USA

[2]Vector Psychometric Group, LLC, Chapel Hill, North Carolina, USA

[3]Albert Einstein College of Medicine, Bronx, New York, USA

[4]NIHR SLaM King's Clinical Research Facility, King's College London, London, UK

[5]Department of Neurology, University of California, Los Angeles, California, USA

[6]Department of Neurology, Mayo Clinic, Scottsdale, Arizona, USA

[7]Atria Institute, New York, New York, USA

[8]Montefiore Medical Center, Bronx, New York, USA

Correspondence
Maya T. Gerstein, Patient Centered Outcomes, OPEN Health Group, 12404 Bobbink Court, Potomac, Bethesda, MD 20854, USA.
Email: maya.tuchman@gmail.com

Funding information
Food and Drug Administration (FDA) of the US Department of Health and Human Services (HHS), Grant/Award Number: UH3FD006795

Abstract

Objectives: To capture patients' perspectives on migraine-related cognitive symptoms during pre-headache, headache, post-headache, and interictal periods.

Background: Migraine-related cognitive symptoms are reported by people with migraine both during and between attacks. Associated with disability, they are increasingly viewed as a priority target for treatment. The Migraine Clinical Outcome Assessment System (MiCOAS) project is focused on developing a patient-centered core set of outcome measures for the evaluation of migraine treatments. The project focuses on incorporating the experience of people living with migraine and the outcomes most meaningful to them. This includes an examination of the presence and functional impact of migraine-related cognitive symptoms and their perceived impact on quality of life and disability.

Methods: Forty individuals with self-reported medically diagnosed migraine were recruited via iterative purposeful sampling for semi-structured qualitative interviews conducted using audio-only web conferencing. Thematic content analysis was performed to identify key concepts around migraine-related cognitive symptoms. Recruitment continued until concept saturation was achieved.

Results: Participants described symptoms consistent with migraine-related deficits in language/speech, sustained attention, executive function, and memory that manifest during pre-headache (36/40 [90%] reported ≥1 cognitive feature), headache (35/40 [88%] reported ≥1 cognitive feature), post-headache (27/40 [68%] reported ≥1 cognitive feature), and interictal periods (13/40 [33%] reported ≥1 cognitive feature). Among participants reporting cognitive symptoms during pre-headache, 32/40 (81%) endorsed 2–5 cognitive symptoms. Findings were similar during the headache phase. Participants reported language/speech problems consistent with, for example, impairments in receptive language, expressive language, and articulation. Issues with sustained attention included fogginess, confusion/disorientation, and trouble with concentration/focus. Deficits in executive function included difficulty processing

Abbreviations: CHAMP, Coalition for Headache and Migraine Patients; CM, chronic migraine; EM, episodic migraine; MiCOAS, Migraine Clinical Outcome Assessment System; MMD, monthly migraine headache day.

information and reduced capacity for planning and decision-making. Memory issues were reported across all phases of the migraine attack.

Conclusions: This patient-level qualitative study suggests that cognitive symptoms are common for persons with migraine, particularly in the pre-headache and headache phases. These findings highlight the importance of assessing and ameliorating these cognitive problems.

KEYWORDS
cognitive symptoms, migraine, patient-centered research, patient-reported outcomes, qualitative research

INTRODUCTION

Migraine is a highly prevalent and potentially severe neurological disease that is associated with significant economic, social, and personal burden.[1,2] It is a chronic disorder, typically with episodic attacks that can impact the functioning of the individual in multiple roles and settings, including occupational, academic, social, familial, and personal.[1–6]

Migraine includes both an ictal (attack) and interictal experience, which involve a constellation of symptoms that occur with varying frequency, intensity, and in varying combinations.[7] Consensus has been gathering that cognitive symptoms, long recognized by clinicians as a clinically relevant component of migraine,[8,9] should be studied, measured, and targeted for treatment.[10–12] A recent examination of data from the American Registry for Migraine Research found that, aside from headache, cognitive dysfunction (when present) was the domain most frequently reported by registry participants as their most bothersome symptom.[13] A review of research related to cognitive dysfunction in migraine cited several studies where subjective cognitive complaints were among the most frequent symptoms reported in the pre-headache and headache phases of the migraine attack.[7,11,14–17] A prospective study of 229 migraine attacks experienced by 100 patients highlighted the role of cognitive dysfunction in attack-related impairment, citing cognitive symptoms as second only to pain in contributing to attack-related disability.[18]

Given the frequency of migraine-related cognitive symptoms (i.e., symptoms that impair a person's ability to think, learn, remember, use judgment, make decisions, or use language) and their reported impact on function and disability, these symptoms are increasingly viewed as a potential target for evaluation and treatment.[10,11] Despite this, recent literature reviews conducted on the outcomes and endpoints used in preventive and acute migraine clinical trials found that patient-reported cognitive function is rarely assessed.[19,20] The Migraine Clinical Outcome Assessment System (MiCOAS) project, a multi-stage program funded by the US Food and Drug Administration, is focused on developing a patient-centered core set of outcome measures/endpoints to be used in the testing of migraine treatments. The project incorporates the experience of people living with migraine, including which outcomes are most meaningful to them. An early action of the MiCOAS project was to capture these experiences through qualitative interviews. Included in this was an examination of the presence and functional impact of migraine-related cognitive symptoms and the role they play in quality of life and migraine-related disability *from the perspective of persons living with migraine*. The qualitative approach undertaken in this study offers a patient-centered perspective not captured in previous examinations of cognitive symptoms in migraine. Previous work in this area has relied on short and/or computerized batteries of replicable close-ended survey questions,[13] simple mechanisms (e.g., checklists) for symptom report,[10] or objective neurocognitive testing.[11] While all of these methods have advantages, qualitative interviews, like those conducted in this study, offer opportunities for an in-depth exploration of each participant's experience with migraine and their perceptions of symptom burden, functional impacts, and quality of life. In addition, we explicitly examined the cognitive effects of migraine in the pre-headache phase (which may include the prodrome/premonitory phase and aura), the headache phase, the post-headache phase (which may include the postdromal phase), and in the interictal period or time between attacks, for reasons outlined in the Methods section. This article describes key findings from this in-depth qualitative inquiry, focusing on results related to the role of cognitive symptoms in migraine.

METHODS

Recruitment and sampling

An announcement and invitation to participate in this qualitative interview study was distributed via existing social media and partner platform communications of the Coalition for Headache and Migraine Patients (CHAMP, https://headachemigraine.org/). CHAMP is a coalition of patient advocacy organizations that is comprised of many headache and migraine advocacy groups and individuals. Recruitment through CHAMP provided an opportunity for people with migraine to be informed about and participate in this patient-centered research effort.

The study announcement directed individuals interested in participating to a designated website where they received more

detailed information on the study, completed an electronic screening questionnaire, provided their informed consent to participate and e-signature, and answered additional questions about their sociodemographic data and headache history.

Eligible participants were US residents self-reporting a medical diagnosis of migraine who had screened positive for migraine on the ID-migraine screener (with ≥2 of the following: disability due to headache ≥1 day in the past 3 months, phonophobia and/or nausea with headache),[21] were able to complete an interview in English, were aged 18–75, and were willing to participate in a 90-min recorded interview. Exclusion criteria were (1) self-report of a medical diagnosis of multiple sclerosis, schizophrenia, bipolar disorder, cognitive impairment, Alzheimer's disease or dementia, or epilepsy; (2) screening positive for alcohol or substance misuse over the past 3 months using the CAGE questionnaire[22]; or (3) self-reported previous or current diagnosis, symptoms, or hospitalization related to COVID-19 infection at the time of screening (July 2020).

Through this recruitment mechanism, we elicited interest and received information from 428 self-selected individuals who were deemed eligible to participate based on their responses to the study screener. From this large potential participant pool, we conducted iterative purposeful sampling to select a diverse sample of 40 interview participants (n = 20 with chronic migraine [CM], defined with modified [Silberstein-Lipton] criteria[23] as an average monthly headache day frequency of ≥15 days among people who meet International Classification of Headache Disorders, 3rd edition, criteria for migraine; n = 20 with episodic migraine [EM] defined as fewer than 15 headache days per month on average for the preceding 3 months) over 8 sampling waves of 4–6 interviews per wave. This approach ensured that collected data were representative of a wide range of experiences, albeit limited by the fact that the participants were identified through an advocacy organization. We targeted specific quotas around headache days per month and variation in the sample by gender, race, ethnicity, age, education, employment status, income, clinical characteristics, and acute and preventive medication use. Based on the research team's substantial experience conducting qualitative data collection and recent methodological research in this area,[24] it was anticipated that a sample of 40 individuals living with migraine carried a strong likelihood of achieving concept saturation in the resulting transcript data.

Data collection

Members of the qualitative research team (M.G., A.U., A.C., N.T., K.M.) conducted a total of 40 semi-structured qualitative interviews using specific techniques designed to elicit rich responses, including broad exploratory questions followed by structured probes, a migraine attack reconstruction, and a web-based visual ranking exercise to assist with discussion of treatment priorities. During the migraine-attack reconstruction exercise, participants were asked to describe their "typical" experience during pre-headache, headache, post-headache, and during the interictal period. These terms were defined for interview participants as: "the period of time between when your migraine attack begins up until the onset of your headache pain" (pre-headache, which may include premonitory symptoms, aura, or both), "the period of time during your migraine attack when you experience headache pain" (headache), "the period immediately after your headache pain subsides" (post-headache), and "the time period in between your migraine attacks" (interictal). One goal of the MiCOAS study is to develop a self-administered, patient-reported measure of cognitive symptoms that can be reliably collected without the careful probing of an experienced clinician. The terms "pre-headache," "headache," and "post-headache" and their accompanying definitions were used during participant interviews in lieu of clinical terms like "premonitory," "aura," "prodrome," and "postdrome" to prioritize patient-centered language and accommodate individuals at all levels of migraine health literacy, in line with the focus of the MiCOAS project.

The interview guide was revised over multiple rounds of review by the research team and study advisory committee and piloted in the field with two participant volunteers prior to data collection. These individuals were not included in the final study sample. Interviews included inquiries about migraine history, symptomology, acute and preventive treatment priorities, and the impact of migraine on emotions, mood, cognition, and daily living/disability/impact. Given the timing of these interviews (July–November, 2020), participants were also provided an opportunity to discuss the impact of the COVID-19 pandemic on various aspects of their experience with migraine (although having COVID-19 was an exclusion criterion for participation). A sub-analysis of this COVID-19-related inquiry is published separately.[25]

All interviewers were trained and observed by senior members of the research team (M.G., K.M.). Interviewers were trained to maintain neutrality and to use techniques for neutral probing. Interviewers followed up on study participants' initial responses using neutral probes about the presence and impact of other cognitive symptoms they did not mention. This provided an opportunity for participants to report cognitive symptoms they may have originally omitted because they did not interpret them as "typical" or because they were uncertain about what may constitute a cognitive symptom. Interviewers also prepared participants on the intention of the interview, which was to gain a better understanding of each person's personal experience living with migraine that may differ from the experiences of others. Interviewees were told up front and reminded as necessary that there are no right or wrong answers or expectations about what they should/would say.

All interviews were conducted through audio-only web-conferencing and targeted 90 min in length. Interviews were recorded with participant consent and transcribed verbatim for use in analysis (identifiers were redacted from the transcripts). Although participants were provided the option to abstain from any interview question, all participants responded to each posed interview prompt. Thus, there were no missing data to account for in this study.

Data analysis

All interviews were coded using a hybrid deductive/inductive approach, where codes are informed both by a preliminary codebook constructed a priori and open codes developed iteratively at each interview wave to reflect the verbatim responses of participants. Four members of the research team (A.C., A.U., M.G., N.T.) participated in data coding. All interview data were managed and coded using Atlas.ti (v8.0) software.[26] To examine the consistency of coding, 10% of the interview transcripts ($n = 4$) were coded independently by two members of the research team. Passages of coded text were then compared across team members using Atlas.ti's inter-rater agreement function. For codes where agreement among team members regarding code attribution (i.e., which codes to attribute to which passages of text) was <80%, discrepancies were reviewed and addressed through research team consensus.[27,28] The research team met regularly throughout the study to discuss coding and address any questions or issues that may have arisen during the coding process. All coded passages were reviewed by a senior member of the research team with significant experience in coding and analysis of qualitative data (M.G.).

Concept frequency counts were calculated to offer a high-level overview of coded content and provide the research team a starting point for additional analysis. Where appropriate, frequency counts were also stratified by migraine phase. Concept frequencies do not provide a full picture of the qualitative experience of individuals living with migraine as was reflected through their thoughtful insights and observations. Thus, thematic content analysis was undertaken to identify key patterns within the data and to categorize coded information into recurrent themes. Coded content was ultimately classified into eight key domains: symptomology, emotions/mood, cognition, daily living, physical limitations, treatment priorities, migraine tracking, and COVID-19 impacts. This article focuses on study findings classified specifically under the domain of cognition and the relationship of those findings to participant-reported concepts identified under daily living and treatment priorities. This is the primary analysis of these data.

Descriptive statistics (i.e., relative frequency) were used to summarize the characteristics of our study sample and calculated using R software version 4.1.1.

Concept saturation

Concept saturation in qualitative research refers to the point in time when the collection and analysis of additional qualitative data does not lead to the identification of new concepts. Concept saturation was assessed by comparing concepts endorsed in each interview wave against previous interview waves to identify the appearance of novel concepts. Saturation grids were constructed to allow for an examination of first coding appearance by transcript and to allow observation of diminishing numbers of newly cited codes in later stages of interviewing.[29] Nearly 400 context and content codes were identified during the coding process, representing a wide range of domains including migraine history, physical symptoms, emotions/mood, cognition, daily living and function, and acute and preventive treatment priorities.

An examination of saturation grids demonstrated that data collection reached concept saturation across all domains. In the domain of cognition, 31 of the 36 concept codes (86%) were identified within the first 30% ($n = 12$) of conducted interviews.

Ethics review

This study was reviewed and approved in its entirety by the WCG Institutional Review Board.

RESULTS

Participant characteristics

Table 1 provides a summary of participant demographics and clinical characteristics. Participants ranged from 21 to 70 years of age (mean = 44). The sample was 78% female, 68% White, and 23% Black or African American. Just over half (53%) of the study sample reported having received a college degree (compared to 38% in the general US population[30]). The sample was composed of both currently employed (55%) and unemployed (45%) individuals. Most of the sample (70%) reported an annual household income of <$100,000. Half of the participants ($n = 20$) reported experiencing ≥15 headache days per month and half ($n = 20$) reported experiencing <15 headache days per month. All participants currently used acute treatment(s) and 88% currently used preventive therapy for migraine.

Cognitive symptoms across phases of the migraine attack

Table 2 summarizes the frequency with which various migraine-related cognitive symptoms were reported to occur within the interview sample. The table presents cognitive symptom frequencies across phases of the attack according to interview participants' descriptions of typical migraine attack experiences. It also presents how many of the 40 participants reported each respective cognitive symptom during at least one phase of their typical migraine attack. An overview of these frequencies suggests that cognitive symptoms are common for persons living with migraine, particularly in the pre-headache and headache phases of attacks. Interestingly, experiences with fogginess, losing words/speech, and difficulty processing information reported during pre-headache were not consistently observed among the same participants during headache (Table 2). This may be due to debilitating and distracting pain during headache

TABLE 1 Demographic, headache, and treatment characteristics of the study sample.

Variable	Category	Interview sample (*N* = 40)	Total respondent sample (*N* = 428)
Age, *n* (%)	18–24 years old	5 (12.5)	18 (4.2)
	25–44 years old	17 (42.5)	174 (40.7)
	45–64 years old	13 (32.5)	208 (48.6)
	65 years and older	5 (12.5)	28 (6.5)
Gender, *n* (%)	Women	31 (77.5)	401 (93.7)
	Men	7 (17.5)	22 (5.1)
	Genderqueer/gender non-binary, transgender person	2 (5.0)	5 (1.2)
Race[a], *n* (%)	White	27 (67.5)	396 (92.5)
	Black or African American	9 (22.5)	18 (4.2)
	American Indian or Alaskan Native	4 (10.0)	9 (2.1)
	Asian	3 (7.5)	8 (1.9)
	Native Hawaiian or Other Pacific Islander	1 (2.5)	1 (0.2)
	Other[b]	1 (2.5)	6 (1.4)
	Prefer not to answer	1 (2.5)	8 (1.9)
Ethnicity/race[a], *n* (%)	Hispanic	9 (22.5)	21 (4.9)
	Non-Hispanic	31 (77.5)	407 (95.1)
Relationship status, *n* (%)	Married or partnered	19 (47.5)	277 (64.7)
	Not married or partnered	21 (52.5)	151 (35.3)
# of other adults in household, *n* (%)	None	8 (20.0)	70 (16.4)
	1–2	27 (67.5)	321 (75.0)
	3 or more	5 (12.5)	37 (8.6)
Children in household, *n* (%)	None	26 (65.0)	296 (69.2)
	1	5 (12.5)	57 (13.3)
	2 or more	9 (22.5)	75 (17.5)
Education, *n* (%)	Grade 12 or GED equivalent	3 (7.5)	11 (2.6)
	Associates degree, technical school, or trade apprenticeship; some college (no degree awarded)	18 (45.0)	130 (30.4)
	College degree or advance degree	19 (47.5)	280 (65.4)
Employment[a], *n* (%)	Paid employment	22 (55.0)	209 (48.8)
	Student	8 (20.0)	28 (6.5)
	Homemaker	3 (7.5)	34 (7.9)
	Retired	6 (15.0)	47 (11.0)
	Unemployed	2 (5.0)	27 (6.3)
	Disabled (disability or leave of absence for any reason)	10 (25.0)	127 (29.7)
	Other	1 (2.5)	13 (3.0)
Household income, *n* (%)	Under $22,000	8 (20.0)	52 (12.1)
	$22,000 to $49,999	10 (25.0)	82 (19.2)
	$50,000 to $99,999	10 (25.0)	135 (31.5)
	$100,000 and over	8 (20.0)	118 (27.6)
	Prefer not to answer	4 (10.0)	41 (9.6)
Migraine subtype by frequency, *n* (%)	<15 headache days per month on average (episodic migraine[c])	20 (50.0)	174 (40.7)
	≥15 headache days per month on average (chronic migraine[c])	20 (50.0)	254 (59.3)

(Continues)

TABLE 1 (Continued)

Variable	Category	Interview sample (*N* = 40)	Total respondent sample (*N* = 428)
Average number of headache days per month, *n* (%)	0–1	0	1 (0.2)
	2–3	6 (15.0)	13 (3.0)
	4–7	8 (20.0)	55 (12.9)
	8–14	6 (15.0)	105 (24.5)
	15–23	18 (45.0)	98 (22.9)
	24 or more	2 (5.0)	156 (36.4)
Over-the-counter or prescription acute pharmacologic treatment (within past year), *n* (%)	Yes	40 (100)	424 (99.1)
Current preventive pharmacologic treatment, *n* (%)	Yes	35 (87.5)	372 (86.9)

[a]Total percent exceeds 100 because participants were able to select more than one race and/or employment status category.

[b]Respondent reported races of "White, South American, and North African" and chose the label "other".

[c]Chronic migraine was defined as an average monthly headache day frequency of ≥15 per month among people who meet criteria for migraine as per Silberstein-Lipton criteria and episodic migraine was the complement. It was not possible to assess the International Classification of Headache Disorders, 3rd edition, criteria.

that dominates the experience, using up attentional resources and reducing bandwidth to identify cognitive symptoms. For example, one participant described the headache phase of their migraine as follows:

> 00-12: I have no activities, no talking. I'm just lying there, I'm in pain. It's not—nothing else is happening. Everything is focused on my body and how it's reacting to it.

An examination of the proportion of individuals reporting *any* cognitive symptoms in the pre-headache, headache, post-headache, and interictal phases further suggests that it is a common experience for persons living with migraine. During pre-headache, 36 out of 40 (90%) participants reported experiencing one or more cognitive features. During headache, 35 out of 40 (88%) participants reported one or more cognitive features. In post-headache, 27 out of 40 (68%) participants reported one or more cognitive features. In the interictal period, 13 out of 40 (33%) participants reported one or more cognitive features (Table 3).

Co-occurrence of multiple cognitive deficits

Among participants reporting cognitive symptoms during pre-headache and/or headache, the vast majority (80% for both periods) endorsed more than one cognitive feature, suggesting that co-occurrence of multiple cognitive deficits during these phases is common. During the post-headache and interictal periods, the proportion experiencing multiple cognitive symptoms was 45% and 10% of the participants, respectively (Table 3).

Impairments to receptive language, language production, and speech production

Migraine-related cognitive symptoms related to language and speech were reported by the majority (29/40; 73%) of participants in the interview sample. Language and speech problems included impairments to (1) receptive language, (2) language production, and (3) speech production (not attributed to difficulties with language). It was not uncommon for individuals to report challenges in two or more of these areas. These cognitive symptoms also served, for some in the sample, as an early indicator of migraine attack onset and as a tool for others in their life to identify that a migraine headache was imminent or had already begun. Few participants reported continued challenges with language and speech in the interictal period (Table 4).

Impact on receptive language

Participants reported challenges in understanding/processing verbal communication during their migraine attacks. For these individuals, information may need to be repeated multiple times to promote comprehension. Participants often described "hearing" the words others were saying but struggling to understand them (Table 4).

Impact on language production

Participants described jumbling words, struggling to form words, and difficulty finding words. Many participants described knowing what they want to convey while being unable to find or form words

TABLE 2 Frequency of perceived migraine-related cognitive symptoms reported by interview participants ($N = 40$) across pre-headache, headache, post-headache, and interictal phases of their typical migraine attacks.

Cognitive symptom	Pre-headache[a], *n* (%)	Headache, *n* (%)	Post-headache[b], *n* (%)	Interictal, *n* (%)	Reported in at least one phase[c], *n* (%)
Trouble with concentration/focus	25 (62.5)	25 (62.5)	11 (27.5)	0 (0.0)	29 (72.5)
Confusion/disorientation	4 (10.0)	3 (7.5)	2 (5.0)	0 (0.0)	6 (15.0)
Avoid making decisions	17 (42.5)	18 (45)	6 (15.0)	0 (0.0)	27 (67.5)
Fogginess	18 (45.0)	9 (22.5)	17 (42.5)	0 (0.0)	24 (60.0)
Losing words/speech	24 (60.0)	12 (30.0)	9 (22.5)	2 (5.0)	29 (72.5)
Memory	12 (30.0)	15 (37.5)	11 (27.5)	12 (30.0)	26 (65.0)
General	3 (7.5)	5 (12.5)	7 (17.5)	9 (22.5)	18 (45.0)
Learning	9 (22.5)	7 (17.5)	5 (12.5)	6 (15.0)	17 (42.5)
Retrieval/recall	3 (7.5)	10 (25.0)	4 (10.0)	1 (2.5)	14 (35.0)
Slurred words/speech	1 (2.5)	3 (7.5)	0 (0.0)	0 (0.0)	3 (7.5)
Difficulty processing information	14 (35.0)	11 (27.5)	7 (17.5)	1 (2.5)	19 (47.5)

[a]Also referred to as prodrome or the premonitory phase but includes aura.

[b]Also referred to as postdrome.

[c]Accounts for how many participants endorsed the cognitive symptom during *at least one phase* of the migraine attack.

TABLE 3 Proportion of participants ($N = 40$) reporting occurrence and co-occurrence of migraine-related cognitive symptoms[a] across pre-headache, headache, post-headache, and interictal phases.

# of endorsed cognitive symptoms	Pre-headache, *n* (%)	Headache, *n* (%)	Post-headache, *n* (%)	Interictal, *n* (%)	Reported in at least one phase[b], *n* (%)
0	4 (10.0)	5 (12.5)	13 (32.5)	27 (67.5)	0 (0.0)
1	4 (10.0)	3 (7.5)	9 (22.5)	9 (22.5)	3 (7.5)
2	9 (22.5)	9 (22.5)	8 (20.0)	2 (5.0)	2 (5.0)
3	6 (15.0)	9 (22.5)	3 (7.5)	2 (5.0)	8 (20.0)
4	8 (20.0)	4 (10.0)	3 (7.5)	0 (0.0)	5 (12.5)
5	6 (15.0)	6 (15.0)	2 (5.0)	0 (0.0)	7 (17.5)
6	3 (7.5)	2 (5.0)	2 (5.0)	0 (0.0)	4 (10.0)
7	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	5 (12.5)
8	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	5 (12.5)
9	0 (0.0)	1 (2.5)	0 (0.0)	0 (0.0)	1 (2.5)

[a]Symptoms include trouble with concentration/focus, confusion/disorientation, decision avoidance, fogginess, losing words/speech, general memory loss, challenges with learning, challenges with retrieval/recall, slurred words/speech, difficulty processing information.

[b]Accounts for how many participants endorsed the cognitive symptom during *at least one phase* of the migraine attack.

to reflect their thoughts. Participants described being unable to express their basic needs or physical sensations during migraine attacks, leading to compounding feelings of frustration, fear, and panic (Table 4).

Impact on speech production

Although distinct, difficulty with speech production often co-occurred with the language production issues described above. Participants with speech production symptoms reported difficulty getting their words out with clarity (e.g., without slurring) (Table 4).

Deficits in sustained attention and executive function

Participants described struggles to sustain attention during migraine attacks including a general and overwhelming sense of "brain fog," vivid descriptions of confusion/disorientation, and trouble maintaining their concentration or focus. For participants in our sample, issues with sustained attention did not seem to linger into the interictal period, but rather, played a prominent role in cognition during the attack itself. Although these cognitive symptoms were reported throughout all phases of the migraine attack, the negative implications of deteriorations in sustained attention were most prominent during the early stages of attack onset (i.e.,

TABLE 4 Key concepts and exemplary quotes: Language/speech impairment.

Concept	Exemplary quote
Language/speech impairment as early indicator of migraine attack onset	00-17: I'll even get to where I'm trying to speak with you right now and words just aren't coming out right. I'm stuttering on my words, I'm trying to think of what word I'm trying to use, stuff like that. And then I'm like, OK, I know I'm fixing to get a migraine because I cannot even speak properly. [pre-headache]
Impact on receptive language	00-23: I cannot tell you how many times I've looked someone straight in the face, tried to read their lips and still did not catch everything that they said. And I'm like, sorry, can you repeat that? But it's like at least two times that I have to ask them for—to repeat it. [post-headache]
Impact on language production	00-17: I cannot form my words. The word is there. I see the word in my head, but when I try to say it, it just does not come out. I cannot—I'll say, help me—like, help me think of the word I'm trying to say. I say that all the time to my husband or to my kids—I'll pretty much describe it to them, what I'm trying to say. [pre-headache]
Frustration, fear, and panic because of impairment to language production	00-01: Inside me, I'm super aware. So that's the problem is that I cannot tell anybody how everything feels because I can barely talk. And everything they—when they touch me, it's hypersensitive. But people are thinking that I'm not aware. [pre-headache] 00-27: It's—that's the biggest frustration, because of my career, because I've worked all my life towards being an academic. I've based my identity on, if not being smart, at least being educated … I could not remember the word head the other day. I said neck-ball. And it's like, if I were lecturing a class of 500 college students—ugh. So it's—that's the—I would deal with the pain every day if it would just not leave me so stupid. [pre-headache]
Dysarthria	00-09: I have started to—depending on the severity of the migraine, I—my speech becomes slow, or I start to stutter. [headache]

TABLE 5 Key concepts and exemplary quotes: Deficits in sustained attention, concentration and brain fog.

Concept	Exemplary quote
Brain fog	00-06: So brain fog feels like—it's almost—if you were to think about—if you are in like a pool and you are trying to walk through waist-high water, it's a lot more difficult to reach your destination, even if it's only a couple feet away. It's like that but with your thoughts. So it's right there but it's a lot farther than it seems. [pre-headache]
Confusion/disorientation	00-12: I'll have a list and everything, I'm not—I'm just randomly walking around the grocery store like a complete idiot, like somebody the other day in XXXX, somebody just walked up to me and said are you OK, because I feel—you looked like you were confused? I was like oh—and I was like no, I'm just looking for some vegetables. She's like can I help you and then she was able to help me, but—so other people notice it too. [pre-headache]
Challenges with concentration/focus	400-10: It becomes very difficult to concentrate. Even focusing's very difficult as well. And I think those are also standards in regards—oh, something's happening … it's like all of a sudden, it's like it comes out of nowhere, and you can be completely involved in a conversation or in a task or—whether it be work or home or friends or whatever, and it's just one of those things where you kind of get this glazed look on your eyes, and you are just really kind of like—you are there, but you are not all there to a certain degree. [pre-headache]

pre-headache) when individuals may still be attempting to maintain a level of function at work, home, school, or social settings (Table 5).

In addition to difficulties with attention, participant-reported migraine-related deficits in executive function included difficulty making decisions and processing information. Participants doubted their capacity for planning or decision-making during the pre-headache and headache phases. Some described struggling to make treatment choices during migraine attacks and a heavy reliance on others to manage medication and health care utilization in these circumstances. Implications of executive function loss were further complicated by participant reports of co-occurring deficits in language/speech production, hindering communication with surrogate medical decision-makers during severe migraine attacks (Table 6).

Issues with memory

Issues with memory were discussed by participants across all phases of a migraine attack and as a key cognitive impact during the interictal period in-between attacks. Participants distinguished between issues related to learning (i.e., forming new memories) and retrieval (i.e., recalling previously learned information).

Impact on learning

Disruptions to learning during the migraine attack itself were often characterized as a complete blackout or partial brownout of events and interactions. This differed from disruptions to learning during the interictal period, which were described as less dramatic

TABLE 6 Key concepts and exemplary quotes: Loss of executive function.

Concept	Exemplary quote
Difficulty making decisions	00-01: I would not say that I'm thinking clearly. What I'm aware of is that I would not say that my executive function is high—is working properly … I would not say that my thinking faculties are working properly. I could not make an executive decision. I used to run an architectural firm with 100 people. I would not want to be the CEO in charge, making decisions then. [pre-headache]
Challenges processing information	00-09: When they are really, really bad, I cannot—things does not make sense to me. I cannot function enough to make sense.
Reliance on surrogate decision-makers during attacks	00–27: I cannot do it at all. I—the—yeah. When—I've had my husband basically forcibly take me to the emergency room when it was bad enough. He'd ask me, do you want to go to the emergency room, and I cannot even decide yes or no. [headache]
Complication of co-occurring deficits in executive function and speech/language production	00-36: Like my sister and I live together, and she's really great in so many other aspects, but sometimes her caretaking skills are a little slackened, and she knows this, and we talk about it, and it's fine. But I just know that, if I do not communicate that to her before of what I need during the attack, when I cannot maybe articulate it as well or even really know exactly what I need, she's not going to be that much help. [headache]

deficiencies in short-term memory, including forgetting recently made plans/responsibilities or conversations (Table 7).

Impact on retrieval/recall

Problems with retrieval/recall manifested during migraine attacks as temporary disruptions to long-term memories such as the names of well-known friends and acquaintances and important, long-held household or family responsibilities. Issues with retrieval/recall were most frequently reported during the headache phase of the attack, suggesting a relationship between head pain and a deterioration in the focus required to recall/retrieve important memories (Table 7).

Beliefs about memory impairment in the interictal period

Participants discussed various theories about the cause of deficiencies in memory during the interictal period. Some participants believe that issues with the formation of new memories and other general concerns about memory loss between attacks are directly related to chronic cognitive deterioration made worse by each migraine attack. Others drew connections to migraine medications whose cognitive side effects made remembering things more challenging. Regardless of the reason behind interictal impacts on memory, participants who experienced problems with memory outside the context of the migraine attack itself viewed this as a highly concerning aspect of their migraine and/or treatment (Table 7).

Relationship of cognitive symptoms and pain

Cognitive symptoms related to language/speech production and processing, sustained attention, executive function, and memory can manifest across all phases of the attack. For many individuals in the sample, cognitive symptoms that interfere with their daily life begin in the pre-headache phase and increase in severity as headache pain intensifies. Many participants viewed cognitive symptoms as having a direct relationship to head pain (i.e., as head pain gets worse, cognition declines; correspondingly, as head pain resolves, so do cognitive symptoms). For some participants, however, migraine-related cognitive symptoms are noticeable outside the context of head pain (i.e., begin before onset of pain and/or linger after pain resolves) (Table 8).

The post-headache period was observed to have the greatest variability in presence and manifestation of cognitive symptoms across and within the participant sample. During some migraine attacks, cognitive symptoms resolved rapidly and early in the post-headache period. During other attacks, cognitive symptoms lingered well beyond head pain into the post-headache period with a more gradual return to a cognitive "baseline" (Table 8).

Cognitive symptoms as a treatment priority

Cognitive symptoms during migraine attacks were reported by participants as a concern and a treatment priority. Most participants in the interview sample experienced cognitive symptoms related to migraine that interfered with their daily life and function. These participants desired a reduction in cognitive symptoms so that they could better accommodate daily responsibilities and activities, including work, school, family, and social life (Table 9). Despite a desired reduction in cognitive burden, some participants in the study were skeptical that migraine treatments could effectively address cognitive symptoms and worried that these therapies may even compound them (Table 9).

Some individuals in the study sample viewed reductions in cognitive symptoms as an extension of pain and other symptom relief and, thus, de-prioritized treatment of cognitive symptoms (Table 9).

Despite variation in how much priority participants placed on addressing cognitive symptoms through acute and/or preventive migraine treatments, all individuals who reported experiencing migraine-related cognitive symptoms viewed them as burdensome

TABLE 7 Key concepts and exemplary quotes: Memory issues.

Concept	Exemplary quote
Deficits in learning prominent during the headache phase	00-10: It's awful. It's—there is absolutely—there's no memory. There's—I mean, there's memory of me going through this and of dealing with it, and you are like, my God, I just want to chop my head off. But as far as everything else, it's just a very—it's like snippets of what may have—what's gone on during that time. [headache]
Perceived deficits in learning during interictal period present as challenges with short-term memory	00-41: So if I made a plan or I set a date for something, I immediately have to put it in my calendar. If I do not, I will completely forget about it. Like I did not have this meeting in my calendar, and I actually forgot about it. And the only reason I remembered last night was because I came across the email … and that's second nature to me these days, because as soon as I—I do not even let the doctor's office give me cards. I am just like this with my phone, putting it in as we are making the appointment, because if I do not, I'll never show up. [interictal]
Deficits in retrieval/recall during the headache phase present as temporary disruptions to long-term memory	00-12: I'll forget their names. I see these people almost every day. So it's like instead of saying whoever that I'm going to see, I do not remember their name. I know them and I'm walking on my—they'll—say somebody will engage in a conversation with me, I'm pretty much looking at them, they are like a stranger, and that's a bad feeling too, because you are trying to connect with me, which is probably what I need. You know what I mean? [headache]
Memory problems in the interictal period are perceived by some patients to be related to history of migraine	00-17: My memory has been affected bad, and I think it has to do with the migraines. But they are not really sure because I'm only 33. I should not be having memory problems the way I do…. I've noticed long-term, as well, I have memory issues, and it's scary because I should not…. My husband has traumatic brain injury from being injured in Afghanistan. He has a reason to be 33 and have memory issues. I do not see where I do unless it's the migraines or whatever that's causing the issues. I should not be having issues he does with memory. [interictal]
Memory problems in interictal period attributed to migraine medication use by some patients	00-26: Well, I know that one of the side effects of the medication that I do take is the memory. That's why I write a lot—that's why I write stuff down. [interictal]

TABLE 8 Key concepts and exemplary quotes: Cognitive symptoms and pain.

Concept	Exemplary quote
Cognitive symptoms increase as headache pain intensifies	00-06: I always notice that, as pain increases, cognitive function goes down. It's directly related. But as pain levels are really high, I sometimes get stuck in a circular pattern of thinking, where I'll just say the same thing over and over and I do not know what's going on. [headache]
Cognitive symptoms outside the context of head pain	00-41: I'll still have brain fog. I actually will still have brain fog for days. And I will not realize it until later. I could be completely fine, have ba—brain fog and work on my report, like my budget or whatever, and come back a couple days later without brain fog and be like, OK, that makes no sense. I do not know why I did that. I must have had brain fog. And I'll have to fix it. [post-headache]
Post-headache variability in cognitive symptoms	00-08: I think it also kind of is situational. So I can think of some times where right after I had a migraine, I was still in that kind of fogginess and confusion or not being able to concentrate and then other times, it seems like I can bounce back quickly and feel like more of a—immediately jumping back into normal life. I do not know that it's—it definitely not always one or the other. [post-headache]

and as a barrier to maintaining or regaining function during migraine attacks (Table 9).

Cognitive interference in individuals with chronic versus episodic migraine

Cognitive symptoms across pre-headache, headache, and interictal phases were similarly reported across chronic and episodic interview subsamples. Thus, it was difficult to distinguish any notable differences in cognitive burden across groups during these stages of migraine. Some variation was noted between the CM and EM subgroups in terms of the reporting of cognitive impacts during the post-headache phase. Individuals in our interview sample with CM reported fogginess, losing words/speech, and difficulty processing information in the post-headache phase more than twice as often as participants with EM. This suggests that individuals with CM may be comparatively more prone to persistent and prolonged cognitive interference that lingers beyond the time point when pain is resolved (Table 10).

DISCUSSION

Findings from this in-depth qualitative interview study align with previously conducted research on migraine-related cognitive symptoms in several important ways. First, this study supports the view that cognitive symptoms are both common and burdensome for people

TABLE 9 Key concepts and corresponding exemplary quotes: Cognitive symptoms as a treatment priority.

Concept	Exemplary quote
Desired reduction in cognitive symptoms to accommodate daily responsibilities	00-09: Only because of the fact that—you know, two kids, two dogs, a senior father, and then I work in finance, I got to have at least some of my mental capacity to function properly with that stuff
Skepticism that migraine treatments can effectively address cognitive symptoms	00-04: I think the brain fog—that always happens when I have migraines, so I just do not—like I said, it's one of those things I just do not think it's ever not going to happen. When you take something that messes with your CNS, you are never going to get something that cures the pain that does not create a side effect. I just do not believe that's ever going to happen
De-prioritization of cognitive symptoms as a treatment priority	00-08: I guess—I think I just was thinking like if I wasn't having as many headaches or wasn't having as severe of headaches, then those [reductions in cognitive impacts] would kind of happen automatically, so that's why they seemed less important
Cognitive symptoms as a barrier to maintaining/regaining function	00-23: Even if I'm able to participate in daily activities, if I've got brain fog, I'm not completely there … there's no point in me being there if I'm not mentally there.

TABLE 10 Frequency of perceived migraine-related cognitive symptoms reported by episodic ($n = 20$) and chronic ($n = 20$) migraine interview participants during the post-headache phase of a typical migraine attack.

	Post-headache[a], *n* (%)	
Cognitive symptom	Episodic ($n = 20$)	Chronic ($n = 20$)
Trouble with concentration/focus	5 (25.0)	6 (30.0)
Confusion/disorientation	1 (5.0)	1 (5.0)
Avoid making decisions	3 (15.0)	3 (15.0)
Fogginess	5 (25.0)	12 (60.0)
Losing words/speech	3 (15.0)	6 (30.0)
Memory	5 (25.0)	6 (30.0)
Slurred words/speech	0 (0.0)	0 (0.0)
Difficulty processing information	2 (10.0)	5 (25.0)

[a]Also referred to as postdrome.

with migraine.[11,13] For example, this study captured a frequency of cognitive symptoms (e.g., 87% during headache) that closely mirrors the results of a previously published prospective survey-data report (e.g., 90% during headache).[10] The current results also agree with previously published conclusions about the outsized expression of cognitive symptoms during the pre-headache and headache phases of the migraine attack with variable persistence of cognitive symptoms in the post-headache period.[14–16] Our qualitative results also provide additional context with which to interpret previously published research correlating cognitive symptoms experienced by patients and changes seen on functional neuroimaging.[31]

Interview data from this study also suggest that return to usual function is a primary priority for individuals living with migraine and that this desire to function at home, school, work, and in social settings underlies the wish for a reduction in cognitive symptoms as an outcome of migraine treatment. This thematic qualitative finding aligns with previously published patient-reported diary data, which placed cognitive symptoms as second, only to pain, in their contribution to attack-related disability.[18]

Cognitive symptoms as a predictor of the headache phase was another corroborated theme, reflected both in the qualitative analysis of this study and in a previously published examination of electronic migraine diary data.[15] In addition, the key manifestations of cognitive symptoms reflected in this study's qualitative analysis (i.e., speech/language, sustained attention, executive function, memory) are further substantiated through a collection of previously published studies reporting similar patterns in patient-reported and testing-based cognitive deficits, including speech difficulties, impaired thinking, distraction, issues with concentration, difficulty with reasoning, and problems with working memory and verbal learning.[16,17,32–35]

In addition to corroborating previous work, this study also contributes novel, in-depth, qualitative insights about cognitive symptoms and migraine. It presents (1) patient perspectives supporting cognitive symptoms as a priority for treatment; (2) a detailed look at the expression of cognitive symptoms within the phases of the attack as well as an examination of cognitive symptoms during the interictal period; and (3) preliminary evidence on the co-occurrence of cognitive symptoms in the pre-headache, headache, post-headache, and interictal phases. The study also offers a valuable contribution in describing how attack-related impairments to speech/language, sustained attention, executive function, and memory are expressed in day-to-day life and perceived by the people who experience them. Finally, this qualitative analysis captured new evidence on the *implications* of migraine-related cognitive symptoms within the context of people's real lives, responsibilities, values, preferences, and challenges.

This study has several limitations. Recruitment through CHAMP's network likely yielded a more severely impacted (longer duration of treatment and more frequent migraine attacks), aggressively treated, and highly health-literate sample of people living with migraine, as demonstrated by research conducted using similar sampling methods.[36] Thus, it is possible that the experience of the study sample may vary from that of the broader migraine population. Because we recruited from a voluntary patient advocacy organization (CHAMP), our sample may be enriched with people who have more severe disease, who have sought more medical care, who are

educated through CHAMP and other scientific and patient advocacy organizations, and who are better attuned to their symptom experience than the general migraine population because of the education they receive through CHAMP and other scientific and patient advocacy organizations, among other factors; however, the MiCOAS project is intended to develop patient-reported outcome measures for use in clinical trials of migraine therapies. This includes trials in both EM and CM and trials of both acute and preventive medications. People who participate in clinical trials are also not broadly representative of the people with migraine in the general population. They are often recruited from neurology or headache subspecialty practices where clinical trials are conducted. Both acute and prevention trials require a minimum number of monthly migraine headache days (MMDs). In acute treatment, this is to optimize the chances of the patient having an eligible acute attack in close proximity to training for the study. For prevention trials, a lower bound on MMDs is designed to provide down-side sensitivity, an opportunity to reduce MMDs without eliminating them completely. People with ≥4 moderate or severe MMDs constitute about 20% to 25% of the total migraine population in the United States while people with CM constitute about 7%–8% of the total US migraine population;[6,37] however, in clinical practice, patients tend to have a higher number of MMDs and in specialty headache care, the majority of patients with migraine have CM. While not fully representative of the general migraine population, we believe our study sample appropriately targeted the groups we wanted to study, and also shed light on the experiences of people with migraine who seek medical care and may use prescription treatments. The interview sample was stratified for EM and CM, migraine with and without aura, and socioeconomic variables, but subsample sizes were insufficient to robustly detail differences across groups. Since we did not ask about aura directly or as an independent phase, we do not know if some symptoms were attributed to the pre-headache or headache phases which may have been due to aura. For example, language difficulties in the pre-headache phase could be premonitory or a manifestation of aura.[38] Without a subsample analysis, our study was unable to distinguish whether participant-reported language deficits are premonitory in nature or related to aura. We did not assess for the presence of cognitive symptoms during the premonitory phase when not followed by headache. It is not possible to determine if cognitive symptoms were due to migraine or were iatrogenic. This study assessed subjective cognition through patient self-report using patient perceptions of cognitive deficits perceived to be due to migraine. Patient perceptions may not align with objective measures of cognition obtained using cognitive tests known to assess specific cognitive domains, and the origin of cognitive symptoms cannot be verified.[39] For example, self-reported difficulties in processing spoken language could reflect aphasia or inattention. Migraine comorbidities, such as depression and anxiety, may also influence subjective cognition.[35,40] Although interviews explored migraine-related impacts on emotions and mood, we did not screen participants for depression or anxiety, and are thus unable to assess the relationship between these psychiatric comorbidities and the cognitive symptoms reported by the study sample. Future work should more explicitly explore the role of depression and anxiety as mediators or moderators of cognitive symptoms in people with EM and CM.

It is also not possible to discern whether cognitive difficulties were due to side effects of treatment, a result of ineffective treatment, or unrelated to treatment. Finally, bringing wider attention to the role of cognitive symptoms in migraine may unintentionally intensify stigmatizing views of persons with migraine. This study was not designed to explore this issue. Future work focused on cognition and migraine should consider the role of stigma.

CONCLUSION

The collection and analysis of interview data from the MiCOAS qualitative study further established the importance of continued monitoring, assessment, and treatment of cognition-related outcomes in the migraine population. The results of this study corroborate existing evidence on the frequent and burdensome nature of cognitive symptoms, and expounds on the real-life implications of cognitive interference from the perspective of persons living with migraine. This study provides evidence to support the role of cognitive symptoms in migraine-related disability and daily function, establishing it as an appropriate target for therapeutic development and evaluations of treatment efficacy.

AUTHOR CONTRIBUTIONS

Study concept and design: Maya T. Gerstein, R. J. Wirth, Carrie R. Houts, James S. McGinley, Dawn C. Buse, Kelly P. McCarrier, Richard B. Lipton. *Acquisition of data*: Maya T. Gerstein, R. J. Wirth, Alyssa A. Uzumcu, Kelly P. McCarrier, Alexis Cooke, Nancy M. Touba. *Analysis and interpretation of data*: Maya T. Gerstein, Alyssa A. Uzumcu, Kelly P. McCarrier, Alexis Cooke, Nancy M. Touba. *Drafting of the manuscript*: Maya T. Gerstein. *Revising it for intellectual content*: R. J. Wirth, Carrie R. Houts, James S. McGinley, Dawn C. Buse, Kelly P. McCarrier, Tracy K. Nishida, Peter J. Goadsby, David W. Dodick, Richard B. Lipton. *Final approval of the completed manuscript*: Maya T. Gerstein, R. J. Wirth, Richard B. Lipton.

ACKNOWLEDGMENTS

The authors would like to thank the US Food and Drug Administration including Robyn Bent, MS, the Coalition for Headache and Migraine Patients (CHAMP) for assisting in recruitment, and Elizabeth Nicki Bush, MHS, Roger K. Cady, MD, Katie M. Golden, BA, and Walter F. Stewart, PhD, MPH.

FUNDING INFORMATION

This manuscript was supported by the Food and Drug Administration (FDA) of the US Department of Health and Human Services (HHS) as part of a financial assistance award (UH3FD006795) totaling $1,599,834, with 100% funded by FDA/HHS. The contents are those of the authors and do not necessarily represent the official views of, nor an endorsement by, the FDA/HHS or the US Government.

CONFLICT OF INTEREST STATEMENT

Maya T. Gerstein is a full-time employee of the Agency for Healthcare Research and Quality. The views expressed in this article are those of the author and no official endorsement by the Agency for Healthcare Research and Quality, the U.S. Department of Health and Human Services, or the Federal government is intended or inferred. **Maya T. Gerstein** was a full-time employee of OPEN Health Group at the time of the study. **Alyssa A. Uzumcu, Alexis Cooke**, and **Nancy M. Touba** were full-time employees of OPEN Health Group at the time of the study. **Carrie R. Houts, Tracy K. Nishida,** and **R. J. Wirth** are full-time employees of Vector Psychometric Group, LLC. **James S. McGinley** is a full-time employee of Vector Psychometric Group, LLC, and has received honoraria/payment/reimbursement from the journal *Cephalalgia* (biostatistics editor) and the American Headache Society (teaching course). **James S. McGinley** has also received research grants/support from Amgen, Inc., and the National Headache Foundation. **Dawn C. Buse** is a part-time employee of Vector Psychometric Group, LLC, and has received grant support from the National Headache Foundation and grant support and honoraria from Abbvie/Allergan, Amgen, Biohaven, Lilly, Lundbeck and Teva. She serves on the editorial board of *Current Pain and Headache Reports*. **Richard B. Lipton** is the Edwin S. Lowe Professor of Neurology at the Albert Einstein College of Medicine in New York. He receives research support from the NIH: 2PO1 AG003949 (mPI), 1RF1 AG057531 (Site PI), RF1 AG054548 (Investigator), 1RO1 AG048642 (Investigator), R56 AG057548 (Investigator), RO1 AG060933 (Investigator), RO1 AG062622 (Investigator), 1UG3FD006795 (mPI), 1U24NS113847 (Investigator), U01 AT011005 (Investigator), 1R01 AG075758 (Pending—Investigator), 1R01 AG077639 (Pending—Investigator), K23 NS107643 (Mentor). He also receives support from the Migraine Research Foundation and the National Headache Foundation, and research grants from TEVA, Satsuma, and Amgen. He serves on the editorial board of *Neurology*, is senior advisor to *Headache*, and associate editor for *Cephalalgia*. He has reviewed for the NIA and NINDS, holds stock and stock options in Biohaven Holdings as well as stock options in Manistee; serves as consultant, advisory board member, or has received honoraria from: Abbvie (Allergan), American Academy of Neurology, American Headache Society, Amgen, Avanir, Axsome, Biohaven, BioVision, Boston Scientific, Dr. Reddy's (Promius), electroCore, Eli Lilly, eNeura Therapeutics, Equinox, GlaxoSmithKline, Grifols, Lundbeck (Alder), Merck, Pernix, Pfizer, Satsuma, Supernus, Teva, Trigemina, Vector, and Vedanta. He receives royalties from *Wolff's Headache*, 7th and 8th editions, Oxford Press University, 2009, Wiley and Informa. **Peter J. Goadsby** reports, over the last 36 months, grants and personal fees from Eli Lilly and Company, a grant from Celgene, and personal fees from Eon Biopharma, Allergan/Abbvie, Amgen, BioDelivery Sciences International, Biohaven Pharmaceuticals Inc., CoolTech LLC, Dr. Reddy's, Epalex, GlaxoSmithKline, Impel Neuropharma, Lundbeck, Novartis, Praxis, Sanofi, Satsuma, and Teva Pharmaceuticals, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI MedPartners, Vector Metric, and fees for educational materials from CME Outfitters, Omnia Education, WebMD, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate, and Wolters Kluwer, and for medicolegal advice in headache, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee. **David W. Dodick** reports interests under the following categoris. Consulting: Amgen, Allergan, Abbvie, Lundbeck, Biohaven, Pfizer, Atria Health, CapiThera Ltd., Cerecin, CoolTech, Ceruvia Lifesciences LLC, Ctrl M, Allergan, Biohaven, GSK, Lundbeck, Eli Lilly, Novartis, Impel, Salvia, Satsuma, Theranica, WL Gore, Nocira, Perfood, Praxis, AYYA Biosciences, Revance. Payment or honoraria for lectures, presentations, educational events: Amgen, Novartis, Eli Lilly, Teva, Allergan, Abbvie, Lundbeck, Biohaven, Pfizer. Participation on a Data Safety Monitoring Board or Advisory Board: Amgen, Novartis, Eli Lilly, Allergan, Abbvie, Lundbeck, Biohaven. Honoraria: Vector Psychometric Group, Clinical Care Solutions, CME Outfitters, Curry Rockefeller Group, DeepBench, Global Access Meetings, KLJ Associates, Academy for Continued Healthcare Learning, Majallin LLC, Medlogix Communications, MJH Lifesciences, Miller Medical Communications, WebMD Health/Medscape, Wolters Kluwer, Oxford University Press, Cambridge University Press. Research support: Department of Defense, National Institutes of Health, Henry Jackson Foundation, Sperling Foundation, American Migraine Foundation, Patient-Centered Outcomes Research Institute (PCORI). Leadership or fiduciary role in other board, society, committee or advocacy group, paid or unpaid: American Migraine Foundation, American Brain Foundation, International Headache Society Global Patient Advocacy Coalition. Stock options/shareholder/patents/Board of Directors: Aural analytics (options), ExSano (options), Man and Science (options), Healint (options), Theranica (options), Second Opinion/Mobile Health (options), Epien (options/board), Nocira (options), Matterhorn (shares/board), Ontologics (shares/board), King-Devick Technologies (options/board), Precon Health (options/board), AYYA Biosciences (options), Atria Health (options). Patent 17189376.1- 1466:v, Title: Botulinum Toxin Dosage Regimen for Chronic Migraine Prophylaxis (non-royalty bearing). Patent application submitted: Synaquell (Precon Health).

ORCID

Maya T. Gerstein https://orcid.org/0000-0003-2035-0828
David W. Dodick https://orcid.org/0000-0002-9486-6790
Richard B. Lipton https://orcid.org/0000-0003-2652-2897

REFERENCES

1. Buse DC, Lipton RB. Global perspectives on the burden of episodic and chronic migraine. *Cephalalgia*. 2013;33:885-890.
2. Hu XH, Markson LE, Lipton RB, Stewart WF, Berger ML. Burden of migraine in the United States: disability and economic costs. *Arch Intern Med*. 1999;159:813-818.
3. American Headache Society. The American Headache Society position statement on integrating new migraine treatments into clinical practice. *Headache*. 2019;59:1-18.
4. Buse DC, Scher AI, Dodick DW, et al. Impact of migraine on the family: perspectives of people with migraine and their spouse/

domestic partner in the CaMEO study. *Mayo Clin Proc*. 2016;91:596-611. doi:10.1016/j.mayocp.2016.02.013
5. Lipton RB, Buse DC, Adams AM, Varon SF, Fanning KM, Reed ML. Family impact of migraine: development of the impact of migraine on partners and adolescent children (IMPAC) scale. *Headache*. 2017;57:570-585.
6. Lipton RB, Stewart WF, Diamond S, Diamond ML, Reed M. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. *Headache*. 2001;41:646-657.
7. Gil-Gouveia R, Martins IP. Cognition and cognitive impairment in migraine. *Curr Pain Headache Rep*. 2019;23:84.
8. Drummond PD, Lance JW. Neurovascular disturbances in headache patients. *Clin Exp Neurol*. 1984;20:93-99.
9. Lance J, Goadsby P. *Mechanism and Management of Headache*. Elsevier; 2005.
10. Gil-Gouveia R, Oliveira AG, Martins IP. Subjective cognitive symptoms during a migraine attack: a prospective study of a clinic-based sample. *Pain Physician*. 2016;19:E137-E150.
11. Gil-Gouveia R, Oliveira AG, Martins IP. Cognitive dysfunction during migraine attacks: a study on migraine without aura. *Cephalalgia*. 2015;35:662-674.
12. Estave PM, Beeghly S, Anderson R, et al. Learning the full impact of migraine through patient voices: a qualitative study. *Headache*. 2021;61:1004-1020.
13. Schwedt TJ, Digre K, Tepper SJ, et al. The American registry for migraine research: research methods and baseline data for an initial patient cohort. *Headache*. 2020;60:337-347.
14. Gil-Gouveia R, Martins IP. Clinical description of attack-related cognitive symptoms in migraine: a systematic review. *Cephalalgia*. 2018;38:1335-1350.
15. Giffin NJ, Ruggiero L, Lipton RB, et al. Premonitory symptoms in migraine: an electronic diary study. *Neurology*. 2003;60:935-940.
16. Quintela E, Castillo J, Muñoz P, Pascual J. Premonitory and resolution symptoms in migraine: a prospective study in 100 unselected patients. *Cephalalgia*. 2006;26:1051-1060.
17. Gil-Gouveia R, Oliveira AG, Martins IP. Assessment of cognitive dysfunction during migraine attacks: a systematic review. *J Neurol*. 2015;262:654-665.
18. Gil-Gouveia R, Oliveira AG, Martins IP. The impact of cognitive symptoms on migraine attack-related disability. *Cephalalgia*. 2016;36:422-430.
19. McGinley JS, Houts CR, Nishida TK, et al. Systematic review of outcomes and endpoints in preventive migraine clinical trials. *Headache*. 2021;61:253-262.
20. Houts CR, McGinley JS, Nishida TK, et al. Systematic review of outcomes and endpoints in acute migraine clinical trials. *Headache*. 2021;61:263-275.
21. Lipton RB, Dodick D, Sadovsky R, et al. A self-administered screener for migraine in primary care: the ID migraine validation study. *Neurology*. 2003;61:375-382.
22. Ewing JA. Detecting alcoholism. The CAGE questionnaire. *JAMA*. 1984;252:1905-1907.
23. Silberstein SD, Lipton RB, Dodick DW. Operational diagnostic criteria for chronic migraine: expert opinion. *Headache*. 2014;54:1258-1266.
24. Turner-Bowker DM, Lamoureux RE, Stokes J, et al. Informing a priori sample size estimation in qualitative concept elicitation interview studies for clinical outcome assessment instrument development. *Value Health*. 2018;21:839-842.
25. Buse DC, Gerstein MT, Houts CR, et al. Impact of the COVID-19 pandemic on people living with migraine: results of the MiCOAS qualitative study. *Headache*. 2022;62:284-293.
26. What is ATLAS.ti. *ATLAS.ti*. https://atlasti.com/product/what-is-atlas-ti/
27. Miles MB, Huberman AM. *Qualitative Data Analysis: An Expanded Sourcebook*. 2nd ed. Sage; 1994.
28. O'Connor C, Joffe H. Intercoder reliability in qualitative research: debates and practical guidelines. *Int J Qual Methods*. 2020;19:1609406919899220.
29. Kerr C, Nixon A, Wild D. Assessing and demonstrating data saturation in qualitative inquiry supporting patient-reported outcomes research. *Expert Rev Pharmacoecon Outcomes Res*. 2010;10:269-281.
30. United States Census Bureau. *Census Bureau Releases New Educational Attainment Data*. Census.gov https://www.census.gov/newsroom/press-releases/2022/educational-attainment.html
31. Karsan N, Goadsby PJ. Imaging the premonitory phase of migraine. *Front Neurol*. 2020;11:140.
32. Farmer K, Cady R, Bleiberg J, Reeves D. A pilot study to measure cognitive efficiency during migraine. *Headache*. 2000;40:657-661.
33. Mulder EJ, Linssen WH, Passchier J, Orlebeke JF, de Geus EJ. Interictal and postictal cognitive changes in migraine. *Cephalalgia*. 1999;19:557-565; discussion 541.
34. Meyer JS, Thornby J, Crawford K, Rauch GM. Reversible cognitive decline accompanies migraine and cluster headaches. *Headache*. 2000;40:638-646.
35. Vuralli D, Ayata C, Bolay H. Cognitive dysfunction and migraine. *J Headache Pain*. 2018;19:109.
36. Morton BA, Brooks C, Lenaburg KJ, Young WB, Lipton RB, Buse DC. Treatment experiences in a high frequency sample of people with migraine: results of the Coalition for Headache and Migraine Patients (CHAMP) headache disease patient access survey. *Headache*. 2021;61:1-77.
37. Buse DC, Manack A, Serrano D, Turkel C, Lipton RB. Sociodemographic and comorbidity profiles of chronic migraine and episodic migraine sufferers. *J Neurol Neurosurg Psychiatry*. 2010;81:428-432.
38. Lucas C. Migraine with aura. *Rev Neurol (Paris)*. 2021;177:779-784.
39. Nasreddine ZS, Phillips NA, Bédirian VA, et al. The Montreal cognitive assessment, MoCA: a brief screening tool for mild cognitive impairment. *J Am Geriatr Soc*. 2005;53:695-699.
40. Lee SH, Kang Y, Cho S-J. Subjective cognitive decline in patients with migraine and its relationship with depression, anxiety, and sleep quality. *J Headache Pain*. 2017;18:77.

How to cite this article: Gerstein MT, Wirth RJ, Uzumcu AA, et al. Patient-reported experiences with migraine-related cognitive symptoms: Results of the MiCOAS qualitative study. *Headache*. 2023;63:441-454. doi:10.1111/head.14484