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ORIGINAL ARTICLE

Neural correlates of pain acceptance and the role of the cerebellum: Functional connectivity and anatomical differences in individuals with headaches versus matched controls

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Abstract

Background: Despite functional connectivity network dysfunction among individuals with headaches, no studies have examined functional connectivity neural correlates and anatomical differences in coping with headaches.

Methods: This study investigated inter-individual variability in whole-brain functional connectivity and anatomical differences among 37 individuals with primary headaches and 24 age- and gender-matched controls, and neural correlates of psychological flexibility (PF) that was previously found to contribute to headache adjustment. Participants (84% women; *M* headache severity = 4/10; *M* age = 43 years) underwent functional magnetic resonance imaging scans and completed questionnaires to examine global and subnetwork brain areas, and their relations with PF components, controlling for age, gender, education, and head-motion.

Results: Seed and voxel-based contrast analyses between groups showed atypical functional connectivity of regions involved in pain matrix and core resting-state networks. Pain acceptance was the sole PF component that correlated with the cerebellum (*x*, *y*, *z*: 28, −72, −34, *p*-false discovery rate <0.001), where individuals with headaches showed higher grey matter density compared to controls.

Conclusions: The cerebellum, recently implicated in modulating emotional and cognitive processes, was indicated to process information resembling what individuals do when practicing pain acceptance. Our findings establish for the first time this connection of the cerebellum and its role in pain acceptance. We propose that pain acceptance might be a behavioural biomarker target that could modulate problematic headache perceptions and brain networks abnormalities.

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Significance: This study highlights the potential use of emerging behavioural biomarkers in headache management, such as pain acceptance, and their role in modifying the headache experience. Notably, grey matter reorganization in the cerebellum and other known brain pain networks, could indicate brain networks that can be modified from targeted behavioural interventions to help decode the nociplastic mechanisms that predominates in headaches.

1 | INTRODUCTION

Behavioural headache interventions include coping processes (McCracken, 2020; Smitherman et al., 2015) that reduce headache disability (Dindo et al., 2014; Vasiliou et al., 2021), improve daily functioning (Vasiliou et al., 2022), quality of life (Dindo et al., 2012), and facilitate headache adjustment (Grazzi et al., 2021). A key intervention process implicated in empirically supported treatments for chronic pain (i.e. acceptance and commitment therapy [ACT]) is pain acceptance; one of the six components of the psychological flexibility (PF) model for chronic pain (McCracken, 2020). Pain acceptance refers to the willingness to experience pain while pursuing valued actions (McCracken et al., 2004). Despite the success of pain acceptance and other PF processes in pain management, their neural correlates with headache-related brain areas remains nascent.

The still limited available findings indicate brain activations in the executive and salience networks associated with acceptance (Ellard et al., 2017; Servaas et al., 2015; Smoski et al., 2015). While the extent of autonomic, cognitive, and brain resource recruitment in acceptance is unknown, existing findings suggest pain acceptance could be a key behavioural biomarker for conditions like primary headaches, involving multiple excitatory brain network. This may result from pain acceptance generating greater brain responses in networks implicated in cognitive control and attention, affecting a wide range of cortical and subcortical functions, but with less executive effort than processes like cognitive reappraisal or suppression and worry (Cary et al., 2020).

Pain neuroimaging studies indicate that processes regulating pain experiences, like pain acceptance, can decouple the sensory and cognitive/affective pain experiences whereby higher pain intensity should not always equate to higher perceptive pain experience (Gard et al., 2012; Grant et al., 2011; Hemington et al., 2018). For example, activation in the anterior/posterior insula (aINS/aMCC) regions of the salient network in which pain acceptance is implicated, suggest these areas are key for processing homeostatically relevant stimuli like headaches (Seeley, 2019). Therefore, targeting processes like pain acceptance, which reflect greater prefrontal activation and improved self-regulation, may improve self-referential cognitive processing of pain inputs (Hudak et al., 2021), leading to better pain modulation.

Similar suggestions result from studies targeting changes in pain acceptance as part of pain interventions (Aytur et al., 2021; Meier et al., 2020). Jensen et al. (2012) found that an ACT-based pain intervention increased activations in the ventrolateral prefrontal/lateral orbitofrontal cortex during a pre-post pressure-evoked pain paradigm with fibromyalgia patients, compared to wait-list controls. Smallwood and colleagues (Smallwood et al., 2016) found reductions in brain activation from pre-to-post, across key networks, including self-reflection (default mode network [DMN]), emotion (salience), and cognitive control (frontal–parietal). These findings were replicated in two other non-randomized studies with chronic musculoskeletal patients (Aytur et al., 2021; Meier et al., 2020).

Neuroimaging studies using resting-state functional connectivity (FC) show altered connectivity in regions involved in primary headache integration (anterior temporal role), affective processing (anterior cingulate cortex), headache regulation (periaqueductal grey), and functional networks, including reduced fluctuations in the default mode, executive, and salience networks (Chong et al., 2019). Brain morphology studies associate migraine with decreased grey matter volume (GMV) and diffusivity abnormalities in brainstem and migraine processing areas (Jia & Yu, 2017; Marciszewski et al., 2018). These neural correlates reflect trigeminal nociceptive inputs that can be tracked and modified (Chong et al., 2019; Lakhan et al., 2013; May, 2017; Schulte et al., 2020), indicating targeted neural structures modulated by headache experiences or coping processes.

This study investigated the neuroanatomical correlates of pain acceptance as a coping process with primary headaches. Using data from our previous randomized controlled trial (RCT) on ACT efficacy for primary headaches (Vasiliou et al., 2021), we examined all six processes of the PF model. First, we examined brain areas with altered functional connectivity without a priori consideration, employing a whole-brain voxel-based

approach to connectivity maps (Buckner et al., 2009; Martuzzi et al., 2011). Second, we examined between-group differences in brain regions and PF responses, using traditional seed-based analyses. We hypothesized that (a) global (voxel-based) functional connectivity patterns of individuals with primary headache, would differ when compared to age and gender-matched controls, and (b) that differences would include brain networks related to PF components and particularly pain acceptance.

2 | METHODS

2.1 | Participants

Participants with primary headaches (headache group) were recruited through private-care Neurologists, referrals from the Cyprus Institute of Neurology and Genetics (CING—main recruiting centre), primary care units, and via our previously conducted studies (Karademas et al., 2017; Vasiliou et al., 2018, 2019). Participants were individuals who took part in a larger headache study for which this study constituted one phase; another phase included a RCT of efficacy of a PF group-based intervention (Vasiliou et al., 2021, 2022). For this study, we only used only the baseline pre-intervention data from the headache group.

Participants in the control group consisted of individuals who were recruited from the Neurocognitive Study on Aging, a multimodal longitudinal study examining modifiable and unmodifiable factors affecting brain health and cognitive aging, such as health, genetic, psychosocial, and demographic factors (Chadjikyprianou et al., 2021). Before enrolling in the study, all eligible participants from the control group were screened for current or past headache, chronic pain conditions, neurological and psychiatric disorders and none were excluded from this screening procedure.

Inclusion criteria for the headache group consisted of adults meeting diagnostic criteria for Primary Headache based on the third edition of the International Classification of Headache Disorders-II-ICHD-III with sufficient Greek reading ability and stable head pain and pharmacotherapy status (both tracked and remained unchanged for 4 weeks before assessment; for more details see Vasiliou et al., 2021). For the control group, inclusion criteria consisted of individuals with no personal or family history of primary headache diagnosis.

Exclusion criteria for both the patient and control group consisted of the presence of unstable psychiatric or other neurological disorders (e.g., active psychosis, suicide ideation, substance misuse—particularly prophylactic, preventive, or abortive medication overuse and based on the beta version of the third edition of the international classification for headache disorders; Headache Classification Committee of the International Headache Society; Olesen, 2018). For this, we conducted a baseline assessment of the frequency and pattern of the prophylactic, preventive, or abortive medication use during the 4 week baseline period and before the magnetic resonance imaging (MRI) scanning. We also assessed for history of seizure, facial neuralgia, or other secondary headache diagnoses, and pregnancy/breastfeeding, presence of metal implants or report of claustrophobia. Finally, for the medication check, the study Neurologists assessed medical prescription history of headaches and used the set criteria, including the prophylactic use as an inclusion criteria, to assess each case's potential preventive medication overuse. The rationale for exclusion of preventive or abortive medication was that excess usage of these medications may modify neural function and pain perception that can confound the results (Hebestreit & May, 2017; Morgan, 2005). One participant from the patient group was excluded due to macroscopic brain T2-visible lesions on MRI scan and was referred for further medical examinations.

2.2 | Study procedures

For the patient group, $n = 164$ expressed an interest and initial eligibility was assessed over the phone. Interested individuals were scheduled for a screening visit at the CING, where a study Neurologist conducted a medical examination and doctoral-level Clinical Psychology trainees carried-out a psychological evaluation. The assessment included examination of inclusion and exclusion criteria and was then followed by scheduling of the MRI scan.

Participants in the control group consisted of $n = 37$ individuals without headaches who were recruited from the Neurocognitive Study on Aging (Chadjikyprianou et al., 2021). A few individuals in the control group were also recruited purposefully from the community after invitation, to match ages and genders of patients. No differences were found between the two recruitment channels of participants in the control group. Individuals who consented to participate visited our laboratory to be assessed for eligibility and complete study questionnaires before scheduling the brain scan at the MRI centre. Participants in the control group were compensated with 35€ for participation travelling expenses.

All study procedures were approved by the Cyprus National Bioethics Committee (#EEBK/EP.2013/05) and the Cyprus Office of the Commissioner for Personal

Data Protection (2.0.18/II). Also, this research was conducted in accordance with the Declaration of the World Medical Association (www.wma.net) and all individuals provided written and signed informed consent for participation.

2.3 | Behavioural measures

All participants completed the same package of behavioural measures, including, sociodemographic, headache-related characteristics, and questionnaires assessing each of the PF components following Hann and McCracken (2014) recommendations.

2.3.1 | Socio-demographics

Gender, age, educational level, family status and monthly income (in euros) were collected.

2.3.2 | Headache-related characteristics

Greek Brief Pain Inventory [G-BPI (Mystakidou et al., 2001); Original (Cleeland & Ryan, 1994)] is an 11-item measure of pain intensity (4 items) and interference (7 items), rated on a scale from 0 = no pain to 10 = pain as bad as you can imagine. For this study as per IMMPACT recommendations (Gewandter et al., 2014), we used only the pain intensity subscale (sum of four items). Cronbach's alpha was 0.78. We also used one item to assess individuals' frequency of headaches during the past month.

Medical Utilization was assessed with three items examining medical visits due to headache over the last 2 months: (a) number of headache-related visits to different physicians; (b) number of primary care visits for headache; and (c) number of emergency department visits for headache. Items are summed to an overall index of headache-related medical utilization.

The Hospital Anxiety and Depression Scale-Greek version [HADS (Michopoulos et al., 2008) original (Zigmond & Snaith, 1983)] assesses levels of Depression (HADS-dep) and Anxiety (HADS-anx) symptomatology in a 14-item questionnaire, rated on a 4-point scale, ranging from 0 to 3. Higher scores in each subscale represent higher levels of depression and anxiety symptoms, unbiased by coexisting medical conditions (Stronks et al., 2004). The Greek version indicates high reliability and validity (Michopoulos et al., 2008). In this study, Cronbach's alpha was 0.75 for depression and 0.84 for anxiety.

2.3.3 | Measures assessing PF facets

The Greek Chronic Pain Acceptance Questionnaire [G-CPAQ (Vasiliou et al., 2018); Original (McCracken et al., 2004)] assesses pain acceptance on two dimensions: (a) Activity engagement (four items), assessing the degree of engagement in meaningful activity even in the presence of pain; and (b) Pain willingness (four items), assessing the degree of experiencing pain without trying to change, control, or struggle with it. Items are rated on a 7-point Likert scale, ranging from 1 = never true to 6 = always true, and yields a total score. Higher scores on G-CPAQ (ranged from 0 to 48) reflect greater pain acceptance. The Greek version shows high reliability and adequate construct validity with theoretically related constructs (Vasiliou et al., 2018). Cronbach's alpha for this study was 0.70.

The Greek Psychological Inflexibility in Pain Scale [G-PIPS-II (Vasiliou et al., 2019); Original (Wicksell et al., 2010)] assesses psychological inflexibility (12 items, rated on a 7-point scale, ranging from 1 = never true to 7 = always true) in two distinct subscales: (a) Avoidance of pain (G-PIPS-avoid.; eight items), assessing behaviours that lead to avoidance of pain and distress and (b) Cognitive fusion (G-PIPS-fus.; four items), assessing the frequency of individuals' fusion with pain-related thoughts that lead to avoidance behaviours. Summed scores in each subscale indicate higher psychological inflexibility in pain or higher individuals' inability to behave effectively based on their chosen values due to the excessive dominance of unwanted internal experiences (e.g., thoughts, emotions, head pain) over behaviour. The scale presents with good psychometric properties in its Greek version, with sufficient reliability in its two sub-factors (Vasiliou et al., 2019). Cronbach's alpha for this study was 0.90 for the total score, 0.90 for G-PIPS-avoid, and 0.68 for the G-PIPS-fus subscales.

Experiences Questionnaire [*EQ* (Fresco et al., 2007)] is a 20-item Likert-type scale assessing decentering (14 items): individuals' ability to step back from their negative thoughts and experience them as temporal phenomena occurring in the mind (Fresco et al., 2007), and rumination (six items): a repetitive, self-focused and passive behaviour. Items range from 1 = never to 5 = happening all the time. The EQ demonstrates adequate internal consistency reliability ($\alpha = 0.83$ and 0.70, respectively) and validity with other theoretically related constructs. For this study, we only used the decentering subscale to assess the self-as-context process of the PF model (Fresco et al., 2007). Cronbach's alpha for this study was 0.90 for the decentering scale.

Committed Action Questionnaire (CAQ) (McCracken, 2013), is an 8-item measure, assessing patterns of behaviours that are intrinsically linked with

values and goals (McCracken, 2013). The scale is rated on a Likert-type scale, ranging from 0 = never true to 6 = always true. The total score reflects an individual's tendency to persist in value-driven behaviours with higher scores reflecting higher committed actions, including higher individuals' persistence and flexibility to pursue goal-directed behaviours. CAQ shows high reliability and sufficient construct validity. Cronbach's alpha for this study was 0.80.

The Valuing Questionnaire (VQ) (Smout et al., 2014) is a 10-item scale, assessing the degree to which individuals act upon their personal values over the past week. The scale uses a 7-point Likert scale, ranging from 0 = not at all true to 6 = completely true, and consists of two distinct dimensions (five items each), assessing either progress in identified values (VQ-Pr) or obstruction of valued living (VQ-Ob). Higher scores in the VQ-Pr reflect pursuing a valued living and higher scores on the VQ-Ob indicate the presence of psychological barriers (i.e., disturbing unwanted experiences, e.g., pain, thoughts, etc.) in pursuing a valued living. VQ demonstrates good convergent validity and high reliability (Smout et al., 2014). Cronbach's alpha for this study was 0.62 for VQ-Ob and 0.87 for VQ-Pr.

The Cognitive Affective Mindfulness Scale-Revised (CAMS-R) (Feldman et al., 2007) assesses affective and cognitive components of mindfulness in a 12-item questionnaire, rated on a 4-point Likert scale, ranging from 1 = rarely to 4 = almost always. Higher total scores reflect greater mindfulness qualities or individuals' ability to bring awareness to what is happening inside and around them via full engagement and non-judgmental stand in the present moment. CAMS-R shows high reliability and adequate construct validity (Feldman et al., 2007). Cronbach's alpha for this study was 0.86.

2.4 | MRI data acquisition

2.4.1 | MRI neuroimaging timing and pain experience

Participants provided momentary levels of pain, prior to, and after the MRI scan, on a scale from 0 = no headache at all to 10 = worst headache. This measure served as an assessment of headache experience and selection criterion check, allowing us to contact the MRI scan for each participant during the ictal phase of their headaches. As expected, some individuals reported momentary pain during the MRI scan. However, because we retained a 2 week baseline period where we tracked headache episode prior to the scan, all participants imaging was considered to be conducted in-between headache attacks (Skorobogatykh et al., 2019).

2.4.2 | MRI settings

MR images were acquired with a 3.0-T scanner (Achieva; Philips Medical Systems, Best, The Netherlands). The built-in quadrature Radio Frequency body coil and a phased array 8-channel head coil were used for proton excitation and signal detection, respectively. An isotropic, three-dimensional, T1-weighted rapid acquisition gradient-echo sequence (fast field echo; repetition time = 25 ms; echo time = 1.85 ms; flip angle = 30°) was utilized to acquire whole brain, transverse MR images with an acquisition/reconstruction voxel of 1.0 mm × 1.0 mm × 1.0 mm (data interpolation was not implemented in any direction to improve resolution and reduce partial volume effects).

The resting-state functional MRI (fMRI) data were acquired using a multi-echo-planar imaging sequence with echo times at 13, 30, and 47 ms (Repetition Time = 2 s, voxel size = 3.75 mm × 3.75 mm × 4.2 mm, image matrix = 64 × 64, slice thickness = 4 mm, slice spacing = 4.2 mm, flip angle = 77°, 32 oblique slices, 187 acquisitions per run), during which participants were instructed not to think of anything in particular and to keep their eyes open. After the scanning session, participants confirmed they had kept their eyes open during the scan and had not fallen asleep. None of the participants underwent an MRI under general anaesthesia or sedation. Participants' head motion was minimized using foam pads placed around the head along with a forehead strap. We employed the same scanner and the same scanning protocol for all participants in both groups.

2.5 | Statistical analyses

2.5.1 | MRI scan analyses

Preprocessing and analyses of imaging data were performed using the Statistical Parametric Mapping 12 (SPM12) software (http://www.fil.ion.ucl.ac.uk/spm/) and Matlab 7.1 (MathWorks, Natick, MA, USA). Two patients had to be excluded from MRI analysis due to head movement and image artefacts, leaving 37 patients for the main analyses. All control group participants were retained for analysis.

Voxel-based morphometry

A whole-brain analysis using voxel-based morphometry was conducted with the aim to identify grey matter (GM) voxels with significant correlation with the behavioural measures. The MR images were first segmented for GM and white matter (WM) using SPM12 (http://www.fil.ion.ucl.ac.uk/spm). A Diffeomorphic Anatomical Registration Through Exponentiated Lie

Algebra (DARTEL) in SPM12 was performed for inter-subject registration of the GM images. During this co-registration pre-processing, local GMVs were conserved by modulating the image intensity of each voxel by the Jacobian determinants of the deformation fields computed by DARTEL. The registered images were smoothed with a Gaussian kernel (Full Width at Half Maximum [FWHM] = 8 mm) and were then transformed to Montreal Neurological Institute stereotactic space using affine and nonlinear spatial normalization implemented in SPM12 for multiple regression.

Pre-processed images were entered into a series of multiple regression models in SPM12. A statistical threshold of $p < 0.05$ corrected for the whole brain volume at a cluster level using the 'Non-Stationary Cluster Extent Correction' toolbox for SPM (http://fmri.wfubmc.edu/cms/NS-General; Hayasaka et al., 2004) was used as an indicator of regions of significant correlation. The design matrix included the study group (patients vs. controls), gender, age, and years of education of the participant as covariates of no interest. The total GMV (for GM analyses) of each individual's brain was also included in the design matrix to regress out any effect attributable to it.

Functional connectivity

First, multi-echo independent component analysis (MEICA) was applied using the ME-ICA software package (version 2.5, beta 11, https://bitbucket.org/prantikk/me-ica) (Kundu et al., 2012). This de-noising technique decomposes the signal into independent components, accepting or rejecting components based on their pattern of signal amplitude decay across echoes. The MEICA algorithm first computed a voxel-wise linear weighted combination of time series for the three echoes (with weights based on voxel-wise estimates of T2*). This step resulted in a new single time series per voxel with maximized contrast-to-noise ratio (Poser et al., 2006), which was then used as input to an independent component analysis (ICA) module that decomposed the data into a series of spatial components and their associated time series. Differences in echo time dependence profiles of artifactual (e.g., no dependence) and non-artifactual (e.g., linear dependence) ICA components were then automatically detected and the artifactual components were removed.

The fMRI data were next processed using CONN18.b (https://www.nitrc.org/projects/conn) and SPM12 (http://www.fil.ion.ucl.ac.uk/spm/). We employed the default pre-processing pipeline in the CONN toolbox which involved structural images: translation, segmentation (into WM), GM, and cerebrospinal fluid (CSF), MNI-space normalization, and smoothing (FWHM 8 mm, Gaussian), and for fMRI images: realignment and unwarp (for head motion correction), translation, slice-time correction, outlier scan detection, segmentation, and MNI-space normalization of fMRI images.

The pre-processed functional images were de-noised by regressing out the confounding effects of WM, CSF, realignment, scrubbing, and the effect of rest. CONN uses CompCor instead of global signal regression (GSR) for denoising to avoid the false anticorrelations introduced by GSR (Whitfield-Gabrieli & Nieto-Castanon, 2012). CompCor uses the first 5 principal components of ROI's time series as covariates in the general linear model during denoising. This was followed by band pass filtering (0.008–0.09 Hz) and linear detrending.

2.5.2 | Behavioural measures

All data were initially analysed to detect possible assumption violations. No variables were found to present serious deviation from normality, as assessed by inspection of histograms, skewness, kurtosis, stem-and-lead, and normality plots to justify the use of nonparametric statistics. Two-sample t-tests were used to examine differences in behavioural measures between the two groups. All comparisons were 2-tailed unless otherwise stated. Correlations of self-report measures were performed using Pearson's correlation coefficient (Pearson's *r*). Also, we assessed group differences between brain areas and the measures assessing the PF facets (G-CPAQ, G-PIPS-II, EQ, CAQ, VQ, CAMS-R), using General Linear Model (GLM) analyses. All results were considered significant at a $p < 0.05$ level, two-tailed. For the behavioural measures all statistical analyses were performed using SPSS software, version 26.0 (IBM, Armonk, NY, USA).

3 | RESULTS

3.1 | Participants' characteristics

Following eligibility assessment for the larger study, $n = 70$ individuals (out of $n = 164$) were excluded. From the remaining $n = 94$, half ($n = 47$) were randomized to receive the intervention in the next phase of the study (Vasiliou et al., 2021). From those $n = 47$ in the headache group, 37 consented to participate in the neuroimaging phase of the trial and were scheduled for a brain MRI scan. For the healthy control group, $n = 37$ were invited to participate in the neuroimaging study. From those, $n = 25$ consented to participate and were schedule for a brain mMRI scan. See Figure S1 for the CONSORT diagram.

Baseline demographic and clinical characteristics of participants are shown in Table 1. Participants in this phase were $n = 37$ individuals with a primary headache diagnosis

TABLE 1 Baseline group comparisons of demographics, headache characteristics, and PF processes.

	Groups[b]				Total
	Headache	Control			
	(*N* = 37)	(*N* = 24)			
Variable	***M* (SD) or %**	***M* (SD) or %**	***t* or χ^2**	***p*[a]**	***N* = 61 (SD)**
Demographics					
Age	43.14 (10.37)	44.58 (11.88)	−2.42	0.11	44.13 (13.82)
Gender (female)	75.70%	70.80%	0.17	0.77	74%
Educational level (# years completed)	-	-	8.60	0.09	-
Primary education (6 years)	2.70%	25.20%	-	-	11%
Middle school (9 years)	2.70%	8.30%	-	-	5%
High or vocational school (12 years)	35.10%	20.80%	-	-	30%
College/University degree (16 years)	27.10%	16.70%	-	-	23%
Postgraduate degree (>16 years)	32.40%	29.20%	-	-	31%
Headache and clinical characteristics					
Pain severity (GBPI)	4.04 (1.80)	1.19 (1.43)	6.30	0.01	2.97 (2.16)
Headache medical utilization	1.25 (2.00)	0.37 (0.82)	2.23	0.05	0.87 (1.65)
Frequency of headache/month	6.68 (5.68)	-	-	-	-
Years since headache onset	19.14 (11.28)	-	-	-	-
Headache diagnosis (IHS criteria)					
Migraine with aura (1.1)	62.7%	-	-	-	-
Chronic migraine (1.2)	7.8%	-	-	-	-
Probable migraine with aura (1.5.1)	9.8%	-	-	-	-
Frequent episodic tension type headache (2.2)	9.8%	-	-	-	-
Probable frequent episodic tension-type headache (2.4.2)	9.8%	-	-	-	-
Medical utilization	1.25 (2.00)	0.37 (0.82)	2.23	0.03	0.87 (1.65)
Depression (HADS-Dep.)	4.76 (3.03)	4.92 (3.04)	−0.16	0.87	4.81 (3.01)
Anxiety (HADS-Anx.)	8.29 (3.99)	8.15 (4.95)	0.10	0.92	8.26 (4.22)
Measures assessing PF facets					
Pain acceptance (G-CPAQ)	29.85 (7.07)	26.46 (11.40)	1.23	0.22	28.91 (8.48)
Fusion with pain (G-PIPS-Fus.)	17.97 (5.62)	19.15 (7.19)	−0.59	0.55	18.30 (6.04)
Avoidance of pain (G-PIPS-Avoid.)	21.68 (9.05)	22.77 (11.45)	−0.34	0.73	21.98 (9.66)
Decentering (EQ)	35.79 (6.47)	34.92 (9.43)	0.22	0.73	35.55 (7.31)
Committed action (CAQ)	30.97 (6.10)	32.33 (7.43)	−0.78	0.43	31.51 (6.63)
Mindfulness (CAMS-R)	35.00 (6.65)	36.85 (5.14)	−0.90	0.37	35.51 (6.27)
Values progress (VQ-Pr.)	21.12 (4.05)	27.91 (2.74)	−5.16	0.01	22.78 (4.77)
Values obstruction (VQ-Ob.)	10.15 (6.16)	6.15 (4.63)	2.11	0.05	9.04 (6.01)

Abbreviations: ACT, acceptance and commitment therapy; CAMS-R, The Cognitive Affective Mindfulness Scale-Revised; CAQ, Committed Action Questionnaire; EQ, Experience Questionnaire; GBPI, Greek Brief Pain Inventory; G-CPAQ, The Greek Chronic Pain Acceptance Questionnaire; G-PIPS-II, The Greek Psychological Inflexibility in Pain Scale; HADS, The Hospital Anxiety and Depression Scale-Greek version; HIS, International Headache Society; PF, psychological flexibility; VQ, The Valuing Questionnaire.

[a]Mean comparisons between groups were executed with Independent *t*-tests for continuous variables and χ^2 for categorical variables.

[b]The scores describe baseline characteristics of the two groups.

(*M* diagnosis years =18.09, SD = 10.71), and *n* = 24, age- and gender-matched, controls. Most participants were females (74%), married (85%), with higher education (about 50% with a college/university degree) and with medium headache severity (4 out of 10 in a VAS scale). Most of the participants had a migraine diagnosis (54.05% migraine without

aura, 8.50% migraine with aura, 11.70% chronic migraine), and 12.64% had a tension-type headache diagnosis. 8.50% reported headache medication overuse.

3.2 | Differences between groups on headache-related and behavioural measures

There were no differences between the two groups in demographic variables at baseline except for pain severity and medical utilization. When compared to controls, individuals with headaches reported higher pain severity and medical utilization (both $p < 0.05$). No significant differences were observed for depression and anxiety between the two groups ($p > 05$ for both). Furthermore, there were no significant differences for the measures assessing PF components, except for values progress (VQ-Pr) and obstruction (VQ-Ob). Patients reported less value progress ($M = 21.12$; SD = 4.05 vs. $M = 27.91$; SD = 2.74; $t_{(54)} = -6.79$, $p < 0.01$) and more presence of psychological barriers toward valued living ($M = 10.15$; SD = 6.16 vs. $M = 6.15$; SD = 4.63; $t_{(45)} = 3.99$, $p < 0.05$).

3.3 | Relationships between behavioural measures

There was an overall significant pattern of correlations between measures of pain-related variables and the PF processes for patients and not for controls. As expected, patients presented significant correlations between anxiety and depression ($r = -0.57$, $p < 0.01$), pain acceptance and depression ($r = -0.40$, $p < 0.02$), and depression and anxiety with de-centering ($rs = -0.47$ and -0.58, $p < 0.01$), committed action ($rs = -0.57$ and 0.64, $p < 0.01$), mindfulness ($rs = -0.47$ and -0.55, $p < 0.01$), value-progress ($rs = -0.44$ and -0.45, $p < 0.01$), and values obstruction ($rs = 0.33$ and 0.47, $p < 0.01$). Significant correlations for patients were also found among the measures assessing the PF components, ranging from $r = 0.33$ to 0.79. The only significant correlations found in controls were between depression with avoidance ($r = 0.80$, $p < 0.001$) and mindfulness ($r = -0.59$, $p < 0.03$), and anxiety with committed actions ($r = -0.68$, $p < 0.01$).

3.4 | Neuroimaging findings

3.4.1 | Voxel-based morphometry

A GLM examined differences between patients and controls, while correcting for multiple comparisons across the whole brain. Findings showed that the healthy controls had higher GM density in a cluster of voxels in the right hemisphere that encompasses the insula (x, y, z: 40, 12, −9) and the putamen (x, y, z: 30, 3, 4). When we run GLM analyses to examine differences in the two groups in the measures assessing the PF components, pain acceptance was the only component showing significant differences between the two groups. Specifically, in a GLM that included pain acceptance, patients presented higher GM density in the cerebellum (x, y, z: 28, −72, −34) that correlated with pain acceptance. In Figure 1, we present the cerebral cluster associated with pain acceptance and in Table 2 the anatomical brain regions associated with the cerebellum.

3.4.2 | Resting state functional connectivity

We tested group differences in resting-state functional connectivity using a voxel-wise approach via a GLM framework which first investigated whole brain differences between patients and controls in seed areas of previously identified functional connectivity networks (using the default CONN network parcellation). Next, we identified differences in functional connectivity between patients and controls in network seed areas that correlate with pain acceptance (CPAQ T-scores). The GLM included demographics (sex, age, and education) as covariates of no-interest.

Table 3 presents the functional connectivity differences in the patients, compared to controls, in the seed-based network analysis. Compared to controls, patients demonstrated increased functional connectivity between: (a) the right lateral sensorimotor network and cerebellum; (b) the left lateral visual network and right occipital pole; (c) the right salience network (rostral prefrontal cortex) and right lingual gyrus; (d) left dorsal attention network (frontal eye field) and the right frontal pole; and (e) between the anterior cerebellar network and the right occipital pole, the right superior temporal gyrus (posterior division), and the right precentral gyrus.

Compared to controls, patients demonstrated decreased functional connectivity between: (a) the left lateral visual network and the right temporal occipital fusiform area; (b) the salience network (anterior cingulate cortex) and the left insular cortex; (c) the right rostral prefrontal salience network and the right cerebellum; (d) the left dorsal attention network (frontal eye field) and the left precentral gyrus; (e) the left and right language network (inferior frontal gyrus) and the left middle temporal gyrus (posterior division); (f) the left language network (superior temporal gyrus, posterior division) with the following three areas: the left middle temporal gyrus (posterior division), the left lateral occipital cortex (superior division), and the right superior temporal gyrus (posterior division);

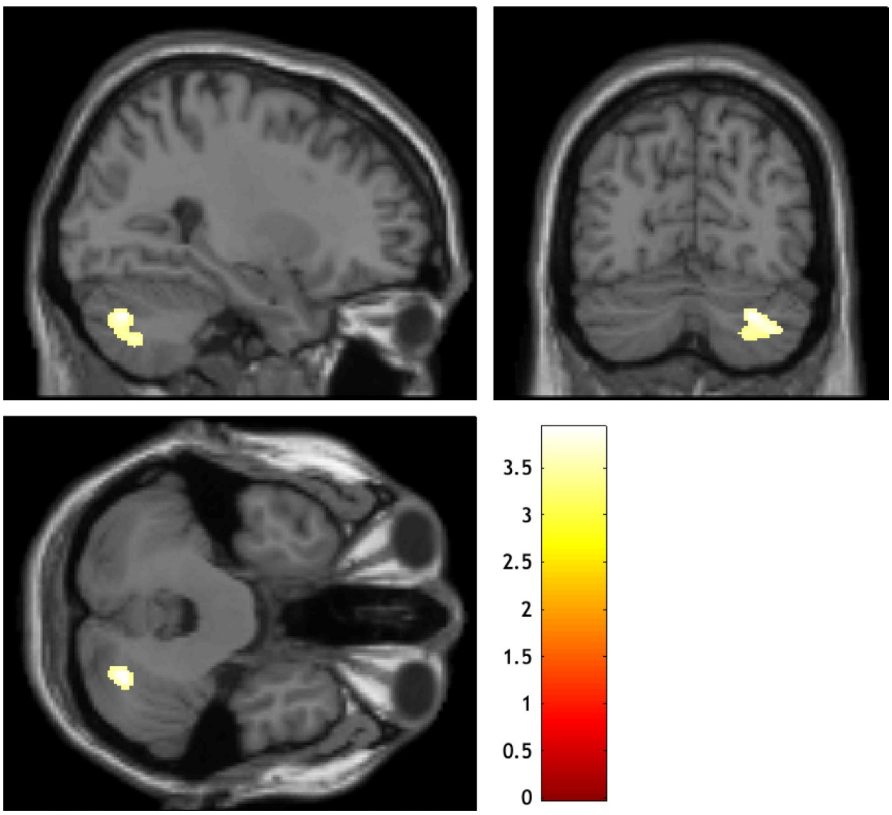

FIGURE 1 Cerebellar cluster associated with pain acceptance in voxel-based morphometry analyses.

TABLE 2 Cluster-level voxel-based morphometry results.

-	Anatomical brain region	MNI coordinates			Cluster size (mm^3)	*Z*	p_{uncorr}	p_{corr}
		x	*y*	*z*				
Control > Headache	Right putamen	31	4	3	1068	4.00	0.001	0.008
	Insular cortex	32	9	−9	-	-	-	-
	Insular cortex	40	12	−9	-	-	-	-
Pain acceptance	Cerebellum right crus I	28	−72	−34	546	3.66	0.001	0.05
	Cerebellum right crus I/II	36	−72	−39	-	-	-	-
	Cerebellum right VIIb	28	−66	−45	-	-	-	-

Note: p_{uncorr}, *p*-value uncorrected; p_{corr}, *p*-value corrected for multiple comparisons using the method of false discovery rate (FDR). Cytoarchitectonic areas were found with SPM Anatomy toolbox (Eickhoff et al., 2005; Zilles & Amunts, 2010).

and (g) the anterior and posterior cerebellar network and the left cerebellum. These findings provide evidence for altered resting-state functional connectivity in the patient group (Figure 2).

Table 4 shows brain regions with significant differences in functional connectivity when comparing patients and controls, with network seed areas that correlate with pain acceptance (CPAQ total scores). Patients were found to have increased functional connectivity compared to controls between the right lateral sensorimotor network and the right cerebellum, the left lateral visual network and the right occipital pole, the right dorsal attention network (intraparietal sulcus) and the right superior temporal gyrus (anterior division) and the right temporo-occipital middle temporal gyrus, the left fronto-parietal network (posterior parietal cortex) and right amygdala.

Conversely, compared to controls, patients exhibited decreased functional connectivity between the right DMN (medial prefrontal cortex) and the left middle temporal gyrus (anterior division), the sensorimotor network (superior) and the right superior frontal gyrus, the right salience network (rostral prefrontal cortex) with the left cerebellum, the right dorsal attention network (intraparietal sulcus) with the left cerebellum, the left and right language network (inferior frontal gyrus) and the left middle temporal gyrus (posterior division), the left language network (posterior superior temporal gyrus) and the left middle temporal gyrus (posterior division), the left lateral

TABLE 3 Between group differences in functional connectivity (Headache vs. Healthy controls seed-based network analysis).

		Seed MNI			Brain region MNI					
Network—seed	**Brain region**	***x***	***y***	***z***	***x***	***y***	***z***	***k***	***p*-unc**[a]	***p*-FDR**[a]
Headache group > Control group										
SM—lateral	Cerebellum	56	−10	29	0	−80	−28	498	**<0.001**	**0.003**
Visual—lateral	OP r	−37	−79	*10*	2	−96	6	522	**<0.001**	**<0.001**
Salience—RPFC	LG r	32	46	27	26	*−56*	6	468	**<0.001**	**0.002**
DA—FEF L	FP l	−27	−9	*64*	42	48	14	186	**0.004**	**0.029**
Cerebellar—anterior	OP r	0	−63	−30	26	−92	16	717	**<0.001**	**<0.001**
	pSTG r	0	−63	−30	64	−18	2	439	**<0.001**	**0.001**
	PreCG r	0	−63	−30	52	−8	54	433	**<0.001**	**0.001**
Control group > Headache group										
Visual—lateral	TOFusC r	−37	−79	−10	36	−56	−8	518	**<0.001**	**<0.001**
Salience—ACC	IC l	0	22	35	−32	16	4	266	**0.002**	**0.028**
Salience—RPFC	Cerebellum	32	46	27	24	−52	−36	363	**<0.001**	**0.010**
DA—FEF L	PreCF l	−27	−9	64	−22	−14	48	197	**0.003**	**0.029**
Language-IFG L	pMTG l	−51	26	2	−46	8	−28	1049	**<0.001**	**<0.001**
Language-IFG R	pMTG l	54	28	1	−54	−16	−8	441	**<0.001**	**0.003**
Language-pSTG L	pMTG l	−57	−47	15	−50	−16	−16	281	**0.002**	**0.023**
	sLOC l				−56	−70	18	251	**0.003**	**0.023**
	pSTG r				66	−22	2	195	**0.007**	**0.039**
Cerebellar—anterior	Cerebellum	0	−63	−30	−14	−82	−46	1853	**<0.001**	**<0.001**
					−22	−50	−6	639	**<0.001**	**<0.001**
Cerebellar—posterior	Cerebellum	0	−79	−32	−2	−64	−50	1076	**<0.001**	**<0.001**

Abbreviations: FEF L, frontal eye-fields, left; FP l, frontal pole, left; IC l, insular cortex, left; LG r, lingual gyrus, right; OP r, occipital pole, right; *p*-FDR, *p*-value, false discovery rate corrected; pMTG l, middle temporal gyrus, posterior division, left; PreCF l, precentral gyrus, left; PreCG r, precentral gyrus, right; pSTG r, superior temporal gyrus, posterior division, right; *p*-unc, *p*-value uncorrected; sLOC l, lateral occipital cortex, superior division, left; TOFusC r, temporal occipital fusiform cortex, right.

Note: Bold values indicate statistically significance.

[a]Cluster-corrected $p > 0.05$.

occipital cortex (superior division), and the left frontal pole, the anterior cerebellar network with the left and right cerebellum and with the left frontal pole, and lastly the posterior cerebellar network with the right cerebellum.

4 | DISCUSSION

Neuroimaging studies can indicate behavioural biomarkers that could modify the headache experience, possibly leading to better headache management. This study found bilateral functional connectivity alterations at global, subnetwork, and regional levels during resting state in a heterogeneous group of individuals with primary headaches. The findings are consistent with the relevant literature pointing to brain network alterations, as indicated by the atypical functional connectivity of regions, associated with the expected pain matrix (Lee et al., 2019; Yang et al., 2018), and multiple core resting state networks, including the executive, attention, limbic, salience, sensorimotor, visual, and DMNs (Cao et al., 2022; Ferrari et al., 2015; Xue et al., 2012). We also identified a neural correlation between pain acceptance as a potential behavioural biomarker and the activation of the cerebellum (Schmahmann, 2019).

Pain acceptance exhibited differential effects between the two groups on GMV, with the group of patients with primary headaches exhibiting higher GM density volume (GMV) in the cerebellum. The cerebellum has been traditionally linked with regulating movement (Timmann et al., 2010) and managing processes of learning and predicting adjustments of tasks (Guell, Gabrieli, & Schmahmann, 2018). New evidence implicates the cerebellum subserving sensory, cognitive, affective, and autonomic functions (Carta et al., 2019; Schmahmann, 2019), as well as anatomically altered brain morphology in individuals with headaches (Hu et al., 2015; Jia & Yu, 2017). Our findings are in line

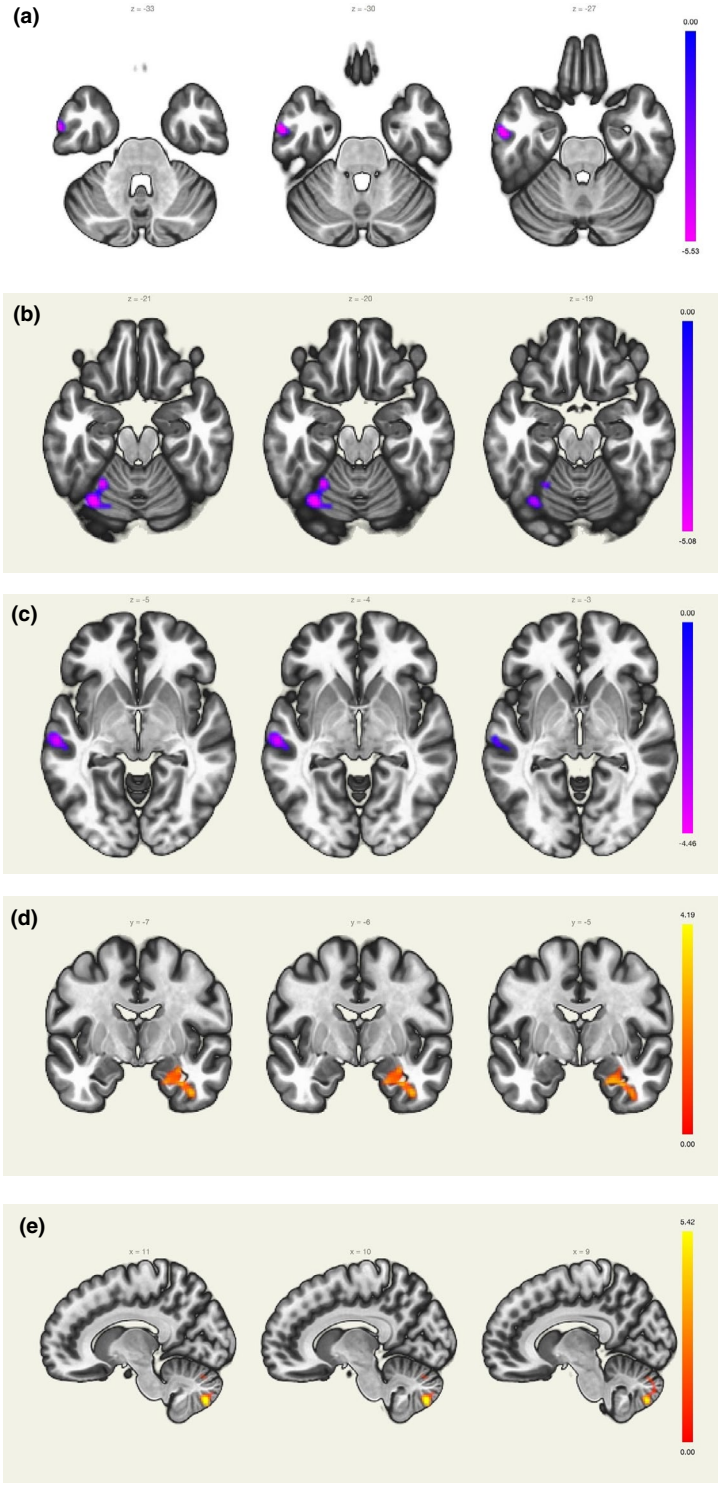

FIGURE 2 Functional connectivity differences correlated with pain acceptance in patients versus controls. (a) Increased DMN-MPFC seed functional connectivity with aMTG in controls compared to patients. (b) Increased DA-IPS seed functional connectivity with cerebellum in controls compared to patients. (c) Increased language-IFG seed functional connectivity with pMTG in controls compared to patients. (d) Increased FP-PPC seed functional connectivity with amygdala in patients compared to controls. (e) Increased SM—lateral seed functional connectivity with cerebellum in patients compared to controls. aMTG, middle temporal gyrus (anterior division); DA-IPS, dorsal attention intraparietal sulcus; DMN-MPFC, default mode network medial prefrontal cortex; FP-PPC, fronto-parietal posterior parietal cortex; language-IFG, inferior frontal gyrus; pMTG, middle temporal gyrus (posterior division); SM, sensori-motor.

with the literature, indicating an increased GMV in the posterior part of the cerebellum (Maleki et al., 2012; Mehnert & May, 2019; Schmidt-Wilcke et al., 2008). The implication of the role of the cerebellum in computing cognitive control and emotional processing information (Schmahmann, 2019) may explain the observed neural correlations between pain acceptance and cerebellum, potentially suggesting a modulating role of this brain area in headache perception (Ruscheweyh et al., 2014). New evidence indicates that the cerebellum is activated as a result of visceral, compared with somatic pain (Claassen et al., 2020). This visceral activation of the cerebellum may also explain the observed connection between the cerebellum and pain acceptance.

A recent meta-analysis (Keren-Happuch et al., 2014; Van Overwalle et al., 2015) provide strong evidence about the role of the cerebellum and its involvement in cognitive and executive behaviours that resemble what

TABLE 4 Brain regions with significant functional connectivity differences with network seeds for pain acceptance (CPAQ total scores) of Headache vs. Healthy controls.

		Seed MNI			Brain region MNI					
Network—seed	**Brain region**	***x***	***y***	***z***	***x***	***y***	***z***	***k***	***p*-unc**	***p*-FDR**
Headache group > Control group										
SM—lateral	Cerebellum	56	−10	29	10	−78	−46	850	**<0.001**	**<0.001**
Visual—lateral	OP r	−37	−79	10	2	−94	6	320	**<0.001**	**0.017**
DA—IPS	aSTG	39	−43	52	66	2	−4	333	**<0.001**	**0.015**
	toMTG	39	−43	52	70	−42	−12	242	**0.003**	**0.030**
FP—PPC	Amygdala	−46	−58	49	38	−6	−36	276	**0.002**	**0.048**
Control group > Headache group										
DMN—MPFC	aMTG	1	55	−3	−60	6	−30	247	**0.002**	**0.038**
SM—superior	SFG	0	−31	67	18	4	60	330	**<0.001**	**0.017**
Salience—RPFC	Cerebellum	32	46	27	−26	−50	−36	424	**<0.001**	**0.003**
DA—IPS	Cerebellum	39	−42	54	−34	−66	−20	303	**0.001**	**0.019**
Language—IFG	pMTG l	−51	26	2	−60	−20	−4	311	**<0.001**	**0.021**
Language—IFG	pMTG l	54	28	1	−56	−14	−8	607	**<0.001**	**<0.001**
Language—pSTG	pMTG l	−57	−47	15	−54	−48	0	508	**<0.001**	**0.002**
	sLOC l	−57	−47	15	−5	−68	18	223	**0.004**	**0.040**
	FP l	−57	−47	15	−18	46	20	209	**0.005**	**0.040**
Cerebellar-anterior	Cerebellum	0	−63	−30	18	−72	−52	2596	**<0.001**	**<0.001**
	Cerebellum				−6	−46	−10	646	**<0.001**	**<0.001**
	FP r				40	42	26	210	**0.005**	**0.043**
Cerebellar-posterior	Cerebellum	0	−79	−32	14	−50	−46	714	**<0.001**	**<0.001**

Abbreviations: aMTG, anterior division of middle temporal gyrus; aSTG, anterior division of superior temporal gyrus; Cer, cerebellar network; CPAQ, Chronic Pain Acceptance Questionnaire; DA, dorsal attention network; DMN, default mode network; FP l, frontal pole left; FP r, frontal pole right; FP, fronto-parietal network; OP r, occipital pole, right; pMTG l, middle temporal gyrus posterior division left; SFG, superior frontal gyrus; sLOC l, lateral occipital cortex, superior division left; SM, sensorimotor network; toMTG, temporooccipital middle temporal gyrus.

Note: Bold values indicate statistically significance.

individuals do when practicing pain acceptance. Pain acceptance involves adopting an open attitude toward pain without trying to eliminate or avoid it, as well as maintaining a flexible pattern of activity even in the presence of pain (McCracken et al., 2004; Vasiliou et al., 2018). Van Overwalle et al. (2015) documented that the cerebellum is activated in processing information called "*event mentalizing*" that encompass momentary intentions and beliefs, resembling what individuals do when practicing pain acceptance (McCracken et al., 2004). For example, it includes making the choice to make room/give some "space" for the experience of headache (e.g., have a headache and not cancelling a social activity; McCracken et al., 2004). Additionally, the cerebellum is also activated when individuals engage in purposeful actions that align with ones stated values, a process named by Van Overwalle et al. (2015) as "person mentalizing" and bears similarities to practicing pain acceptance (McCracken et al., 2004).

Further evidence about the neural correlation of pain acceptance shows an activation of sub-areas of the cerebellum in processing behaviours, resembling pain acceptance. Recent evidence shows an activation of three sub-areas of the cerebellar posterior lobe (including lobule VI and Crus I and lobules VIIb and IX/X) (Guell, Gabrieli, & Schmahmann, 2018) that are involved in non-primary motor processing, including meta-cognitive function and awareness (Claassen et al., 2020; Guell, Schmahmann, et al., 2018; Mehnert & May, 2019; Qin et al., 2019; Stoodley & Schmahmann, 2018). These processes resemble what individuals do when practicing pain acceptance (Goldin et al., 2019), such as getting a meta-cognitive curiosity about emotions seen as transient phenomena (Goldin et al., 2019). Moreover, these sub-areas are activated during sensory discrimination tasks of movements (Claassen et al., 2020; Restuccia et al., 2006) and responses to visceral, compared with somatic pain (Claassen et al., 2020); all behaviours

relevant to pain acceptance (e.g., individuals engage in behaviours toward value-based activities even in the presence of headache).

Further evidence about the neural connection of pain acceptance with the cerebellum are supported by recent research from the Human Connectome Project (Guell, Gabrieli, & Schmahmann, 2018), showing cerebellar activation during processes involving expansion of awareness to non-painful stimuli (Dindo et al., 2015; Foote et al., 2016; Kratz et al., 2017; Lillis et al., 2017). Evidence from the dynamic pain conectome project indicates that individuals with higher levels of pain might experience altered pain-related cognition because the DMN and sensorimotor networks (SMN) are abnormally functionally connected within-DMN connectivity. Practicing resilience may influence the impact of emotional event (e.g., pain inputs) by modifying pain related cognition in such way so that pain adaptation occurs. Pain acceptance is theorized to reduce the hyperconnectivity at this level of networks—the DMN and SMN that during pain processing function, abnormally (Cao et al., 2022; Messina et al., 2021).

The insights gained in the current investigation may be useful to understand further the neural interaction of certain behavioural interventions for headaches. For example, psychological interventions, such as ACT (Hayes et al., 2011; McCracken et al., 2022) show improvements in daily functioning owing to pain acceptance (Cathcart et al., 2014; Dindo et al., 2014; Grazzi et al., 2021; Raggi et al., 2018; Vasiliou et al., 2021, 2022; Wells et al., 2014), potentially opening up a new line of research toward the neural correlations of pain acceptance or other key psychological processes, such as activity pacing.

Our findings are noteworthy, yet exploratory and speculative in nature, thus, there are several limitations and future directions to be discussed. Firstly, our sample included a community mixed headache group, and we did not examine how the neural correlations might be in individuals with different headache diagnoses (e.g., migraine, tension-type headache, medication-overuse headaches) or subpopulations (e.g., male and females or older and younger individuals) (Xin et al., 2019). Similarly, we did not exclude individuals who had in addition to headache other comorbid chronic pain conditions, which research indicates may show different brain network FC patterns (Davis et al., 2017; Martucci & Mackey, 2018; Morton et al., 2016; Van Der Miesen et al., 2019). We also did not conduct group-based analyses of headache type (e.g., migraine with aura, migraine without aura, tension type headache), and with distinct frequencies (episodic migraine and chronic migraine) which constitutes a logical next step, given recent literature indicating distinct fMRI signatures (Chou et al., 2023; Faragó et al., 2017; Kincses et al., 2019; Wang et al., 2022).

Furthermore, we only examined the topography of pain acceptance with neural correlates during rest, without exploring how the cerebellum reacts during pain acceptance practice in individuals undergoing a resting state fMRI scan. There is still a debate about the consistency of findings, indicating neural correlates between certain headache coping techniques (e.g., pain acceptance) and increases in GMV following a sensory input. Indeed, these neural correlates result in more diffuse perceptual experiences (e.g., event and person mentalizing) which are more subtle to be captured or observed and need a more robust sample and/or refined methods (Mehnert & May, 2019). They also involve the severity and disease duration of the headache experience which often is not controlled. Finally, the findings regarding comparisons with seeds in areas correlated with pain acceptance may have been driven by other reasons rather than pain acceptance itself, since that did not differ between patients and controls (reverse inference bias; see Davis et al., 2017). However, we note that while pain acceptance scores did not reach statistical significance, subtle, non-significant differences in how the two groups experience and cope with pain could still be present and may manifest in the observed brain connectivity patterns.

While decreases in GMV are noted in headaches, especially in the frontal cortex and cingulate gyrus (Jia & Yu, 2017; Neumann et al., 2023; Schmidt-Wilcke et al., 2008), our study suggests increased GMV and its neural correlations with pain acceptance. Given the main inhibitory role of the cerebellum in nociception (Ruscheweyh et al., 2014), one could speculate that the increased GMV, observed in the cerebellar microstructures of our sample and its neural correlations with headache acceptance may be the result of a complex integration of trigeminal nociception and multimodal information integration due to nociplastic pain (Kuner & Flor, 2017). This indicates the need for examining how brain network dynamics correlate with behavioural biomarkers for headaches (Kotikalapudi et al., 2023; Paban et al., 2019), not just pain acceptance but expanding on other potential components of the PF model (e.g., values and mindfulness), and exploring multi-scale topological interactions of brain activations and behavioural responding (Betzel & Bassett, 2017; Messina et al., 2021).

In conclusion, this study delineated a certain neural correlation between headache acceptance and a specific altered brain morphology in the cerebellum. It underscores the cerebellum's role in pain circular networks and its contribution to higher-order functions, specifically in regulating fronto-cerebellar connections. The findings pave the way of personalized non-pharmacological

interventions where behavioural biomarkers can serve as indicators of normalizing targeted excitatory brain networks in headaches.

AUTHOR CONTRIBUTIONS

VSV led the writing of this manuscript, drafted the introduction, methods, and discussion, and revised the manuscript. NK conducted the neuroimaging data analyses and wrote part of the results. YC and SP conducted the clinical assessments of the sample and recruitment. FC provided the control group and assisted in MRI scanning protocol. EH supervised the neuroimaging scanning. IS developed the full MRI protocol and assisted in data interpretation. MK concepted the study, reviewed the manuscript, and provided overall supervision of the project. All authors conceived and approved the manuscript.

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CONFLICT OF INTEREST STATEMENT

VSV have consultancy/advisory board with Wanax Ltd., Behavioural Health Care solutions and is an Associate editor of the Journal of Contextual and Behavioural Science (JCBS). No other conflicts of interest are declared.

DATA AVAILABILITY STATEMENT

All the data are available upon request from the corresponding author.

ANALYSIS PREREGISTRATION

The conducted research study was not *preregistered with an analysis plan* in an independent, institutional registry, but a previous version of the final submitted manuscript has been uploaded in the OSF repository: https://osf.io/4n8kc.

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