Perceiving less or perceiving unreliably? Disentangling thermosensory sensitivity and precision in the contexts of ageing and neuropathy

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Abstract

Thermal perception is determined not only by sensitivity but also by precision, yet the latter is often overlooked in thermosensation and pain research. This study examined how ageing and diabetic polyneuropathy (DPN) affect the sensitivity and precision of thermal perception and whether combining these parameters can aid in distinguishing patients from healthy controls. Using a Bayesian hierarchical modelling approach, we estimated psychometric function thresholds (sensitivity) and slopes (precision) for cold detection, warm detection, cold pain, and heat pain in 86 healthy adults (aged 21–80) and 34 patients with DPN. We assessed age- and neuropathy-related effects on these parameters. Using simulated classification analyses, we also tested their utility in discriminating patients from controls. Ageing was associated with elevated detection and cold pain thresholds and reduced precision of cold detection. Patients with DPN showed similar patterns: higher detection thresholds and lower cold detection slopes while pain-related parameters were largely unaffected. These findings indicate that ageing and neuropathy produce qualitatively similar changes in thermosensory function, particularly affecting cold detection sensitivity and precision. Classification based on detection thresholds and cold detection slope successfully discriminated patients from controls, with cold detection slope offering the best performance. Combining threshold and slope parameters did not significantly improve classification accuracy. Accurate classification was not possible based on pain thresholds and slopes. Modelling both thresholds and slopes provides a more comprehensive view of sensory decline and may enhance the detection of early or subtle sensory dysfunction.

Keywords: Thermosensation, Pain, Ageing, Neuropathy, Diabetic polyneuropathy, Small fibre neuropathy, Diabetes mellitus, QST, Psychophysics, Thermal threshold, Psychometric Function, Bayesian modelling

Introduction

Sensitivity and precision are fundamental parameters of sensory processing, determining which stimuli we are able to feel and how we perceive them. Sensitivity can be quantified by psychophysical thresholds, the smallest stimulus intensity that is perceived at least half of the time. Precision, indexed by the slope of the psychometric function relating stimulus intensity to perception probability, reflects the reliability of perceptual judgements. A steep slope indicates a clear boundary between perceived and non-perceived intensities, whereas a shallow slope reflects greater variability in perception. Thresholds are routinely investigated in thermosensation and pain studies but slopes are usually overlooked. However, the assessment of both threshold (sensitivity) and slope (precision) would offer complementary information on how individuals detect and interpret thermal stimuli, potentially revealing differences that remain hidden when focusing on thresholds alone.

Ageing leads to progressive changes in somatosensory function, including thermosensation and nociception. Older adults often exhibit elevated thermal detection and pain thresholds, suggesting that they are less sensitive to temperature changes [18,21,34,41]. These age-related differences may stem from factors such as diminished peripheral nerve conduction velocity, reduced density of cutaneous receptors, and alterations in central sensory processing [7,11,24,32].

Thermal thresholds are often further elevated in patients with diabetic polyneuropathy (DPN), a frequent complication of *diabetes mellitus* [30]. In these patients, chronic hyperglycemia and hyperlipidemia lead to progressive nerve damage affecting all types of peripheral nerve fibres, including those subserving thermosensation and nociception [14,37]. As a result, individuals with DPN exhibit decreased conduction velocities, reduced intra-epidermal nerve fibre density, and aberrant patterns of spontaneous activity, which contribute to these changes in thermal perception [14,30,37].

Although the literature extensively documents how both healthy ageing and DPN affect thermal thresholds, little research has examined the influence of these conditions on the precision of thermosensory processing. To address this gap, we evaluated the thresholds and slope for cold and warm detection, as well as cold and heat pain perception, across the adult lifespan (20 to 80 years) and between healthy controls and individuals with DPN. We hypothesized that ageing and neuropathy are associated with reduced sensitivity (elevated thresholds) and precision (decreased slope), to different extents for different modalities. Further, we expected that incorporating both measures of perceptual sensitivity and precision may enhance our ability to distinguish patients from healthy controls, ultimately improving assessments of age- and neuropathy-related changes in thermosensory function. These analyses also allowed us to examine whether thermosensory alterations associated with age and neuropathy reflect a shared phenotype or are qualitatively distinct changes, as well as to explore how thresholds and slopes relate to each other across modalities.

2. Methods

2.1. Design

The study employed a single-session, cross-sectional design to examine the impact of ageing and neuropathy on thermosensation. Participants completed three tasks aimed at assessing thermal sensitivity and precision (detection and pain thresholding), paradoxical heat sensation, and spatial aspects of thermal perception [13]. In addition, all participants completed survey measures related to handedness [43], mental health [28,33], and pain sensitivity [15,36]. Patients also completed surveys on neuropathic pain symptoms [4,5].

Each participant's session lasted approximately four hours and data were collected between April and October 2024. This project was approved by the Region Midtjylland Ethics Committee (Denmark) and adhered to the current version of the Helsinki Convention (2013). Participants provided informed consent prior to their participation in the study. In accordance with Danish ethical guidelines, healthy controls received financial compensation for their participation. Patients were not compensated directly, but the costs associated with their travel and related arrangements were reimbursed.

This paper focuses on a specific subset of the data, related to thermal detection and pain perception across the lifespan and in individuals with diabetic neuropathy.

2.2. Participants

To ensure balanced representation across the adult lifespan, the control group was stratified into four age cohorts (20-35, 36-50, 51-65 and 66-80 years) with the aim of including 15 to 25 individuals in each cohort. Patients with DPN were recruited from a pool of patients diagnosed as having probable neuropathy based on the Toronto consensus grading system, as part of other projects within the framework of the Danish National Type 2 Diabetes (DD2) Cohort [6,8,19,39,42].

Inclusion criteria required all participants to be between 20 and 80 years old and fluent in Danish and/or English. Exclusion criteria included pregnancy or lactation, recent jet lag or sleep deprivation, non-diabetes-related skin diseases such as eczema or psoriasis, a history of alcohol or drug abuse, cannabis use within the previous four weeks, and alcohol consumption within the previous 48 hours. For healthy controls, having a physical condition and/or medication that might influence pain perception was also an exclusion criteria.

A total of 86 healthy controls and 34 patients with probable diabetic polyneuropathy (DPN) completed the thresholding tasks. Following a secondary review of participant reports and prior to data analysis, we excluded ten control participants due to potential confounding factors: use of medications potentially affecting temperature perception (n = 7), history of epilepsy (n = 1), diagnosis of Reynaud syndrome (n = 1), and diagnosis of ankylosing spondylitis (n = 1). We also excluded one patient due to a history of thermal injury at the stimulation site, related to their professional occupation. After visualizing the data but before formal analysis, one additional control participant was excluded due to poor data quality (see below). A detailed overview of participant recruitment and exclusions is presented in Fig. 1.

The final analyzed sample included 75 healthy controls (30 M and 45 F; age range: [21- 80]) and 33 patients with neuropathy (18 M and 15 F; age range: [47 - 79]; years since *diabetes* diagnosis as mean±SD: 13.0± 2.2)

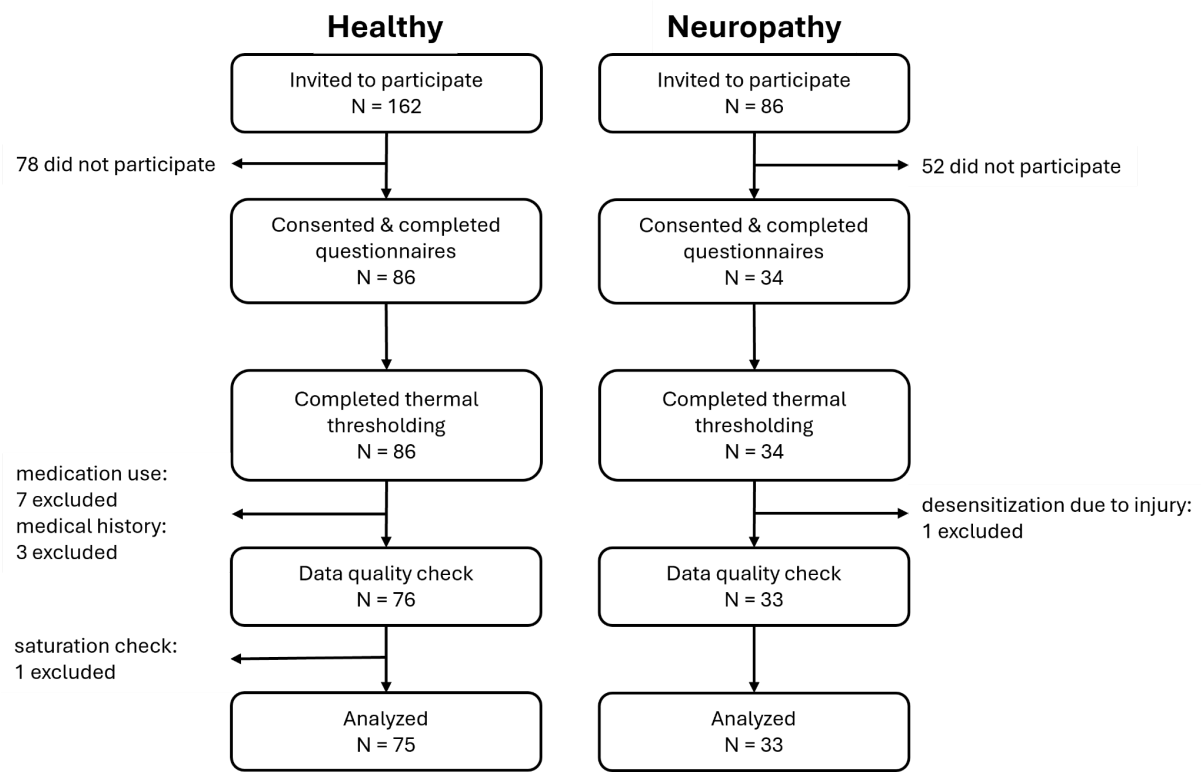

Figure 1. Recruitment flow chart
Recruitment flow chart detailing participant inclusions, exclusions, and final sample sizes for analysis.

2.3. Thresholding tasks

Thermal sensitivity was assessed with four brief computerized tasks designed to measure the participants' ability to detect cooling and warming, as well as their sensitivity to painful cold and heat. These tasks were always performed after the end of the surveys and in the same order: cold detection followed by warm detection on the non-dominant volar forearm, then cold pain followed by heat pain on the dominant volar forearm (Fig. 2).

All thermal stimuli were delivered using the TCS-II (QST.Lab, Strasbourg, France), a Peltier effect contact stimulator. More specifically, we used the T11 probe which has a total stimulation surface of 90 mm^2 split into five independently controlled zones of 7.4 x 24.2 mm and a maximum rate of temperature change of 100℃/s. For the whole duration of the experiment, all zones of the probe were kept to the neutral temperature of 30℃ except during stimulation.

Each trial began with a randomized 1-3 s baseline period, during which all zones remained at 30℃. This was followed by an increase in temperature in two adjacent stimulation zones (randomly selected from the four possible combinations) at a rate of 2.5℃/s. Once the target temperature was reached, it was maintained for 1.5 s, before return to baseline at a rate of 80℃/s. The temperature of each zone was continuously recorded from the onset of the temperature change until the end of the plateau. After each stimulus, participants reported whether they felt cold (yes or no) for cold detection, warm (yes or no) for warm detection, or a burning sensation (yes or no) for pain perception assessment. Their chosen answer was displayed for 0.5 s before the next trial began. For all tasks, participants had a maximum of 10 s to respond, using the left or right arrow keys of the computer's keyboard (left = yes, right = no). Each detection thresholding task comprised 30 trials and lasted between 5 and 7 minutes. Each pain thresholding task comprised 50 trials and lasted between 10 and 15 minutes.

For all modalities, participants were informed that each trial would involve a temperature change, followed by a question: "Did you perceive a cold sensation?" for cold detection, "Did you perceive a warm sensation?" for warm detection, and "Did you perceive a burning sensation?" for pain assessments. They were instructed to respond as quickly and accurately as possible. To clarify the concept of 'burning,' participants were given examples such as holding a very hot cup of coffee or an ice cube for too long.

The task was programmed using Psychtoolbox-3 [26] in MATLAB R2021a (The MathWorks, USA).

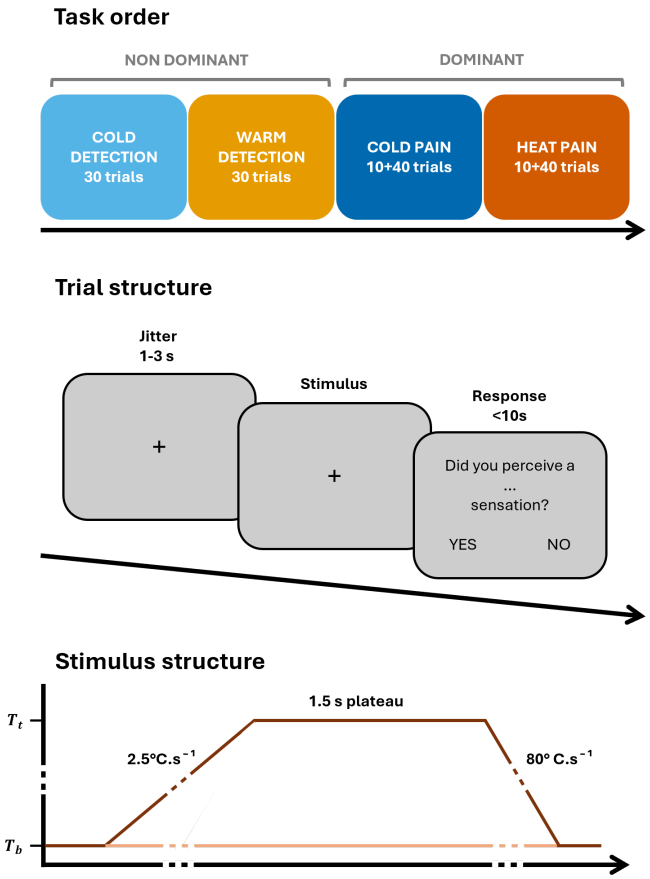

Figure 2. Task design
The top row illustrates the sequence of tasks, including the number of trials for each and the forearm to which the stimulator was applied. The middle row illustrates the structure of a single trial: first a baseline period, during which the stimulator was held at 30℃ for a pseudo-random duration, followed by the stimulus itself, and finally a response period. The bottom row illustrates the temperature profile over time during stimulation: all zones started at baseline temperature T_b, two zones then reach the target temperature T_t at a rate of 2.5℃/s, remain at T_t for 1.5 s, and finally return to T_b at a rate of 80℃/s.

2.4. Adaptive stimulus intensity selection

We used an adaptive algorithm to select stimulus intensities on each trial based on the participants' responses in previous trials of the same task. This approach ensured that stimulus intensities were calibrated to individual sensitivity, limiting the number of trials at uninformative (never or always detected) or excessively painful intensities. As a result, it reduced the number of trials needed to attain a given level of estimation precision and the risk of habituation or sensitization.

Specifically, we used the Ψ (psi) method, a Bayesian adaptive algorithm implemented in Palamedes [25,27]. This method keeps track of an approximate probability distribution for the threshold and the slope of a psychometric function (PF), which describes the relationship

between stimulus intensity and the probability of detection or pain perception. At the start of each trial, this probability distribution is used to select the stimulus intensity that maximizes information gain. This distribution is updated after each participant's response based on the outcome of the trial. Courtin *et al*. demonstrated that this approach effectively estimates cold and warm detection thresholds and slopes in as few as 30 trials [10].

In all cases, the algorithm modeled the PF as a Gaussian cumulative density function. The guess and lapse rates, corresponding to the probability of reporting a detection at very low intensities and not reporting a detection at very high intensities respectively, were both set to .05. For cold detection and cold pain assessments, possible stimulus values ranged from 29.9℃ to 0.1℃ in 0.1℃ increments. For warm detection and heat pain assessments, possible stimulus intensities ranged from 30.1℃ to 50℃ in 0.1℃ increments. In all cases, the algorithm kept track of the approximate joint posterior distribution for slope and threshold values on a 51 by 51 grid, with possible threshold values uniformly distributed across the stimulus range and possible log_{10} slope values uniformly distributed between $log_{10}(0.001°C^{-1})$ and $log_{10}(6°C^{-1})$ (inclusive). We used uniform priors for all parameters.

$$\Theta(x; \alpha, \beta, \gamma, \lambda) = \gamma + (1 - \gamma - \lambda)\, \Phi(\beta(x - \alpha))$$

where Θ is the probability of reporting the target perception, x is the absolute temperature deviation from baseline, α is the threshold, β is the slope, λ is the lapse rate, γ is the guess rate, and Φ is the standard Gaussian distribution cumulative density function

Out of the 50 trials used to assess pain sensitivity, the first 10 were familiarization trials, for which stimulus intensities were selected using an up-down staircase algorithm. This ensured that the participant had some time to stabilize their strategy regarding what they reported as burning. These trials were not included in the analysis.

2.5. Statistical analyses

The pre-registered data processing and analysis plan for this experiment can be found on the project's OSF repository: https://osf.io/dvz94. Data and analysis scripts can be found on the project's GitHub page: https://github.com/Body-Pain-Perception-Lab/lifespan-and-neuropathy-sensitivity-and-precision

Deviations from the pre-registered plan were minor and included an adjusted criterion for assessing the quality of temperature recordings, the use of simplified models due to sampling issues, and the addition of Bayes Factors to evaluate evidence for the absence of effects in parallel with posterior probability tests. Full details and justifications are available in the OSF repository.

2.5.1. Data quality assessment

Before analyzing the dataset, we performed several control checks to ensure data quality and, if necessary, to exclude specific trials or participants according to predefined criteria.

The Michigan Neuropathy Screening Instrument (MNSI) questionnaire was used as a tool for neuropathy screening [15,20]. No control participants had a MNSI score larger or equal to seven, which would have been indicative of potential neuropathy.

To account for potential deviations between delivered and target temperatures, we modelled stimulus intensities based on the probe temperature recorded during the last 1 s of stimulation at target temperature (i.e., plateau). Additionally, we checked whether, at any time during this recording, the temperature deviated by more than 1℃ from the target (two out of 15,260 trials) or more than 0.2℃ from the mean recording (180 out of 15,260 trials). Flagged trials were excluded from further analysis.

For control participants, we also inspected the cumulative mean of their responses as a function of stimulus intensity to ensure that detection responses saturated at a lower intensity than pain responses. One control participant was excluded because they showed the opposite pattern (i.e., pain responses saturated before detection responses), suggesting abnormal sensory processing. This criterion was not applied to patients, as they might experience pain before clearly identifying any temperature change due to sensory disturbances caused by neuropathy.

2.5.2. Model specification

The dataset consisted of stimulus temperatures and the binary yes/no responses provided by participants, with responses grouped by modality within participants. To estimate thresholds and slopes for each modality and participant while accounting for this nested structure, we used hierarchical Bayesian psychometric function (PF) models.

2.5.2.1. Effects of age on thermal perception

We first assessed how ageing affects thermal perception, limiting our analyses to data from healthy controls. Specifically, we tested whether thresholds increase and slopes decrease with age, across thermosensory modalities. This analysis also aimed to investigate the shapes of the psychometric function and of the relationship between age and threshold.

Rather than choosing a single model formulation a priori, we compared three different versions to determine which best explained the data (Fig. 3). The PF was either a Gaussian cumulative distribution function, assuming symmetry around the threshold (model 1 and 2), or a modified Weibull cumulative distribution function known as the Quick function, allowing asymmetry around the threshold (model 3). Although the Quick function is theoretically more appropriate given that the stimulus values are strictly positive [25], the cumulative Gaussian was successfully applied in previous studies and aligns with the formulation assumed by the adaptive stimulus selection algorithm used in this experiment [9,12].

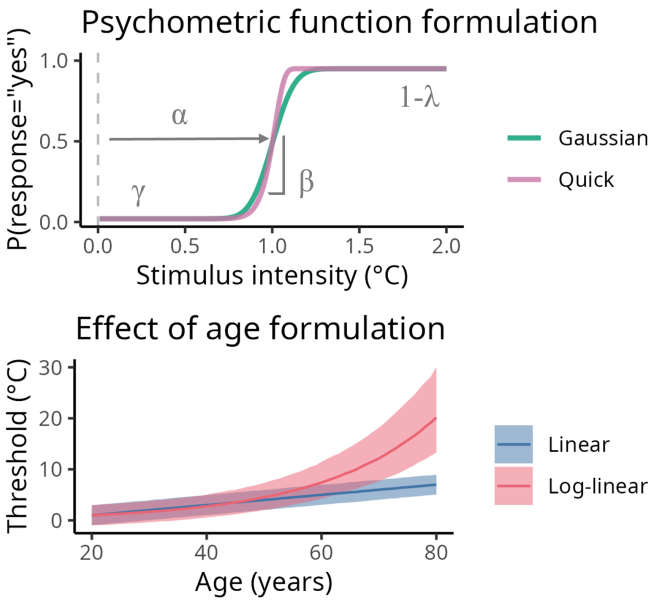

Figure 3. Model space
Top: Example psychometric functions under the Gaussian (models 1 & 2) and Quick formulations (model 3). The plot illustrates how the threshold α, the slope β, the guess rate γ, and the lapse rate λ relate to the psychometric function. Bottom: Example age-threshold relationships under the two tested formulations: a linear (model 1) and a log-linear trend (models 2 & 3). Shaded areas represent dispersion.

The relationship between age and threshold was modelled as either linear (model 1) or log-linear (model 2 and 3). Previous studies investigating the effect of age on the thresholds assumed a linear relationship. However, published data suggests a geometric increase of thresholds with age, accompanied by an increase of their variance, which may indicate a log-linear relationship instead [21].

Because the Quick function requires strictly positive thresholds, enforced through exponentiation in the hierarchical model, the linear model was only tested with the cumulative Gaussian (model 1), while the log-linear model was tested with both the cumulative Gaussian (model 2) and Quick (model 3) formulations of the PF:

$$[model\ 1\ \&\ 2]\ Gaussian\colon\ \Theta(x;\alpha,\beta,\gamma,\lambda) = \gamma + (1-\gamma-\lambda)\,\Phi(\beta(x-\alpha))$$

$$[model\ 3]\ Quick\colon\ \Theta(x;\alpha,\beta,\gamma,\lambda) = \gamma + (1-\gamma-\lambda)\left(1-2^{-\left(\frac{x}{\alpha}\right)^{\beta}}\right)$$

$$[model\ 1]\ Linear\colon \alpha = \kappa_{0,\alpha} + \kappa_{a,\alpha}\cdot Age + \epsilon_{i,\alpha}$$

$$[model\ 2\ \&\ 3]\ Log-linear\colon ln(\alpha) = \kappa_{0,\alpha} + \kappa_{a,\alpha}\cdot Age + \epsilon_{i,\alpha}$$

$$ln(\beta) = \kappa_{0,\beta} + \kappa_{a,\beta}\cdot Age + \epsilon_{i,\beta}$$

$$logit(\gamma) = \kappa_{0,\gamma} + \epsilon_{i,\gamma}$$

$$logit(\lambda) = \kappa_{0,\lambda} + \epsilon_{i,\lambda}$$

where Θ is the probability of reporting the target perception, x is the absolute temperature deviation from baseline, α is the threshold, β is the slope, λ is the lapse rate, γ is the guess rate, Φ is the standard Gaussian distribution cumulative density function, κ's are main effects and ϵ's are random intercept effects on the relationship between age and PF parameters, for participant i and Age.

We assumed that all PFs (cold detection, warm detection, cold pain, heat pain) had the same shape. They were therefore estimated using a single hierarchical multivariate model for each model specification, incorporating data from all modalities.

Thresholds and slopes were modelled as varying across participants and modalities. Guess and lapse rates were allowed to vary between participants but remained constant across modalities, as they represent an individual's overall tendency to make errors. The slopes and thresholds were modeled as affine functions of the participant's age, with a random intercept. To improve model interpretability, age was centered at 20 years, ensuring that the intercept corresponded to parameter values for the youngest possible participant. The relationship between age and slope was assumed to be log-linear, ensuring that an increase in stimulus intensity leads to an increase in probability of perception. Guess and lapse rates were modelled in logit space, constraining their values to the 0 to 0.5 range.

2.5.2.2. Effects of neuropathy on thermal perception

After assessing the effects of ageing in healthy controls, we investigated how neuropathy alters thermal perception by including data from both healthy controls and patients. This allowed us to test our hypothesis that neuropathy further increases thresholds and reduces slopes, beyond the effects of ageing alone.

To account for the combined effects of age and neuropathy, the models described in the previous section were extended to differentiate between healthy controls and patients. Participant status was indexed by a dummy variable (0 for controls, 1 for patients).

$$[model\ 1]\ Linear\colon \alpha = \kappa_{0,\alpha} + \kappa_{s,\alpha}\cdot Status + \kappa_{a,\alpha}\cdot Age + \epsilon_{i,\alpha}$$

$$[model\ 2\ \&\ 3]\ Log\ -\ linear: ln(\alpha) = \kappa_{0,\alpha} + \kappa_{s,\alpha} \cdot Status + \kappa_{a,\alpha} \cdot Age + \epsilon_{i,\alpha}$$

$$ln(\beta) = \kappa_{0,\beta} + \kappa_{s,\beta} \cdot Status + \kappa_{a,\beta} \cdot Age + \epsilon_{i,\beta}$$

where Status is the dummy variable indexing whether participant i is a control (0) or a patient (1).

2.5.3. Model estimation:

The models were implemented in *Stan* and estimated using the *CmdStanR* package for *R*, using the *Rstudio* interface [1,16,40]. Justification of the chosen priors can be found in the Supplementary Materials.

Each model was sampled using four chains of 2,000 warm-up and 2,000 sampling iterations, with a target average acceptance probability of .99 and a maximum tree depth of 12. Initial values for hyperparameters μ and τ were randomly selected from the priors. Initial values for the other parameters were randomly sampled from a uniform distribution on the [-2, 2] interval.

To ensure proper model sampling, we relied on a series of conventional diagnostic checks [40]. None of the post-warm-up chains showed divergent transitions and all Estimated Bayesian Fractions of Missing Information (E-BFMI) were higher than 0.3, indicating adequate sampling of the posterior. All parameters had $\widehat{R}$ diagnostic values below the conventional cut-off of 1.05, indicating convergence of the chains to a common solution. Finally, all group-level parameters had sufficient bulk and tail effective sample sizes (bulk-ESS and tail-ESS), indicating an adequate number of independent draws for inference.

2.5.4. Model selection:

We used model comparison to test hypotheses about the shape of the PF and the shape of the age-threshold relationship. To do so, we used approximate leave-one-out cross-validation (LOO-CV), as implemented in the *loo* package [44], to quantify how well the different models explained the data, as indexed by the expected log pointwise predictive densities (ELPD), and whether one outperformed the others.

We relied on Pareto-k diagnostics to assess the reliability of ELPD estimates and their standard errors. As regular LOO-CV showed a substantial amount of problematic Pareto-k values, we switched to moment matching LOO-CV, as recommended in the *loo* documentation. This reduced the number of problematic Pareto-k values to an acceptable level: for the ageing only models, 1 out of 10,355 for model 1, 0 for model 2, and 1 for model 3; for the ageing and neuropathy models, 4 out of 14,912 for model 1, 0 for model 2, and 1 for model 3.

We used the following pre-registered criteria for the interpretation of LOO-CV results. Absolute ELPD differences below four were considered too small to be meaningful. If the difference between the model with the highest ELPD and all other models was larger than four and larger than two times their standard error, the model with the highest ELPD was considered significantly better than the others. If these criteria were not met, we reported a tie, and specified which models were involved. In such cases, we still used the model with the highest ELPD for inference. To provide a graded assessment of model differences, we also reported the probability that the ELPD difference was larger than zero (i.e., the probability that the best model is worse than the comparison model), assuming a Gaussian error distribution.

The primary model comparison was conducted on all trials pooled across modalities (cold detection, warm detection, cold pain, and heat pain). As a robustness check, we also repeated the comparisons separately for each modality. The results of the modality-specific comparisons were consistent with those from the pooled analysis.

2.5.5. Interpretation of group-level parameters

2.5.5.1. Hypothesis tests using posterior probabilities

Pre-registered hypothesis tests were conducted by comparing the posterior probability of null hypotheses (H0), with a cut-off determined using the Holm-Bonferroni procedure, to ensure that the family-wise error rate did not exceed .05. This inference strategy is similar to the use of corrected p-values in frequentist statistics.

To test the prediction that thresholds increase with age, we assessed whether the group-level age effects on thresholds ($\kappa_{a,\alpha}$ for cold detection, warm detection, cold pain, and heat pain) were smaller than or equal to zero, using estimates from the ageing only models.

To test whether the slope of thermal perception decreases with age, we assessed whether the group-level age effect on slopes in the ageing only models ($\kappa_{a,\beta}$ for all modalities) were larger than or equal to zero.

To test the prediction that patients with neuropathy have higher thresholds than age-matched healthy controls, we assessed whether the group-level effects of neuropathy on thresholds ($\kappa_{s,\alpha}$ for all modalities) were smaller than or equal to zero, using estimates from the ageing and neuropathy models.

Finally, to test whether neuropathy increases the variability of thermal perception, we assessed whether the group-level effects of neuropathy on slopes ($\kappa_{s,\beta}$ for all modalities) were larger than or equal to zero, using estimates from the ageing and neuropathy models.

2.5.5.2. Tests for an absence of effect using Bayes Factors

As some of the tests described in the previous section were not significant, we also computed Bayes factors for the absence of an effect (i.e., BF_{01}) using the Savage-Dickey density ratio method [45]. Following Jeffrey's scale, we interpreted $\log_{10}(BF_{01})$ values between -0.5 and 0.5 as indicating insufficient evidence to draw conclusions. Values above 0.5 were taken as substantial evidence for the absence of an effect, while values below -0.5 were interpreted as substantial evidence for the presence of an effect [22].

2.5.6. Analysis of participant level parameters

2.5.6.1. Discrimination between healthy controls and patients

We investigated whether the thresholds and slopes of the psychometric functions (cold detection, warm detection, cold pain, and heat pain) provided useful and complementary information to distinguish patients from healthy controls, beyond the group-level differences in these parameters. Specifically, we tested whether classification based on age-adjusted scores incorporating the threshold, the slope, or both, either for individual modalities or across all modalities, achieved above chance accuracy (0.5).

To this end, we simulated 1,000 datasets, each containing 2,000 patients and 2,000 controls. Ages were randomly sampled between 40 and 80 years and PF parameters were sampled from the posterior predictive distribution of the ageing and neuropathy version of model 1.

Each dataset was split into a training set of 1,000 patients and 1,000 controls and a test set of 1,000 patients and 1,000 controls. For each score, we fit a logistic regression (using the *glm* function in R) to the training set, predicting participant status (patient or control) based on the parameters of interest (threshold and/or slope for a single modality or all

modalities) and their interactions with age. We then used the resulting coefficients to compute scores for the participants in the test set and evaluated classification performance based on these scores.

For each score, we assessed sensitivity and specificity at 101 cut-off values evenly spaced between the minimum and maximum scores in the test set. These values were used to calculate an estimate of the Area Under the Receiver Operating Characteristics Curve (AUROC), providing an index of classification accuracy.

AUROC values across the 1,000 simulated datasets were summarized by their mean and .05 and .95 quantiles, providing an estimate of the true AUROC and its 90% confidence interval (CI), and by the proportion of draws with an AUC lower or equal to 0.5, reflecting the posterior probability that classification was not better than chance. To assess if one parameter allowed better classification than the other, we also computed the mean difference in AUC and corresponding 95% CI for scores including only threshold vs. only slope vs. both, separately for each modality.

2.5.6.2. Association between PF parameters

To investigate associations between PF parameters beyond the effects of age and neuropathy, we inspected the correlation matrix estimated within the hierarchical model. This reflects the associations between parameters after accounting for these explanatory variables. We summarized the posterior draws for each cell of the residual correlation matrix as the mean and the .025 and .975 quantiles, providing estimates of the correlation coefficients and their 95% CI.

2.5.7. Sample size justifications

The sample size was selected based on previous experiments reported in the literature and available resources. There is no analytical solution for sample size calculation for Bayesian hierarchical models. Simulation-based sample size analyses are possible but computationally expensive and the validity of their results is dependent on the accuracy of arbitrary choices when setting up the simulations.

3. Results

3.1. Model selection

We used model comparison to determine which formulation of the psychometric function (PF) and age–threshold relationship best explained the data (Table 1).

For the reduced model including only healthy controls, the Gaussian PF with a linear effect of age on the threshold (Model 1) performed best, although the difference was not significant. For the full dataset including both patients and controls, the same model outperformed the alternatives and the difference was significant. All subsequent analyses of age and neuropathy effects on thresholds and slopes used Model 1.

Table 1
Model comparison

Model	ΔELPD	SE ΔELPD	Z	P(ΔELPD>0)
Ageing only				
Model 1: Gaussian - Linear	0	0	NA	NA
Model 2: Gaussian - Log-linear	-5.60	8.5	-0.66	0.255
Model 3: Quick - Log-linear	-0.67	11.4	-0.06	0.476
Ageing and neuropathy				
Model 1: Gaussian - Linear	0	0	NA	NA
Model 2: Gaussian - Log-linear	-66.5	13.0	-5.11	0.000
Model 3: Quick - Log-linear	-53.8	15.4	-3.50	0.000

Note. ΔELPD = expected log pointwise predictive density difference; SE = standard error; NA = not applicable

3.2. Effect of age on temperature perception

Increasing age was associated with a significant increase of cold detection (posterior mean κ = 0.02, 90% credible interval (CI) [0.01,0.03], $P(\kappa \leq 0)$ = .001, $\log_{10}(BF_{01})$ = -2.03), warm detection (κ = 0.04, 90% CI [0.01,0.06], $P(\kappa \leq 0)$ = .010, $\log_{10}(BF_{01})$ = -0.85), and cold pain thresholds (κ = 0.13, 90% CI [0.05,0.22], $P(\kappa \leq 0)$ = .006, $\log_{10}(BF_{01})$ = -1.03), reflecting reduced thermal sensitivity (Fig. 4). Additionally, the cold detection slope significantly decreased with age (κ = -0.01, 90% CI [-0.02,-0.01], $P(\kappa \geq 0)$ = .005, $\log_{10}(BF_{01})$ = -0.99), indicating reduced sensory precision (Fig. 4). In contrast, there was substantial evidence ($\log_{10}(BF_{01}) > 0.5$) supporting the absence of an age effect on heat pain thresholds (κ = 0.00, 90% CI [-0.02,0.02], $P(\kappa \leq 0)$ = .422, $\log_{10}(BF_{01})$ = .54). All other comparisons showed inconclusive results. To visualize these effects, we display group-level psychometric functions estimated at ages 20 and 80, corresponding to the bounds of the inclusion criteria, at the bottom of Fig. 4.

3.3. Effect of neuropathy on temperature perception

Patients with neuropathy showed higher cold detection (posterior mean κ = 0.84, 90% CI [0.24,1.44], $P(\kappa \leq 0)$ = .012, $\log_{10}(BF_{01})$ = -0.87) and warm detection thresholds (κ = 1.97, 90% CI [0.71,3.24], $P(\kappa \leq 0)$ = .005, $\log_{10}(BF_{01})$ = -0.97) compared to age-matched controls, indicating reduced sensitivity to innocuous thermal stimuli (Fig. 5). Cold detection slopes

were also lower in patients (κ = -0.57, 90% CI [-0.98,-0.17], $P(\kappa \geq 0)$ = .010, $\log_{10}(BF_{01})$ = -0.50), indicating less reliable perception (Fig. 5). In contrast, there was substantial evidence supporting the absence of an effect of neuropathy on heat pain slopes (κ = -0.07, 90% CI [-0.44,0.30], $P(\kappa \geq 0)$ = .369, $\log_{10}(BF_{01})$ = 0.53). All other comparisons showed inconclusive results. To illustrate these effects, group-level psychometric functions were estimated at age 50 for patients and controls (Fig. 5).

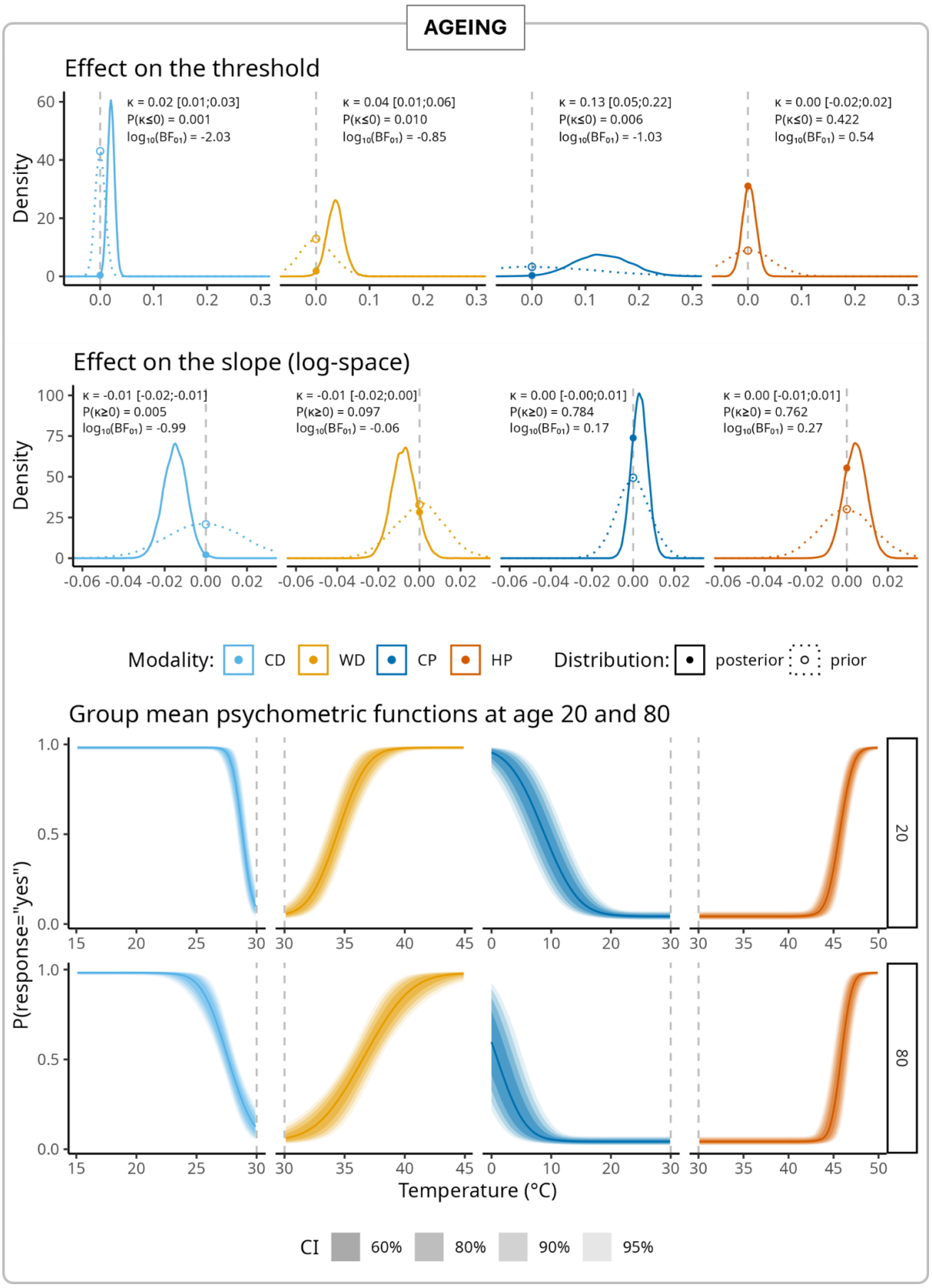

Figure 4. Effect of age on psychometric function parameters

Posterior distributions of age effects on threshold (top row) and log-transformed slope (second row) parameters across four sensory modalities: cold detection (CD), warm detection (WD), cold pain (CP), and heat pain (HP). For each distribution, we report the posterior probability of an effect ($P(x > 0)$ or $P(x < 0)$) and the Bayes Factor in favor of the null hypothesis (BF_{01}). We also display the group-level psychometric functions estimated

at ages 20 and 80 for each modality (bottom rows). Shaded areas represent 60%, 80%, 90%, and 95% credible intervals (CI).

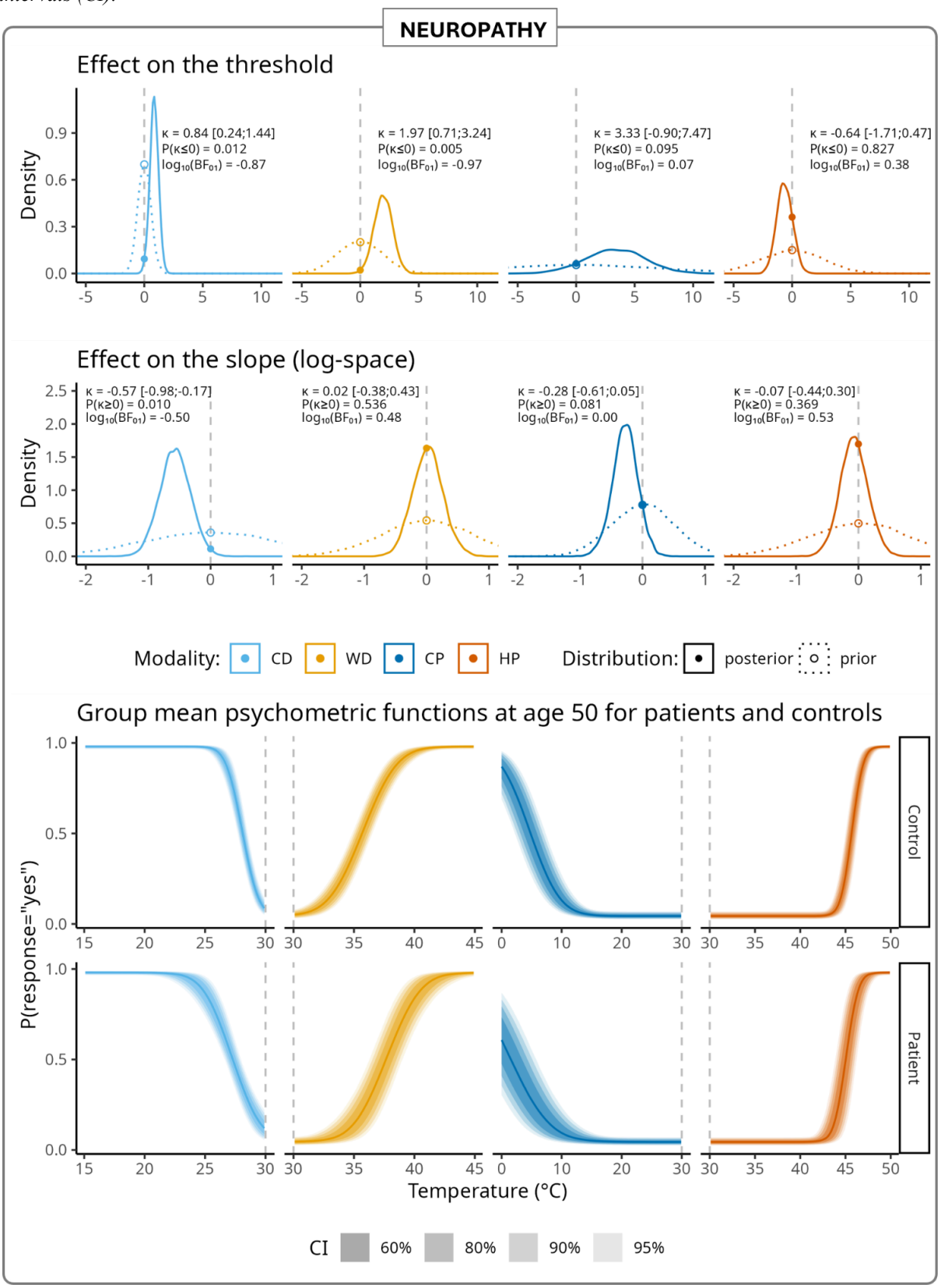

Figure 5. Effect of neuropathy on psychometric function parameters
Posterior distributions of neuropathy effects on threshold (top row) and log-scaled slope (second row) parameters across four sensory modalities: cold detection (CD), warm detection (WD), cold pain (CP), and heat pain (HP). For each distribution, we report the posterior probability of an effect (P(x > 0) or P(x < 0)) and the

Bayes Factor in favor of the null hypothesis (BF_{01}). We also display the group-level psychometric functions estimated at age 50 for patients and controls across all modalities (bottom rows). Shaded areas represent 60%, 80%, 90%, and 95% credible intervals (CI).

3.4. Discrimination between healthy controls and patients with neuropathy

PF parameters afforded varying levels of discrimination between patients and controls, depending on the modality and whether threshold, slope, or both were included in the score used for classification (Fig. 6). Threshold-based mean AUROC values ranged from .54 to .65, slope-based from .50 to .68, and combined scores from .54 to .66.

Classification was significantly better than chance (AUROC > .5) when using scores based on cold detection threshold (AUROC = .62, 95% confidence interval [CI] [.51, .71], $P(AUROC \leq .5)$ = .019), cold detection slope (AUROC = .68, 95% CI [.52, .80], $P(AUROC \leq .5)$ = .018), cold detection slope and threshold (AUROC = .66, 95% CI [.51, .80], $P(AUROC \leq .5)$ = .022), warm detection threshold (AUROC = .65, 95% CI [.52, .76], $P(AUROC \leq .5)$ = .014), and warm detection threshold and slopes (AUROC = .63, 95% CI [.47, .76], $P(AUROC \leq .5)$ = .050) but not when using scores including warm detection slope only or pain parameters.

Furthermore, classification accuracy was not significantly different between the different scores based on cold detection parameters. The mean difference in AUC between threshold-only and slope-only scores was -0.06 (95% CI [-0.22, 0.11]), the difference between threshold-only and combined scores was -0.04 (95 CI% [-0.20, 0.11]), and the difference between the combined and slope-only scores was 0.00 (95% CI [-0.13, 0.05]). Similarly, there was no difference between scores including only the warm detection threshold and those including both threshold and slope (difference = 0.01, 95% CI [-0.04, 0.13]).

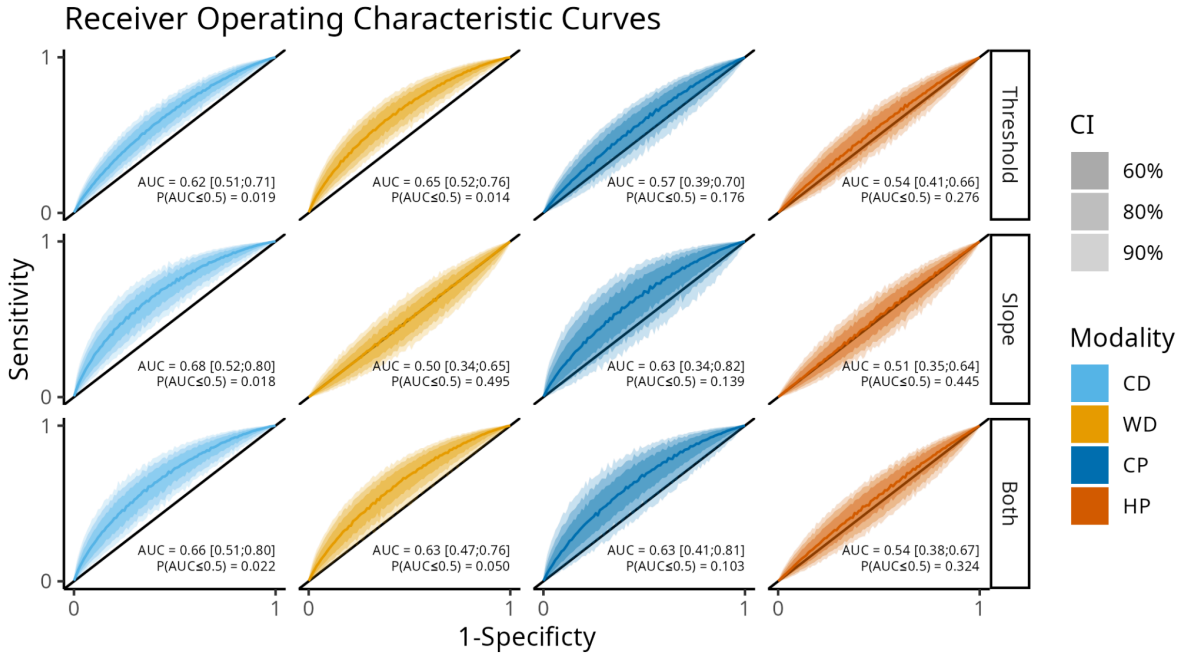

Figure 6. Discriminability of patients and controls based on combinations of psychometric function parameters

Receiver operating characteristic (ROC) curves showing classification performance based on threshold-only (top row), slope-only (middle row), or combined threshold and slope (bottom row) scores for each modality: cold detection (CD), warm detection (WD), cold pain (CP), and heat pain (HP). Scores were corrected for age. The posterior mean Area Under the ROC Curve (AUROC) is reported for each model, with 90% credible intervals shown in brackets. Shaded regions represent 60%, 80%, and 90% credible intervals for the ROC curves.

3.4. Association between parameters

Partial correlation analysis, controlled for age and patient status, revealed a moderate anticorrelation between cold detection thresholds and cold detection slopes (posterior mean ρ = -0.58, 95% CI [-0.77, -0.32]), as well as weak correlations between cold and warm detection thresholds (ρ = 0.22, 95% CI [0.03 ; 0.42]), cold and heat pain detection thresholds (ρ = 0.35, 95% CI [0.16 ; 0.51]), cold pain thresholds and heat pain slopes (ρ = 0.23, 95% CI [0.00 ; 0.46]), and heat pain thresholds and slopes (ρ = 0.33, 95% CI [0.08 ; 0.54]). All other correlations did not differ significantly from 0.

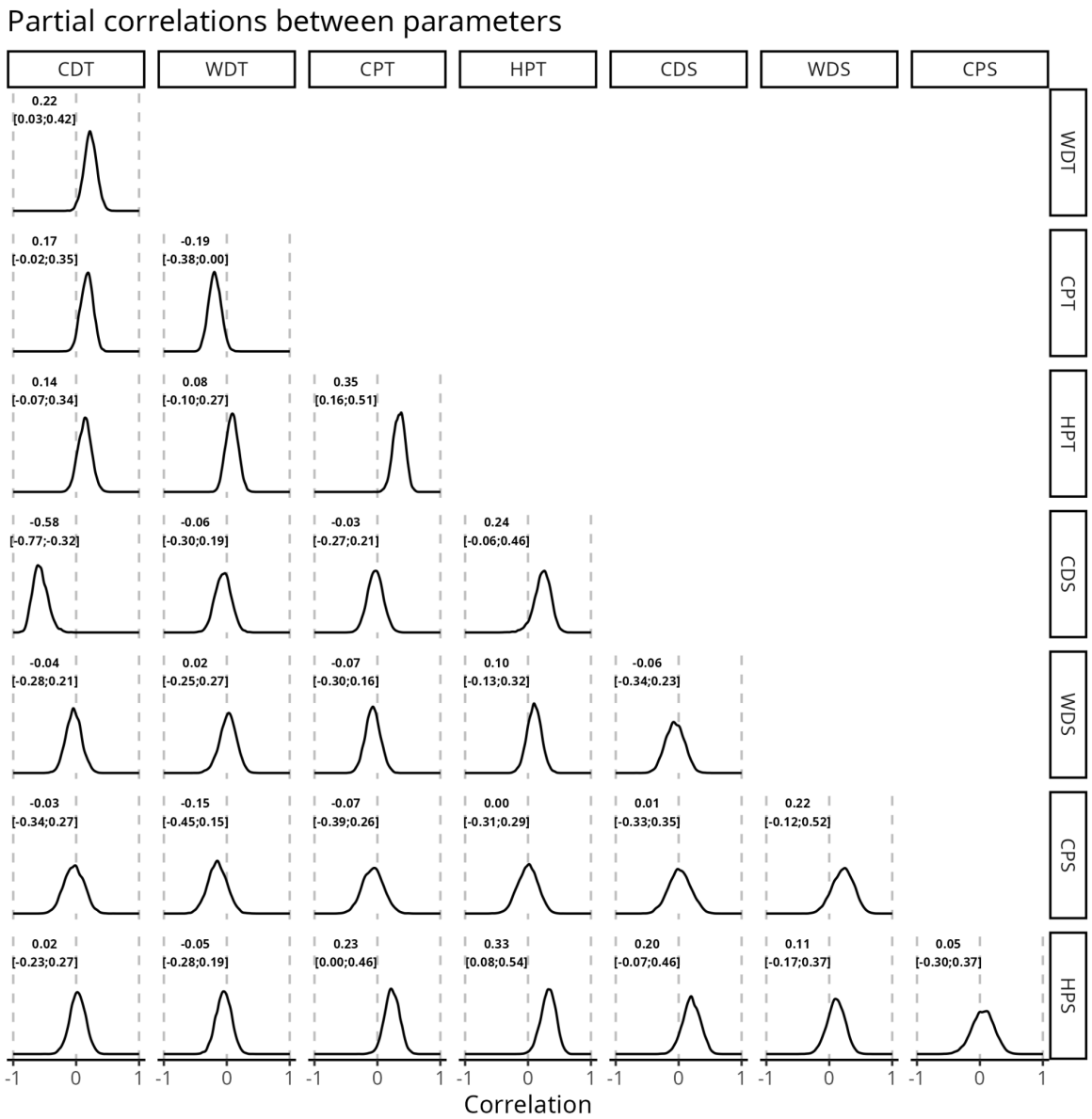

Figure 7. Partial correlation matrix
Matrix of posterior densities for the partial correlation coefficients, adjusted for age and patient status. Included in the matrix are associations between cold detection thresholds (CDT), warm detection thresholds (WDT), cold pain thresholds (CPT), heat pain thresholds (HPT), cold detection log-slopes (CDS), warm detection log-slopes (WDS), cold pain log-slopes (CPS), and heat pain log-slopes (HPS). The posterior mean correlation coefficient is reported for each cell, with 95% credible intervals shown in brackets.

4. Discussion

This study investigated how ageing and diabetic polyneuropathy (DPN) affect the sensitivity and precision of thermal perception, using the thresholds and slopes of psychometric functions across four modalities: cold detection, warm detection, cold pain, and heat pain. We also examined whether these parameters could differentiate patients with DPN from healthy controls and whether they correlated with each other.

We report four key findings. First, ageing was associated with higher thresholds in multiple modalities and flatter cold detection slopes. Second, DPN had a similar effect, increasing detection thresholds and flattening cold detection slopes. Third, accurate discrimination between patients and controls was possible based on detection thresholds and cold detection slope, with the latter affording the best classification performance. Finally, detection and pain parameters appeared to form two separate ensembles, with significant correlations within but not between them.

Consistent with previous findings, we observed age-related increases in thermal detection and cold pain thresholds, suggesting reduced sensitivity to temperature changes with increasing age [18]. Importantly, our results extend these findings by showing that ageing reduces the precision or reliability of cold detection, as indicated by a flatter psychometric function (reduced slope). This means that older adults not only require more intense stimuli to detect skin cooling but also experience greater variability in whether and how they perceive it.

We found no significant age-related effects on the slope of warm detection or pain modalities. This may suggest that ageing disproportionately affects specific thermosensory pathways, potentially due to differences in small-fiber subtypes vulnerability or central processing. However, the Bayes Factors indicated insufficient evidence to conclude a true absence of effect, so these null findings may also reflect limited power due to greater interindividual variability.

Our analysis revealed substantial evidence against an age-related effect on heat pain thresholds, possibly reflecting preserved function of heat-sensitive nociceptive fibers in older adults. Notably, our findings contrast with previous large studies reporting either decreases [21] or increases [29,34] of heat pain thresholds with age. While some discrepancies may be due to differences in test site (*e.g.*, hand *vs* forearm), they also highlight limitations of the conventional threshold measurement using the method of limits. In such tasks, a continuously increasing stimulus is applied and participants press a button as soon as they perceive it [35]. The average intensity at the time of button press across three trials is taken as the threshold measure. Because this depends on response timing, differences in response speed can bias the threshold estimate, even when perception is identical. Moreover, since perception can occur well above or below the actual threshold and since only a few trials are averaged, the estimate is variably influenced by both the true threshold and the slope. In contrast, our tasks do not rely on when participants reply, preventing contamination by response time, whilst jointly estimating thresholds and slopes, preventing their conflation. Eliminating these confounds may explain why we found substantial evidence against an effect of age on heat pain threshold.

On average, patients with DPN had higher cold and warm detection thresholds and lower cold detection slopes compared to age-matched controls. These results are consistent with known peripheral nerve fiber degeneration in DPN [3,17,23]. Interestingly, pain thresholds and slopes were either clearly not affected by neuropathy (heat pain slope) or not clearly different between patients and controls (cold pain threshold and slope, heat pain threshold). One possibility is that nociceptive pathways are less susceptible to neuropathic damage or more variable in their impairment, reducing our statistical power to detect these

changes. Alternatively, heat pain thresholds may have been truly unaffected in our sample, contrasting with a large number of studies finding heat pain threshold increases in DPN [38]. This could be due to improved methodology, as discussed above, or this discrepancy could reflect differences in test site, as DPN is thought to be length-dependent and we tested the volar forearm, a more proximal location than the foot dorsum used in most prior studies [14].

Taken together, our results suggest that the effects of DPN on thermal detection closely parallel those observed in healthy ageing, both in direction and magnitude. For cold detection thresholds, cold detection slopes and warm detection thresholds (the three parameters which were significantly affected by neuropathy) the impact of DPN was roughly equivalent to the impact of 40 years of healthy ageing. This alignment suggests that neuropathy may accelerate ageing-like changes in the thermosensory system, rather than induce a qualitatively different pattern of impairment. In this view, DPN compresses or amplifies the trajectory of sensory decline typically seen with age. This interpretation aligns with broader theories proposing that chronic conditions such as diabetes mimic or hasten normal ageing processes in peripheral and central nervous systems [2,31]. However, because our study is cross-sectional, we cannot determine whether neuropathic alterations truly reflect accelerated ageing in thermal perception. Longitudinal data will be needed to test this hypothesis directly.

One of our hypotheses was that indices of sensitivity (threshold) and precision (slope) would provide complementary information, such that combining them would improve discrimination between patients and controls. When evaluating the classification performance of different psychometric function parameters, we found that scores including detection thresholds or cold detection slopes yielded better-than-chance discrimination. Cold detection slope, in particular, showed the highest discrimination accuracy, underscoring its relevance for assessing thermosensory alterations in DPN. However, combining cold detection slopes and thresholds did not further improve classification, contradicting the idea that these measures offer complementary information. This contrasts with our previous study, which reported a large, albeit non-significant, increase in discrimination accuracy when combining cold detection thresholds and slopes to distinguish diabetic patients without neuropathy from age-matched controls [10]. Previously, we used stimuli that were considerably faster (cooling rate: 300°C. s^{-1} vs 2.5°C. s^{-1}), shorter (plateau: ~0.1 s vs 1.5 s), and smaller (stimulation surface area: 0.38 cm^2 vs 9 cm^2), likely making detection more difficult. These design differences may have amplified the impact of neuropathic alterations on performance, resulting in better discriminability. Notably, the reported classification accuracies were overall higher than in the present study, suggesting that optimizing stimulus design may be key to enhancing the diagnostic utility of psychophysical measures in DPN.

Finally, while many studies have examined associations between thermal thresholds and various biological or psychological variables, few have investigated how different thermal thresholds relate to each other, or to the slope, in the absence of external explanatory factors. Our partial correlation analysis revealed several associations among these parameters, beyond shared effects of neuropathy or age. Interestingly, significant correlations were only observed between detection metrics or between pain metrics. This indicates a certain separation between pure thermosensation and thermonociception, rather than a smooth continuum encompassing all temperature perception. These findings also suggest that assessing both cold and warm detection (or pain) parameters does not provide entirely independent information, which could have implications for test selection in clinical or experimental settings.

5. Conclusion

In summary, our results indicate that ageing and diabetic polyneuropathy weaken thermosensory function in strikingly similar ways: both elevate cold and warm detection thresholds and flatten the cold detection slope, while leaving pain measures largely intact. This overlap suggests that neuropathy accelerates the normal trajectory of sensory ageing rather than introducing a fundamentally different pattern of impairment. By modelling thresholds and slopes together, our study provides a more nuanced picture of thermosensory decline and lays the groundwork for refined quantitative sensory tests that can better track neuropathic change.

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Competing interests
Authors declare that they have no competing interests.

Data and materials availability
Data and analysis code for this study is available at
https://github.com/Body-Pain-Perception-Lab/lifespan-and-neuropathy-sensitivity-and-precision

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