Decoding Meditation Mechanisms underlying Brain Preservation and Psycho-affective Health in Older Expert Meditators and Meditation-Naive Participants

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1. Supplementary results

1.1. **Supplementary Table S1 | Cluster details for significant differences in brain volume between older expert meditators and older controls**

Number of voxel	Volume (mm^3)	Significance maximum (T)	Significance maximum (x,y,z)	p-value (uncorrected)	p-value (FWE corrected)	Brain regions
650	1,635.3	4.5	6 -44 30	0.003	0.1	PCC
317	705.5	4.33	-18 57 -18	0.03	0.65	OFC
561	1,276.1	3.71	-36 52 -4	0.047	0.86	IFG (R), IFG (L)

Abbreviations: FWE Family Wise Error, R Right, L Left, IFG Inferior Frontal Gyrus, OFC OrbitoFrontal Cortex, PCC Posterior Cingulate Cortex.

1.2. **Supplementary Table S2 | Cluster details for significant differences in brain perfusion between older expert meditators and older controls**

Number of voxel	SUVR	Significance maximum (T)	Significance maximum (x,y,z)	p-value (uncorrected)	p-value (FWE corrected)	Brain regions
3,446	1.17	4.17	56 -51 -12	0.001	**0.01**	inferior and middle temporal gyrus (R), inferior and middle occipital gyrus (R), fusiform gyrus (R), Angular gyrus (R)
2,825	1.16	4.53	-36 -86 6	0.002	**0.03**	inferior, middle, superior temporal gyrus (L), inferior and middle occipital gyrus (L)
1,192	1.15	3.94	-58 -54 22	0.03	0.34	Middle and superior temporal gyrus (L), Angular gyrus (L)
1,149	0.94	3.55	-45 -26 -30	0.03	0.37	Hippocampus, amygdala, inferior temporal gyrus (L), fusiform gyrus (L)

Abbreviations: FWE Family Wise Error, R Right, L Left, Suvr Standard uptake value ratio.

1.3. Supplementary Table S3 | Group differences (ANCOVAs) for psycho-affective scores and meditation mechanisms

Psycho-affective scores	*F*-value	*p*-value
Positive psycho-affective score	19.93	<0.0001
Negative psycho-affective score	17.87	<0.0001
Meditation mechanisms		
Attentional	28.16	<0.0001
Constructive	22.85	<0.0001
Deconstructive	37.69	<0.0001

Abbreviations: ANCOVA ANalysis of COVAriance. Covariates: Age, Sex, Level of education

1.4. Supplementary Table S4 | Multiple linear regressions between each meditation mechanism and both psycho-affective scores, with the group added as a covariate

Meditation mechanisms	b	SE	β	*Adjusted r²*	*t*-value	*p*-value
Positive psycho-affective score ~ Attentional mechanism	0.30	0.08	0.30	0.17	3.73	0.0003
Negative psycho-affective score ~ Attentional mechanism	-0.12	0.09	-0.12	0.13	-1.39	0.17
Positive psycho-affective score ~ Constructive mechanism	0.33	0.07	0.35	0.2	4.44	<0.0001
Negative psycho-affective score ~ Constructive mechanism	-0.02	0.08	-0.02	0.13	-0.21	0.83
Positive psycho-affective score ~ Deconstructive mechanism	0.53	0.07	0.55	0.34	7.55	<0.0001
Negative psycho-affective score ~ Deconstructive mechanism	-0.67	0.06	-0.69	0.52	-11.02	<0.0001

Abbreviations: SE Standard Error

1.5. **Supplementary Table S5 | Comparisons of the correlation coefficients of the associations between meditation mechanisms and psycho-affective scores with the group added as a covariate (with residuals)**

	Positive psycho-affective score[1] ~ Attentional mechanism VS Negative psycho-affective score[1] ~ Attentional mechanism	Positive psycho-affective score[1] ~ Constructive mechanism VS Negative psycho-affective score[1] ~ Constructive mechanism	Positive psycho-affective score[1] ~ Deconstructive mechanism VS Negative psycho-affective score[1] ~ Deconstructive mechanism
Pearson and Filon's z (1898)	z=2.21, p=0.01	z=4, p<0.0001	z= -1.98, p=0.02
Dunn and Clark's z (1969)	z=2.18, p=0.01	z=3.9, p<0.0001	z= -1.98, p=0.02
Meng, Rosenthal, and Rubin's z (1992)	z=2.16, p=0.02	z=3.9, p<0.0001	z= -1.97, p=0.02
Hittner, May, and Silver's z (2003)	z=2.7, p=0.01	z=3.9, p<0.0001	z= -1.97, p=0.02

Comparisons of the correlation coefficients between the two psycho-affective scores and each meditation mechanism were performed on R-studio. Statistical values were obtained after testing the alternative hypothesis "greater" for the attentional and constructive mechanisms and "less" for the deconstructive mechanism and were considered significant when $p<0.05$.

[1] Statistical values were obtained by comparing correlation coefficient between each meditation mechanism and residuals of multiple linear regressions between the psycho-affective scores and the covariates (age, sex and education).

1.6. **Supplementary Table S6 | Multiple linear regressions between each meditation mechanism and both psycho-affective scores in the meditator population**

Meditation mechanisms	**b**	**SE**	**β**	***Adjusted r²***	***t*-value**	***p*-value**
Positive psycho-affective score ~ Attentional mechanism	0.74	0.31	0.45	0.18	2.40	0.03
Negative psycho-affective score ~ Attentional mechanism	-0.49	0.32	-0.32	0.05	-1.53	0.14
Positive psycho-affective score ~ Constructive mechanism	0.57	0.10	0.76	0.6	5.73	<0.0001
Negative psycho-affective score ~ Constructive mechanism	-0.48	0.12	-0.68	0.42	-4.16	0.0005
Positive psycho-affective score ~ Deconstructive mechanism	0.67	0.19	0.59	0.29	3.55	0.002
Negative psycho-affective score ~ Deconstructive mechanism	-0.75	0.17	-0.70	0.40	-4.49	0.0002

Abbreviations: SE Standard Error

1.7. **Supplementary Table S7 | Correlation coefficients comparisons of the associations between meditation mechanisms and psycho-affective scores in the meditator population (with residuals)**

	Positive psycho-affective score[1] ~ Attentional mechanism VS Negative psycho-affective score[1] ~ Attentional mechanism	Positive psycho-affective score[1] ~ Constructive mechanism VS Negative psycho-affective score[1] ~ Constructive mechanism	Positive psycho-affective score[1] ~ Deconstructive mechanism VS Negative psycho-affective score[1] ~ Deconstructive mechanism
Pearson and Filon's z (1898)	z=1.5, p=0.07	z=1.06, p=0.15	z= -1.01, p=0.16
Dunn and Clark's z (1969)	z=1.43, p=0.08	z=1.03, p=0.15	z= -0.98, p=0.16
Meng, Rosenthal, and Rubin's z (1992)	z=1.42, p=0.08	z=1.02, p=0.15	z= -0.97, p=0.17
Hittner, May, and Silver's z (2003)	z=1.42, p=0.08	z=1.02, p=0.15	z= -0.97, p=0.17

Comparisons of correlations coefficient between psycho-affective scores and each meditation mechanism (with residuals) were performed on R-studio. Statistical values were obtained after testing the alternative hypothesis "greater" for the attentional and constructive mechanisms and "less" for the deconstructive mechanism and were considered significant when p<0.005.

[1] Statistical values were obtained by comparing correlation coefficient between each meditation mechanism and residuals of multiple linear regressions between the psycho-affective scores and covariate as a mean to take into account covariates (age, sex and education).

1.8. **Supplementary Table S8 | Forward linear regressions showing the brain regions significantly associated with each meditation mechanism**

Meditation mechanisms	**Coefficient [95% CI]**	***p*-value**
Attentional Score ~ Temporo-parietal perfusion	0.31 [0.15, 0.47]	0.0002
Constructive Score ~ Temporo-occipital perfusion	0.2 [0.03, 0.37]	0.03
Constructive Score ~ Inferior frontal volume	0.22 [0.05, 0.40]	0.01
Deconstructive Score ~ Temporo-occipital perfusion	0.32 [0.15, 0.48]	0.0002
Deconstructive Score ~ Inferior frontal volume	0.16 [-0.01, 0.33]	0.06
Deconstructive Score ~ Orbitofrontal volume	0.16 [-0.02, 0.33]	0.07

Abbreviations: CI Confidence Interval. Forward stepwise regressions were performed to identify which perfusion region was the best predictor of each meditation composite score.

1.9. **Supplementary Table S9 | Forward linear regressions showing the brain regions significantly associated with each meditation mechanism with the group as a covariate**

Meditation mechanisms	**Coefficient [95% CI]**	***p*-value**
Attentional Score ~ Temporo-parietal perfusion	0.27 [0.09, 0.46]	0.004
Deconstructive Score ~ Temporo-parietal perfusion	0.18 [0.01, 0.36]	0.04

Abbreviations: CI Confidence Interval. Forward stepwise regressions were performed to identify which perfusion region was the best predictor of each meditation composite score. The forward regression revealed no significant region as a predictor of the constructive mechanism.

1.10. **Supplementary Table S10 | Forward linear regressions showing the brain regions significantly associated with each meditation mechanism in the meditator population**

Meditation mechanisms	**Coefficient [95% CI]**	***p*-value**
Attentional Score ~ Temporo-parietal perfusion	0.31 [0.02, 0.59]	0.035
Constructive Score ~ Temporo-parietal perfusion	0.74 [0.17, 1.31]	0.014

Abbreviations: CI Confidence Interval. Forward stepwise regressions were performed to identify which perfusion region was the best predictor of each meditation composite score. The forward regression revealed no significant region as a predictor of the deconstructive mechanism.

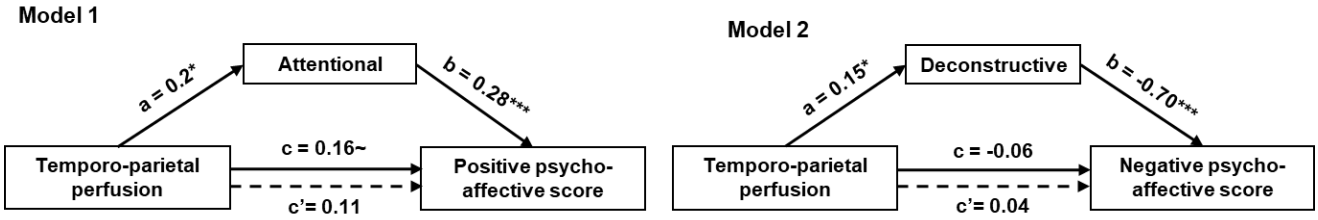
1.11. **Supplementary Table S11 | Detailed statistics of the mediation analyses with the group as a covariate**

	ADE			ACME		
	Estimate	95% CI	*p* Value	Estimate	95% CI	*p* Value
Model 1	0.11	[-0.05, 0.28]	0.16	0.06	[0.01, 0.14]	**0.016**
Model 2	0.04	[-0.1, 0.19]	0.6	-0.11	[-0.22, 0]	**0.046**

Abbreviations: ADE = Average Direct Effect; ACME = Average Causal Mediation Effect; CI = Confidence Interval.

In models 1 and 2, temporo-parietal perfusion was entered as the independent variable. In model 1, the positive psycho-affective composite score was entered as the dependent variable while the attentional mechanism was entered as the mediator. In model 2, the negative psycho-affective composite score was entered as the dependent variable while the deconstructive mechanism was entered as the mediator.

1.12. **Supplementary Figure S1 | Mediation analyses of the associations between brain integrity and psycho-affective scores with the group added as a covariate**



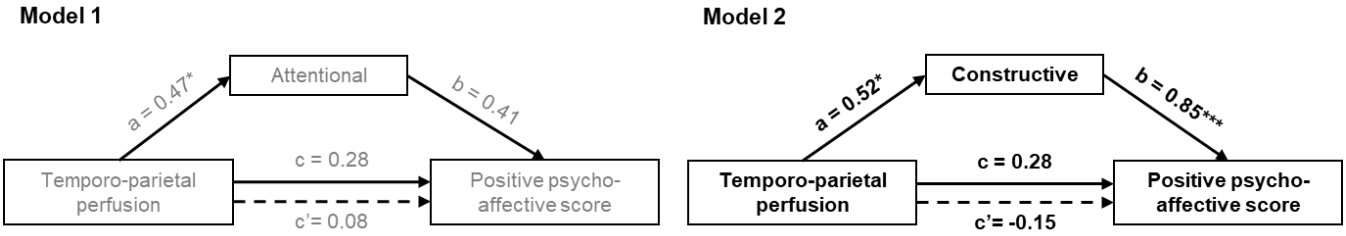
*Direct effects in filled arrows (simple regressions between variables) are expressed as standardized regression coefficients and indirect effects in dotted arrows (multiple regressions in which the predictor and the mediator are both added in the model) as partial correlation coefficients. Significant models are highlighted in bold black. All regressions are adjusted for age, sex, and education. *p<0.05, **p<0.01, ***p<0.001.*

1.13. **Supplementary Table S12 | Detailed statistics of mediation analyses in the meditator population**

	ADE			ACME		
	Estimate	95% CI	*p* Value	Estimate	95% CI	*p* Value
Model 1	0.09	[-0.53, 0.79]	0.8	0.21	[-0.08, 0.71]	0.16
Model 2	-0.17	[-0.54, 0.29]	0.37	0.47	[0.17, 0.99]	**<0.0001**

Abbreviations: ADE = Average Direct Effect; ACME = Average Causal Mediation Effect; CI = Confidence Interval.
In models 1 and 2, temporo-parietal perfusion was entered as the independent variable and the positive psycho-affective score was included as the dependent variable. In model 1, the mediator was the attentional mechanism while it was the constructive mechanism in model 2.

1.14. **Supplementary Figure S2 | Mediations analyses of the associations between brain integrity and psycho-affective scores in the meditator population**



*Direct effects in filled arrows (simple regressions between variables) are expressed as standardized regression coefficients and indirect effects in dotted arrows (multiple regressions in which the predictor and the mediator are both added in the model) as partial correlation coefficients. Significant models are highlighted in bold black while the non-significant one is in gray. All regressions are adjusted for age, sex, and education. ~p<0.1, *p<0.05, **p<0.01, ***p<0.001.*

1.15. Supplementary analyses testing the alternative hypothesis of an effect of meditation mechanisms on brain differences mediated by the differences in the psycho-affective scores

To test the alternative hypothesis of the meditation mechanisms predicting brain integrity through the psycho-affective factors, we conducted the same procedure of variable selection before performing the mediation analysis as a mean to avoid multiple testing. Thus, we selected i) the brain regions the most strongly associated with each psycho-affective score; and ii) the meditation mechanism the most predictive of each psycho-affective score. These analyses were conducted on the whole sample (with and without the group as a covariate) and in meditators only. Based on the results of these selection analyses, in the whole sample, 5 mediation models were tested, while no model was tested in the whole sample with the group as a covariate nor in the meditators only as the regressions revealed no link between the psycho-affective factors and brain integrity in those two conditions.

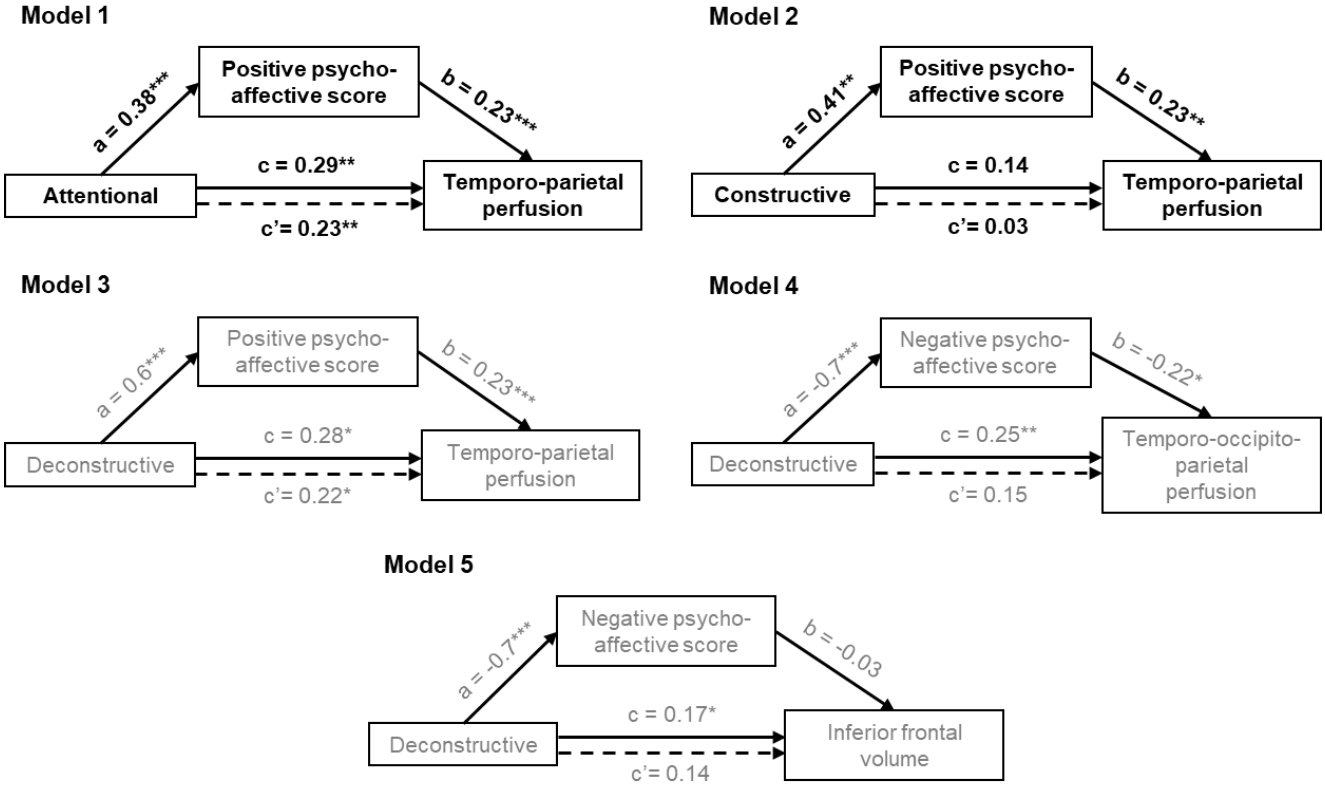
1.16. Supplementary Table S13 | Detailed statistics of mediation analyses in the alternative hypothesis of an effect of meditation mechanisms on brain differences mediated by the differences in the psycho-affective scores

	ADE			ACME		
	Estimate	95% CI	*p* Value	Estimate	95% CI	*p* Value
Model 1	0.23	[0.07, 0.41]	<0.001	0.06	[0.002, 0.13]	**0.036**
Model 2	0.03	[-0.14, 0.20]	0.74	0.09	[0.02, 0.16]	**0.002**
Model 3	0.2	[0.04, 0.36]	0.014	0.6	[-0.3, 0.16]	0.18
Model 4	0.14	[-0.04, 0.32]	0.12	0.07	[-0.06, 0.21]	0.28
Model 5	0.13	[-0.09, 0.34]	0.27	0.02	[-0.1, 0.16]	0.74

Abbreviations: ADE = Average Direct Effect; ACME = Average Causal Mediation Effect; CI = Confidence Interval.

In model 1, the attentional mechanism was entered as the independent variable. In model 2, the constructive mechanism was included as the independent variable. In models 3, 4 and 5, the deconstructive mechanism was entered as the independent variable. In models 1, 2 and 3, the mediator was the positive psycho-affective score while the negative psycho-affective score was included as mediator in models 4 and 5. In models 1, 2 and 3, the temporo-parietal perfusion was included as the dependent variable. In model 4, the temporo-occipito-parietal perfusion was entered as the dependent variable. In model 5, the inferior frontal volume was included as dependent variable. inferior frontal volume.

1.17. Supplementary Figure S3 | Diagram of the mediation models illustrating the predictors (attentional, constructive and deconstructive mechanisms), potential mediators (positive and negative psycho-affective scores) and outcomes (grey matter volume, perfusion)



*Direct effects in filled arrows (simple regressions between variables) are expressed as standardized regression coefficients and indirect effects in dotted arrows (multiple regressions in which the predictor and the mediator are both added in the model) as partial correlation coefficients. Significant models are highlighted in bold black while non-significant one are in gray. All regressions are adjusted for age, sex, and education. *p<0.05, **p<0.01, ***p<0.001.*

2. Supplementary methods

2.1. **Questionnaires used for the construction of the positive psycho-affective score**

The positive psycho-affective score is a composite score built by averaging the scaled scores of 4 questionnaires (Compassion For Self[1], Emotion Regulation Questionnaire[2] – Reappraisal, Satisfaction with life[3] and Well-being[4]).

Compassion was measured by the Compassion For Self-short form (SCS-SF, scores ranging from 12 to 60) which is designed to assess typical action towards one's self in difficult times. This scale measures several aspects of compassion towards oneself such as self-indulgence, self-judgment or mindfulness. This measure uses a 5-point Likert scale ranging from 1 (almost never) to 5 (almost always), a higher score indicating higher self-compassion.

Emotion regulation was assessed using Emotion Regulation Questionnaire (ERQ, scores from 4 to 28 for suppression and from 6 to 42 for cognitive reappraisal), divided in 2 sub-scales: cognitive reappraisal, measuring a cognitive change strategy that involves reinterpreting emotional situations and expressive suppression, measuring a response modulation strategy that involves restricting behavioural displays of emotion. The reappraisal subscale was used in the positive psycho-affective score as it is thought to reflect a positive strategy towards emotional balance while suppression is considered as a non-efficient or even detrimental strategy[2]. This measure uses a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), a higher score indicating higher use of each emotional regulation strategy.

Satisfaction was measured using the Satisfaction with life questionnaire (scores ranging from 5 to 35). The Satisfaction with Life questionnaire uses a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree) to assess global life satisfaction. Total satisfaction was derived by summing all item scores with higher score reflecting higher satisfaction.

Well-being was assessed using the Ryff 7 item Well-Being Scale (scores ranging from 1 to 7). This scale uses a 7-point Likert scale ranging from 1 (strongly disagree) to 7 (strongly agree), a higher score indicating higher well-being.

2.2. **Questionnaires used for the construction of the negative psycho-affective score**

The Negative psycho-affective score is a composite score built by averaging the scaled scores of 5 questionnaires (Penn State Worry Questionnaire[5], State Trait Anxiety Inventory Form Y–A[6], death depression scale[7], the Attentional Style Questionnaire[8] and the Rumination Response Scale[9] – Brooding).

Worry was measured using the Penn State Worry Questionnaire (PSWQ, scores ranging from 16 to 80). The Penn State Worry Questionnaire uses a 5-point Likert scale ranging from 1 (not at all typical of me) to 5 (very typical of me). We used total worry as it represents pervasive negative thoughts and is intricately linked to mood disorders. Total worry score is derived by summing all the respective item scores with higher scores indicating higher levels of worry.

Rumination was measured using the Rumination Response Scale (RRS, scores ranging from 22 to 88). The Rumination Response Scale describes responses to depressed mood that are self-focused, symptom focused and focused on the possible consequences and causes of the mood and can be divided in 2 subscales: reflective rumination and brooding rumination. It was the Brooding subscale (scores ranging from 5 to 20) that was used in the negative psycho-affective score as it involves anxious or gloomy thinking and is thought to be maladaptive and is associated to depression[9]. The Rumination Response Scale uses a 4-point Likert scale ranging from 1 (almost never) to 4 (almost always). Brooding rumination score is derived by summing all the respective item scores with higher scores indicating higher levels of brooding.

Anxiety was measured using the State Trait Anxiety Inventory Form Y (STAI, scores from 20 to 80) and is divided in 2 subscales: STAI B assessing the long-standing quality of "trait

anxiety" and STAI A measuring the temporary condition of "state anxiety". The essential qualities evaluated by the STAI-Anxiety scale are feelings of apprehension, tension, nervousness, and worry. This measure uses a 4-point Likert scale ranging from 0 (No) to 3 (Yes), a higher score relating to higher level of anxiety.

Depression was assessed by the Death Depression Scale (DDS, scores from 21 to 105) which measure depression sadness or somber reflections associated with death. Four aspects of death depression are assessed: death sadness, anergia, existential vacuum and anhedonia. The death depression scale uses a 5-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree), a higher score relating to more depressive symptoms.

The Attentional Style Questionnaire (ASQ, scores from 12 to 72) is a questionnaire allowing the assessment of attentional style along a bottom-up versus top-down attentional dimension while distinguishing between external versus internal origins of potential attentional distractors. We used the total score which reflect difficulties in concentration as well as how easily an individual may be distracted from both internal and external distractors. Distraction is known to interfere with ongoing activities and has been associated to rumination such that this mental process may be detrimental to normal functioning and well-being. The ASQ uses a 6-point Likert scale ranging from 1 (strongly disagree) to 6 (strongly agree), a higher score indicating higher tendency to be distracted and concentration difficulties.

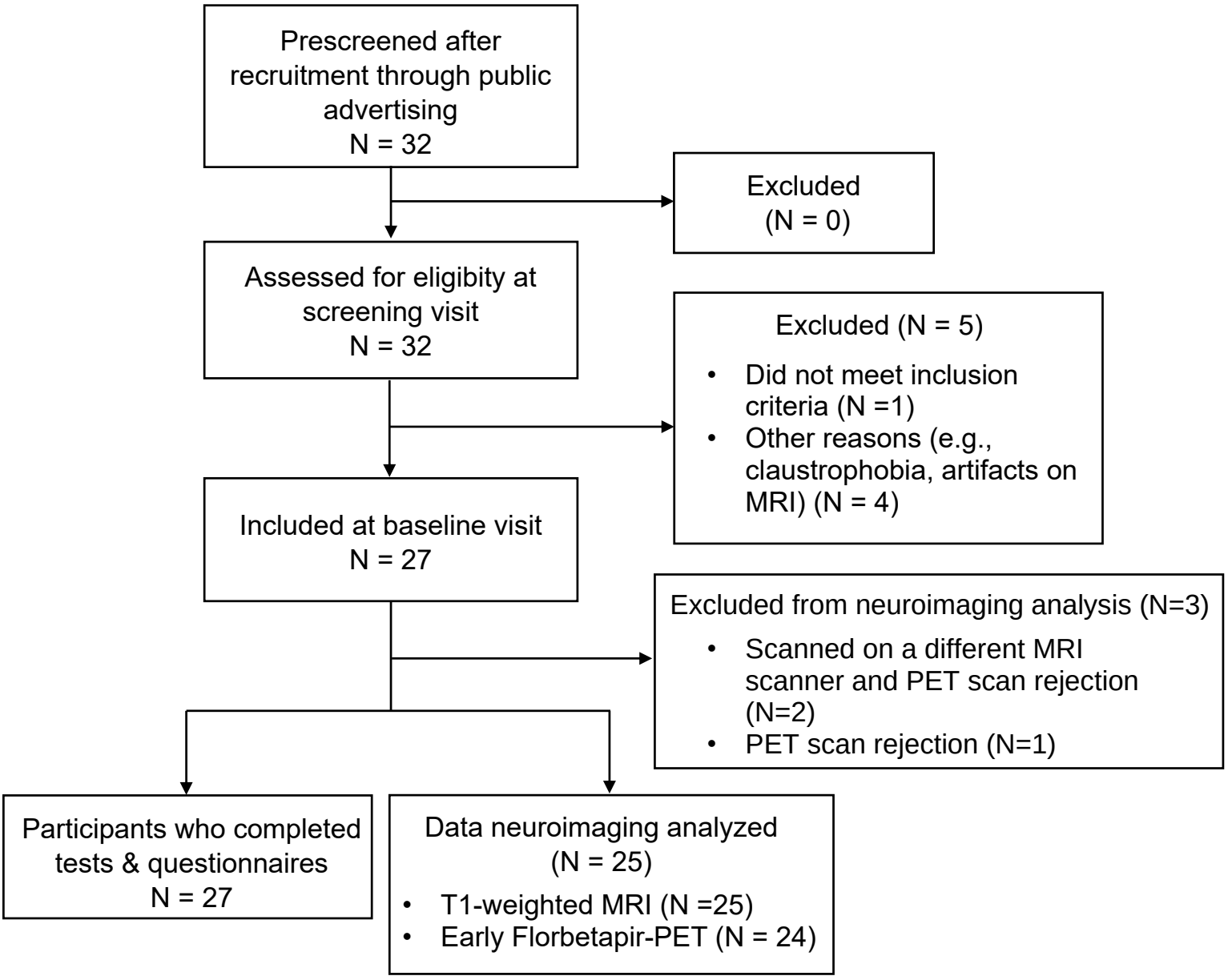
2.3. Questionnaires used for the construction of the meditation mechanisms composite scores

The questionnaires used for the construction of the attentional mechanism were the noticing, attention regulation, emotional awareness, self-regulation, and body listening subscores of the Multidimensional Assessment of Interoceptive Awareness (MAIA) and the observe and acting with awareness subscores of the Five Facet Mindfulness Questionnaire (FFMQ).

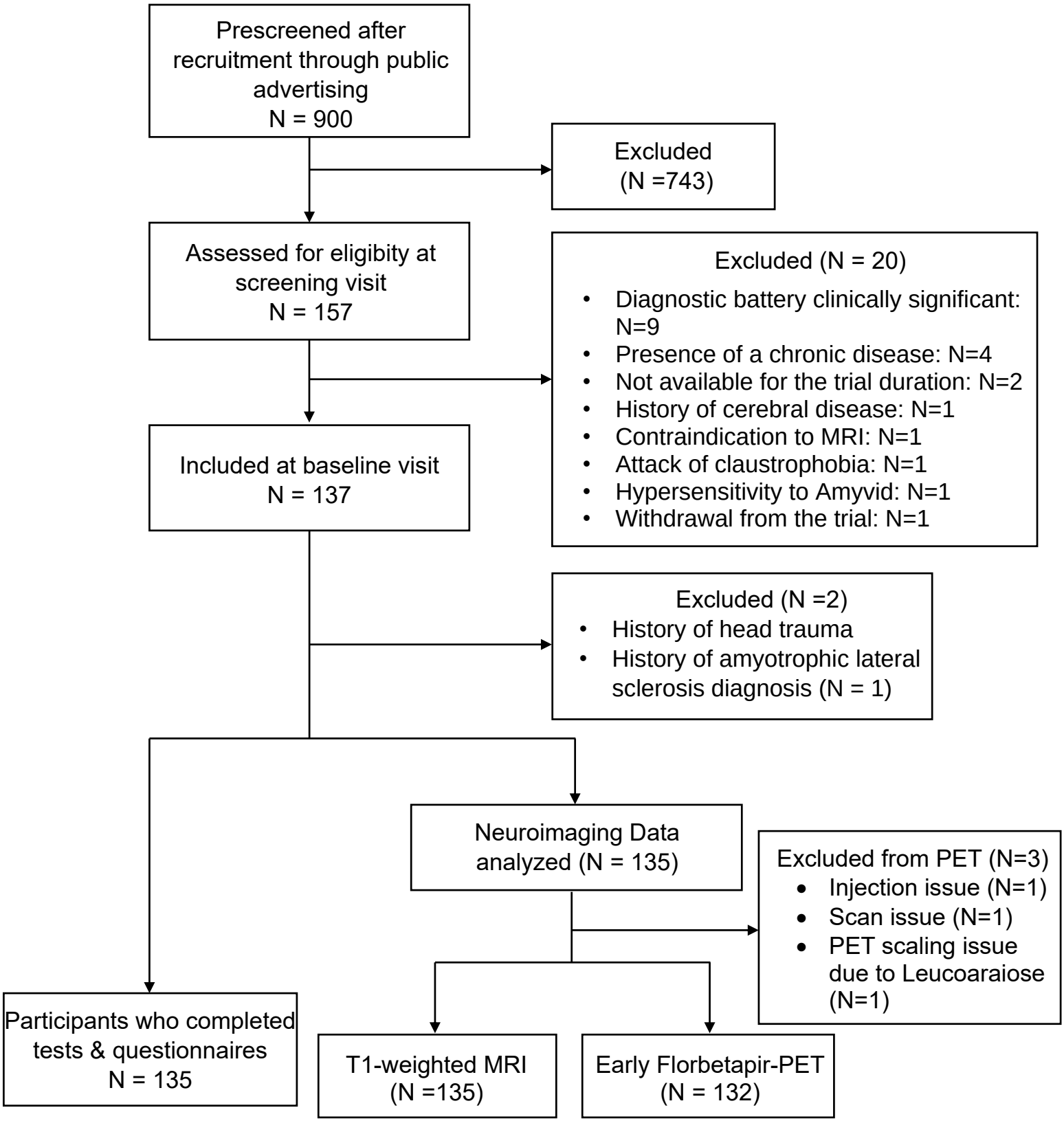
The questionnaires used for the construction of the constructive mechanism were the Compassion for Others Scale, the empathic concern and perspective-taking subscores of the Interpersonal Reactivity Index (IRI) and the Prosocialness Scale.

The questionnaires used for the construction of the deconstructive mechanism were the Drexel Defusion Scale, the non-judging and non-reactivity subscores of the FFMQ and the distress subscore of the IRI.

2.4. **Supplementary Figure S4: Flow chart of the expert meditator population**



2.5. **Supplementary Figure S5: Flow chart of the older control population**



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